

PERIOPERATIVE APPLICATIONS OF PERIPHERAL NERVE BLOCKS

Okolooperacyjne zastosowanie blokady nerwów obwodowych

Terese T. Horlocker

Mayo Clinic, Rochester, Minnesota, USA

Peripheral nerve blocks are well described, but not universally accepted or utilized. In a national survey of 409 anesthesiologists evaluating the use of peripheral nerve blocks. Hadzic et al., [1998] reported that while nearly all respondents perform regional techniques, less than half performed more than five peripheral nerve blocks per month. Importantly, lower extremity blocks other than ankle blocks were seldom used. This is unfortunate, since lower extremity blocks have many advantages over neuraxial techniques, and represent alternatives for both intraoperative anesthesia and postoperative analgesia. Anesthesiologists in Europe have already shifted their practice towards peripheral blocks. A prospective study of 103.730 regional anesthetics performed in France over a five-month period included 21.278 peripheral blocks.

Lower extremity blocks may be accomplished when neuraxial blockade is contraindicated. Spinal and epidural anesthesia are often avoided in the anticoagulated or febrile patient because of the catastrophic consequences of bleeding or infection in the central nervous system. Although it is difficult to quantitate the incidence of hemorrhagic or infectious complications of peripheral nerve blocks, the lack of case reports suggests the risk of serious morbidity is minimal.

Although not commonly used in the outpatient setting, ambulatory surgical patients are ideally suited for peripheral blocks. Advantages include reduced recovery room admissions, decreased nausea/emesis and urinary retention, and improved postoperative analgesia. These benefits may translate into shortened hospital stays, fewer unplanned admissions, and reduced hospital costs and patient charges. It is likely that a major impetus toward peripheral blocks will be economic. However, timely and efficient (as well as successful) performance is paramount if these techniques are to supplant neuraxial and general anesthesia as the anesthetic/analgesic of choice.

Despite these many advantages, peripheral nerve blocks have not been widely used in the United States. Peripheral blocks are more technically demanding than neuraxial techniques, often requiring multiple injections, increased onset time, and larger volumes of local anesthetic. Advances in

needle and catheter technology, refinement of devices to localize neural structures, as well as the introduction of longer-lasting encapsulated local anesthetics will improve the acceptance and popularity of peripheral techniques.

This lecture will describe upper and lower extremity peripheral nerve blocks focusing on innovations of existing techniques, descriptions of new approaches, and pearls for improved success. Importantly, applications of peripheral nerve blocks, which contribute to, improved patient outcomes will be highlighted.

Lower extremity joint replacement

Major orthopedic surgery is associated with marked and prolonged postoperative pain. The most commonly accepted methods used to control pain during the postoperative period include intravenous and oral analgesics and continuous epidural analgesia. However, each technique has distinct advantages and disadvantages. For example, opioids do not consistently provide adequate pain relief and often cause sedation, constipation, nausea/vomiting, and pruritus. Epidural infusions containing local anesthetics (with or without an opioid) provide superior analgesia but are associated with hypotension, urinary retention, motor block limiting ambulation [Singelyn, 1998; Capdevila, 1999] and hematoma secondary to anticoagulation [Horlocker, 1998].

Recently, single dose and continuous peripheral nerve techniques which block the lumbar plexus (femoral, femoral 3-in-1, psoas blocks) and/or sciatic nerve have been utilized among this patient population [Allen, 1998; Allen, 1998; Ganapathy, 1999]. Unilateral lower extremity blockade provides superior analgesia, allows rehabilitation and ambulation, and minimizes the side effects of neuraxial opioids and local anesthetics. Of the possible approaches to the lumbar plexus, the psoas technique results in a more comprehensive block of all branches (femoral, lateral femoral cutaneous, and obturator nerves) and theoretically provides improved analgesia compared to the femoral approach [Chayen, 1976]. However, with the exception of hip fracture, previous investigations have focused on the femoral 3-in-1 technique for blockade of the lumbar plexus.

Hip fracture

Femoral neck fracture occurs in elderly patients who often have multiple medical co-morbidities. Complications include thromboembolic events, confusion, and pulmonary infections. In addition, quadriceps spasm contributes to perioperative pain and the need for opioid analgesia. Several studies have evaluated the use of continuous lumbar plexus block (psoas approach) in the pre-, intra-, and postoperative management of hip fracture.

An early study performed in 1978 included 21 patients with femoral neck fracture. Continuous psoas catheters were placed, using a loss of resistance technique, upon arrival to the ward. The catheters were used intraoperatively, combined with a general anesthetic, and removed 48 hours postoperatively. During this time, the catheters were intermittently bolused with 15–20 ml of 0.5% bupivacaine. Eighty percent of patients had adequate analgesia and did not require supplementation [Brands, 1978]. Similar results were reported in a more recent study by Chudinov et al., [1999]. Forty patients undergoing stabilization of femur fracture were randomized to receive a continuous psoas block (implemented 16–48 h preoperatively and continued 72 h postoperatively) or meperidine. The lumbar plexus block was inadequate for surgical anesthesia in 85% of patients. VAS scores were lower and patient satisfaction was higher in the psoas group. These studies suggest that continuous psoas block is an effective perioperative analgesic technique, but supplementation is required during surgical repair. In addition, possible improvement in patient outcomes has not been formally investigated.

Total hip arthroplasty

The usefulness of peripheral nerve blocks for total hip arthroplasty (THA) has not been clearly established. Innervation to the joint involves both the lumbar and sacral plexi. Therefore, while a lumbar plexus block may reduce pain postoperatively, it would not be sufficient to provide surgical anesthesia. A study in the orthopedic literature (Twyman, 1990) demonstrated reduced intraoperative blood loss (310 ± 81 ml vs 617 ± 230 ml) in THA patients that received a single-shot psoas block (0.42 ml/kg of 0.375% bupivacaine). No other outcomes were monitored.

Stevens et al., [2000] prospectively studied 60 patients undergoing THA who were randomized to receive general anesthesia with or without a psoas block. Blocks were performed using a nerve stimulator and 0.4 ml/kg of 0.5% bupivacaine with epinephrine was injected. The need for intraoperative supplemental fentanyl occurred three times more often in the control group. Pain scores and morphine consumption remained less in the psoas group for six hours postoperatively. Perioperative blood loss was also modestly decreased in the psoas group. There was epidural spread in 3 of 28 patients, but no other side effects were noted. It is possible that a continuous psoas technique would further facilitate the rehabilitation of patients undergoing THA. However, currently there are no data to support (or refute) this theory.

Total knee arthroplasty

Patients undergoing total knee arthroplasty (TKA) experience significant postoperative pain. Failure to provide adequate analgesia impedes aggressive physical therapy and rehabilitation, which is critical to maintaining joint range of motion and potentially delays hospital dismissal.

Although numerous methods of providing postoperative analgesia after total knee arthroplasty have been reported, the optimal technique based on efficacy, number/type of side effects, surgical outcome, and resource utilization is unknown. Several European studies have suggested that aggressive postoperative analgesic techniques maintained for 48–72 hours result in a shorter rehabilitation period and increased joint mobility. Singelyn et al., [1998] assessed the influence of three analgesic techniques (patient-controlled analgesia, continuous femoral 3-in-1 block, and epidural analgesia) on postoperative knee rehabilitation after TKA. Patients receiving regional analgesic techniques reported significantly lower pain scores, better knee flexion (until 6 weeks after surgery), faster ambulation, and shorter hospital stay compared to patients receiving intravenous morphine. However, these benefits did not affect outcome at 3 months.

Table 1. Knee flexion and duration of stay during rehabilitation after total knee arthroplasty

Knee mobility in degrees median (25 th –75 th percentile)	Patient-controlled analgesia (PCA) N=19	Continuous femoral block (CFB) N=20	Continuous epidural analgesia (CEA) N=17
Day 5	60 (50–70)*	80 (65–85)	85 (75–100)
Day 7	80 (65–90)*	90 (70–95)	90 (78–100)
1-month	90 (85–100)	95 (95–100)	105 (100–120)
3-month	125 (100–125)	125 (105–125)	130 (115–130)
Days of rehabilitation, Median (range)	50 (30–80)*	40 (31–60)	37 (30–45)

*P<0.05 vs CFB and CEA. Adapted from Capdevila et al. 1999.

Capdevila et al., [1999] also evaluated the effect of postoperative analgesia on surgical outcome and rehabilitation following TKA. Patients were randomized to receive one of three postoperative analgesia techniques for 72 hours: continuous epidural infusion, continuous femoral block, or intravenous patient-controlled morphine. Pain was assessed at rest and during continuous passive motion using a visual analog scale. To evaluate functional outcome, the maximal amplitudes were measured again on postoperative day 5, at hospital discharge (day 7), and at 1- and 3-month follow-up examinations (Table 1). When the patients left the surgical ward, they were admitted to a rehabilita-

tion center, where their length of stay depended on prospectively determined discharge criteria. The continuous epidural infusion and continuous femoral block groups showed significantly lower visual analog scale scores at rest and during continuous passive motion compared with the patient-controlled morphine group. The early postoperative knee mobilization levels in both continuous epidural infusion and continuous femoral block groups were significantly closer to the target levels prescribed by the surgeon than in the patient-controlled morphine group. The durations of stay in the rehabilitation center were significantly shorter in the regional analgesic groups compared to the patient-controlled morphine group. Side effects were encountered more frequently in the continuous epidural infusion group.

These landmark studies demonstrate the long-term effects of an aggressive postoperative analgesic technique following orthopedic surgery – continuous femoral and epidural analgesia hastened rehabilitation and improved joint mobility [Todd, 1999]. Additional studies are required to assess these outcomes in a managed care environment with shorter hospital stays of approximately five days, and discharge to home, rather than a rehabilitation center for an extended period as is the standard in Europe. For example, the median duration of hospital stay (including rehabilitation unit) in the study by Singelyn et al. was 19 days, while the patients in the investigation by Capdevila et al., were hospitalized for as long as 80 days postoperatively.

An additional relevant result of these investigations is the finding that continuous femoral block provides a quality of analgesia and surgical outcomes similar to that of continuous epidural analgesia, but is associated with fewer side effects. This suggests that continuous peripheral techniques may be the optimal analgesic method following total knee arthroplasty. However, further studies are needed to determine the resource utilization based on surgical outcome. The modest and temporary improvement in joint mo-

bility may not justify the cost of invasive analgesic techniques.

Knee arthroscopy and anterior cruciate ligament repair

Outpatient knee surgery may be performed under a variety of regional anesthetic techniques. Traditionally, neuraxial anesthesia was utilized. However, prolonged lower extremity weakness and/or urinary retention delayed hospital discharge. Furthermore, concerns over transient neurologic symptoms propelled a search for an alternative to intrathecal lidocaine. Unfortunately, the reliable sensory and motor block (of limited duration) associated with lidocaine has not been duplicated. Lower extremity peripheral blocks provide adequate analgesia intraoperatively, with the added benefit of postoperative analgesia.

Diagnostic knee arthroscopy is a relatively minor procedure that may be performed under local anesthesia with sedation. The performance of a single dose or continuous lower extremity block is probably not warranted in the majority of patients. Several studies have failed to demonstrate a clinically significant difference in patient outcome with respect to anesthetic technique. De Andres et al., [1993] compared intraarticular bupivacaine, continuous lumbar plexus block for 24 hours, and intraarticular morphine for patients undergoing knee arthroscopy. VAS scores were reduced in the 3-in-1 block group 16 and 24 hours postoperatively. However, patients in all groups required little supplemental analgesia. Similar results were reported by Schwarz et al., [1999]. The authors noted that the addition of a femoral 3-in-1 block to intraarticular ropivacaine did not reduce analgesic requirements following arthroscopic knee surgery. Few data exist on the use of lower extremity blocks for patients undergoing anterior cruciate ligament repair. However, preliminary studies suggest that a lumbar plexus block (combined with a spinal or sciatic block) dramatically reduces postoperative opioids requirements as well

Table 2.
Anesthetic techniques for common foot and ankle operations

	Surgical Procedure	Regional Technique	Comments
Forefoot*	Hallux valgus	Metatarsal, ankle, popliteal blockade	Sural nerve block not necessary for surgery
	Amputations	Ankle, popliteal blockade	Popliteal blockade is the technique of choice in the presence of infection or swelling
Midfoot*	Transmetatarsal amputations	Popliteal, ankle blockade	
Hindfoot*	Ankle arthroscopy	Spinal, epidural or general anesthesia	Operation typically requires good muscle relaxation for manipulation; thigh tourniquet
	Achilles tendon repair	Spinal, epidural, or popliteal blockade	Spinal or epidural anesthesia whenever thigh tourniquet is required
	Triple arthrodesis	Spinal or epidural	Neuraxial technique preferred for bone graft harvesting; popliteal blockade for postoperative analgesia

*Femoral or saphenous block required if the incision extends to the medial aspect of the foot or ankle. From Hadzic and Vloka, 1999 [3:113].

as opioid related side-effects [Matheny, 1993]. Thus for outpatient procedures, the complexity/duration of the surgical procedure will determine the usefulness of peripheral blocks compared to neuraxial or general anesthesia.

Surgery to the ankle and foot

Innervation of the foot is provided by the femoral nerve (via the saphenous nerve) and by the sciatic nerve (via the posterior tibial, sural, deep and superficial peroneal nerves). Therefore, central neuraxial blockade and peripheral nerve blocks at the upper leg, knee or ankle are appropriate regional anesthetic techniques for foot surgery. Common surgical procedures are discussed in the table 2.

The selection of the regional technique is based upon the surgical site, use of a calf or thigh tourniquet, degree of weight-bearing/ambulation, and the need for postoperative analgesia. For example, inflation of a thigh tourniquet for longer than 15 to 20 minutes necessitates a general or neuraxial anesthetic, regardless of surgical site. The distal surgical site and the ability to block the pain pathways at multiple sites gives regional anesthesia an advantage over general anesthesia for surgery to the ankle and foot. The main disadvantage of peripheral blocks is the technical expertise (and theoretically, the associated complications) required for consistent success rate; neuraxial techniques are a suitable alternative.

Upper extremity techniques

Upper extremity regional anesthesia consists mainly of brachial plexus techniques. Numerous studies have documented the improved analgesia, reduced hospital stays and fewer unplanned hospital admissions with these approaches. Indeed, axillary blocks, compared to lower extremity blocks, are often performed in the ambulatory setting. New applications of upper extremity peripheral techniques involve placement of continuous catheters to facilitate rehabilitation and avoid hospital admission. More patients are being discharged with disposable pumps set to deliver a local anesthetic infusion or bolus for approximately 24–48 hours [Klein, 1999]. Ongoing studies will soon reveal the optimal use of these devices. In addition to innovations in block technology, several new approaches to the brachial plexus have been described – the midhumeral [Bouaziz, 1997] and intersternocleidomastoid [Pham Dang, 1997] techniques. The clinician is urged to read the descriptions of these blocks by the original authors and apply them to their individual practice as appropriate.

In summary, peripheral nerve blocks are valuable regional anesthetic techniques. Additional outcome studies are required to define their role in ambulatory and inpatient procedures. It is also imperative that prior to attempting the new approaches and continuous catheters, anesthesiologists thoroughly review neural anatomy and practice with meticulous regional anesthetic technique to improve success rate and avoid neurologic complications.

References

- Allen HW, Liu SS, Ware PD. Peripheral nerve blocks improve analgesia after total knee replacement surgery. *Anesth Analg* 1998; 87: 93–97.
- Allen JG, Denny NM, Oakman N. Postoperative analgesia following total knee arthroplasty: a study comparing spinal anesthesia and combined sciatic femoral 3-in-1 block. *Reg Anesth Pain Med* 1998; 23: 142–146.
- Benzon HT, Kim C, Benzon HP. Correlation between evoked motor response of the sciatic nerve and sensory blockade. *Anesthesiology* 1997; 87: 547–552.
- Bouaziz H, Narchi P, Mercier FJ, Labaille T, Zerrouk N, Girod J, Benhamou D. Comparison between conventional axillary block and a new approach at the midhumeral level. *Anesth Analg* 1997; 84: 1058–1062.
- Brands E, Callanan VI. Continuous lumbar plexus block—analgesia for femoral neck fractures. *Anaesthesia* 1978; 6: 256–258.
- Capdevila X, Barthelet Y, Biboulet P, Rykwaert Y, Rubernovitch J, d’Athys F. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. *Anesthesiology* 1999; 91: 8.
- Chayen D, Nathan H, Chayen M. The psoas compartment block. *Anesthesiology* 1976; 45: 95–99.
- Chelly JE, Delaunay L. A new anterior approach to the sciatic nerve block. *Anesthesiology* 1999; 91: 1655–1660.
- Chudinov A, Berkenstadt H, Salai M, Cahana A, Perel A. Continuous psoas compartment block for postoperative analgesia in patients with hip fractures. *Reg Anesth Pain Med* 1999; 24: 563–568.
- Farny J, Drolet P, Girard M. Anatomy of the posterior approach to the lumbar plexus block. *Can J Anaesth* 1994; 41: 480–485.
- Farny J, Girard M, Drolet P. Posterior approach to the lumbar plexus combined with a sciatic nerve block using lidocaine. *Can J Anaesth* 1994; 41: 486–491.
- Ganapathy S, Wasserman RA, Watson JT, et al. Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty. *Anesth Analg* 1999; 89: 1197–1212.
- Hadzic A, Vloka JD. A comparison of the posterior versus lateral approaches to the block of the sciatic nerve in the popliteal fossa. *Anesthesiology* 1998; 88: 1480–1486.
- Hadzic A, Vloka JD. Anesthesia for Ankle and Foot Surgery. *Techniques in Regional Anesthesia and Pain Management*; 1999; 3: 113.
- Horlocker TT. Peripheral nerve blocks—regional anesthesia for the new millennium [editorial]. *Reg Anesth Pain Med* 1998; 23: 237–240.
- Horlocker TT, Wedel DJ. Neuraxial block and low-molecular-weight heparin: balancing perioperative analgesia and thromboprophylaxis. [Review]. *Reg Anesth Pain Med* 1998; 23: 164–177.
- Klein SM, D’Ercole F, Greengrass RA, Warner DS. Enoxaparin associated with psoas hematoma and lumbar plexopathy after lumbar plexus block. *Anesthesiology* 1997; 87: 1576–1579.
- Klein SM, Greengrass RA, Gleason DH, Nunley JA, Steele SM. Major ambulatory surgery with continuous regional anesthesia and a disposable infusion pump. *Anesthesiology* 1999; 91: 563–565.
- Lynch NM, Cofield RH, Silbert PL, Hermann RC. Neurologic complications after total shoulder arthroplasty. *J Shoulder Elbow Surg*; 1996; 5: 53.
- Matheny JM, Hanks GA, Rung GW, Blanda JB, Kalenak A. A comparison of patient-controlled analgesia and continuous lumbar plexus block after anterior cruciate ligament reconstruction. *Arthroscopy* 1993; 9: 87–90.
- McLeod DH, Wong DH, Vaghadia H, Claridge RJ, Merrick PM. Lateral popliteal sciatic nerve block compared with ankle block for analgesia following foot surgery. *Can J Anaesth* 1995; 42: 765–769.
- Paqueron X, Bouaziz H, Macalou D, Labaille T, Merle M, Laxenaire MC, Benhamou D. The lateral approach to the sciatic nerve at the popliteal fossa: one or two injections? *Anesth Analg* 1999; 89: 1221–1225.
- Pham-Dang C, Gunst JP, Gouin F, Poirier P, Touchais S, Meunier JF, Kick O, Drouet JC, Bourreli B, Pinaud M. A novel supraclavicular approach to brachial plexus block. *Anesth Analg* 1997; 85: 111–116.
- Schwarz SK, Franciosi LG, Ries CR, Regan WD, Davidson RG, Nevin K, Escobedo S, MacLeod BA. Addition of femoral 3-in-1 blockade to intra-articular ropivacaine 0.2% does not reduce analgesic requirements following arthroscopic knee surgery. *Can J Anaesth* 1999; 46: 741–747.
- Seeberger MD, Urwyler A. Paravascular lumbar plexus block: block extension after femoral nerve stimulation and injection of 20 vs. 40 ml mepivacaine 10 mg/ml. *Acta Anaesthesiol Scand* 1995; 39: 769–773.
- Singelyn FJ, Deyaert M, Joris D, Pendeville E, Gouverneur JM. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative

pain and knee rehabilitation after unilateral total knee arthroplasty. *Anesth Analg* 1998; 87: 88.

