

DOI: 10.26693/jmbs04.02.021

UDC 57.084.1+599.323.45

Kyselova A. A.¹, Kravtsova E. S.², Mishchenko D. O.², Chernishova E. R.²**MODERN ASPECTS OF TREATMENT OF DEPRESSION**¹SWPS: University of Social Sciences and Humanities, Warsaw, Poland²Dnipropetrovsk State Medical Academy, Dnipro, Ukraine

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Nowadays depression is a very serious problem for modern society. It influences not only how a person feels, but also it can interfere with his or her thoughts and behavior. Different life events such as stress at work, traumatic accident, divorce, and so on can lead to depression. According to the fifth edition of Diagnostic and Statistical Manual of Mental Disorders to be diagnosed with depression several symptoms (the most important of them are depressed mood and loss of pleasure and interest in life) must be present during at least 2 weeks. There are two main types of treatment of depression which are used in therapy. However, still it is not enough, and scientists have not stopped, and are continuing working on developing new methods of treatment.

The aim of this article was to review articles, Internet sources, chapters from textbooks connected with the main topic of our article. All these materials were used to show the most common ways of treatment of depression and alternative methods, which are becoming very popular nowadays.

The material of research was in 19 native and foreign sources (articles, Internet sources, chapters from textbooks) which are connected with the main theme of this article.

Results and discussion. There are two main branches of treatment of depression. They are psychological treatment (which divides into interpersonal psychotherapy, cognitive therapy, cognitive-behavioral therapy, behavioral activation, behavioral couples therapy), and biological treatment (electroconvulsive therapy, medications, transcranial magnetic stimulation). Every method has its advantages and disadvantages; however, still we have those patients who are treatment-resistant. And at the moment scientists focus on these patients and try to administer new alternative method (such as ketamine, hatha yoga, acupuncture, psilocybin, and so on) to decrease the level of side effects.

Keywords: depression, medications, selective serotonin reuptake inhibitors, cognitive-behavioral therapy, interpersonal psychotherapy, behavioral activation, transcranial magnetic stimulation, ketamine.

Introduction. Nowadays depression is a very serious problem for modern society. More than 25% of all people around the world suffer from it [17, 16]. And still scientists do not know exactly correct answer what can be ideal treatment for their patients, and are working on the way of treatment of depression which is not so harmful and have little amount of side effects [18, 19]. And in this article we would like to describe well-known methods of treatment of depression, and in addition, we would like to cover some new researches and studies in which alternative methods are described.

Therapists and scientists divide all methods of treatment into several categories [15]:

1. Psychological Treatment (here we would like to present several subtypes which are focus on helping to relieve depression during several months of regular weekly meetings) [6, 10, 11]:

a. Interpersonal Psychotherapy (ITP) is connected with the idea that depression is linked to interpersonal problems (for instance, interpersonal conflicts, bereavement, interpersonal isolation, and so on). During such type of meetings both therapist and client focus on not more than two problems. They try to identify patient's feeling connected with these issues, how he or she can solve problems and make decision. Usually, it lasts not more than 16 meetings. In many studies it was proven that ITP can be useful for relieving symptoms of depression, and it prevents relapse during recovery stage. Therapists can use such techniques:

1. discussion of interpersonal problems;
2. exploring negative feelings;
3. encouraging patient to express his or her negative emotions;
4. problem solving;
5. suggestion of better models of behavior to patients;

b. Cognitive Therapy (CT) is connected with altering maladaptive thought patterns. At the beginning, patients can learn how our thoughts may influence on mood, and that is why negative thought about yourself can lead to low mood. To have a better picture of patient's mood a therapist asks their patients to

complete daily monitoring homework where they must write about their negative thoughts during a week. And then it is visible for patients that their negative thoughts can really influence on their mood. During the next stage therapists help patients to change their opinion about self and not to have a lot of negative assumptions about self. Therapists ask patients to generalize this idea and use it in everyday life. In addition, therapists suggest doing more pleasant activities which can increase amount of positive thoughts. At the moment, scientists are working on developing on a computer-administered version of CT. One advantage of using it instead of simple CT is connected with better supporting for homework. And finally there is also a mindfulness-based cognitive therapy (MBCT) which is based on idea of prevention of relapse after successful treatment for recurrent episode of major depressive episode. Scientists believe that patients become vulnerable to relapse due to continuous connection between negative mood and patterns of self-devaluating. So that is why after treatment some patients with depression can start to think in the same way as they thought when they had an episode of depression. And as a result, new episode can be present. Because of this patients must be taught how they can recognize changes in their mood and how they can deal with it - view their thoughts as "mental events" not as a core aspects of the self (for example, they can say to themselves: "thoughts are not facts!"). However, it is not so useful if the patient had only one episode of depression.

