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MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
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QUALIFICATION WORK
on the topic: **«CLINICAL AND PHARMACOLOGICAL ANALYSIS OF ANTIDEPRESSANT USE FROM THE GROUP OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS»**

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ANNOTATION

In the qualification work, the issues of clinical and pharmaceutical analysis of antidepressants from selective serotonin reuptake inhibitors group in depression-associated diseases treatment have been considered; clinical and pharmacological characteristics of different groups of antidepressants have been given; analysis results of selective serotonin reuptake inhibitors off-label use have been presented; the results of pharmacists and pharmacy visitors surveys regarding their awareness of selective serotonin reuptake inhibitors' rational use have been provided; recommendations for pharmacists and patients with depression with an emphasis on the criteria of effectiveness and safety of this group of drugs use have been developed.

Key words: depression, antidepressants, selective serotonin reuptake inhibitors, efficacy criteria, and safety criteria

АНОТАЦІЯ

У кваліфікаційній роботі розглянути питання клініко-фармацевтичного аналізу антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну при лікуванні захворювань, пов'язаних з депресією; дана клініко-фармакологічна характеристика різних груп антидепресантів; представлені результати аналізу застосування селективних інгібіторів зворотного захоплення серотоніну не за призначенням (off-label); надані результати опитування фармацевтів та відвідувачів аптек щодо їх інформованості про аспекти раціонально селективних інгібіторів зворотного захвату серотоніну; розроблено рекомендації для фармацевтів та хворих на депресію з акцентом на критерії ефективності та безпеки застосування цієї групи препаратів.

Ключові слова: депресія, антидепресанти, селективні інгібітори зворотного захвату серотоніну, критерії ефективності, критерії безпеки

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ABBREVIATION LIST

WHO	−	World health organization
PTSD	−	Post-traumatic stress disorder
SSRIs	−	Selective serotonin reuptake inhibitors
SNRIs	−	Serotonin and norepinephrine reuptake inhibitors
ADHD	−	Attention deficit hyperactivity disorder
OCD	−	Obsessive-compulsive disorder
TCAs	−	Tricyclic antidepressants
MAOIs	−	Monoamine oxidase inhibitors
MAOIs	−	Monoamine oxidase inhibitors
NaSSAs	−	Noradrenaline and specific serotoninergic antidepressants

INTRODUCTION

Relevance of the topic. Depression is a psychiatric disorder characterized by significant and persistent loss of pleasure, anhedonia, and decreased interest. To date, no specific biological markers have been found for the diagnosis of depression. Therefore, in clinics, the diagnosis of depression is mainly carried out by psychiatrists through structured interviews based on diagnostic manuals (e.g., DSM-IV). With the development of artificial intelligence technology, pattern recognition technology based on machine learning has been widely studied in the recognition or diagnosis of depression. [1].