Singelyn FJ, Gouverneur JM. Extended „three-in-one” block after total knee arthroplasty: Continuous versus patient-controlled techniques. *Anesth Analg* 2000; 91: 176–180.

Stevens RD, Van Gessel E, Flory N, Fournier R. Lumbar plexus block reduces pain and blood loss associated with total hip arthroplasty. *Anesthesiology* 2000; 93: 115–121.

Todd MM, Brown DL. Regional anesthesia and postoperative pain management: long-term benefits from a short-term intervention [editorial]. *Anesthesiology* 1999; 91: 1–2.

Twyman R, Kirwan T, Fennelly M. Blood loss reduced during hip arthroplasty by lumbar plexus block. *J Bone Joint Surg [British]* 1990; 72: 770–771.

Vloka JD, Hadzic A, Drobnik L, Ernest A, Reiss W, Thys DM. Anatomical landmarks for femoral nerve block: a comparison of four needle insertion sites. *Anesth Analg* 1999; 89: 1467–1470.

Vloka JD, Hadzic A, Kitain E, Lesser JB, Kuroda M, April EW, Thys DM. Anatomic considerations for sciatic nerve block in the popliteal fossa through the lateral approach. *Reg Anesth* 1996; 21: 414–418.

Vloka JD, Hadzic A, Mulcare R, Lesser JB, Koorn R, Thys DM. Combined popliteal and posterior cutaneous nerve of the thigh blocks for short saphenous vein stripping in outpatients: an alternative to spinal anesthesia. *J Clin Anesth* 1997; 9: 618–622.

INFLUENCE OF THE NEW ANTI-PLATELET MEDICATIONS ON REGIONAL ANAESTHESIA

Nowe leki przeciwplatetkowe w regionalnej anestezji

Terese T. Horlocker

Mayo Clinic, Rochester, Minnesota, USA

Antiplatelet therapy has been considered a relative contraindication to central neural blockade by some authors due to the associated prolongation of the bleeding time and theoretically greater risk of spinal hematoma formation. Although the actual incidence of spinal hematoma is unknown, the incidence cited in the literature is estimated to be less than 1 in 150,000 epidural and less than 1 in 220,000 spinal anesthetics [Tryba, 1993]. In a review of the literature between 1906 and 1994, Vandermeulen et al [1994] reported only 61 cases of spinal hematoma associated with epidural or spinal anesthesia, including three patients who received antiplatelet medications (aspirin, indomethacin, ticlopidine) immediately before or after the neuraxial anesthetic [Greensite and Katz, 1980; Mayumi and Dohi, 1983; Williams et al., 1990]. Two subsequent cases have been published [Benzon et al., 1999; Gerancher et al., 1997].

The recent introduction of new, more potent antiplatelet agents, including ticlopidine and clopidogrel have once again raised issues regarding the safety of neuraxial techniques in patients that are receiving these medications perioperatively.

Antiplatelet pharmacology

Non-steroidal anti-inflammatory drugs (NSAIDs) medications inhibit platelet cyclooxygenase and prevent the synthesis of thromboxane A_2 . Thromboxane A_2 is not only a potent vasoconstrictor, but also facilitates secondary platelet aggregation and release reactions. Platelets from patients who have been taking these medications have normal platelet adherence to subendothelium and normal primary hemostatic plug formation. Thus an adequate, although potentially fragile, clot may form. While such plugs may be satisfactory hemostatic barriers for smaller vascular lesions, they may not ensure adequate perioperative hemostatic clot formation. With aspirin, the effect is irreversible and present for the life of the platelet. Other nonsteroidal analgesics (naproxen, piroxicam, ibuprofen) produce a short-term

defect which normalizes within 1–5 days [Cronberg et al., 1984].

Depending on the dose administered, aspirin may produce opposing effects on the hemostatic mechanism. Platelet cyclooxygenase is inhibited by low-dose aspirin (60–325 mg/d). However, larger doses (1.5–2 g/d) will also inhibit the production of prostacyclin (a potent vasodilator and platelet aggregation inhibitor) by vascular endothelial cells. Therefore, low-dose aspirin produces a greater antiplatelet effect than larger doses – hence the “baby aspirin a day” to prevent cerebro- or cardiovascular events.

It has been suggested that the Ivy bleeding time is the most reliable predictor of abnormal bleeding in patients receiving NSAIDs. However, the „post-aspirin” bleeding time is not a reliable indicator of platelet function. Although the bleeding time may normalize within three days after aspirin ingestion, platelet function as measured by platelet response to ADP, epinephrine, and collagen may take a week to return to normal. There is no evidence to suggest that a bleeding time can predict hemostatic compromise; studies have failed to show a correlation between aspirin-induced prolongation of the bleeding time and surgical blood loss [Rodgers and Levin, 1990]. Therefore, measurement of an Ivy bleeding time before induction of spinal or epidural anesthesia may not identify those patients at increased risk for hemorrhagic complications and is clinically not indicated. Special platelet function assays are also available to monitor platelet aggregation and degranulation.

Several new classes of antiplatelet agents have been recently introduced. The antiplatelet effect of the thienopyridine derivatives, ticlopidine and clopidogrel, results from inhibition of ADP-induced platelet aggregation. Because of their extended plasma-half lives, clopidogrel must be discontinued 5–7 days and ticlopidine 10–14 days before normal platelet function is restored. Platelet glycoprotein IIb/IIIa receptor antagonists, such as abciximab, eptifibatide and tirofiban, not only inhibit platelet aggregation, but also interfere with platelet-fibrinogen binding and subsequent platelet-platelet interactions. Time to normal plate-

let aggregation following discontinuation of therapy ranges from eight hours (eptifibatid, tirofiban) to 48 hours (abciximab). The pharmacologic differences of the thienopyridine derivatives, glycoprotein IIb/IIIa inhibitors and NSAIDs makes it impossible to extrapolate between the groups of drugs regarding the practice of neuraxial techniques. However, the increase in perioperative bleeding in patients undergoing cardiac and vascular surgery after receiving ticlopidine, clopidogrel and glycoprotein IIb/IIIa antagonists warrants concern regarding the risk of spinal hematoma. There have been two spinal hematomas attributed to neuraxial techniques and thienopyridine derivatives, including one patient undergoing a series of epidural steroid injections.

Antiplatelet therapy and neuraxial blockade

Several large studies have demonstrated the relative safety of central neural blockade in combination with NSAIDs therapy. The Collaborative Low-dose Aspirin Study in Pregnancy (CLASP) Group included 1422 high-risk obstetric patients administered 60 mg aspirin daily who underwent epidural anesthesia without any neurologic sequelae. However, no data regarding difficulty or bleeding during epidural needle or catheter were reported [CLASP, 1994].

Horlocker et al. [1990] retrospectively reported 1013 spinal and epidural anesthetics in which NSAIDs were taken by 39% of the patients including 11% of patients who were on multiple NSAIDs. While no patient developed signs of spinal hematoma, patients on NSAIDs showed a higher incidence of blood aspirated through the spinal or epidural needle or catheter. This study was subsequently performed prospectively on an additional 1000 patients, 39% of whom reported preoperative NSAIDs [Horlocker et al., 1995]. As before, there were no spinal hematomas. Blood was noted during needle or catheter placement in 22% of patients, including 7% of patients with frank blood. Preoperative NSAIDs were not a risk factor for bloody needle or catheter placement. However, many patient and anesthetic variables including female gender, increased age, a history of excessive bruising or bleeding, continuous catheter technique, large needle gauge, multiple needle passes, and difficult needle placement were significant risk factors. The lack of correlation between NSAIDs and bloody needle or catheter placement (producing clinically insignificant collections of blood within the spinal canal) is strong evidence that preoperative NSAIDs are not a significant risk factor for the development of neurologic dysfunction from spinal hematoma in patients who undergo spinal or epidural anesthesia while receiving these medications.

Epidural steroid injection is often performed on an outpatient-basis. These patients also report a significant history of NSAID use. Horlocker et al. [2002] prospectively studied 1035 individuals undergoing 1214 epidural steroid injections to determine the risk of hemorrhagic complications. A history of bruising or bleeding was present in 176 (15%) patients. NSAIDs were reported by 383 (32%) patients, including 34 patients on multiple medications. Aspi-

rin was the most common NSAID and was noted by 158 patients, including 104 patients on 325 mg or less per day. There were no spinal hematomas. NSAIDs did not increase the frequency of minor hemorrhagic complications. However, increased age, needle gauge, needle approach, needle insertion at multiple interspaces, number of needle passes, volume of injectate, and accidental dural puncture were all significant risk factors for minor hemorrhagic complications. These results confirm those of previous studies performed in obstetric and surgical populations which document the safety of neuraxial techniques in patients receiving NSAIDs.

There has been no published series of patients documenting the safety or risk of neuraxial blockade in the presence of ticlopidine and clopidogrel. There have been two spinal hematomas attributed to neuraxial techniques the ADP receptor blockers [Mayumi and Dohi, 1983; Benzon et al., 1999].

Regional anesthetic management of the patient receiving antiplatelet medications

NSAIDs, by themselves, appear to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia. However, the concurrent use of medications that affect other components of the clotting mechanisms, such as oral anticoagulants, standard heparin, and LMWH, may increase the risk of bleeding complications for patients receiving NSAIDs. Assessment of platelet function prior to performance of neuraxial block is not recommended. However, careful preoperative assessment of the patient to identify alterations of health that might contribute to bleeding is crucial [Urmeý and Rowlingson, 1998].

The pharmacologic differences of ticlopidine/clopidogrel and NSAIDs makes it impossible to extrapolate between the two groups of drugs regarding the practice of regional anesthesia. The risk associated with ticlopidine and clopidogrel is most likely increased, relative to the nonsteroidal antiinflammatory medications. Given the prolonged duration of the antiplatelet effect, it may be most prudent to avoid neuraxial blocks in patients who have recently received a ADP receptor antagonists. This decision should be made on an individual basis. Alternative anesthetic and analgesic techniques exist for patients considered to be at an unacceptable risk.

Patients should be monitored in the perioperative period for early signs of cord compression. If spinal hematoma is suspected, the treatment of choice is immediate decompressive laminectomy. Recovery is unlikely if surgery is postponed for more than 8–12 hours; less than 40% of the patients in Vandermeulen's series had partial or good recovery of neurologic function [Vandermeulen et al., 1994]

References

Benzon HT, Wong HY, Siddiqui T, Ondra S. Caution in performing epidural injections in patients on several antiplatelet drugs. *Anesthesiology* 1999; 91: 1558–1559.

CLASP (Collaborative Low-Dose Aspirin Study in Pregnancy) Collaborative Group. CLASP: a randomized trial of low-dose aspirin for the prevention

and treatment of pre-eclampsia among 9364 pregnant women. *Lancet* 1994; 343: 619–629.

Cronberg S, Wallmark E, Soderberg I. Effect on platelet aggregation of oral administration of 10 non-steroidal analgesics to humans. *Scand J Haematol* 1984; 33: 155–159.

Gerancher JC, Waterer R, Middleton J. Transient paraparesis after postdural puncture spinal hematoma in a patient receiving ketorolac. *Anesthesiology* 1997; 86: 490–494.

Greensite FS, Katz J. Spinal subdural hematoma associated with attempted epidural anesthesia and subsequent continuous spinal anesthesia. *Anesth Analg* 1980; 59: 72–73.

Horlocker TT, Bajwa ZH, Ashraft Z. Risk assessment of hemorrhagic complications associated with nonsteroidal anti-inflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. *Anesth Analg* 2002; 95: 1691–1697.

Horlocker TT, Wedel DJ, Offord KP. Does preoperative antiplatelet therapy increase the risk of hemorrhagic complications associated with regional anesthesia? *Anesth Analg* 1990; 70: 631–634.

Horlocker TT, Wedel DJ, Schroeder DR. Preoperative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia. *Anesth Analg* 1995; 80: 303–309.

Mayumi T, Dohi S. Spinal subarachnoid hematoma after lumbar puncture in a patient receiving antiplatelet therapy. *Anesth Analg* 1983; 62: 777–779.

Rodgers RPC, Levin J. A critical reappraisal of the bleeding time. *Semin Thromb Hemost* 1990; 16: 1–20.

Tryba M. Rückmarksnahe regionalanästhesie und niedermolekulare heparine: Pro. *Anästh Intensivmed Notfallmed Schmerzther* 1993; 28: 179–181.

Urmey WF, Rowlingson J. Do antiplatelet agents contribute to the development of perioperative spinal hematoma? *Reg Anesth Pain Med* 1998; 23: 146–151.

Vandermeulen EP, Van Aken H, Vermeylen J. Anticoagulants and spinal-epidural anesthesia. *Anesth Analg* 1994; 79: 1165–1177.

Williams KN, Jackowski A, Evans PJ. Epidural haematoma requiring surgical decompression following repeated cervical epidural steroid injections for chronic pain. *Pain* 1990; 42: 197–199.

POSTOPERATIVE PAIN MANAGEMENT – THE ROLE OF ACCEPTABLE PAIN SCORES (APS)

Leczenie bólu pooperacyjnego – rola skal bólu

Narinder Rawal

Örebro University Hospital, Sweden

In spite of major advances in our understanding of the pathophysiology of acute pain and the development of new analgesic medications and drug delivery techniques, significant number of patients continue to suffer from unrelieved postoperative pain. Historically, the treatment of postoperative pain has been given low priority by both surgeons and anesthesiologists. Therefore, patients accepted pain as an inevitable in their postoperative experience. Reports of unrelieved pain do not invariably result in corrective measures, and physicians and nurses have not traditionally been held accountable for poor analgesia. Even today, many patients do not receive adequate postoperative pain relief because of staff failures to routinely assess pain and pain relief [Puig et al., 2001]. Several reports indicate that the implementation of guidelines and introduction of APS are associated with improved standards of care [Wheatley et al., 1991; Miaskowski et al., 1999; Tighe et al., 1998]. However, more than a decade after their introduction, many institutions still do not have acceptable pain scores (APS) [Puig et al., 2001; Rawal and Allvin, 1998; Winsor et al., 1996].

In a survey of German hospitals published by Stamer et al; reviewed the literature on APS and stated that in spite of guidelines, most APS worldwide did not meet basic quality criteria, which were defined as: regular assessment and documentation of pain scores at least once a day, written protocols for pain management, personnel assignment for APS, and policies for postoperative pain management during nights and weekends [Stamer et al., 2002]. These quality criteria should represent requirements at the time of introduction of APS. A good APS should include much more.

Defining maximum acceptable pain scores and “making pain visible”

In the absence of formal, documented pain assessment, many medical and nursing staff continue to believe that patients who do not report pain do not feel pain. It is therefore essential that a maximum acceptable pain score is defined and pain intensity is routinely documented before and after treatment. Documentation also provides data for audit and facilitates review and improvement of care. Traditionally, patients have assumed that pain after surgery is inevitable, they are unlikely to be aware of the standard of care they can expect to receive and the potential benefits of effective pain relief. Quality assurance measures can no longer be ignored; patients should be informed that their pain will be maintained at or below of predefined threshold level (generally 3 on a 10-grade Visual Analog Scale) and that pain scores in excess of the threshold will trigger interventions to reduce pain.

Although each institution will have different requirements for its APS and modifications of published models will be necessary to accommodate local conditions, the main components of an APS should include the following: 1). designated personnel responsible for 24-hour APS (in small hospitals 1 or 2 individuals may be adequate), 2) regular pain assessment at rest and movement, maintaining pain scores below predetermined threshold level, and documentation (“make pain visible”), with appropriate scales for children and patients with cognitive impairment, 3). active cooperation with surgeons and ward nurses for development of protocols and critical pathways to achieve preset goals for postoperative mobilization and rehabilitation, 4). ongoing teaching programs for ward nurses for provision of safe and cost-effective analgesic techniques, 5). patient

education regarding pain monitoring and treatment options, goals, benefits and adverse effects, and 6). regular audit of cost-effectiveness of analgesic techniques on surgical wards and patient satisfaction of inpatients and day case patients.

The Joint Commission has recognized some of these issues on Accreditation of Healthcare Organizations (JCAHO), and independent not-for-profit organization that sets healthcare standards in the US. From 2001, accreditation of healthcare facilities in the United States will be determined, in part, by how they adhere to the JCAHO standards of pain assessment and care. Under the new rules, healthcare facilities must recognize that patients have the right to assessment and management of their pain. JCAHO standards require that hospitals assess, treat, and document patients' pain, guarantee the competence of their staff in pain assessment and management, and educate patients and families about effective pain management. Hospitals must also consider the needs of ambulatory surgery patients for information and guidelines about pain management after discharge from the hospital. The mandatory JCAHO requirements are a reflection of widespread dissatisfaction with pain management and a failure of pain services to address the issue by implementing hospital-wide quality assurance programs. In the US, it is expected that consumer demand will play an important role in bringing about the long-awaited changes in pain management.

Upgrading the role of ward nurses

Ward nurses have the responsibility for assessing the patient's pain intensity, monitoring the extent of regional block, administering prescribed analgesic treatments, and monitoring their efficacy and adverse effects. Recent studies have demonstrated that importance of the key role that nurses have in improving the efficacy of analgesic regimens. Specialist nurses or Acute Pain Nurses (APN) with particular training in pain management are increasingly being appointed as part of an acute pain team. They can educate nurses, give necessary support, and help initiate and supervise analgesia. They also improved collaboration among surgeons, anesthesiologists, and nurses on surgical wards.

The nursing role must be upgraded if postoperative pain management is to improve on surgical wards. In many countries and institutions, ward nurses are not allowed to inject opioids in intravenous (IV) lines or epidural catheters. They are expected to call APS physicians every time PCA and epidural doses need adjustments. This is time consuming, unrealistic, cost-ineffective, and unnecessary. These restrictions for ward nurses seem strand in view of the increasing trends towards self-treatment by patients. Outsi-

de hospitals, diabetic children are allowed to self-administer injections of potentially dangerous doses of insulin, and cancer patients are allowed to self-administer epidural and intrathecal drugs for pain relief. The use of home ventilators, home dialysis, home PCA devices, and opioids in non-cancer pain is increasingly accepted. Notably, in many hospitals, midwives are allowed to top-up epidural catheters for labor pain, but ward nurses are not allowed to do the same for postoperative pain. There is convincing evidence from many countries and institutions that with appropriate teaching and training, ward nurses are able to dose-titrate, monitor, and manage analgesic modalities, such as PCA and epidural on surgical wards. Nurse education is widely recognized as an important priority in pain management.