c. Behavioral Activation (BA). The main purpose of using BA is connected with idea that different risk factors for depression can interfere with obtaining positive reinforcement. For instance, low social contact or marital distress can lead to low positive reinforcement. In addition, after first symptoms of depression occur, inactivity withdrawal, unfold and so on decrease the level of positive reinforcement further. The BA can be a component of CT which was described above, and after using it patients can have no relapse during 2-year period. By the way, a group version of the BA can also be used, and again in all versions and all ways of psychological treatment the main aspect is to change negative thoughts about self and have more positive thoughts and feelings.

d. Behavioral Couples Therapy: in this type of treatment therapists work with both partners to improve their relation satisfaction and communication. Especially, it is useful, if a patient with depression experiences marital distress

2. Biological Treatment:

a. Electroconvulsive Therapy (ECT) is used to treat depression if other methods are used, but there is no effect from them (especially, if patients have psy-

chotic symptoms). It entails deliberately including the momentary seizure which passes a 70- to 130-volt current through the brain. At the beginning of usage of this method electrodes were placed on both sides of the forehead (bilateral electroconvulsive therapy). However, now only one electrode is used (unilateral electroconvulsive therapy), because side effects are less severe in comparison to bilateral one. During procedure, patients are given a muscle relaxation, that is why they fall asleep during the therapy and the convulsion spasms of muscles are barely perceptible. After therapy patients wake up with no idea what was during the procedure. Patients usually receive from 6 till 12 such treatments, including several free days between procedures. The biggest side effects of this method of treatment is connected with short-term confusion and loss of memory, and these side effects can last during 6-month period after finishing of receiving treatment.

b. Medications. Therapists differentiate all antidepressant drugs of into 3 categories: monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs). The MAOIs are not so popular nowadays, due to very severe side effects, but, on the other hand, SSRIs have become more common at the moment because they have fewer disadvantages. Based on several studies, it was proven that there is decreasing of symptoms in near 50–70% of patients. Despite the type of medications, it must be present during at least 6-month period or even more, because it was proven that continuous usage of antidepressants lower risks of remission for patients to 20–40%. However, it is essential to mention that if patients have mild form of depression drugs are not so effective in comparison to other methods of treatment.

c. Transcranial Magnetic Stimulation is a method which can be used if usage of antidepressants does not lead to decreasing of symptoms. During this procedure an electromagnetic coil is placed against the scalp, and then intermittent pulses are produced which influence on activity of dorsolateral prefrontal cortex. Usually one procedure lasts near 30 minutes, and it is administered during 5–10 days without pauses. According to different researches, transcranial magnetic stimulation can be used in cases of treatment-resistant depression.

By the way, researchers think that there is a genetic predisposition how antidepressant can influence on patient [2]. This idea was provided after experiment in which reaction of animals (in this case they were mice) to antidepressants was measured. In addition, they found that glucocorticoid receptors, which play a very important role in fine-tuning the stress hormone system, can influence on reaction to antidepressants.

In the future, scientists believe that their findings can improve treatment for patients with depression.

In addition, nowadays scientists are working on developing alternative methods of treatment of depression, and one of them is acupuncture [1]. The main principle is based on fact that acupuncture can affect the releasing of different neurotransmitters such as norepinephrine, dopamine, and serotonin. It was shown that if therapists advise their patients to combine acupuncture with antidepressants, decreasing of symptoms is much higher than if only antidepressants are used. For instance, in study done by Xiaoyun Wang patients were administered the combination of abdominal acupuncture and fluoxetine (Prozac). As a result patients had a significant improvement in depression. Xiaoyun Wang mentioned: "Our findings demonstrate the additive effect of acupuncture to antidepressant treatment and suggest that this effect may be achieved through the limbic system, especially the amygdala and the ACC."

Another alternative method for depression treatment is hatha yoga [3, 4]. In the study "Treating major depression with yoga: A prospective, randomized, controlled pilot trial" conducted by Renee Rivera, Ashly Cochran and colleagues, it was proven that in adults with mild or moderate form of depression hatha yoga can result in significant decreasing of symptoms severity and better well-being (in this study 90-minute hatha yoga was used during 2 months twice a week).

