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MINIREVIEW

TREATMENT OF DEPRESSION: CLINICAL ASPECTS

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Depressive disorders are nowadays one of the most disabling medical illnesses. In spite of the great progress in the field of their treatment, still many therapeutic problems are not resolved. In this paper, available methods of treatment as well as most important clinical principles of treatment implementation are reviewed.

Key words: *depressive disorders, psychotherapy, pharmacotherapy*

Recurrent depression is usually overwhelmingly burdensome. The World Health Organization ranked major depressive disorder the fourth most disabling illness. WHO projected that by 2010 major depression will be ranked second unless meaningful improvements occur in prevention, diagnosis and treatment [10]. So big burden of depression is caused by the high prevalence of the disorder, mortality rates from suicide, personal and familial consequences, financial costs. Kessler et al. [7] determined that as much as 12.7% of males have a lifetime risk of major depression, whereas in women it is 21.3%

However, depressive disorders are often underdiagnosed and undertreated. Various estimates suggest that fewer than 10% of individuals with major depression have ever seen a psychiatrist, 10–20% of patients do not want an antidepressant, approximately one in five depressed patients do not fill their first antidepressant prescription and only about half of patients continue to take prescribed medication after 5–6 months [2].

In spite of the great progress in the field of pharmacotherapy and over 30 antidepressants present on our market, still many therapeutic problems are not resolved.

First, we will concentrate on methods available in the treatment of depression. Generally they can be divided into two groups: biological and psychological ones.

Psychotherapy of depressive disorder has shown its efficacy, especially in patients with less severe, non-psychotic depression. However, in conjunction with antidepressants it has proved to be more effective than either treatment alone. As classical insight-oriented psychoanalysis does not meet expectations of depressive individuals, short-term psychotherapeutic approaches developed. The most important are: Cognitive Therapy based on correcting distortions in thinking, Interpersonal Therapy emphasing ongoing current interpersonal unresolved problems, and Behavior Therapy aimed at correction of undesired behaviors. Other forms of psychological interventions used in the management of depression are: family therapy, group therapy, supportive psychotherapy.

Biological treatments include electroconvulsive therapy, transcranial magnetic stimulation, vagus nerve stimulation, sleep deprivation, phototherapy and of course the most important pharmacotherapy.

The first antidepressants were discovered over 50 years ago. These early agents acted either by inhibiting the enzyme monoamine oxidase (MAOI) or by non-selective blocking the reuptake of norepinephrine and serotonin (tricyclic antidepressants – TCI). These agents dominated the treatment of depression for almost 30 years, from the late 1950s until the late 1980s when the selective serotonin reuptake inhibitors (SSRI) were introduced [15].

The SSRIs were a milestone in the treatment of depression for many reasons. First of all, their safety and tolerability are much higher that those of TCI or MAOI. They are not lethal when overdosed, which is particularly important for individuals with suicidal tendencies, treated as out-patients. Also, cardiac toxicity and anticholinergic side effects are absent. SSRIs can be administered once daily, which ameliorates compliance in long-term preventive treatment. Another advantage is broad therapeutic profile of SSRIs, extending far beyond antidepressant action. SSRIs are effective in panic disorder, general anxiety disorder, obsessive compulsive disorder, bulimia, dysthymia, PTSD (post-traumatic stress disorder), premenstrual dysphoric disorder, social fobia. However, SSRIs cannot be perfect solution for all patients. They cause development of sexual dysfunctions, in the beginning of treatment can cause agitation, they are nor free of bothersome side effects as nausea, vomiting. It is important to notice that SSRIs are five distinctive therapeutic agents and they differ in causing adverse events.

Thus, currently several new classes of antidepressants are available, whose action involves other neurotransmitter mechanisms than the SSRIs. Those classes include: selective serotonin and norepinephrine reuptake inhibitors (SNRI – e.g. venlafaxine, milnacipram), noradrenergic and specific serotonergic antidepressant (NaSSA – mirtazapine), noradrenaline reuptake inhibitors (reboxetine), selective reversible MAO-A inhibitors (RIMA – e.g. moclobemide) and tianeptine.

However, no subsequently developed antidepressant can surpass classical agents in overall efficacy in clinical trials, and a lot of clinical problems and needs are still unanswered.

Nowadays, we understand that neither psychosocial interventions, nor biological treatment are sufficient for patients with depressive disorders. Symptoms of depression have many dimensions: physiological (e.g. insomnia, weight loss, amenorrhea), affective (e.g. depressed mood, anxiety, an-

ger), cognitive (e.g. low self-esteem, hopelessness, helplessness), behavioral (e.g. reduced activity, withdrawal, suicidal tendencies), interpersonal (e.g. withdrawal from social activities). Some of these manifestations are better treated with pharmacotherapy, others with psychotherapy [4]. Moreover, in some cases biological variables may override psychological ones, or the reverse. The recent study by Keller et al. showed the most robust benefit from the combination therapy. In this study, combination treatment increased response rates from approximately 50% to approximately 85% [6]. Thus, the best solution would be a highly individualized approach to meet each depressed patient's needs and an integrative model to combine psychotherapy with biological treatment should be promoted.