In summary, the answer to the question: "Is there a need for APS?" is a definite yes. A decade after their introduction, it is clear that APS are here to stay, however, their ideal structure and cost-effectiveness need to be established. Recent surveys continue to show that significant numbers of patients experience unacceptable levels of postoperative pain. Developing an APS is a process, not an event. In the next phase of APS development, several issues need to be addressed. These include implementation of quality assurance measures on a 24-hours hospital-wide basis, structured patient and staff education programs, and regular audits of cost-effectiveness of analgesic techniques. The integration of effective analgesia into general surgical care should be mandatory to improve outcome and will depend on close cooperation between the surgeons and anesthesiologist. APSs will also have to document their value and demonstrate the justification of allotted resources and expertise. The credibility of APS will be tested by organisations, such as JCAHO and consumers demanding better pain relief.

References

- Miaskowski C, Crews J, Ready LB, Paul SM, Ginsberg B. Anesthesia-based pain services improve the quality of postoperative pain management. *Pain* 1999; 80: 23–29.
- Puig MM, Montes A, Marrugat J. Management of postoperative pain in Spain. *Acta Anaesthesiol Scand* 2001; 45: 465–470.
- Rawal N, Allvin R, the European Acute Pain Working Party. Acute pain services in Europe: A 17-nation survey of 105 hospitals. *Eur J Anaesth* 1998; 15: 354–363.
- Stamer UM, Mpasios N, Stuber F, Maier C. A survey of acute pain services in Germany and a discussion of international survey data. *Reg Anesth Pain Med* 2002; 27(2):125–131.
- Tighe SQM, Bie JA, Nelson RA, Skues MA. The acute pain service: Effective or expensive care. *Anaesthesia* 1998; 53: 397–403.
- Wheatley RG, Madej TH, Jackson IJB, Hunter D. The first year's experience of an acute pain service. *Br J Anaesth* 1991; 67: 353–359.
- Winsor AM, Glynn CJ, Mason DG. National provision of acute pain services. *Anaesthesia* 1996; 51: 228–231.

EXTENDING CATHETER REGIONAL TECHNIQUES AT HOME

Ciągłe techniki RA w opiece domowej

Narinder Rawal

Örebro University Hospital, Sweden

Postoperative pain is one of the most common complaints after surgery and continues to be a challenge for anesthesiologists. Contrary to the common belief that day surgery is followed by mild pain, recent studies have shown that under-treatment of pain is common. About 30–45 % of discharged outpatients may suffer from moderate to severe pain during the first 24–48 h [Rawal et al., 1997; Bearegaard et al., 1998]. A recent systematic review and analysis of post discharge symptoms after day surgery has shown that 45 % patients experience postoperative pain at home [Wu et al., 2002].

Effective management of pain may make the difference between surgery being performed on an in-patient or day care basis. Although non-steroid anti-inflammatory drugs (NSAID's), paracetamol and weak opioids such as codeine and dextropropoxyphene are adequate for mild to moderate pain, these drugs may be ineffective in many patients with moderate to severe pain [Rawal et al., 2001].

By avoiding opioids regional anesthesia techniques provide excellent analgesia in an alert, co-operative patient untroubled by nausea. These techniques are among the most effective and versatile means for providing relief of acute pain.

Peripheral nerve catheter techniques for postoperative pain relief after ambulatory surgery

Peripheral nerve blocks can provide excellent analgesia over a limited field and with minimal systemic effect. Such blocks allow early ambulation and are indicated in increasing number of day surgery patients. Regional techniques are particularly useful in paediatric patients because they reduce or eliminate the need for repeated injections of parenteral opioids. Although peripheral blocks have been used satisfactorily as single-shot techniques, they have not gained widespread acceptance for prolonged postoperative analgesia because it has been assumed that they must be repeated every few hours. This assumption is not necessarily correct, because it has been found that a catheter can be inserted through the fascial sheaths which surround neurovascular compartments. Catheter techniques are possible for nearly all nerve blocks. In general peripheral nerve blocks are easy to perform, inexpensive and safe but are underused for postoperative analgesia [Horlocker, 1998]. In recent years several authors have demonstrated that perineural catheter techniques are feasible, safe, and effective for postoperative analgesia after ambulatory surgery of upper and lower extremities [Rawal et al., 2002; Ilfeld et al., 2002a,b; Klein et al., 2000; Chelly et al., 2002; Enneking and Ilfeld; 2002]. An editorial suggested that extending such regional techniques to the patients' home could

be next stage in the development of regional techniques in pain management [Klein, 2002].

Incisional and intra-articular catheter techniques

Although they are effective, peripheral blocks have a potential for significant complications. They also have the disadvantage of requiring needle placement and sensory and motor block of the entire arm preventing postoperative neurological assessment. Incisional and intra-articular use of local anesthetic drugs to treat postoperative pain is an attractive technique because of its simplicity, safety and low cost. The use of local anesthetic in the wound or joint has several advantages over peripheral blocks for postoperative analgesia. Incisional catheter techniques by intermittent boluses or continuous infusions have been used for postoperative analgesia after different surgical procedures such as hernia repair, major abdominal surgery, laparoscopic cholecystectomy and skeletal surgery (iliac crest bone harvesting, maxillo-facial). The technique has also been used in the management of chronic pain and cancer pain. Catheters have been placed subcutaneously, subfascially, supraperiosteally, intra-articularly and intraperitoneally. Controlled studies of incisional analgesia by intermittent boluses of local anesthetics have shown effective analgesia following inguinal hernia repair, shoulder surgery, hysterectomy and section [Vintar et al., 2002, Zohar et al., 2001; Gupta et al., 2002, Axelsson et al., 2003; Fredman et al., 2000]. Incisional and intraarticular catheter techniques have been shown to be safe and effective in the patients' home [Axelsson et al., 2003; Rawal et al., 1998].

The technique of PCRA at home

We have described a technique using an elastometric balloon pump, which allows the patient to self-administer local anesthetic analgesia at home [Rawal et al., 1998]. The technique involves the placement of a multihole, thin (22-gauge) epidural or Perifix brachial plexus catheters subcutaneously into the surgical wound, subacromially, intraarticularly or in the axillary brachial plexus sheath (Table 1). The catheter is tunnelled 4–5 cm subcutaneously by the surgeon and firmly secured on the skin by sterile tape. Axillary brachial plexus catheters are placed and secured in position by anesthesiologists. The catheters are introduced 3–5 cm within the sheath and secured to the skin by transparent dressing and tape.

Using aseptic technique the catheters are connected to a 50 ml or 100 ml elastometric (balloon) pump with the appropriate concentration and volume of local anaesthetic drug (Home pump®, I-Flow Corporation, Lake Forest, CA, USA). The balloon pump is filled with a volume of local

anesthetic to provide 10 doses for postoperative pain management. Postoperatively, when the patient feels pain he starts the local anesthetic infusion by opening the clamp. The patient stops the infusion by closing the clamp after the prescribed time (usually 6 min) or earlier if he is satisfied with pain relief. When the patient does not need analgesia any further, he removes the tape, pulls out the catheter and discards the pump. In most cases the patient self-administers the first dose in the PACU.

Bupivacaine 0.125 % was used in brachial plexus catheters, in all other catheters 0.25 % concentration was used. The 0.125 % solution was used to reduce or avoid the risk of possible injury due to excessive motor block. The maximum volume of local anesthetic allowed for each administration was 2.5 ml for maxillofacial surgery, 5–10 ml for surgical wounds, 10 ml for the remaining procedures. An appropriate pump (50 ml or 100 ml) filled with local anesthetic to provide 10 doses at home was given to the patient before discharge. The patient was instructed to avoid using the pump more than once every hour. Follow-up consisted of evaluation of pain relief at home, pump function, use of rescue medication and overall satisfaction/dissatisfaction with the technique.

Pain relief was graded good to excellent by 90 % of patients. Onset of analgesia was experienced within 5 min, the duration of analgesia after each administration of local anesthetic varied from 2–8 h. Patient follow-up did not reveal any infection or any other major problem with the technique, patient satisfaction was very high. To date over 1000 patients undergoing a variety of surgical procedures (Table 1) have been treated with patient controlled regional anesthesia (PCRA) without any major complications. A recently completed double-blind study comparing 0.125 % bupivacaine versus 0.125 % ropivacaine brachial plexus PCRA showed that both drugs provided effective analgesia after hand

surgery. In this study ropivacaine was superior to bupivacaine. Patient satisfaction was high, 87 % patients would prefer PCRA at home again [Rawal et al., 2002]. In other controlled studies PCRA was demonstrated to be effective for incisional analgesia following Caesarean section [Fredman et al., 2000], hysterectomy [Zohar et al., 2001], and inguinal surgery [Vintar et al., 2002]. Controlled trials are also in progress to compare this technique with traditional methods and to evaluate the optimal concentration and volume of local anesthetic. The importance of adequate patient information is emphasised (Table 2).

Table 2

Patient instructions for postoperative PCRA at home

<p>Inform the patient about the technique and how “balloon pump” works (oral and written information). Information should also include the following:</p> <ul style="list-style-type: none"> • Importance of opening and closing the clamp at prescribed times (use of a timer is encouraged). • Removal of catheter at the end of treatment. • Importance of good hygiene near the wound area.
<p>Provide the name and telephone (and beeper) number(s) of physician to be contacted in case of local anaesthetic toxicity symptoms or other problems.</p>
<p>Ask patient to return follow-up data about technique and satisfaction in self-addressed envelope.</p>
<p>Telephone follow-up day after surgery by a nurse or physician.</p>

The possible risk of local anesthetic toxicity with the pump described here can be prevented with newer devices which allow a continuous infusion of local anesthetic at a pre-set rate. For example a 100 ml elastometric pump can provide adequate analgesia at home for two days when the local anesthetic is infused at a rate of 2 ml/hour. However, this is not PCRA. Newer lightweight pumps with appropriate safety features and disposable cassettes for local anesthetic solutions are now available to provide safe PCRA in the patients’ home environment. Currently there are several elastomeric and battery-driven pumps available for self-administration of local anesthetic analgesia at home. A recent study comparing elastomeric and electronic pumps has shown that the simple elastomeric pumps are preferred by patients [Capdevila et al., 2003]. Further studies are necessary to establish the efficacy and safety of this promising new technique of PCRA at home after ambulatory surgery. It is also emphasised that although the technique of home PCRA is simple it should only be used if there is a 24-hour access to a physician and the patient (and escort) is well informed about possible risks (Table 2).

Reference

Axelsson K, Johanson E, Gupta A, et al. Intra-articular administration of ketolorac, morphine, and ropivacaine combined with patient-controlled regional analgesia (PCRA) for pain relief during shoulder surgery. *Acta Anaesth Scand* 2003 (in press).

Bauregard L, Pomp A, Choinière M. Severity and impact of pain after day-surgery. *Can J Anaesth* 1998; 45: 304–1301.

Capdevila X, Macaire P, Aknin P, Dadure C, Bernard N, Lopez S. Patient-controlled perineural analgesia after ambulatory orthopedic surgery: a comparison of electronic versus elastomeric pumps. *Anesth Analg* 2003; 96: 414–417.

Table 1

Type of surgery and site of catheter placement for PCRA

Surgery	Site of catheter placement
Hand surgery	<ul style="list-style-type: none"> • Brachial plexus sheath • Surgical wound
Shoulder surgery	<ul style="list-style-type: none"> • Interscalene block • Subacromial • Intraarticular
Breast surgery (augmentation, mastectomy)	<ul style="list-style-type: none"> • Surgical wound
Bone harvesting	<ul style="list-style-type: none"> • Supra periosteal (iliac crest)
Inguinal hernia	<ul style="list-style-type: none"> • Surgical wound (subcut., subfascial)
Maxillo-facial surgery	<ul style="list-style-type: none"> • Supra periosteal
Obst. Gyn. Surgery	<ul style="list-style-type: none"> • Surgical wound (C. section, hysterectomy)
Miscellaneous	<ul style="list-style-type: none"> • Surgical wound

Chelly JE, Delaunay L, Williams B, Borghi B. Outpatient lower extremity infusion. *Best Practice & Research. Clinical Anaesthesiology* 2002; 16(2): 311–320.

Enneking FK, Ilfeld BM. Major surgery in the ambulatory environment: continuous catheters and home infusions. *Best Practice & Research. Clinical Anaesthesiology* 2002; 16(2): 285–294.

Fredman B, Shapiro A, Zohar E. The analgesic efficacy of patient-controlled ropivacaine instillation after cesarean delivery. *Anesthesia & Analgesia* 2000; 91: 1436–1440.

Gupta A, Thörn SE, Axelsson K. Postoperative pain relief using intermittent injections of 0.5 % ropivacaine following laparoscopic cholecystectomy. *Anesth Analg* 2002; 95: 450–456.

Horlocker TT. Peripheral nerve blocks – regional anaesthesia for the new millennium (Editorial). *Reg Anesth Pain Med* 1998; 23: 237–240.

Ilfeld B, Morey T, Enneking F. Continuous infraclavicular brachial plexus block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. *Anesthesiology* 2002a; 96: 1297–1304.

Ilfeld BM, Morey TE, Wang RD, Enneking FK. Continuous popliteal sciatic nerve block for postoperative pain control at home: a randomised, double-blinded, placebo-controlled study. *Anesthesiology* 2002b; 97(4): 959–965.

Klein S, Grant S, Greengrass R, Nielsen K, Speer K, White W, Warner D, Steele S. Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. *Anesth Analg* 2000; 91: 563–565.

Klein SM. Beyond the hospital. Continuous peripheral nerve blocks at home. *Anesthesiology* 2002; 96: 1283–1285.

Rawal N, Allvin R, Amilon A, Ohlsson T, Hallén J. Postoperative analgesia at home after ambulatory hand surgery: A controlled comparison between tramadol, metamizol, and paracetamol. *Anesth Analg* 2001; 92: 347–351.

Rawal N, Allvin R, Axelsson K, Hallén J, Ekback G, Ohlsson T, Amilon A. Patient-controlled regional analgesia (PCRA) at home: Controlled comparison between bupivacaine and ropivacaine brachial plexus analgesia. *Anesthesiology* 2002; 96: 1290–1296.

Rawal N, Axelsson K, Hylander J, Allvin R, Amilon A, Lidgran G, Hallén J. Postoperative patient-controlled local anesthetic administration at home. *Anesth Analg* 1998; 86: 86–89.

Rawal N, Hylander J, Nydahl P-A, Olofsson I, Gupta A. Survey of postoperative analgesia following ambulatory surgery. *Acta Anaesthesiol Scand* 1997; 41: 1017–22.

Vintar N, Rawal N, Po•lep G. Incisional analgesia by self-administration of local anaesthetic solution on demand after inguinal hernia repair: a comparison of bupivacaine and ropivacaine. *Can J Anaesth* 2002; 49: 481–486.

Wu Christopher L, Berenholtz Sean M, Pronovost Peter J, Fleisher Lee A. Systematic review and analysis of postdischarge symptoms after outpatient surgery. *Anesthesiology* 2002; 96: 994–1003.

Zohar E, Fredman B, Phillipov A. The analgesic efficacy of patient-controlled bupivacaine wound instillation after total abdominal hysterectomy with bilateral salpingo-oophorectomy. *Anesth Analg* 2001; 93: 482–487.

EYE BLOCKS

Blokady oka

Anthony Rubin

Wellington Eye Unit, London, UK

A detailed understanding of the anatomy of the orbit and surrounding structures is essential to the safe practice of eye blocks. Much new information has been obtained by the use of cadaveric orbital fixing and more recently the use of CT and MRI scanning [Johnson, 1995]. The aim is to deposit local anaesthetic in sites where sensory and motor block may be achieved without damaging the globe, blood vessels, the lacrimal apparatus, muscles or the optic nerve and its dural cuff.

The globe occupies the front half of the orbit, and is about 7 cc in volume and 23 – 25 mm long (the axial length is the distance from the front of the cornea to the retina). Myopic eyes may be longer (more than 26 mm), have thinner sclerae and even develop bulges (staphylomata) especially posteriorly in the inferotemporal compartment. Thus they are at greater risk of perforation by a needle. The equator is about half way back on the globe.

The orbit itself is a four-sided pyramidal cavity with its apex placed posteromedially and its base being the quadrilateral anterior opening bounded by the orbital margins. It has a total volume of about 30 ml. The base is 4 cm horizontally and 3,5 cm vertically. The two orbits are about 2.5 cm apart, and have parallel medial walls and lateral walls that are perpendicular to each other. The thin medial wall is formed by the maxilla, lacrimal, ethmoid and body of the sphenoid posteriorly. It runs backward parallel to the sagittal plan. The thick lateral wall is formed by the zygomatic anteriorly and the greater wing of the sphenoid posteriorly. It runs inwards at 45 degrees. The lateral orbital rim is set

back 12 – 18 mm behind the corneal apex, allowing easier access to the orbital fat in the inferotemporal region. The roof is formed anteriorly by the orbital plane of the frontal bone and posteriorly by the lesser wing of the sphenoid. It is horizontal. Between the roof and the lateral wall lies the superior orbital fissure. The floor which is formed by the maxillary bone medially, the zygomatic laterally and the palatine bone posteriorly, runs upwards at about 10 degrees. The orbital cavity may be divided for descriptive purposes into three regions: anterior (between the lids and the insertion of the recti muscles), mid (between the insertion of the recti muscles to 10mm behind the globe), and posterior (from 10mm behind the globe to the optic foramen). In the posterior orbit the arteries, veins and nerves are all tightly compressed against each other and are vulnerable targets if needles are inserted deeply. The optic foramen lies posteromedially and carries the optic nerve and ophthalmic artery from the middle cranial fossa to the orbit. The globe may be closer to the roof than to the floor of the orbit, and also closer to the lateral than the medial wall. The visual axis in primary gaze differs from the orbital axis by about 23 degrees. The exact position of the front of the globe in relation to the orbital opening may vary in different individuals and with pathology.

The four recti muscles arise from the annulus of Zinn at the back of the orbit and run forwards to insert into the globe just anterior to its equator. The muscle cone is considered to form a boundary between two compartments, the central (retrobulbar) space and the peripheral (peribulbar)

space. However the orbital fat, while divided by fine septa into compartments, is continuous both inside and outside the cone and solutions spread freely from one space to the other. Within the cone is the optic nerve, the trunk of the ophthalmic artery, the ciliary ganglion and the nerves to the muscles. All these structures are vulnerable to trauma, decreased blood supply or pressure. To have the best chance of avoiding them, needles should be short so that they cannot be inserted too far into the orbit. The eyelids protect the eye from injury and excessive light, and allow tears to spread over the surface of the eyeball. They may need to be paralysed for intraocular surgery by blocking the oculomotor innervation of the levator palpebrae superioris and the terminal facial nerve supply to the orbicularis oculi. This can be done from within the orbit as dehiscences above and below the medial orbital septum allow forward movement of solution, so that a separate facial nerve block is no longer required.