The same idea about how therapists can find and use a specific treatment for specific patient was covered in another study where researchers wanted to find if there was a link between brain scans and treatment of depression [5]. Helen Mayberg said: "All depressions are not equal and like different types of cancer, different types of depression will require specific treatments. Using these scans, we may be able to match a patient to the treatment that is most likely to help them, while avoiding treatments unlikely to provide benefit". And it is true, because in her and her colleagues study it was proven that the individual treatment depends on specific biological characteristics of patient which can be noticed using brain scans methods.

Herbal therapy is another alternative way of relieving depressive symptoms, only if your symptoms are not severe [9]. And one of these herbs is *Rhodiola rosea*, or roseroot. In the study conducted by Jun J. Mao, MD, MSCE, associate professor of Family Medicine, Community Health and Epidemiology and colleagues at the Perelman School of Medicine of University of Pennsylvania, during 12 weeks all participants with depression were divided into 3 groups and administered three different substances: roseroot, extract, sertraline, or placebo. Not surprisingly, in group who received sertraline improvements were

much more significant than in group who received roseroot. However, patients taking roseroot showed fewer side effects in comparison to patients taking sertraline (in this group the most common side effects were sexual dysfunction and nausea). Doctor Mao mentioned: "These results are a bit preliminary but suggest that herbal therapy may have the potential to help patients with depression who cannot tolerate conventional antidepressants due to side effects. Larger studies will be needed to fully evaluate the benefit and harm of *R. rosea* as compared to conventional antidepressants."

Another substance that has a very interesting effect on depressive patients is psilocybin [8]. It is a hallucinogenic substance which people can get from mushrooms. This substance works on serotonin receptors, as other well-known antidepressants, but due to different chemical structure, it works faster than antidepressants. In the experiment conducted by doctor Robin Carhart-Harris in Imperial College London (the United Kingdom), a small amount of psilocybin was used together with supportive therapy. As a result, patients with treatment-resistant depression had improvements and decreasing of the level of symptoms. He said: "This is the first time that psilocybin has been investigated as a potential treatment for major depression. Treatment-resistant depression is common, disabling and extremely difficult to treat. New treatments are urgently needed, and our study shows that psilocybin is a promising area of future research. The results are encouraging and we now need larger trials to understand whether the effects we saw in this study translate into long-term benefits, and to study how psilocybin compares to other current treatments."

Finally, the most interesting findings come from another study. Here it was demonstrated that esketamine (a component of the general anesthetic ketamine) can lead to improvements and decreasing of depressive symptoms in patients who do not have any changes after using other methods of treatment [7, 14]. In this study done by Jaskaran Singh from Janssen Research & Development, LLC in San Diego, California and colleagues all patients were divided into two groups: those who received ketamine, and those who received placebo. 3 days after near 60% of patients who were administered ketamine showed improvements in depressive symptoms. Murray Stein, from the University of California San Diego and a deputy editor of *Biological Psychiatry*, said: "The study shows clear benefits of the drug over placebo and suggests that the lowest of the two doses may be equally efficacious but also safer".

In addition, according to the pilot study done at Washington University School of Medicine in St. Louis,

nitrous oxide, or laughing gas, was used, and as a result in two-third of all participants who are treatment-resistant there were noticed improvements in comparison to group where placebo was used [12]. Peter Nagele who was one of the researchers in this team mentioned: "Our findings need to be replicated, but we think this is a good starting point, and we believe therapy with nitrous oxide eventually could help many people with depression". Scientists believe that more studies must be done in this field because if nitrous oxide can really influence symptoms of the depression, this method can be administered to treatment-resistant patient.

Nevertheless, there were some other innovative methods of treatment which were developed but no addition studies which could support those ideas were not conducted [13]. One of them is nasal spray which works as a delivery of peptide treatment. Unfortunately, in this case only laboratory experiments were done.

Conclusions. To sum up, we would like to say that unfortunately but at the moment we do not have one way of treatment of depression. None of all methods which were described in this article can lead to complete remission. However, we believe that in the future scientists will create and find totally new method which can help patients with depression to throw off this illness. But today the only thing which we can do is to combine the most effective methods to relieve patients' symptoms.

Prospects for future research. Despite the fact that at the moment we have already found reliable methods of treatment (for instance, medications or cognitive behavioral therapy), scientist still are working on developing new ways of treatment of depression, and we believe that in the future researchers must pay more attention on patients with treatment-resistant cases, go beyond and find new medications in other well-known drugs as it was with ketamine.