Principles of the treatment of depression

With the number of available methods, the choice of the best one is a real challenge. In clinical practice, there exist several rules according to which the optimal therapy is selected.

First of all, careful psychiatric examination must be performed. It can be divided into three parts: interview with the patient, observation of patient's behavior and, if possible, interview with somebody from patient's environment. It is important to learn about previous depressive episodes and previous successful treatment. Generally, if during the previous episode the patient responded to certain medication, we try to prescribe the same one. Also if patient's family member was treated for major depression, we should assess what medication was efficient for him/her. During psychiatric examination of depressed person, it is essential to estimate the risk of suicide [13].

Depressive disorders often coexist with a medical illness. This has strong negative influence on the treatment and prognosis of both conditions and in many cases determinate the choice of therapy. That is why physical examination and obtaining information about any comorbid disorders and treatments should never been omitted.

One of examples is depression in coronary artery disease. Major depression affects approximately 16–22% of patients after recent myocardial infarction. It is also common in subjects who have never had a myocardial infarction, but who have angiographically proven coronary artery disease. The prevalence of depression is estimated to be about 18% in these patients. Depressed mood in patients with coronary artery disease can complicate recovery, increases the risk of further cardiac mortality and morbidity and affects patient' quality of life. Heart disease obviously influence the choice of medication, with preference to newer agents, free of anticholinergic mechanisms [1].

Necessary condition to implement successful treatment is establishing therapeutic contract and compliance. The patient must be aware of prodromal symptoms and signs, recurrent nature of the disorder and the course of treatment. It is particularly important to inform the patient about the delay of action of antidepressant (minimum 14 days from the administration of antidepressant to first signs of improvement) and about the need to continue pharmacotherapy after symptomatological improvement (in first episode of depression the treatment should be maintained for about six months and in recurrent depression – indefinitely and sometimes even for lifetime).

Treatment of depression aims to achieve complete symptom remission and complete restoration of day-to-day functioning with as minimal side effects burden as possible. Failure to achieve remission is associated with both functional impairment and poorer prognosis [11]. For example, in the study of Judd et al. the presence of persistent symptoms of depression was a primary risk factor for relapse [3]. In another study, Paykel et al. found that the presence of residual symptoms of depression was associated with a relapse rate of 76% in comparison to a rate of 25% among individuals without residual symptoms [12].

Thus, one of more important principles in the treatment of depression should be optimizing therapy to avoid residual symptoms. First of all, adequate antidepressant dose should be considered. This is quite easy with newer antidepressants (e.g. SSRIs) where usually single tablet is the adequate daily dose. However, with classical TCIs, the most common mistake is prescribing doses < 150 mg/day.

Second most common mistake is inadequate duration of treatment. According to general rules of treatment, lack of efficacy after 3 weeks of treatment is an indication to increase the dose, and the change of medication should be considered only after 6–8 weeks without therapeutic effect.

Inadequate antidepressant treatment is significantly associated with the risk of relapse and recur-

rence [9]. Moreover, relapsing patients may be at greater risk of not receiving care for subsequent episodes of major depression or failing to respond to treatment [7]. There is an additive risk for developing chronic depression with each subsequent episode. For each episode about 8% of patients would still be depressed within 5 years. The more episodes of depression a patient has, the more likely it will be for him to develop chronic depression [5].

Depressive disorders are frequently complicated by substance abuse. In the Epidemiologic Catchment Area study, 32% of individuals with an affective disorder also had a substance use disorder [8, 14]. Alcohol intake often is the most popular "self medication" to counteract the anxiety, sadness and other symptoms. By contrast, benzodiazepins abuse is often the consequence of inadequate treatment given by general practitioner. On the other hand, depression can be secondary to psychoactive substances dependence. Thus, careful psychiatric examination should be performed to detect coexisting substance abuse/dependence.

Also, other concurrent psychiatric disorders should be diagnosed and treated (as anxiety, personality disturbances).

Last, but not least factor is psychosocial situation of the patient, that always must be considered. Major depressive disorder is frequently associated with functional impairments in many areas, including interpersonal relationships, work, living conditions etc. Implementation of successful treatment requires to identify difficulties in those areas, which can be both the consequence of the disease and the cause of its worse course.

Conclusions

Major depression is overwhelmingly burdensome and frequently life-threatening disorder. However, when properly treated, it can be well controlled, thus preventing much of secondary problems. The growing number of available methods makes the treatment choice a particular challenge, requiring doctor's knowledge, experience and careful evaluation of many individual variables of the patient.

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