The orbital fat compartment is similar to the epidural space or brachial plexus sheath in containing fat, connective tissue septa and blood vessels. The least vascular areas are found in the inferotemporal, nasal and superotemporal areas and it is usual to prefer these sites for the insertion of the needles [Hamilton et al., 1998].

The sensory supply of the orbit is provided by the lacrimal, frontal and nasociliary branches of the ophthalmic division of the trigeminal nerve (V), each of which enters the orbit through the superior orbital fissure. Autonomic fibres run from the ciliary ganglion, which is situated within the cone near to the orbital apex. The oculomotor nerve (III) supplies the superior, inferior and medial rectus muscles as well as the inferior oblique and levator palpebrae superioris; the trochlear nerve (IV) supplies the superior oblique; the abducent nerve (VI) supplies the lateral rectus; and the facial nerve (VII) the orbicularis oculi. After traversing the stylohyoid foramen the facial nerve passes through the parotid gland, and its temporal and zygomatic branches innervate the orbicularis oculi muscle.

The eye is covered with conjunctiva and deep to the conjunctiva is Tenon's capsule, a fibrous sheath of tissue, which is very developed in young people but in the elderly tends to blend with the conjunctiva. Beneath Tenon's capsule is the sub-Tenon's or episcleral space, which is traversed by fine bands of connective tissue. Tenon's capsule posteriorly blends with the sheaths of the recti muscles. The injection of local anaesthetic into the Sub-Tenon's space by means of a blunt cannula is becoming a very popular method of local anaesthesia, and has been shown to act by the solution entering the anterior retrobulbar space behind the globe. It may combine efficacy with a suggested lower rate of complications than sharp needle blocks such as peribulbar or retrobulbar injections [Thind and Rubin, 2001].

Thus knowledge of anatomy allows the development of techniques of eye blocks which maximise efficacy and reduce the risk of complications to a minimum. Administration of local anaesthetic can be particularly challenging in those with shallow orbits or deep-set eyes, prominent brow and nasal bridge, previous orbital fractures, and previous

surgery involving extraocular implants such as encircling bands.

While many cataract operations are now performed with only topical drops with or without subconjunctival injections or intracameral infusion of local anaesthetic, this abstract concentrates on retrobulbar and peribulbar blocks (sharp needle techniques) and sub-Tenon's block (a blunt cannula technique).

Retrobulbar and peribulbar blocks

Although retrobulbar and peribulbar blocks are usually considered separately, the injection is made into the same adipose tissue compartment and it is merely a matter of needle length and direction. Most of the structures to be blocked are in a central location and so the more central blocks work quicker and more effectively (Hamilton et al., 1988). Thus the more peripheral blocks usually take longer to work, require larger volumes of local anaesthetic, and more injections.

Techniques have been devised to be as painless as possible. The preferred route is through the conjunctiva, which is easily anaesthetised with drops. However if the patient has a deep-set eye, a narrow palpebral fissure, or is unable to stop screwing up the eye, the transcutaneous approach may be safer.

The patient lies supine or semi-sitting and the eye looks straight-ahead ("primary gaze position"). This allows the optic nerve to remain behind the globe and not rotate towards the needle. With the conjunctiva anaesthetised with Benoxinate 0.4% or Proxymetacaine 0.5% and the lower eyelid pulled downwards and outwards, about 1 ml of 0.2% lignocaine ("painless local anaesthetic solution" made up with 2% lignocaine mixed with ten times its volume of balanced salt solution) is injected with a 1 cm 30 g needle in the inferotemporal region of the inferior conjunctival fornix as far temporal as possible. A more temporal approach reduces the chance of damaging or injecting into the inferior oblique muscle. The needle is inserted at the tangent to the globe and the injection should go into the fat and not lift the conjunctiva. This injection should be painless and make the subsequent injections equally painless. About two minutes later, a 25 g 2.5 cm sharp disposable needle is inserted through the same entry point and after going tangentially is aligned parallel to the orbital floor. The injection may be made at a depth of 1 to 2 cm ("peribulbar") or the needle, once the tip has passed the equator, angled upwards and inwards to enter the more central region just behind the globe ("shallow retrobulbar") [Hamilton, 1996]

After careful aspiration, up to 5 ml of solution should be injected very slowly. It should be painless and without resistance. The upper lid may be seen to fill and drop (ptosis) and this is a good sign. The pressure within the globe must be assessed, and if it rises, the injection should be stopped. Normally the globe should feel soft and move freely within the orbit, and there should not be proptosis. There may be some filling of the lower lid and some sub-conjunctival swelling (chemosis). If either is excessive, the needle should be repositioned before the injection is continued.

The choice of local anaesthetic depends on the required duration, both lignocaine and bupivacaine or a mixture of the two being most commonly used. High concentrations e.g. lignocaine 2% or bupivacaine 0.75% are preferred to achieve optimal motor block. Studies have confirmed the suitability of levobupivacaine or ropivacaine as well, [McLure and Rubin, 1998; McLure et al., 1999]. Hyaluronidase (not more than 15 iu/ml) is often added to help spread and thereby improve the onset and quality of the block. It may also help absorption of the fluid so that any rise in pressure is transient. Long duration means prolonged corneal anaesthesia and motor block, necessitates postoperative eye padding and leads to a high incidence of postoperative diplopia often lasting into the next day.

Great care should be taken to choose the least vascular areas, to withdraw the needle very carefully and to apply gentle pressure on the closed eye immediately to control any potential haemorrhage. The anaesthetised cornea must be protected from possible damage at all times and kept moist.

Within five minutes, significant akinesia should be apparent. If there is failure to block the medial rectus or the orbicularis oculi, the same needle may be inserted in to the nasal (medial) compartment [Hustead et al., 1994]. The needle is inserted through the conjunctiva between the caruncle and the skin of the medial canthus, and directed straight back parallel to the medial orbital wall. The resistance of the medial orbital septum will be felt and once it has been pierced, and after negative aspiration, a further 3 – 5 ml is injected at a depth of 1.5 – 2 cm. Some of the solution will remain deep to the medial orbital septum and improve the peribulbar block, while some will come forwards through foramina above and below the septum to fill the eyelids and block the orbicularis oculi. If the needle is inserted too far there is a risk of it entering the central space and damaging the optic nerve or the injection going into its sheath. If the first inferotemporal injection was central, and is followed by the nasal injection, only about 2% will require a further injection. However if it was peripheral, the number rises to about 25% if full akinesia is required. The further injection is done according to the clinical deficiency. A need for further block of the medial rectus or orbicularis oculi warrants a nasal injection, while failure to block adequately the superior rectus or levator palpebrae superioris may justify a superotemporal injection through the skin of the closed upper lid in line with the lateral limbus. The superotemporal injection must go upwards towards the orbital roof to avoid the globe as there is only limited space between the globe and the orbital roof. Not more than 3 ml of solution is required. If there is failure to block several muscles, the inferotemporal injection should be repeated.

These subsequent injections should be painless because the initial one is likely to produce adequate anaesthesia even if not total akinesia. Each injection should be followed by a period of firm pressure, and adequate akinesia and low intraocular pressure achieved before the patient is offered for surgery. However only as much akinesia as the surgeon

requires is warranted, and it must be stressed that every additional injection carries risks.

Sub-tenon's block

In the last few years, continuing concern over the rare but serious complications of sharp needle blocks, in particular globe perforation and retrobulbar haemorrhage, has led to the rediscovery and increasing use of sub-Tenon's block [Stevens, 1992; Smerdon, 2001; Thind and Rubin, 2001]. After the application of topical anaesthesia and full asepsis, a very small incision is made in the inferonasal conjunctiva about 5 mm from the limbus. Blunt dissection with spring scissors opens the space around the globe between Tenon's fascia and the sclera. A blunt cannula is passed along this track towards the back of the globe and about 5 ml of solution injected. The solution should largely remain behind the eye and not come forwards through the incision or produce excessive chemosis. There will be rapid onset of anaesthesia and akinesia, the latter being volume dependent.

Complications

Complications may be due to systemic toxicity or allergic reactions. Bruising (ecchymosis), sub-conjunctival haemorrhage, orbital (retrobulbar) haemorrhage, globe penetration or perforation, temporary loss of vision, direct damage to the optic nerve or injection or haemorrhage within the optic nerve sheath, central spread of local anaesthetic, external ocular muscle palsies and subconjunctival oedema (chemosis) may all occasionally be seen [Davis and Mandel, 1994; Hamilton, 1999].

References

- Davis DB II, Mandel MR. Efficacy and complication rate of 16,224 consecutive peribulbar blocks: A prospective multicenter study. *J Cataract Refract Surg* 1994; 20: 327–337.
- Hamilton RC, Gimbel HV, Strunin L. Regional anaesthesia for 12,000 cataract extraction and intraocular lens implantation procedures. *Can J Anaesth* 1988; 35: 615–623.
- Hamilton RC. Retrobulbar block revisited and revised. *Journal of Cataract & Refractive Surgery* 1996; 22:1147–1150.
- Hamilton RC. Complications of ophthalmic regional anaesthesia, W: Finucaine B (red.). *Complications of regional anaesthesia* Churchill Livingstone, New York: 1999.
- Hustead RF, Hamilton RC, Loken RG. Periocular local anaesthesia: Medial orbital as an alternative to superior nasal injection. *J Cataract Refract Surg* 1994; 20: 197–201.
- Johnson RW. Anatomy for ophthalmic anaesthesia. *Brit J Anaesth* 1995; 75: 80–87.
- McLure HA, Rubin AP. Comparison of 0.75% levobupivacaine with 0.75% racemic bupivacaine for peribulbar anaesthesia. *Anaesthesia* 1998; 53: 1160–1164.
- McLure HA, Rubin AP, Westcott M, Henderson H. A comparison of 1% ropivacaine with a mixture of 0.75% bupivacaine and 2% lignocaine for peribulbar anaesthesia. *Anaesthesia* 1999; 54: 1178–1182.
- Stevens JD. A new local anaesthesia technique for cataract extraction by one quadrant sub-Tenon's infiltration. *Br J Ophthalmol* 1992; 76: 670–674.
- Smerdon D. Needle local anaesthesia for cataract surgery: A chip off the old block? *Eye* 2001; 15: 439–440.
- Thind GS, Rubin AP. Local anaesthesia for eye surgery – no room for complacency. *Brit J Anaesthesia* 2001; 86: 473–476.

LEVOBUPIVACAINE IN REGIONAL ANAESTHESIA – CLINICAL EXPERIENCE

Rola lewobupiwakainy w regionalnej anestezji – doświadczenia kliniczne

Jan Jacek Rykowski

ANIVA, Pain Management Unit, University Hospital Orebro, Sweden

Bupivacaine has remained in use in regional anaesthesia over three decades. **Levobupivacaine** and **ropivacaine** are two new amide type local anaesthetics introduced into the clinical practice as potential replacement for bupivacaine. They were developed in response to circulatory toxic complications – based on anecdotal cardiac arrest reports – associated with the inadvertent administration of bupivacaine overdoses [Albright, 1979].

Already during the early investigations and exploration of bupivacaine toxicity the significance of chirality and stereochemistry of their structure became apparent. Administration of a racemate can give rise to a range of diverse effects, depending on the pharmacological profile of each enantiomer and its distribution and metabolism and differences between the isomers [McLeod and Burke, 2001; Groban, 2003]. **All three compounds** are very similar in chemical structure (a four-carbon side-chain of bupivacaine and levobupivacaine is replaced with a three-carbon side-chain of ropivacaine), however bupivacaine is prepared as a racemic mixture while levobupivacaine and ropivacaine are prepared in the almost pure L-isomer form. Animal toxicity testing revealed from the beginning that the toxic lethal doses (LD50) were significant lower for the R(+) than for S(-) isomer of bupivacaine, where S(-) bupivacaine had a stronger protein binding and resulted in longer duration of anaesthesia after skin infiltration and produced in vitro stronger inhibition of sodium channels in peripheral nerves [McLeod and Burke, 2001; Groban, 2003].

Although the mechanism remains unknown, the S-isomer of racemic bupivacaine binds to cardiac sodium channels more intensely than do the R+isomers of levobupivacaine or ropivacaine. In particular, the persistence of the inhibition and the block of sodium channels slows myocardial conduction and predisposes the heart to re-entrant arrhythmias. The dissociation time constant for bupivacaine is around ten times longer than that of lidocaine, and S (-) bupivacaine has a considerable greater cardiac depressant effect than is suggested by its relative potency at sodium channels compared to lidocaine [McLeod and Burke, 2001; Groban, 2003].

As a result, levobupivacaine and ropivacaine are reportedly less cardiotoxic than bupivacaine and additionally, ropivacaine has the reported advantage of producing less motor blockade than bupivacaine. Are these benefits enough significant to replace bupivacaine in modern clinical practice with newer agents?

Levobupivacaine in clinical studies

Peripheral nerve blocks/brachial plexus block – Levobupivacaine was compared in two concentrations (0.25% and 0.5%) with racemic bupivacaine 0.5% in 76 patients

undergoing hand surgery under supraclavicular **plexus block** [Cox et al., 1998]. A standard volume of 0.4 ml/kg was used for all patients. Higher dermatomes were blocked more consistently and complete block was achieved in higher percentage of patients receiving levobupivacaine 0.5% (81%) than in those who received levobupivacaine 0.25% (68%) or bupivacaine 0.5% (74%). It was not possible to demonstrate a dose-response effect, although there was a tendency for levobupivacaine 0.25% to have a slower onset, shorter duration and lower overall success rate than levobupivacaine 0.5% or bupivacaine 0.5%. Mean (SD) duration of sensory analgesia was longer for levobupivacaine 0.5% – 1039 (317) min without significance in between levobupivacaine 0.25% – 892 (250) min vs. bupivacaine 0.5% – 896 (284) min.

Spinal anaesthesia – levobupivacaine plain (i.e. glucose-free) 0.5% 3 ml was administered for spinal anaesthesia in 20 patients scheduled to undergo lower limb surgery [Burke et al., 1999]. Satisfactory surgical anaesthesia was achieved in 18 patients with complete motor block but variable spread of analgesia were noted, largely attributed to the fact that plain levobupivacaine at 37°C is hypobaric!

Epidural anaesthesia – two studies have been performed on surgical patients. The first comparing levobupivacaine in two concentrations 0.5% and 0.75% and racemic bupivacaine 0.5% in patients undergoing lower limb vascular surgery or arthroscopy [Cox et al., 1998]. **Time to onset** of block and **duration** of sensory and motor block were similar with 0.5% preparations. Longer time of sensory and motor blocks in the 0.75% preparations indicates a dose response effect with the 0.5% and 0.75% concentrations of levobupivacaine. In the second study [Kopacz et al., 2000] 15 ml of the 0.75% preparations were compared to assess adequacy of anaesthesia for major abdominal surgery. There was no difference in the speed of onset of sensory or motor block but there was a significant longer mean duration of sensory block with levobupivacaine, 551 (88) min. vs. 506 (71) min while motor block was 355 (83) and 376 (71) min for levobupivacaine and bupivacaine respectively. There was no difference in Relaxation of Abdominal Muscle score (RAM).

Caesarean section – two studies by Bader et al., [Bader et al., 1999] and by Datta compared **epidural** bupivacaine 0.5% 30 ml and levobupivacaine 0.5% 30 ml for elective Caesarean section in 60 women aged 18–40 years. Assessment of sensory block showed **no difference** between two solutions in the time to reach bilateral T4-T6 sensory block. Time to regression of the block to T10 and time to complete offset of sensory block were not significantly different. All patients experienced motor blockade-Bromage score of 2 or 3 within 30 min and the mean time to complete offset of the motor blockade was 241 min for levobupivacaine

group and 265 min. for the bupivacaine group. In the other similar study where the protocol was slightly different 62 patients received 25 ml of either levobupivacaine 0.5% or bupivacaine 0.5% with an optional 5 ml of rescue dose to obtain adequate anaesthesia level. **No difference** was noted in onset or duration of sensory block between the two solutions. The motor block was significantly more pronounced in the levobupivacaine group (77%) than in the bupivacaine group (58%)!

Labour analgesia – Comparison of the relative potency of drugs by interpretation of clinical efficacy studies is difficult. To compare the relative potency of the drugs one should determine the Median effective Local Anaesthetic Concentration (MLAC) of the drug that produce a desired clinical effect in 50% of those treated and extrapolate this results to 95% of the group [Columb and Lyons, 1995].

In order to compare the relative potencies of levobupivacaine and bupivacaine, 60 women in early labour were given 20 ml of either drug by the epidural route, at concentrations ranging from 0.05% to 0.12%, and an effective or ineffective outcome was determined [Lyons et al., 1998]. This study showed **no difference** between the MLAC of levobupivacaine (0.083%) and bupivacaine (0.081%).

A multicenter study by Burke et al., evaluated levobupivacaine and bupivacaine when

used to provide epidural analgesia in 137 women for labour as top-up injection of 10 ml of 0.25% solution [Burke et al., 1999]. The study found levobupivacaine and bupivacaine to have an **equivalent** analgesic efficacy. Following the initial injection both drugs had the same median onset time of 12 min. and very **similar** median **duration**, 49 min. and 51 min. for levobupivacaine and bupivacaine respect. The first top-up injection gave median onset time of 7 min. and median duration of 82 min for levobupivacaine and 76 min. for bupivacaine. Motor blockade was similar between the groups, with a higher proportion of both groups having a Bromage score of 0 after the initial injection (levobupivacaine 84% and bupivacaine 83%) with increased motor block values after first top-up injection of 66% and 63% for levobupivacaine and bupivacaine respectively. A study comparing epidural infusion of levobupivacaine 0.125% and bupivacaine 0.125% for continuous labour analgesia was conducted in 80 patients [Convery et al., 1999]. Levobupivacaine and bupivacaine were found to be **equally** effective providing **analgesia** and **duration** of pain free hours with mean total dose received 28.3 mg/h for levobupivacaine and 27.2 mg/h for bupivacaine. It is of interest to note that there was a trend towards less motor block in patients receiving levobupivacaine.

Ten levobupivacaine patients maintained a Bromage score of 0 compared to five in the bupivacaine group, while only one levobupivacaine group patient, compared to six bupivacaine group patients reached a score of 3 after top-ups.

Pharmacokinetics, maternal-fetal distribution. In comparative studies of levobupivacaine and racemic bupivacaine in obstetric patients, no significant differences in maximum plasma concentrations (Cmax.) or (AUC) values have

been found [Bader et al., 1999; Henderson et al., 1998]. Of further concern for the safe use of local anaesthetics in pregnancy is the effect of local anaesthetic on **uterine blood flow** and extent of uptake of the **drug by the fetus**. These factors were examined in a study comparing bupivacaine, levobupivacaine and ropivacaine in animal model [Santos, 1999]. All three drugs were shown to cross the placenta and were taken up into fetal tissues. Fetal serum concentrations and fetal tissue distribution were **similar** for each agent and were not associated with any important haemodynamic changes. Clinical measurements of bupivacaine concentrations in maternal and fetal plasma showed low fetal/maternal ratios after epidural administration, with umbilical vein to maternal vein ratios of approximately 0.3 being consistently reported [McLeod et al., 2000]. In clinical obstetric studies, infants were assessed using both NAC score system and Apgar Scores [Bader et al., 1999; Polley et al., 1999]. The results indicate that the favourable profile of bupivacaine, in terms of outcome of labour and well-being of the newborn, is also seen with levobupivacaine. **No differences** were found between levobupivacaine and bupivacaine treated patients in either mode of delivery or infant NAC and Apgar scores.