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УДК 57.084.1+599.323.45

СУЧАСНІ АСПЕКТИ ЛІКУВАННЯ ДЕПРЕСІЇ

Кисельова А. А., Кравцова Є. С., Міщенко Д. О., Чернишова К. Р.

Резюме. Нині депресія є дуже серйозною проблемою для сучасного суспільства. Вона впливає не тільки на те, як людина відчуває себе, але й вона втручається у його думки та поведінку. Різні життєві події, такі як стрес на роботі, травматична аварія, розлучення можуть призвести до депресії. Відповідно до п'ятого видання Діагностичного і статистичного посібника з психічних розладів (DSM V) для діагностики депресії кілька симптомів (найважливіші є пригнічений настрій, втрата задоволення та інтересу до життя) повинні бути присутніми протягом принаймні 2 тижнів. Існують два основних типи лікування депресії, які використовуються в терапії. Проте навіть цього недостатньо, і вчені не зупиняються і продовжують працювати над розробкою нових методів лікування.

Метою даної статті став літературний огляд статей, інтернет-джерел, глав з підручників, пов'язаних з основною темою нашої статті. Всі ці матеріали були використані для демонстрації найбільш поширених способів лікування депресії і альтернативних методів, які стають дуже популярними в наші дні.

Результати та обговорення. Існує два основних напрямки лікування депресії. Це психологічне лікування (яке поділяється на міжособистісну психотерапію, когнітивну терапію, когнітивно-поведінкову терапію, поведінкову активацію, поведінкову терапію пар) і біологічне лікування (електросудорожна терапія, медикаменти, транскраніальна магнітна стимуляція). Кожен метод має свої переваги і недоліки; тим не менш, все ще зустрічаються пацієнти, стійкі до лікування. І в даний час вчені зосереджуються на цих пацієнтах, і намагаються застосувати нові альтернативні методи, такі як кетамін, хатха-йога, акупунктура, псилоцибін і т. д., з метою зменшити рівень побічних ефектів.

Ключові слова: депресія, медикаменти, селективні інгібітори зворотного захоплення серотоніну, когнітивно-поведінкова терапія, міжособистісна психотерапія, поведінкова активація, транскраніальна магнітна стимуляція, кетамін.

УДК 57.084.1+599.323.45

СОВРЕМЕННЫЕ АСПЕКТЫ ЛЕЧЕНИЯ ДЕПРЕССИИ

Киселева А. А., Кравцова Е. С., Мищенко Д. О., Чернышова Е. Р.

Резюме. В настоящее время депрессия является очень серьезной проблемой для современного общества. Это влияет не только на то, как человек себя чувствует, но и вмешивается в его мысли и поведение. Различные жизненные события, такие как стресс на работе, травматический несчастный случай, развод могут привести к депрессии. Согласно пятому изданию Диагностического и статистического руководства по психическим расстройствам (DSM V) для диагностики депрессии, в течение не менее 2 недель должны присутствовать несколько симптомов (наиболее важными являются подавленное настроение, потеря удовольствия и интереса к жизни). Существует два основных типа лечения депрессии, которые используются в терапии. Однако этого все же недостаточно, и ученые не останавливаются и продолжают работать над разработкой новых методов лечения.

Целью данной статьи стал литературный обзор статей, интернет-источников, глав из учебников, связанных с основной темой нашей статьи. Все эти материалы были использованы для демонстрации наиболее распространенных способов лечения депрессии и альтернативных методов, которые становятся очень популярными в наши дни.

Результаты и обсуждение. Существует два основных направления лечения депрессии. Это психологическое лечение (которое подразделяется на межличностную психотерапию, когнитивную терапию, когнитивно-поведенческую терапию, поведенческую активацию, поведенческую терапию пар) и биологическое лечение (электросудорожная терапия, медикаменты, транскраниальная магнитная стимуляция). Каждый метод имеет свои преимущества и недостатки; тем не менее, все еще встречаются пациенты, устойчивые к лечению. И в настоящее время ученые сосредотачиваются на этих пациентах, и пытаются применить новые альтернативные методы, такие как кетамин, хатха-йога, иглоукалывание, псилоцибин и т. д., с целью уменьшить уровень побочных эффектов.

Ключевые слова: депрессия, медикаменты, селективные ингибиторы обратного захвата серотонина, когнитивно-поведенческая терапия, межличностная психотерапия, поведенческая активация, транскраниальная магнитная стимуляция, кетамин.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of coauthors of the article.

Стаття надійшла 10.02.2019 р.

Рекомендована до друку на засіданні редакційної колегії після рецензування