Vasoactivity – Local anaesthetics not only block ion channels but also exert a vaso-active effects on blood vessels, where vasoconstriction can provide additional safety benefits by limiting systemic uptake of local anaesthetics. In a study by Aps and Reynolds [Aps et al., 1978] there were no differences noted between the two isomers of bupivacaine at subclinical concentrations (0.016%). Analgesic and anaesthetic concentrations of levobupivacaine (0.125%, 0.255%, 0.5%, 0.75%) were compared in a study by Newton et al. [2000]. All injections, including controls, produced a rapid increase in skin blood flow, and all except bupivacaine 0.75%, had recovered back to baseline levels by 40 min.

Bupivacaine and levobupivacaine have been found to have a biphasic effect on the skin microcirculation, with the exception of bupivacaine 0.75%, but levobupivacaine is consistently associated with less vasodilation.

Conclusions – The studies reviewed in the literature show levobupivacaine to be less toxic than bupivacaine. Bupivacaine produces excitatory CNS effects/convulsions at a lower dose than levobupivacaine. Although they both cause effects on the heart, the dose that results in myocardial depression and ultimately fatal arrhythmias, is higher with levobupivacaine than bupivacaine. This is of particular concern in the obstetric population since this group of patients is most vulnerable in the event of toxic reaction and even cardiac arrest. In the evaluation programmes for both ropivacaine and levobupivacaine, intravascular injections occurred with an incidence of 1:500 to 1:600, despite all measures undertaken and procedures provided by experts in a controlled, elective setting [Kopacz et al., 1999].

Subsequent changes in practice of regional anaesthesia with use of incremental low doses of local anaesthetics, repeated use of test doses and continuous infusions of low concentrations of local anaesthetics, particularly bupivacaine, together with the increased awareness of the relation-

ship between stereoselectivity and toxicity were able to reduce abruptly the risk and incidence of severe toxicity especially in obstetrics and postoperative pain relief. Such measures could not guarantee however safety in the event of accidental intravascular injection.

Increasing utilization of regional anesthesia techniques, often conducted by non experts, increase the need for a long acting local anaesthetic that enjoy the benefits of bupivacaine but with lower potential for toxicity. Clinical studies indicate that **levobupivacaine** is well tolerated and has an efficacy equivalent to bupivacaine for both anaesthesia and analgesia across a wide spectrum of indications, including obstetrics and post operative pain management. This would indicate that, when using levobupivacaine in clinical practice, a simple substitution for the same concentration of bupivacaine is all that is required. A small increase in duration of sensory block with levobupivacaine may be attributed to the relative vasoconstriction properties of levobupivacaine compared to bupivacaine but the laboratory data on this subject is still limited. Initial licensing of levobupivacaine recommends a maximum dose of 150 mg and a maximum dose over 24 hours of 400 mg, however there are reports of levobupivacaine single doses for brachial plexus of 300 mg, or > 3 mg/kg with plasma concentrations as high as 3.74 µg/ml without adverse reactions or evidence of CNS/cardiovascular toxicity, indicating that levobupivacaine is well tolerated at a high doses. Doses of > 500 mg and > 600 mg for postoperative analgesia over 24 hours were tolerated as well without sign of toxicity [Auroy et al., 1997; Cox et al., 1998].

Generally, based on the review of clinical studies, levobupivacaine has shown a **similar efficacy** but an **enhanced safety** profile compared to bupivacaine.

References

Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology* 1979; 51: 285–287.

Aps C, Reynolds F. An intradermal study of the local anaesthetic and vascular effects of the isomers of bupivacaine. *Br. J Clin Pharm* 1978; 6: 63–68.

Auroy Y, Narchi P, Messiah A, Litt L, Rouvier B, Samii K. Serious complications related to regional anesthesia: results of a prospective survey in France. *Anesthesiology* 1997;87: 479–486.

Bader AM, Tsen LC, Camann WR, Nephew E, Datta S. Clinical effects and maternal and fetal plasma concentrations of 0.5% epidural levobupivacaine versus bupivacaine for cesarean delivery. *Anesthesiology* 1999; 90: 1596–1601.

Burke D, Kennedy S, Bannister J. Spinal anesthesia with 0.5% S(-)-bupivacaine for elective lower limb surgery. *Regional An Pain Med* 1999; 24: 519–523.

Burke D, Henderson DJ, Simpson AM, Faccenda KA, Morrison LM, McGrady EM, McLeod GA, Bannister J. Comparison of 0.25% S(-)-bupivacaine with 0.25% RS-bupivacaine for epidural analgesia in labour. *Br J Anaesth* 1999; 83:750–755.

Columb MQ, Lyons G. Determination of the minimum local analgesic concentrations of epidural bupivacaine and lidocaine in labor. *Anesth Analg* 1995; 81: 833–837.

Convery P. et al. *Int J Obst. Anaesth* 1999; 8: 197–197.

Cox CR, Checketts MR, Mackenzie N, Scott NB, Bannister J. Comparison of S(-)-bupivacaine with racemic (RS)-bupivacaine in supraclavicular brachial plexus block. *Br J Anaesth* 1998; 80: 594–598.

Cox CR, Faccenda KA, Gilhooly C, Bannister J, Scott NB, Morrison LM. Extradural S(-)-bupivacaine: comparison with racemic RS-bupivacaine. *Br J Anaesth* 1998; 80: 289–293.

Groban L. Central nervous system and cardiac effects from long-acting amide local anesthetic toxicity in the intact animal model. *Reg Anesth Pain Med* 2003; 28(1): 3–11.

Henderson DJ. et al. *Int Mon Reg Anaesth* 1998; 10: 115.

Kopacz DJ, Allen HW, Thompson GE. A comparison of epidural levobupivacaine 0.75% with racemic bupivacaine for lower abdominal surgery. *Anesth Analg* 2000; 90: 642–648.

Kopacz DJ, Allen HW. Accidental intravenous levobupivacaine. *Anesth Analg* 1999; 89:1027–1029.

Lyons G, Columb M, Wilson RC, Johnson RV. Epidural pain relief in labour: potencies of levobupivacaine and racemic bupivacaine. *Br J Anaesth* 1998; 81: 899–901.

McLeod G. et al. Abstract. 12 W. Cong Anaesth 2000; p. 98

McLeod GA, Burke D. Levobupivacaine. *Anaesthesia* 2001; 56: 331–341.

Newton DJ, Burke D, Khan F, McLeod GA, Belch JJ, McKenzie M, Bannister J. Skin blood flow changes in response to intradermal injection of bupivacaine and levobupivacaine, assessed by laser Doppler imaging. *Reg An Pain Med* 2000; 25: 626–631.

Polley LS, Columb MO, Naughton NN, Wagner DS, van de Ven CJ. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor: implications for therapeutic indexes. *Anesthesiology* 1999; 90: 944–950.

Santos AC, Karpel B, Noble G. The placental transfer and fetal effects of levobupivacaine, racemic bupivacaine, and ropivacaine. *Anesthesiology* 1999; 90: 1698–1703.

CSE – AN EVOLVING TECHNIQUE IN LABOUR ANALGESIA: TECHNICAL AND PHARMACOLOGICAL ISSUES

CSE – rozwijająca się technika w analgezji położniczej: uwarunkowania techniczne i farmakologiczne

Rudolf Stienstra

Department of Anesthesiology, Leiden University Medical Center, Leiden, The Netherlands

CSE in labour analgesia

CSE is a technique that is becoming increasingly popular in obstetrics, both in labour analgesia as well as for Caesarean section. The first report on CSE for labor analgesia was published in 1991 [Abouleish et al., 1991]. The claimed forte of CSE is that it combines the advantages of spinal and epidural analgesia. In labour analgesia, whereas the onset of analgesia with traditional epidural analgesia will

take some time, the spinal component of CSE will provide immediate and profound pain relief.

The spinal loading dose may consist of a local anesthetic, an opioid or the combination of both. An opioid alone will provide adequate pain relief during the first stage of labour without any motor block, thus allowing unimpaired ambulation of the parturient. When analgesia of the spinal opioid wears off or becomes insufficient, analgesia can be reinforced via the epidural catheter. Opioids most widely used

for CSE labour analgesia are sufentanil or fentanyl. Given spinally without local anesthetic, both sufentanil [Camann et al., 1993; D'Angelo et al., 1994] and fentanyl [Honet et al., 1992] have been shown to provide rapid analgesia, although duration is short.

The initial spinal loading dose can also be given with a local anesthetic or a combination of local anesthetic and opioid. The combination of bupivacaine and fentanyl [Collis et al., 1993, 1995] or sufentanil [Campbell et al., 1995, 1997] for the spinal loading dose has been shown to be effective and longer lasting than either opioid or local anesthetic alone.

Compared to epidural analgesia, the total dose of local anesthetic administered to the parturient during labour is lower when using CSE. It has been claimed that this lower local anesthetic dose provides better conditions for ambulation, but this view has been challenged [McLoughlin, 1998]. Indeed, many epidural regimens (with fentanyl or sufentanil, alone or in combination with low dose bupivacaine or ropivacaine) that allow ambulation of the parturient have been reported in the literature and it seems that ambulation is not a prerogative of CSE [Breen et al., 1993; Dunn et al., 1998; Cohen et al., 2000; Campbell et al., 2000; Connelly et al., 2000].

The ability to ambulate has received much attention. It has been speculated that ambulation will likely reduce instrumental delivery and Caesarean section rates, but so far this assumption is not supported by data from the literature. On the contrary, three studies investigating this issue found that ambulation has no effect on the mode of delivery [Bloom et al., 1998; Collis et al., 1999; Nageotte et al., 1997]. A recent study designed to compare CSE and epidural analgesia with respect to obstetric outcome and anesthetic complications found no differences and concluded that either technique provides safe and effective analgesia [Norris, 2001].

Although some authors report a (tendency to a) higher maternal satisfaction with CSE as compared to conventional epidural analgesia [Davies et al., 1997; Van de Velde et al., 1999], it should be emphasized that "maternal satisfaction" is a diffuse entity and difficult to define; others failed to find a difference in this respect [Dresner et al., 1999; Hepner et al., 2000; Price et al., 1998].

Some authors have commented on the low incidence of postdural puncture headache (PDPH) associated with the CSE technique [Stacey et al., 1993; Rawal et al., 1997] and several explanations for this observation have been put forward. However, comparing the low incidence of PDPH associated with CSE with an average unintentional dural tap incidence associated with conventional epidural analgesia is not exactly fair. Where PDPH associated with epidural analgesia usually results from an accidental dural tap, the CSE technique is only used after correct placement of the Tuohy needle in the epidural space, i.e. in the absence of an accidental dural tap. In these patients, the risk of PDPH will be extremely low, and the subsequent piercing of the dura with the spinal needle can only increase this incidence.

Therefore, compared with conventional epidural analgesia, the incidence of PDPH associated with CSE will in fact always be higher, but given the low incidence of PDPH, large numbers of parturients would have to be included to unveil a statistically significant difference.

Thus, the main advantage of CSE compared to epidural analgesia is the speed of onset of pain relief. CSE has disadvantages as well [Eisenach, 1999]. The use of intrathecal fentanyl [Clarke et al., 1994] and sufentanil [Gambling et al., 1998] as been associated with fetal bradycardia. It has been suggested that the rapid onset of intrathecal pain relief results in a decrease in circulating epinephrine levels, reducing β -adrenergic uterine input; this leads to a shift in norepinephrine-mediated predominance of α -activity, resulting in increased uterine tonus and contractions [Segal et al., 1998]. However, three retrospective studies found no increased incidence of fetal heart rate abnormalities associated with CSE [Eberle et al., 1998; Nielsen et al., 1996; Palmer et al., 1999]. A large retrospective analysis looking at the incidence of emergency Caesarean section found no difference between women receiving CSE analgesia and women without central neuraxis analgesia [Albright and Forster, 1997].

The intrathecal administration of fentanyl or sufentanil will be accompanied by a dose-dependent decrease in ventilation and may result in manifest respiratory depression [[Hays and Palmer, 1994; Herman et al., 1999; Norris et al., 1998]. A common side effect of opioids in central neuraxis analgesia is pruritus; however, the incidence and severity are significantly more profound after spinal as compared to epidural administration [Dunn et al., 1998; Norris et al., 1994].

CSE for caesarean section

CSE is a suitable technique for Caesarean section [Davies et al., 1997; Rawal et al., 1998; Thoren et al., 1994]. In analogy of CSE for labour and delivery, CSE for Caesarean section combines the advantages of both spinal and epidural anesthesia. The profound, intense block associated with spinal anesthesia provides excellent surgical conditions and patient comfort, whereas the epidural catheter may be used for postoperative analgesia.

Contrary to expectations, there are no comparative studies showing that the incidence of hypotension is lower with CSE; although the onset of hypotension is slower in epidural and CSE anesthesia and would theoretically allow more time for compensatory mechanisms, the incidence and magnitude of the decrease in systemic blood pressure is similar [Norris et al., 1994; Thoren et al., 1994].

Compared to single shot spinal anesthesia, CSE allows the anesthesiologist to titrate a low subarachnoid dose of local anesthetic, alone or in combination with an opioid, because the epidural catheter is a back up in case of insufficient spread.

At our institution, we increasingly use the CSE technique for elective Caesarean section rather than spinal anesthesia, administering a subarachnoid dose of 6–7.5 mg plain

bupivacaine in combination with 5 mg sufentanil or 20 mg fentanyl. Although we have not done a randomized comparison between CSE and our standard single shot spinal anesthesia with 12.5 mg plain bupivacaine, we have observed that, contrary to the earlier mentioned literature, using the CSE technique results in a dramatic reduction in the incidence of hypotension.

Single segment or double segment technique

The technical issues of CSE have been reviewed extensively [Rawal et al., 2000]. The single segment, or needle-through-needle, technique is the simplest and most widely used method for CSE. The epidural space is identified with a standard epidural needle; a long spinal needle is advanced through the epidural needle into the subarachnoid space. After injection of local anesthetic in the subarachnoid space the spinal needle is withdrawn and an epidural catheter is threaded through the epidural needle.

With the double segment technique the epidural catheter is inserted first in one interspace, followed by spinal anesthesia at another interspace.

There has been much debate about which is the better technique because each method has advantages and disadvantages. The advantage of the needle-through needle technique is that it requires only one lumbar puncture and it is fast in onset. A disadvantage is that when epidural catheter insertion appears to be difficult or impossible, a second lumbar puncture at another interspace may be necessary. However, the subarachnoid dose has already been given and if the patient is in the sitting position the inevitable delay associated with a second lumbar puncture may be undesirable. For that reason a paramedian approach may be preferable, because the steeper angle of entry of the epidural needle associated with this approach renders the problem of being unable to introduce an epidural catheter to virtually non-existent.

Some people feel uncomfortable with introducing an epidural catheter after prior administration of a subarachnoid dose of local anesthetic, because of difficulty in testing the epidural catheter in the presence of spinal anesthesia. However, testing for an intravenous catheter position is still possible using a β 1-sympathomimetic drug. Careful aspiration and fractionating the epidural dose should be sufficient in preventing unintentional subarachnoid injection of a large local anesthetic dose.

Standard or special equipment

Double-barrel needles have been developed to separate the course of the epidural catheter and the spinal needle. The ratio for this is threefold.

1. The separate lumina of these needles allow for the epidural catheter to be inserted prior to subarachnoid puncture and thus provide the advantage of the double segment technique.

2. Some authors have expressed fear for the possibility that the catheter may penetrate through the hole made in

the dura mater by the previous passage of the spinal needle when using the needle-through-needle technique. The chances of this happening are reduced when using a double-barrel needle, firstly because the epidural catheter may be inserted prior to subarachnoid puncture, and secondly because the exit of the epidural catheter from the needle is angled away from the exit of the spinal needle. The fear of the epidural catheter going through the hole made by the spinal needle seems unfounded. It should be remembered that there is always a risk of inadvertent subarachnoid catheter placement, but this applies to both CSE and traditional epidural anesthesia. In an experimental cadaver study using epiduroscopy it was clearly demonstrated that it is next to impossible to pass 16 or 18 gauge epidural catheters through the hole in the dura made by 27 or 25 gauge spinal needles [Holmstrom et al., 1995]. Also in clinical practice, there is no indication of an increased incidence of accidental subarachnoid placement of the epidural catheter when using the needle-through-needle technique.

3. When using conventional equipment, the spinal needle has to follow the curve at the tip of the Tuohy needle and it has been suggested that the tip of the spinal needle may scrape against the inner wall of the epidural needle, introducing metallic particles into the subarachnoid or epidural space. This seems farfetched, especially when using a spinal needle with a conical tip, and indeed this concern has been shown to be groundless [Herman et al., 1996].

Double-barrel needles have several disadvantages. They are expensive, they have a larger outer diameter compared to standard epidural needles and they handle differently during epidural needle placement. From a safety perspective, it is preferable to use identical equipment with the same characteristics whenever possible, and using different needles for CSE and conventional epidural anesthesia is not in line with this concept. Since there are no studies demonstrating an increased patient safety or decreased complication rate associated with double-barrel needles, their use seems more founded on personal preference than on scientific data.

When introducing the spinal needle through the Tuohy needle with the needle-through-needle technique, the spinal needle is not supported by tissue as in traditional spinal anesthesia. As a consequence, the needle is very mobile with the inherent risk of displacement of the needle tip during manipulation. Several companies have introduced locking devices to overcome this problem, fixing the spinal needle to the epidural needle. Apart from the extra cost, the downside is that with some of these devices the typical feeling of penetrating the dura with the spinal needle is lost and this may result in pushing the needle too far inside, causing paresthesia. The need for these locking devices is debatable and highly dependent on personal taste. In my opinion fixing the spinal needle to the epidural needle between thumb and index finger requires some skill, but once mastered it obviates the need for special locking devices.

References

Abouleish E, Rawal N, Shaw J, Lorenz T, Rashad MN. Intrathecal morphine 0.2 mg versus epidural bupivacaine 0.125% or their combination: effects on parturients. *Anesthesiology* 1991; 74(4): 711–716.

- Albright GA, Forster RM. Does combined spinal-epidural analgesia with subarachnoid sufentanil increase the incidence of emergency cesarean delivery? *Reg Anesth* 1997; 22(5): 400–405.
- Bloom SL, McIntire DD, Kelly MA, Beimer HL, Burpo RH, Garcia MA, Leveno KJ. Lack of effect of walking on labor and delivery. *N Engl J Med* 1998; 339(2): 76–79.
- Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. Epidural anesthesia for labor in an ambulatory patient. *Anesth Analg* 1993; 77(5): 919–924.
- Camann WR, Minzter BH, Denney RA, Datta S. Intrathecal sufentanil for labor analgesia. Effects of added epinephrine. *Anesthesiology* 1993; 78(5): 870–874.
- Campbell DC, Banner R, Crone LA, Gore-Hickman W, Yip RW. Addition of epinephrine to intrathecal bupivacaine and sufentanil for ambulatory labor analgesia. *Anesthesiology* 1997; 86(3): 525–531.
- Campbell DC, Camann WR, Datta S. The addition of bupivacaine to intrathecal sufentanil for labor analgesia. *Anesth Analg* 1995; 81(2): 305–309.
- Campbell DC, Zwack RM, Crone LA, Yip RW. Ambulatory labor epidural analgesia: bupivacaine versus ropivacaine. *Anesth Analg* 2000; 90(6): 1384–1389.
- Clarke VT, Smiley RM, Finster M. Uterine hyperactivity after intrathecal injection of fentanyl for analgesia during labor: a cause of fetal bradycardia? *Anesthesiology* 1994; 81(4): 1083.
- Cohen SE, Yeh JY, Riley ET, Vogel TM. Walking with labor epidural analgesia: the impact of bupivacaine concentration and a lidocaine-epinephrine test dose. *Anesthesiology* 2000; 92(2): 387–392.
- Collis RE, Baxandall ML, Srikantharajah ID, Edge G, Kadim MY, Morgan BM. Combined spinal epidural analgesia with ability to walk throughout labour. *Lancet* 1993; 341(8847): 767–768.
- Collis RE, Davies DW, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labour. *Lancet* 1995; 345(8962): 1413–1416.
- Collis RE, Harding SA, Morgan BM. Effect of maternal ambulation on labour with low-dose combined spinal-epidural analgesia. *Anaesthesia* 1999; 54(6): 535–539.
- Connelly NR, Parker RK, Vallurupalli V, Bhopatkar S, Dunn S. Comparison of epidural fentanyl versus epidural sufentanil for analgesia in ambulatory patients in early labor. *Anesth Analg* 2000; 91(2): 374–378.
- D'Angelo R, Anderson MT, Philip J, Eisenach JC. Intrathecal sufentanil compared to epidural bupivacaine for labor analgesia. *Anesthesiology* 1994; 80(6): 1209–1215.
- Davies SJ, Paech MJ, Welch H, Evans SF, Pavy TJ. Maternal experience during epidural or combined spinal-epidural anesthesia for cesarean section: a prospective, randomized trial. *Anesth Analg* 1997; 85(3): 607–613.
- Dresner M, Bamber J, Calow C, Freeman J, Charlton P. Comparison of low-dose epidural with combined spinal-epidural analgesia for labour. *Br J Anaesth* 1999; 83(5): 756–760.
- Dunn SM, Connelly NR, Steinberg RB, Lewis TJ, Bazzell CM, Klatt JL, Parker RK. Intrathecal sufentanil versus epidural lidocaine with epinephrine and sufentanil for early labor analgesia. *Anesth Analg* 1998; 87(2): 331–335.
- Eberle RL, Norris MC, Eberle AM, Naulty JS, Arkoosh VA. The effect of maternal position on fetal heart rate during epidural or intrathecal labor analgesia. *Am J Obstet Gynecol* 1998; 179(1): 150–155.
- Eisenach JC. Combined spinal-epidural analgesia in obstetrics. *Anesthesiology* 1999; 91(1): 299–302.
- Gambling DR, Sharma SK, Ramin SM, Lucas MJ, Leveno KJ, Wiley J, Sidawi JE. A randomized study of combined spinal-epidural analgesia versus intravenous meperidine during labor: impact on cesarean delivery rate. *Anesthesiology* 1998; 89(6): 1336–1344.
- Hays RL, Palmer CM. Respiratory depression after intrathecal sufentanil during labor. *Anesthesiology* 1994; 81(2): 511–512.
- Hepner DL, Gaiser RR, Cheek TG, Gutsche BB. Comparison of combined spinal-epidural and low dose epidural for labour analgesia. *Can J Anaesth* 2000; 47(3): 232–236.
- Herman NL, Choi KC, Affleck PJ, Calicott R, Brackin R, Singhal A, Andreasen A, Gadalla F, Fong J, Gomillion MC, Hartman JK, Koff HD, Lee SH, Van Decar TK. Analgesia, pruritus, and ventilation exhibit a dose-response relationship in parturients receiving intrathecal fentanyl during labor. *Anesth Analg* 1999; 89(2): 378–383.
- Herman NL, Molin J, Knape KG. No additional metal particle formation using the needle-through-needle combined epidural/spinal technique. *Acta Anaesthesiol Scand* 1996; 40: 227–231.
- Holmstrom B, Rawal N, Axelsson K, Nydahl PA. Risk of catheter migration during combined spinal epidural block: percutaneous epiduroscopy study. *Anesth Analg* 1995; 80(4): 747–753.
- Honet JE, Arkoosh VA, Norris MC, Huffnagle HJ, Silverman NS, Leighton BL. Comparison among intrathecal fentanyl, meperidine, and sufentanil for labor analgesia. *Anesth Analg* 1992; 75(5): 734–739.
- McLoughlin L. The combined spinal-epidural technique. *Reg Anesth Pain Med* 1998; 23(5): 521–524.
- Nageotte MP, Larson D, Rumney PJ, Sidhu M, Hollenbach K. Epidural analgesia compared with combined spinal-epidural analgesia during labor in nulliparous women. *N Engl J Med* 1997; 337(24): 1715–1719.
- Nielsen PE, Erickson JR, Abouleish EI, Perriatt S, Sheppard C. Fetal heart rate changes after intrathecal sufentanil or epidural bupivacaine for labor analgesia: incidence and clinical significance. *Anesth Analg* 1996; 83(4): 742–746.
- Norris MC, Fogel ST, Conway-Long C. Combined spinal-epidural versus epidural labor analgesia. *Anesthesiology* 2001; 95: 913–920.
- Norris MC, Fogel ST, Holtmann B. Intrathecal sufentanil (5 vs. 10 microg) for labor analgesia: efficacy and side effects. *Reg Anesth Pain Med* 1998; 23(3): 252–257.
- Norris MC, Grieco WM, Borkowski M, Leighton BL, Arkoosh VA, Huffnagle HJ, Huffnagle S. Complications of labor analgesia: epidural versus combined spinal epidural techniques. *Anesth Analg* 1994; 79(3): 529–537.
- Palmer CM, Maciulla JE, Cork RC, Nogami WM, Gossler K, Alves D. The incidence of fetal heart rate changes after intrathecal fentanyl labor analgesia. *Anesth Analg* 1999; 88(3): 577–581.
- Price C, Lafreniere L, Brosnan C, Findley I. Regional analgesia in early active labour: combined spinal epidural vs. epidural. *Anaesthesia* 1998; 53(10): 951–955.
- Rawal N, Holmstrom B, Van Zundert A, Crowhurst JA. The combined spinal-epidural technique. In: Birnbach DJ, Gatt SP, Datta S, editors. *Textbook of obstetric anesthesia*. New York: Churchill Livingstone, 2000; 157–182.
- Rawal N, Schollin J, Weststrom G. Epidural versus combined spinal epidural block for cesarean section. *Acta Anaesthesiol Scand* 1988; 32(1): 61–66.
- Rawal N, Van Zundert A, Holmstrom B, Crowhurst JA. Combined spinal-epidural technique. *Reg Anesth* 1997; 22(5): 406–423.
- Segal S, Csavoy AN, Datta S. The tocolytic effect of catecholamines in the gravid rat uterus. *Anesth Analg* 1998; 87(4): 864–869.
- Stacey RG, Watt S, Kadim MY, Morgan BM. Single space combined spinal-epidural technique for analgesia in labour. *Br J Anaesth* 1993; 71(4): 499–502.
- Thoren T, Holmstrom B, Rawal N, Schollin J, Lindeberg S, Skeppner G. Sequential combined spinal epidural block versus spinal block for cesarean section: effects on maternal hypotension and neurobehavioral function of the newborn. *Anesth Analg* 1994; 78(6): 1087–1092.
- VandeVelde M, Mignolet K, Vandermeersch E, Van Assche A. Prospective, randomized comparison of epidural and combined spinal epidural analgesia during labor. *Acta Anaesthesiol Belg* 1999; 50(3): 129–136.

THE ROLE OF ROPIVACAINE AND LEVOBUPIVACAINE IN REGIONAL ANESTHESIA. TOXICITY

Rola ropiwakainy i lewobupiwakainy w regionalnej anestezji. Toksyczność

Rudolf Stienstra

Department of Anesthesiology, Leiden University Medical Center, Leiden, The Netherlands

Introduction

Ropivacaine and levobupivacaine have been introduced as safer alternatives to racemic bupivacaine. The aim of these new local anesthetics is to provide a similar clinical profile, but a reduced systemic toxicity compared to racemic bupivacaine.

The lower central nervous system toxicity of ropivacaine compared to racemic bupivacaine is illustrated by the higher dose of ropivacaine needed to provoke convulsions in all animal species studied [Feldman et al., 1989; Morishima et al., 1985; Nancarrow et al., 1989; Santos et al., 1991, 1995]. Ropivacaine has a lower cardiotoxicity than racemic bupivacaine in in-vitro as well as in animal studies [Reiz et al., 1989; Pitkänen et al., 1992; Sztark et al., 1998] and in human volunteers, ropivacaine is better tolerated than bupivacaine [Scott et al., 1989; Knudsen et al., 1997].

Levobupivacaine is less cardiotoxic than racemic bupivacaine in both in-vitro [Graf et al., 1997; Harding et al., 2001; Mazoit et al., 1993; Valenzuela et al., 1995] and animal studies [Huang et al., 1998]. In human volunteers, levobupivacaine produced significantly fewer effects on cardiovascular function than racemic bupivacaine [Bardsley et al., 1998].

Two issues are at stake here. Levobupivacaine has a clinical profile that is more or less similar to racemic bupivacaine. However, ropivacaine is less potent and of course a difference in potency has to be brought into the equation when comparing toxicity. The second question is how the reduction in cardiotoxicity of levobupivacaine relative to racemic bupivacaine compares to the reduction in cardiotoxicity of ropivacaine relative to racemic bupivacaine.

Potency and toxicity

Potency

Originally ropivacaine was believed to be equipotent to bupivacaine with respect to sensory blocking capacity and less potent regarding motor blocking characteristics. This assumption was based on one in vitro study, in which it was demonstrated that in equal doses the depressant effect of bupivacaine on A-fibers was 16 % greater than that of ropivacaine, but only 3 % greater on C-fibers [Bader et al., 1989]. Later, this sensory equipotency has been questioned and the issue of potency has become the subject of intense debate.

Initial studies comparing ropivacaine and racemic bupivacaine for epidural anesthesia in concentrations of 0.5 % and 0.75 % found sensory block characteristics to be similar [Brown et al., 1990; Brockway et al., 1991; Kerckamp et al., 1990; Morrison et al., 1991], although duration of sen-

sory blockade was significantly shorter in some studies [Brown et al., 1990; Kerckamp et al., 1990] and showed a trend toward shorter duration in other studies. In brachial plexus anesthesia, ropivacaine and racemic bupivacaine have been found to be equally efficacious [Hickey et al., 1991, 1992; Klein et al., 1998; McGlade et al., 1998; Vanionpää et al., 1995]. Two studies comparing equal volumes of ropivacaine 0.2 % and racemic bupivacaine 0.25 % for caudal epidural analgesia in children found both drugs to be equally effective and duration of ropivacaine analgesia slightly longer, indicating that ropivacaine would be slightly more potent than bupivacaine [Ivani et al., 1998, 1999].

On the other hand, a study comparing ropivacaine and racemic bupivacaine for spinal anesthesia, found ropivacaine to be 50 % less potent, and this finding has been confirmed in a volunteer study [McDonald et al., 1999]. Two studies aimed at determining the ED₅₀ of epidural ropivacaine and racemic bupivacaine in parturients by an up-down sequential allocation method found ropivacaine to be 40 % less potent [Capogna et al., 1999; Polley et al., 1999]. Overlooking the present literature, a confusing picture regarding the potency of ropivacaine thus arises: it seems that ropivacaine is more potent than racemic bupivacaine when used for caudal epidural analgesia in children, but 50 % less potent when used for spinal anesthesia! Obviously, something is wrong with this picture. A confounding factor is that sensory equipotency in clinical terms is a qualitative, and not a quantitative endpoint: surgical anesthesia is adequate or inadequate. Assuming a potency difference between ropivacaine and bupivacaine, there is a fair chance that the dose-response curves will overlap especially at the high end, and together with the absence of a precise quantitative measuring tool, this will obscure differences in potency. A potency difference will be more visible in the lower dose-range, as demonstrated by ED₅₀ studies in laboring women [Capogna et al., 1999; Polley et al., 1999]. However, although the ED₅₀ studies claiming a 40 % potency difference are elegant in design, they have a strong limitation in that they only permit conclusions about one point of the dose-response curve and it is questionable whether or not an existing difference at the ED₅₀-level may be extrapolated to other parts of the dose-response curve. In sharp disagreement with the conclusions of the two ED₅₀-studies mentioned above is that none of the other labor studies comparing racemic bupivacaine and ropivacaine have substantiated a 40 % potency difference. By contrast, most of these studies that were aiming for adequate pain relief in all parturients and therefore compared the two drugs at the higher end of the dose-response curve, came up with the same conclusion: equal doses yield similar analgesia and the amount of drug used per unit of time is similar. Recon-

caling these clinical findings with a potency difference of 40 % is clearly impossible. Moreover, from a clinical point of view the ED₅₀ is irrelevant, as providing adequate pain relief in only 50 % of the patients is not an acceptable goal anyway. Therefore, the clinical relevance of a potency difference that is only obvious at the ED₅₀ level is questionable. At least in obstetrics the question of a difference in potency is irrelevant, the clinical picture being that ropivacaine provides similar pain relief but less motor block compared to bupivacaine and is associated with less instrumental deliveries [Campbell et al., 2000; Writer et al., 1998].

Another confounding factor in assessing differences in potency arises when the clinical endpoint used for assessment is susceptible for bias, for example pain scores. Patients often become very appreciative of the extra medical attention associated with participation in a trial, and may become "eager to please".

A third confounding factor is that ropivacaine has a shorter duration of action than bupivacaine. Generally speaking, there is an inverse relation between tachyphylaxis and duration of action, and this may obscure the picture when the drugs are administered over a longer time period, such as in postoperative epidural analgesia. Looking at the studies that compared both drugs in this field, it seems obvious that bupivacaine is more potent than ropivacaine. This difference with obstetrics is most likely explained on the basis of tachyphylaxis, as duration in obstetric analgesia seldom exceeds 10 h, whereas postoperative epidural analgesia is often administered for several days.

Our own experience supports the notion of a potency difference becoming more obvious over time. We have used a mixture of ropivacaine 0.1 % + sufentanil 0.5 mg/mL for both postoperative and labor epidural pain relief for several years. Whereas this mixture provides excellent analgesia in more than 95 % of laboring women without additional interventions and is consequently still in use today, it was not equally successful in providing adequate postoperative analgesia and based on an evaluation showing that interventions were necessary in approximately 50 % of the postoperative patients we have increased the concentrations of ropivacaine and sufentanil in our postoperative mixture to respectively 0.2 % and 1 mg/ml.

Toxicity

Ropivacaine is less toxic than racemic bupivacaine. However, if ropivacaine is also less potent, the question is if the reduction in toxicity is significant, i.e., is ropivacaine still less toxic even when used in higher doses? Moreover, since levobupivacaine has become available, a comparison between the two newer drugs should be made as well. Like ropivacaine, levobupivacaine also has a better toxicity profile but unlike ropivacaine, levobupivacaine seems to be equipotent to racemic bupivacaine. The important issues here are therefore twofold: Is the reduction in toxicity associated with ropivacaine compared to racemic bupivacaine still there when taking a potency difference into account, and is there a difference in safety profile between ropivacaine and levobupivacaine?

Cardiotoxicity of local anesthetics has several components. The blocking of sodium channels may interfere with cardiac impulse conduction and thus affect cardiac rhythm. In a study comparing the direct cardiotoxicity of the isomers of bupivacaine and ropivacaine, it was shown that in equal doses, both isomers of bupivacaine prolong AV conduction time significantly more than the ropivacaine isomers [Graf et al., 2002]. In a study comparing the effects of ropivacaine, levobupivacaine and racemic bupivacaine on QRS-prolongation after intracoronary injection in anesthetised swine, it was found that ropivacaine induced the least degree of QRS and Q-T interval widening, but there was no difference in the lethal dose between levobupivacaine and ropivacaine [Morrison et al., 2000]. In the isolated rabbit heart it has been shown that racemic bupivacaine, levobupivacaine and ropivacaine induce an increase in QRS duration in the ratio of 1:0.4:0.3 [Mazoit et al., 2000].

In a study in anesthetized dogs it was demonstrated that the cumulative dose necessary to cause cardiovascular collapse was significantly larger for ropivacaine compared to both levobupivacaine and racemic bupivacaine [Groban et al., 2001]; resuscitation was unsuccessful in 10 % of the ropivacaine animals as opposed to 30 % and 50 % of the dogs receiving levobupivacaine or racemic bupivacaine respectively.

In a comparative study in pregnant and nonpregnant ewes, the risk of systemic toxicity was greatest for racemic bupivacaine, intermediate for levobupivacaine and least with ropivacaine [Santos et al., 2001]. A study comparing the systemic toxicity in rats demonstrated that the cardiac toxicity of levobupivacaine was intermediate between that of racemic bupivacaine and ropivacaine, and resuscitation in ropivacaine-induced asystole required a smaller amount of epinephrine as compared to both levobupivacaine and racemic bupivacaine [Ohmura et al., 2001].

As stated above, if ropivacaine and bupivacaine are not equipotent, then the difference in potency has to be brought into the equation when comparing systemic toxicity. Although the relationship between potency and systemic toxicity is not linear, differences in systemic toxicity found at equivalent doses may disappear at equipotent doses. Assuming a 50 % difference in potency, Dony and colleagues [Dony et al., 2000] compared different doses of ropivacaine and racemic bupivacaine in Wistar rats and found that even at a 50 % larger dose, ropivacaine still showed a wider therapeutic index. Similar results were obtained in a study where ropivacaine in a 50 % larger dose affected ventricular conduction less than bupivacaine [Lefrant et al., 2001]; this is an important observation because apart from haemodynamic depression, cardiac death as a result of systemic local anesthetic toxicity is thought to occur by the slowing of ventricular conduction which in turn facilitates reentrant ventricular arrhythmias & fibrillation [de La Coussaye et al., 1992].

Cardiotoxicity of local anesthetics is also attributed to their ability to interfere with mitochondrial respiration. In a study comparing the effects of ropivacaine and (racemic) bupivacaine on mitochondrial energy metabolism in rat heart

isolated mitochondria, it was shown that ropivacaine depresses mitochondrial ATP-synthesis less than racemic bupivacaine [Sztark et al., 1998]. The same observation has been confirmed in a study comparing inhibition of ATP-synthesis in rat liver mitochondria [Scutari et al., 1998]. The observed difference between ropivacaine and racemic bupivacaine in inhibiting ATP-synthesis has been attributed to their difference in lipid solubility. Since the lipid solubility of levobupivacaine is similar to racemic bupivacaine, the interference of levobupivacaine with mitochondrial respiration will be similar to that of racemic bupivacaine, an expectation that has recently been confirmed [Sztark et al., 2000].

The fact that ropivacaine interferes with mitochondrial respiration to a lesser extent than both racemic and levobupivacaine suggests that recovery from cardiac ropivacaine intoxication will be easier, and this has been observed in two studies [Groban et al., 2001; Ohmura et al., 2001].

Recently, Groban et al., [2002] studied the effects of lidocaine, ropivacaine, racemic bupivacaine and levobupivacaine on parameters of myocardial depression in dogs receiving escalating doses until cardiovascular collapse; all local anesthetics produced concentration dependent decreases in left ventricular end-diastolic pressure, dP/dtmax, ejection fraction, fractional shortening and cardiac output, but the effects of ropivacaine were significantly less compared to both racemic and levobupivacaine; whereas there was no difference in the estimated effective concentration of levobupivacaine and racemic bupivacaine to produce a 35 % decrease in dP/dtmax and fractional shortening, ropivacaine concentrations to produce this decrease were respectively 65 % and 130 % higher. The authors suggested that molecular size and not stereoselectivity determines cardiotoxicity in terms of myocardial depression.

Summary

Both ropivacaine and levobupivacaine have a lower systemic toxicity than racemic bupivacaine. While some studies indicate that the reduction in toxicity of ropivacaine and levobupivacaine (compared to racemic bupivacaine) is similar, a number of studies clearly show that ropivacaine is less toxic than levobupivacaine. Especially with respect to interference with mitochondrial respiration as well as myocardial depression, it seems that there is little or no difference between levobupivacaine and racemic bupivacaine.

Ropivacaine is less potent than bupivacaine and has a shorter duration of action. This difference in potency however is not clearly quantified and differs with varying anesthetic techniques. The lower systemic toxicity of ropivacaine compared to bupivacaine is not offset by a lower potency, as ropivacaine in a 50 % higher dose is still less cardiotoxic.

References

Bader AM, Datta S, Flanagan H, Covino BG. Comparison of bupivacaine- and ropivacaine- induced conduction in blockade in the isolated rabbit vagus nerve. *Anesth Analg* 1989; 68(6): 724–727.

Bardsley H, Gristwood R, Baker H, Watson N, Nimmo W. A comparison of the cardiovascular effects of levobupivacaine and rac- bupivacaine following intravenous administration to healthy volunteers. *Br J Clin Pharmacol* 1998; 46(3): 245–249.

Brockway MS, Bannister J, McClure JH, McKeown D, Wildsmith JAW. Comparison of extradural ropivacaine and bupivacaine. *British Journal of Anaesthesia* 1991; 66: 31–37.

Brown DL, Carpenter RL, Thompson GE. Comparison of 0.5 % ropivacaine and 0.5 % bupivacaine for epidural anesthesia in patients undergoing lower-extremity surgery. *Anesthesiology* 1990; 72: 633–636.

Campbell DC, Zwack RM, Crone L-AL, Yip RW. Ambulatory labor epidural analgesia: bupivacaine versus ropivacaine. *Anesth Analg* 2000; 90: 1384–1389.

Capogna G, Celleno D, Fusco P, Lyons G, Columb M. Relative potencies of bupivacaine and ropivacaine for analgesia in labour. *Br J Anaesth* 1999; 82: 371–373.

de La Coussaye JE, Brugada J, Allessie MA. Electrophysiologic and arrhythmogenic effects of bupivacaine. A study with high-resolution ventricular epicardial mapping in rabbit hearts. *Anesthesiology* 1992; 77(1): 132–141.

Dony P, Dewinde V, Vanderick B, Cuignet O, Gautier P, Legrand E, Lavand'homme P, De Kock M. The comparative toxicity of ropivacaine and bupivacaine at equipotent doses in rats [In Process Citation]. *Anesth Analg* 2000; 91(6): 1489–1492.

Feldman HS, Arthur GR, Covino BG. Comparative systemic toxicity of convulsant and supraconvulsant doses of intravenous ropivacaine, bupivacaine and lidocaine in the conscious dog. *Anesth Analg* 1989; 69: 794–801.

Gautier PE, De Kock M, Van Steenberge A, Poth N, Lahaye-Goffart B, Fanard L, Hody JL. Intrathecal ropivacaine for ambulatory surgery. *Anesthesiology* 1999; 91(5): 1239–1245.

Graf BM, Abraham I, Eberbach N, Kunst G, Stowe DF, Martin E. Differences in cardiotoxicity of bupivacaine and ropivacaine are the result of physicochemical and stereoselective properties. *Anesthesiology* 2002; 96(6): 1427–1434.

Graf BM, Martin E, Bosnjak ZJ, Stowe DF. Stereospecific effect of bupivacaine isomers on atrioventricular conduction in the isolated perfused guinea pig heart. *Anesthesiology* 1997; 86(2): 410–419.

Groban L, Deal DD, Vernon JC, James RL, Butterworth J. Cardiac resuscitation after incremental overdosage with lidocaine, bupivacaine, levobupivacaine, and ropivacaine in anesthetized dogs. *Anesth Analg* 2001; 92(1): 37–43.

Groban L, Deal DD, Vernon JC, James RL, Butterworth J. Does local anesthetic stereoselectivity or structure predict myocardial depression in anesthetized canines? *Reg Anesth Pain Med* 2002; 27(5): 460–468.

Harding DP, Collier PA, Huckle RM, Gristwood R, Spridgen E. Comparison of the cardiotoxic effects of bupivacaine, levobupivacaine and ropivacaine. An in vitro study in guinea-pig and human cardiac muscle. *Regional Anesthesia and Pain Medicine* 2001; 23 (Suppl), 6.

Hickey R, Hoffman J, Ramamurthy S. A comparison of ropivacaine 0.5 % and bupivacaine 0.5 % for brachial plexus block. *Anesthesiology* 1991; 74: 639–642.

Hickey R, Rowley CL, Candido KD, Hoffman J, Ramamurthy S, Winnie AP. A comparative study of 0.25 % ropivacaine and 0.25 % bupivacaine for brachial plexus block. *Anesth Analg* 1992; 75: 602–606.

Huang YF, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous levobupivacaine and bupivacaine in sheep. *Anesth Analg* 1998; 86(4): 797–804.

Ivani G, Lampugnani E, De Negri P, Lonnqvist PA, Broadman L. Ropivacaine vs bupivacaine in major surgery in infants. *Can J Anaesth* 1999; 46(5 Pt 1): 467–469.

Ivani G, Lampugnani E, Torre M, Calevo-Maria G, DeNegri P, Borometti F, Messeri A, Calamandrei M, Lonnqvist PA, Morton NS. Comparison of ropivacaine with bupivacaine for paediatric caudal block. *British Journal of Anaesthesia* 1998; 81: 247–248.

Kerckamp HEM, Gielen MJM, Edström H. Comparison of 0.75 % ropivacaine with epinephrine and 0.75 % bupivacaine with epinephrine in lumbar epidural anesthesia. *Reg Anesth* 1990; 15: 204–207.

Klein SM, Greengrass RA, Steele SM, D'Ercole FJ, Speer KP, Gleason DH, DeLong ER, Warner DS. A comparison of 0.5 % bupivacaine, 0.5 % ropivacaine, and 0.75 % ropivacaine for interscalene brachial plexus block. *Anesth Analg* 1998; 87: 1316–1319.

Knudsen K, Beckman-Suurkula M, Blomberg S, Sjövall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. *British Journal of Anaesthesia* 1997; 78: 507–514.

Lefrant JY, de La Coussaye JE, Ripart J, Muller L, Lalourcey L, Peray PA, Mazoit X, Sassine A, Eledjam JJ. The comparative electrophysiologic and hemodynamic effects of a large dose of ropivacaine and bupivacaine in

- anesthetized and ventilated piglets. *Anesth Analg* 2001; 93(6): 1598–1605.
- Mazoit JX, Boico O, Samii K. Myocardial uptake of bupivacaine: II. Pharmacokinetics and pharmacodynamics of bupivacaine enantiomers in the isolated perfused rabbit heart. *Anesth Analg* 1993; 77(3): 477–482.
- Mazoit JX, Decaux A, Bouaziz H, Edouard A. Comparative ventricular electrophysiologic effect of racemic bupivacaine, levobupivacaine, and ropivacaine on the isolated rabbit heart. *Anesthesiology* 2000; 93(3): 784–792.
- McDonald SB, Liu SS, Kopacz DJ, Stephenson CA. Hyperbaric spinal ropivacaine: a comparison to bupivacaine in volunteers. *Anesthesiology* 1999; 90(4): 971–977.
- McGlade DP, Kalpokas MV, Mooney PH, Chamley D, Mark AH, Torda TA. A comparison of 0.5 % ropivacaine and 0.5 % bupivacaine for axillary brachial plexus anaesthesia. *Anaesth Intensive Care* 1998; 26: 515–520.
- Morishima HO, Pedersen H, Finster M, Hiraoka H, Tsuji A, Feldman HS, Arthur GR, Covino BG. Bupivacaine toxicity in pregnant and nonpregnant ewes. *Anesthesiology* 1985; 63: 134–139.
- Morrison LMM, Emanuelsson B-M, McClure JH, Pollok AJ, McKeown DW, Brockway MS, Jozwiak H, Wildsmith JAW. Efficacy and kinetics of extradural ropivacaine: Comparison with bupivacaine. *British Journal of Anaesthesia* 1994; 72: 164–169.
- Morrison SG, Dominguez JJ, Frascarolo P, Reiz S. A comparison of the electrocardiographic cardiotoxic effects of racemic bupivacaine, levobupivacaine, and ropivacaine in anesthetized swine. *Anesth Analg* 2000; 90(6): 1308–1314.
- Nancarrow C, Rutten AJ, Runciman WB, Mather LE, Carapetis RJ, McLean CF, Hipkins SF. Myocardial and cerebral drug concentrations and the mechanisms of death after fatal intravenous doses of lidocaine, bupivacaine and ropivacaine in the sheep. *Anesth Analg* 1989; 69: 276–283.
- Ohmura S, Kawada M, Ohta T, Yamamoto K, Kobayashi T. Systemic Toxicity and Resuscitation in Bupivacaine-, Levobupivacaine-, or Ropivacaine-Infused Rats. *Anesth Analg* 2001; 93(3): 743–748.
- Pitkänen M, Feldman HS, Arthur GR, Covino BG. Chronotropic and inotropic effects of ropivacaine, bupivacaine and lidocaine in the spontaneously beating and electrically paced isolated, perfused rabbit heart. *Reg Anesth* 1992; 17: 183–192.
- Polley LS, Columb MO, Naughton NN, Wagner DS, Van de Ven CJM. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor. *Anesthesiology* 1999; 90: 944–950.
- Reiz S, Häggmark S, Johansson G, Nath S. Cardiotoxicity of ropivacaine – a new amide local anaesthetic agent. *Acta Anaesthesiol Scand* 1989; 33: 93–98.
- Santos AC, Arthur GR, Pederson H, Morishima HO, Finster M, Covino BG. Systemic toxicity of ropivacaine during ovine pregnancy. *Anesthesiology* 1991; 75: 137–141.
- Santos AC, Arthur GR, Wlody D, De Armas P, Morishima HO, Finster M. Comparative systemic toxicity of ropivacaine and bupivacaine in pregnant and non-pregnant ewes. *Anesthesiology* 1995; 82: 734–740.
- Santos AC, DeArmas PI. Systemic Toxicity of Levobupivacaine, Bupivacaine, and Ropivacaine during Continuous Intravenous Infusion to Nonpregnant and Pregnant Ewes. *Anesthesiology* 2001; 95(5): 1256–1264.
- Scott DB, Lee A, Fagan D, Bowler GMR, Bloomfield P, Lundh R. Acute toxicity of ropivacaine compared with that of bupivacaine. *Anesth Analg* 1989; 69: 563–569.
- Scutari G, Marian M, Bindoli A, Rigobello MP, Deoni D, Vincenti E, Bragadin M. Mitochondrial effects of l-ropivacaine, a new local anesthetic. *Biochem Pharmacol* 1998; 56: 1633–1637.
- Sztark F, Malgat M, Dabadie P, Mazat JP. Comparison of the effects of bupivacaine and ropivacaine on heart cell mitochondrial bioenergetics. *Anesthesiology* 1998; 88: 1340–1349.
- Sztark F, Nouette-Gaulain K, Malgat M, Dabadie P, Mazat JP. Absence of stereospecific effects of bupivacaine isomers on heart mitochondrial bioenergetics. *Anesthesiology* 2000; 93(2): 456–462.
- Vainionpää VA, Haavisto ET, Huha TM, Korpi KJ, Nuutinen LS, Hollmén AI, Jozwiak HM, Magnusson AA. A clinical and pharmacokinetic comparison of ropivacaine and bupivacaine in axillary plexus block. *Anesth Analg* 1995; 81: 534–538.
- Valenzuela C, Snyders DJ, Bennett PB, Tamargo J, Hondeghem LM. Stereoselective block of cardiac sodium channels by bupivacaine in guinea pig ventricular myocytes. *Circulation* 1995; 92(10): 3014–3024.
- Writer D, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, Joyce TH, Hedlund CC, Heeroma K, Selander D. Neonatal outcome and mode of delivery after epidural analgesia for labour with ropivacaine and bupivacaine: a prospective meta-analysis. *Br J Anaesth* 1998; 81: 713–717.

WHAT IS 'NEW' IN REGIONAL ANESTHESIA FOR CESAREAN SECTION?

Co nowego w regionalnej anestezji do cięcia cesarskiego?

Marcel Vercauteren

University Hospital Antwerp, Belgium

Hypotension: volume preloading: pro and contra

Following spinal anesthesia even up to 2000 ml of crystalloids may reduce but not eliminate hypotension. In addition, greater volumes of crystalloids may even increase the risk of hypotension due to decreases of the afterload caused by secretion of Atrial Natriuretic Peptide. Administering the amount of crystalloids over a shorter did not decrease the risk of hypotension. Recently it was shown that cooling of the fluid may increase MAP by \pm 5 mmHg but it may be questioned whether this increase is clinically important [Jorgenson et al., 2000]. Rout et al., demonstrated that the incidence of hypotension decreased from 71% to 55% for unpreloaded vs preloaded (crystalloids) subjects [Rout et al., 1993] without effect on neonatal outcome and biochemistry.

In addition two other studies showed that the use of 1000 ml of crystalloids alone does not appear to be better than

no prehydration at all or preloading with only 200 ml [Jackson et al., 1995; Husaini and Russell, 1998]. The incidence of hypotension was still considerable despite the infusion of ephedrine. Prehydration may induce pulmonary edema, a risk which may be reduced by the use of colloids since these maintain the oncotic pressure of plasma and less volume is required. The properties of the available colloids may differ considerably. Hydroxyethylstarch (HES) 6% may offer several advantages such as venous thrombosis prophylaxis and significantly less allergic potential than gelatins and dextrans. HES seems to be safe with regard to placental transfer which has been found to be almost negligible [Marcus et al., 1995].

In obstetrics the superiority of a crystalloid-HES combination has been shown and confirmed as compared to crystalloids alone [Riley et al., 1995; Vercauteren et al., 1996; Ueyama et al., 1999]. A study performed in our department in 90 Cesarean sections under CSE-anesthesia reve-

aled that the incidence of hypotension (SBP<90 mmHg) following 1000 ml of Ringer's lactate with up to 1000 ml of HES 6% was only 10% a compared to 30% in those treated with HES 1000 ml alone or 1000 ml Ringer's lactate with up to 1000 ml of modified gelatin 3% [Vercauteren et al., 1996]. Ephedrine requirements were also the lowest in the Ringer's Lactate-HES combination (\pm 2.5 mg as opposed to 6–7.5 mg in the other two groups). This is still much less than the ephedrine doses up to 50 mg reported in other studies [Jackson et al., 1995; Husaini and Russell, 1998]. A recent study using invasive hemodynamic monitoring demonstrated that 1000 ml HES 6% caused less hypotension than only 500 ml HES or 1500 ml crystalloids [Ueyama et al., 1999]. Whereas 100% of the colloid remained intravascularly, only 28% of the crystalloid remained in the vascular space. The 6% concentration may be preferred in obstetrical practice since, as opposed to the 10% concentration, its volume retaining effect in excess of 100% lasts only 30 minutes which is ideal to cover the interval between administration and delivery.

Baricity: does it affect hypotension or the success of the block?

The substance used for spinal anesthesia in most obstetric departments is hyperbaric bupivacaine. In a non-pregnant population, most studies have shown that with hyperbaric substances the cephalad spread is significantly greater than with plain substances. Consequently, enhanced rostral may also have hemodynamic repercussions. Isobaric solutions have been regarded as more unpredictable as well. The previous findings may not be identical for pregnant patients requiring less bupivacaine. Baricity-related differences in upper sensory level could not be evidenced in two studies using 12.5–15 mg bupivacaine [Russell and Holmqvist, 1989; Richardson et al., 1998]. We performed a study using small doses of bupivacaine (6.6 mg) to which was added 3.3 μ g sufentanil [Vercauteren et al., 1998]. More hypotension was registered with the plain solution while the mean upper sensory level was identical for both groups. The hyperbaric substance however resulted in a more reliable block while the plain solution caused more incidental excessive rostral spread. Our results are in contradiction with a recent study by Khaw using 25 mg ropivacaine, plain versus hyperbaric [Khaw et al., 2002]. This study found hyperbaric ropivacaine to result in more hypotension than the plain solution but with the latter a 25% failure rate was noticed (which might explain why there was also less hypotension in this group).

Is it time to use other vasopressors ?

Gutsche et al demonstrated that 25–50 mg given intramuscularly within 30 min of instituting a subarachnoid block, significantly decreased the incidence of hypotension [Gutsche, 1976]. Placental transfer of such high ephedrine doses may result in higher neonatal catecholamine levels, fetal acidosis and rebound hypertension. Not every study

has found benefit to prophylactic administration of ephedrine.

The intravenous route for administering ephedrine either as an incremental dose or by infusion may be more effective and predictable than the IM route. Many studies have shown that ephedrine prophylaxis offers the same benefit as crystalloid preloading [Chan et al., 1997; Gajraj, 1993]. We performed a study in prehydrated parturients and receiving low dose spinal anesthesia to evaluate the value of a small ephedrine dose (5 mg) [Vercauteren et al., 2000]. Patients receiving ephedrine showed more hemodynamic stability than the placebo group. Despite identical ephedrine requirements the placebo treated patients had a higher incidence and severity of hypotension and nausea.

Subsequently studies have tried to define the optimal ephedrine dose when administered as a prophylactic bolus. Two studies found the 10 mg dose to be ineffective while only 30 mg reduced the incidence of hypotension but at the expense of reactive hypertension when 20 mg or higher were given.

Other studies demonstrated that ephedrine compared favorably with other vasopressors such as phenylephrine and angiotensin II [Hall et al., 1994; Ramin et al., 1994]. Phenylephrine treated parturients may often require atropine because of bradycardia [Thomas et al., 1996]. Studies with phenylephrine and angiotensin II have found less fetal acidosis as well [Vincent et al., 1998] but it should be emphasized that many studies use too large doses of ephedrine (up to 50 mg). A recent meta-analysis has confirmed the superiority of phenylephrine in the treatment of hypotension [Lee et al., 2002].

Nevertheless, despite this convincing evidence, I was never able to read anywhere that ephedrine should be forgotten now for ever. Due to the theoretical advantages with respect to uterine blood perfusion and the lack of bradycardia, we can only ask ourselves what we are doing wrong in the use of ephedrine and how we can use it in a more optimal way to obtain similar neonatal pH values as with phenylephrine.

Low dose spinals and EVE

Whereas previously bupivacaine dose for spinal anesthesia ranged between 12 and 15 mg, some even more, the addition of adjuvant drugs has enabled to decrease this dose. Unfortunately too little number of colleagues have discovered that 5 to 6 mg with an opioid is more than sufficient to perform a C-section. Such a low dose will reduce the incidence and severity of hypotension while the motor block induced may wear off by the end of surgery allowing faster discharge out of recovery. A recent study pointed out that bupivacaine 5 mg + fentanyl 25 μ g decreased the incidence of hypotension, vasopressor requirement and nausea/vomiting [Ben-David et al., 2000].

Some colleagues believe that epidural volume extension (EVE) with saline after a low dose spinal is better for reducing cardiovascular effects but this is highly speculative and has never been demonstrated in a nicely designed study.

Ropivacaine and levobupivacaine

Although spinal application of these local anesthetics will not be inspired by their lower toxicity, a few number of studies has focused on the possible clinical differences. For ropivacaine, due to a lower potency as compared to bupivacaine, the ED_{50/95} values have been found to be 17/27 mg [Khaw et al., 2001]. However in our experience we could use 10mg after adding sufentanil 3–4 µg (equivalent to 12–15 µg fentanyl). The lower motor block potency may be beneficial but it is difficult to compare this effect with bupivacaine as mostly different doses are used. Hyperbaric substances are not commercially available. Levobupivacaine on the other hand is practically equipotent and is licensed for spinal use in Europe. The few abstracts actually published reveal that it may cause less motor block and less hypotension than racemic bupivacaine.

Severe pre-eclampsia: is a spinal safe?

Until some years ago a spinal (and it supposed greater risk of hypotension and bradycardia) was considered dangerous and consequently an epidural technique was regarded as the technique of choice. The reasons why spinal was considered unsafe were risk of pulmonary edema (prehydration), existing hypovolemia and low cardiac output further aggravated by hypotension. Few recent studies have demonstrated that spinal do not cause more hypotension [Hood and Curry, 1999; Ramanathan et al., 2001]. There are however many problems with studies as all studies up to now were either retrospective, non-randomized, low sample-sized with variable severity of preeclampsia. Epidurals on the other hand, were thought to be dangerous as well in case of coagulation problems such as in HELLP syndrome. However some reports have described their experience with epidurals without the development of a spinal hematoma [Beilin et al., 1997; Vigil-De Gracia et al., 2001]. The value of thrombo-elastography (TEG) remains controversial as well as the effect of preeclampsia on TEG or platelet function. It should not be forgotten that besides platelet count, aspirin intake, thrombo-embolic prophylaxis with LMWH, hepatic dysfunction and DIC may further compromise coagulation.

The best compromise actually seems to be a Combined Spinal Epidural technique, starting with a low dose local anesthetic and supplemented as necessary. If platelets are too low, a single dose spinal, using larger doses, has to be weighed against general anesthesia. A CSE technique may also be the technique of choice in severe cardiac disease as more and more case reports have applied this in these conditions. A continuous spinal may also be an attractive alternative but its popularity is surely fading during the last years.

HIV+ parturients and locoregional anesthesia

These patients are likely to present for C-section, even elective to reduce the risk of vertical transmission. Although this is far from proven, the question arises whether locoregional anesthesia is safe in these subjects. Actually

the best way to prevent vertical transmission is a combination of retroviral therapy to decrease the viral load, eventually to be combined with surgical delivery to further decrease this risk, if this is still possible. Retroviral therapy may decrease the clearance of some drugs used by anesthesiologists (e.g. fentanyl). Provided they are cooperative and without fever, locoregional anesthesia can be performed but it should be remembered that a wet tap is always possible and that an epidural blood patch (EBP) may be suggested sooner or later. As CSE has been reported by several case reports to cause meningitis, even if this is difficult to explain, it is not sure, despite a growing experience of locoregional techniques in these patients, if CSE will not increase the risk of meningitis. Colleagues having performed an EBP claim that it can be done safely without development of meningitis. In case of fever or sepsis, waiting is the message while the headache may have gone before reconsidering EBP. More information will be created when more and more severely ill AIDS parturients will present.

References

- Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm⁻³. *Anesth Analg* 1997; 85: 385–388.
- Ben-David B, Miller G, Gavriel R, Gurevitch A. Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. *Reg Anesth Pain Med* 2000; 25: 235–239.
- Chan WS, Irwin MG, Tong WN, Lam YH. Prevention of hypotension during spinal anaesthesia for caesarean section: ephedrine infusion versus fluid preload. *Anaesthesia* 1997; 52: 908–913.
- French GW, White JB, Howell SJ, Popat M. Comparison of pentastarch and Hartmann's solution for volume preloading in spinal anaesthesia for elective caesarean section. *Br J Anaesth* 1999; 83: 475–477.
- Gajraj NM, Victory RA, Pace NA, Van Elstraete AC, Wallace DH. Comparison of an ephedrine infusion with crystalloid administration for prevention of hypotension during spinal anesthesia. *Anesth Analg* 1993; 76: 1023–1026.
- Gutsche BB. Prophylactic ephedrine preceding spinal analgesia for cesarean section. *Anesthesiology* 1976; 45: 462–465.
- Hall PA, Bennett A, Wilkes MP, Lewis M. Spinal anaesthesia for caesarean section: comparison of infusions of phenylephrine and ephedrine. *Br J Anaesth* 1994; 73: 471–474.
- Hood D, Curry R. Spinal versus epidural anesthesia for cesarean section in severely preeclamptic patients: a retrospective survey. *Anesthesiology* 1999; 90: 1276–1282.
- Husaini SW, Russell IF. Intrathecal diamorphine compared with morphine for postoperative analgesia after caesarean section under spinal anaesthesia. *Int J Obst Anesth* 1998; 7: 76–81.
- Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at caesarean section. *Br J Anaesth* 1995; 75: 262–265.
- Jorgenson et al. *Int J Obstet Anesth* 2000; 9: 20–25.
- Kee WD, Khaw KS, Lee BB, Lau TK, Gin T. A dose-response study of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg* 2000; 90: 1390–1395.
- Khaw K, Ngan Kee WD, Wong EL, Liu JY, Chung R. Spinal ropivacaine for cesarean section: a dose-finding study. *Anesthesiology* 2001; 95: 1346–1350.
- Khaw KS, Ngan Kee WD, Wong M, Ng F, Lee A. Spinal ropivacaine for cesarean delivery: a comparison of hyperbaric and plain solutions. *Anesth Analg* 2002; 94: 680–685.
- Lee A, Ngan Kee WD, Gin T. Prophylactic ephedrine prevents hypotension during spinal anesthesia for Cesarean delivery but does not improve neonatal outcome: a quantitative systematic review. *Can J Anaesth* 2002; 49: 588–599.
- Marcus M, Vertommen JD, Van Aken H. Hydroxyethyl starch versus lactated Ringer's solution in the chronic maternal-fetal sheep preparation: a pharmacodynamic and pharmacokinetic study. *Anesth Analg* 1995; 80: 949–954.

Ramanathan J, Vaddadi AK, Arheart KL. Combined spinal and epidural anesthesia with low doses of intrathecal bupivacaine in women with severe preeclampsia: a preliminary report. *Reg Anesth Pain Med* 2001; 26: 46–51.

Ramin SM, Ramin KD, Cox K, Magness RR, Shearer VE, Gant NF. Comparison of prophylactic angiotensin II versus ephedrine infusion for prevention of maternal hypotension during spinal anesthesia. *Am J Obstet Gynecol* 1994; 171: 734–739.

Richardson MG, Illins HV, Wissler RN. Intrathecal hypobaric versus hyperbaric bupivacaine with morphine for cesarean section. *Anesth Analg* 1998; 87(2): 336–340.

Riley ET, Cohen SE, Rubenstein AJ, Flanagan B. Prevention of hypotension after spinal anesthesia for cesarean section: six percent hetastarch versus lactated Ringer's solution. *Anesth Analg* 1995; 81: 838–842.

Rout CC, Rocke DA, Levin J, Gouws E, Reddy D. A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. *Anesthesiology* 1993; 79: 262–269.

Russell I & Holmqvist E. *Br J Anaesth* 1989; 59: 347–353.

Siddik SM, Aouad MT, Kai GE, Sfeir MM, Baraka AS. Hydroxyethylstarch 10% is superior to Ringer's solution for preloading before spinal anesthesia for Cesarean section. *Can J Anaesth* 2000; 47: 616–621.

Thomas DJ et al. *Br J Anaesth* 1996; 76: 61–65.

Tsen LC, Boosalis P, Segal S, Datta S, Bader AM. Hemodynamic effects of simultaneous administration of intravenous ephedrine and spinal anesthesia for cesarean delivery. *J Clin Anesth* 2000; 12: 378–382.

Ueyama H, He YL, Tanigami H, Mashimo T, Yoshiya I. Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective Cesarean section. *Anesthesiology* 1999; 91: 1571–1576.

Vercauteren M, Coppejans HC, Hoffmann VL, Saldien V, Adriaensen HA. Small-dose hyperbaric versus plain bupivacaine during spinal anesthesia for cesarean section. *Anesth Analg* 1998; 86: 989–993.

Vercauteren M, Hoffmann V, Coppejans HC, Van Steenberge AL, Adriaensen HA. Hydroxyethylstarch compared with modified gelatin as volume preload before spinal anaesthesia for Caesarean section. *Br J Anaesth* 1996; 76: 731–733.

Vercauteren MP, Coppejans HC, Hoffmann VH, Mertens E, Adriaensen HA. Prevention of hypotension by a single 5-mg dose of ephedrine during small-dose spinal anesthesia in prehydrated cesarean delivery patients. *Anesth Analg* 2000; 90: 324–327.

Vigil-De Gracia P, Silva S, Montufar C, Carrol I, De Los Rios S. Anesthesia in pregnant women with HELLP syndrome. *Int J Gynaecol Obstet* 2001; 74: 23–27.

Vincent RD Jr, Werhan CF, Norman PF, Shih GH, Chestnut DH, Ray T, Ross EL, Bofill JA, Shaw DB. Prophylactic angiotensin II infusion during spinal anesthesia for elective cesarean delivery. *Anesthesiology* 1998; 88: 1475–1479.

THE EFFECT OF LOCOREGIONAL ANALGESIA UPON THE PROGRESS OF LABOUR

Wpływ regionalnej analgezji na postęp porodu

Marcel Vercauteren

University Hospital Antwerp, Belgium

Since several decades the debate is going on whether epidural or spinal techniques during vaginal delivery affect the progress of labour. This may be expressed as prolongation of first and/or second stage, dystocia, instrumental delivery, Caesarean section (C-section). Epidurals may theoretically influence this progress due to the local anaesthetics, opioids or other adjuvant drugs administered either by a direct pharmacodynamic effect or by muscle relaxation.

Otherwise during the second stage the parturient may cooperate better despite a lack of bearing down feeling. The most important problem more than one decade ago was the lack of **randomised studies** as these were considered to be unethical. In addition, even with a randomised design, it is difficult to blind the obstetrician while the criteria to apply instrumental or surgical delivery differ considerably as well as the definitions of first and second stage. However since the early nineties, several randomised studies have been done some of them demonstrating either a prolongation of the first or the second stage, a higher incidence of C-section whether or not related to dystocia whereas later on a majority of them contested these results as they were unable to show a difference [Ramin et al., 1995; Sharma et al., 1997; Thorp et al., 1993]. Despite a good alternative analgesic regimen (iv PCA) there were still many patients who violated the protocol. A meta-analysis demonstrated that "epidural" mothers were more satisfied, had somewhat longerlasting labours, required more oxytocin but more importantly neonates of mothers treated with iv

opioids did significantly less well [Halpern et al., 1998]. It is remarkable that most of these kind of studies, as well as others trying to put epidurals in a bad daylight, have been published in 'non-anaesthesiological' journals. Even more remarkable is the acceptance of studies in major journals reporting the comparison of epidural populations with historical controls.

Another issue casting some doubt on the safety of locoregional analgesia for labour was the finding that epidurals may cause **fever** and as a consequence the incidence of C-section, septic workups, maternal and neonatal antibiotic therapy [Lieberman et al., 1997]. Subsequent studies have confirmed this but they all agree that temperature increases are mainly noticed with longerlasting labours, that this is not related to infection, neonatal sepsis or positive culturing. Opioids may play a crucial role especially when administered epidurally, more than intravenously but also this hypothesis remains controversial.

Due to all previous studies, it has been suggested that there are plenty of reasons now to ask **informed consent** from the parturient after having explained all possible drawbacks of labour pain treatment.

Nevertheless anaesthetists have always tried to avoid any enhanced risk of instrumental delivery or influence of their techniques upon labour progress. **Delayed or prolonged pushing** was found to be ineffective while stopping the epidural at 8 cm cervical dilation also did not appear to be beneficial either. In several studies it was also shown that

epidurals may be started early in labour and that waiting until cervical dilation has reached 5 cm does not make sense [Chestnut et al., 1994].

The **addition of adjuvant drugs** such as opioids, clonidine, adrenaline... ect. to the local anaesthetic may theoretically prolong the duration of analgesia or allow a decrease in its concentration, thus resulting in less LA consumption, less motor block and as a consequence less instrumental deliveries. This has been demonstrated in 2 studies [Vertommen et al., 1991; Olofsson et al., 1998], unfortunately not confirmed in later studies.

PCEA (Patient Controlled Epidural Analgesia) techniques although requiring less drug than continuous infusion has never been able to provide evidence of better obstetric outcome. A recent meta-analysis of PCEA protocols without basal rate versus continuous epidural infusion has confirmed less analgesic requirements but without effect upon obstetrical and neonatal outcome [Van der Vyver et al., 2002].

CSE techniques, although possible without the initial use of local anaesthetics, and despite significant less dose requirement of the local anaesthetic were not able to further reduce the incidence of instrumental deliver or C-section. Only one study found a faster dilation rate [Tsen et al., 1999] but this has not been confirmed later on. Opposed to a dose sparing effect of CSE, there has been raised some concern with respect to possible foetal heart rate changes (FHR) which might even result in more C-sections [Van der Velde et al., 2001]. Although the effect of CSE upon FHR remains controversial, in most studies this has not resulted in adverse obstetrical or neonatal outcome.

Related to CSE, though equally possible with low dose epidurals, **ambulation** during labour was thought to be able to shorten labour duration and positively influencing its progress by decreasing FHR changes, reducing urinary retention and the need for analgesics. Randomised studies have resulted in conflicting findings [Vallejo et al., 2001; Karraz, 2003] but it may be concluded that ambulation will only increase maternal satisfaction while other benefits should not be expected too strongly. In most studies it is far from clear whether the obtained benefits are the consequence of ambulation per se or rather the selected drug combination [Wilson et al., 2002].

Even the **newer local anaesthetics**, having less motor block properties did not seem to affect labour progress although only in a meta-analysis [Writer et al., 1998] some significance could be obtained. Actually only one out of four studies has been able to demonstrate less motor block in labouring patients.

In conclusion, although I'm sure that the foregoing discussion will go on for ever, anaesthetist have tried all they could to make locoregional analgesia for the parturient safer, to reduce the side-effects as much as possible while minimising its effect upon obstetric and neonatal outcome. Low dose techniques either by addition of other substances, PCEA or CSE techniques, the use of safer local anaesthetics, all intended to maintain maternal muscle capacity, regardless of ambulation or not, have all contributed to

a pain management of the labouring mother, close to perfection.

References

- Chestnut DH, Vincent RD Jr, McGrath JM, Choi WW, Bates JN. Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are receiving intravenous oxytocin? *Anesthesiology* 1994; 80: 1193–200.
- Halpern SH, Leighton BL, Ohlsson A, Barrett JF, Rice A. Effect of epidural vs parenteral opioid analgesia on the progress of labor: a meta-analysis. *JAMA* 1998; 280: 2105–2110.
- Karraz MA. Ambulatory epidural anesthesia and the duration of labor. *Int J Gynaecol Obstet* 2003; 80(2): 117–122.
- Lieberman E, Lang JM, Frigoletto F Jr, Richardson DK, Ringer SA, Cohen A. Epidural analgesia, intrapartum fever, and neonatal sepsis evaluation. *Pediatrics* 1997; 99: 415–419.
- Olofsson C, Ekblom A, Ekman-Ordeberg G, Irestedt L. Obstetric outcome following epidural analgesia with bupivacaine-adrenaline 0.25% or bupivacaine 0.125% with sufentanil—a prospective randomized controlled study in 1000 parturients. *Acta Anaesthesiol Scand* 1998; 42: 284–292.
- Ramin SM, Gambling DR, Lucas MJ, Sharma SK, Sidawi JE, Leveno KJ. Randomized trial of epidural versus intravenous analgesia during labor. *Obstet Gynecol.* 1995; 86(5): 783–789.
- Sharma SK, Sidawi JE, Ramin SM, Lucas MJ, Leveno KJ, Cunningham FG. Cesarean delivery: a randomized trial of epidural versus patient-controlled meperidine analgesia during labor. *Anesthesiology* 1997; 87: 487–94.
- Thorp JA, Hu DH, Albin RM, McNitt J, Meyer BA, Cohen GR, Yeast JD. The effect of intrapartum epidural analgesia on nulliparous labor: a randomized, controlled, prospective trial. *Am J Obstet Gynecol* 1993; 169: 851–858.
- Tsen LC, Thue B, Datta S, Segal S. Is combined spinal-epidural analgesia associated with more rapid cervical dilation in nulliparous patients when compared with conventional epidural analgesia? *Anesthesiology* 1999; 91: 920–925.
- Vallejo MC, Firestone LL, Mandell GL, Jaime F, Makishima S, Ramanathan S. Effect of epidural analgesia with ambulation on labor duration. *Anesthesiology* 2001; 95: 857–861
- Van der Velde M et al. *RAPM* 2001; 26: 257–62.
- Van der Vyver M, Halpern S, Joseph G. Patient-controlled epidural analgesia versus continuous infusion for labour analgesia: a meta-analysis. *Br J Anaesth.* 2002; 89: 459–465.
- Vertommen JD, Vandermeulen E, Van Aken H, Vaes L, Soetens M, Van Steenberghe A, Mourisse P, Willaert J, Noorduyn H, Devlieger H. The effects of the addition of sufentanil to 0.125% bupivacaine on the quality of analgesia during labor and on the incidence of instrumental deliveries. *Anesthesiology* 1991; 74: 809–814.
- Wilson MJ, Cooper G, MacArthur C, Shennan A. Randomized controlled trial comparing traditional with two „mobile“ epidural techniques: anesthetic and analgesic efficacy. *Anesthesiology* 2002; 97: 1567–1575.
- Writer WD, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, Joyce TH, Hedlund C, Heeroma K, Selander D. Neonatal outcome and mode of delivery after epidural analgesia for labour with ropivacaine and bupivacaine: a prospective meta-analysis. *Br J Anaesth* 1998; 81(5): 713–777.