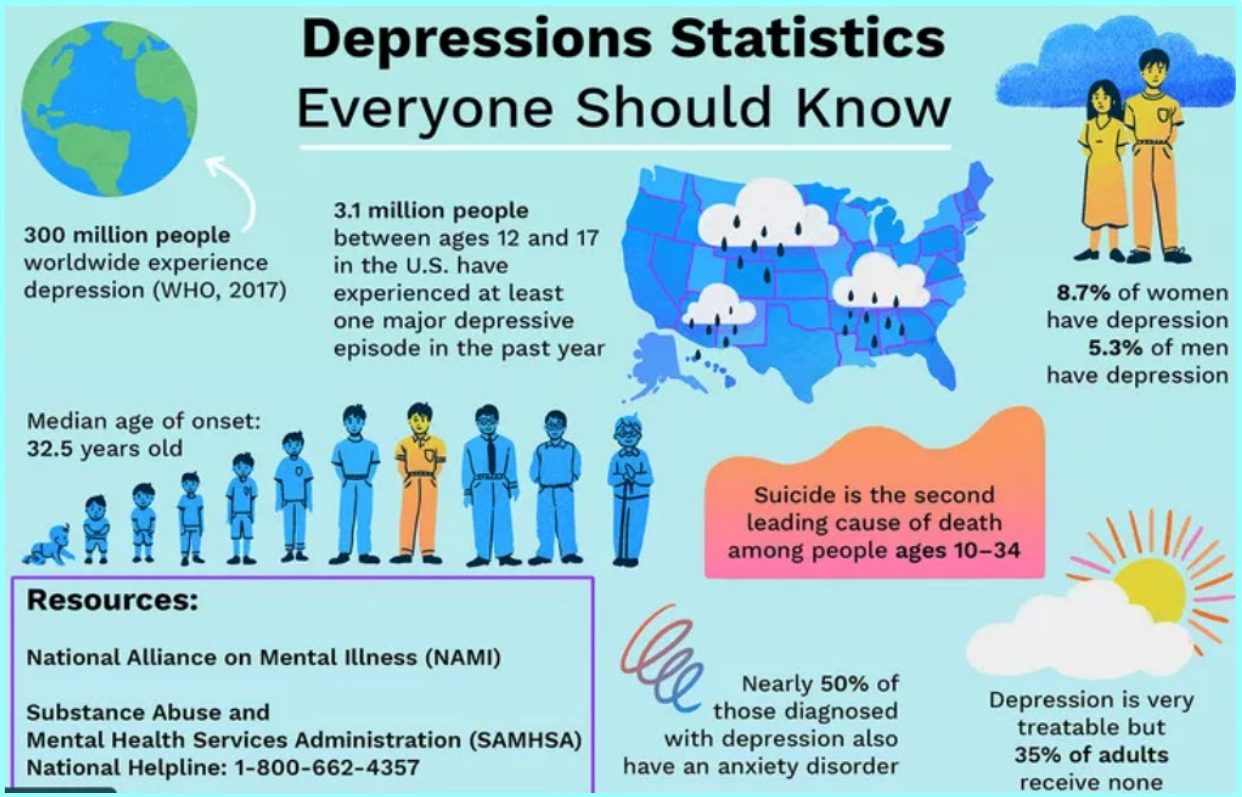

Fig. 1. Depression statistics: everyone should know [1-3]

According to statistics from the World Health Organization (WHO), hundreds of millions of people worldwide suffer from various manifestations of depression [1-8]. In Lebanon, according to official data, medical conditions associated with depression affect about 13% of the population, unofficial data - from 20 to 30% depending on the environment, climate, production, and development in certain

regions of the country [1]. These diseases significantly impair the quality of life, and negatively affect the socio-economic well-being of society [2, 9, 10].

Depression is a common and serious medical illness that negatively affects how you feel, think, and act. Fortunately, it is also treatable. Depression causes feelings of sadness and a loss of interest in activities you once enjoyed. It can lead to various emotional and physical problems and decrease your ability to function at work and home [2-8].

Depression symptoms can vary from mild to severe and can include [5, 9-13]:

- feeling sad or having a depressed mood;
- loss of interest or pleasure in activities once enjoyed;
- changes in appetite – weight loss or gain unrelated to dieting;
- trouble sleeping or sleeping too much;
- loss of energy or increased fatigue;
- increase in purposeless physical activity (e.g., inability to sit still, pacing, handwringing) or slowed movements or speech (these actions must be severe enough to be observable by others);
- feeling worthless or guilty;
- difficulty thinking, concentrating, or making decisions;
- thoughts of death or suicide.

Symptoms must last at least two weeks and must represent a change in your previous level of functioning for a diagnosis of depression.

Also, medical conditions (e.g., thyroid problems, a brain tumor, or vitamin deficiency) can mimic symptoms of depression. So, it is important to rule out general medical causes.

Patients with chronic medical illnesses have two to threefold higher rates of major depression compared to age- and gender-matched primary care patients. Colleagues found that 4% of those with one or more medical conditions have developed major depression over a 2-year period [14]. Wells and colleagues found a 41% increase in the risk of having any recent psychiatric disorder [15]. Von Korff

and colleagues have shown that childhood adversity and depression that occurs in adolescence and early adulthood are independent risk factors for developing a range of medical problems in adulthood [16]. A meta-analysis of 13 studies found that depression predicted the subsequent development of diabetes, with a pooled relative risk of 1.60 [17, 18]. A 5-year prospective study examined factors associated with major depression at 5-year follow-up in 3000 patients with diabetes, with baseline minor and major depression, number of diabetes symptoms, and having one or more cardiac procedures being independent predictors [19]. A systematic review found 8 studies that examined the risk of depression for subsequent onset of myocardial infarction [20].

According to the literature data analysis results, we did not find published data on the national prevalence and treatment of mental disorders in the Arab region.

The aim of the study. Therefore, the study's aim is to conduct clinical and pharmaceutical analysis of antidepressant use from the group of selective serotonin reuptake inhibitors.

The objectives of the study. To achieve the study goals it was necessary to solve the following tasks:

1) consider the epidemiology and medico-social significance of medical conditions associated with depression;

2) analyze international and domestic recommendations for modern approaches to the treatment of medical conditions associated with depression;

3) create a questionnaire to conduct a survey for pharmacists **a**bout awareness of escitalopram's rational use in depression treatment;

4) create a questionnaire to conduct a survey for pharmacy visitors create a questionnaire to conduct a survey for pharmacists **a**bout awareness of escitalopram's rational use in depression treatment;

5) develop practical recommendations for all participants of the treatment process about escitalopram's rational use in depression treatment.

The study object. The role and place of selective serotonin reuptake inhibitors in the treatment of medical conditions associated with depression.

The study subject. Clinical and pharmaceutical analysis of selective serotonin reuptake inhibitors for the treatment of medical conditions associated with depression.

The research methods. To achieve this goal, the following research methods were used:

- sociological methods of survey and questionnaire;
- methods of theoretical research;
- mathematical and statistical research methods.

Publications:

Perspectives of selective serotonin reuptake inhibitors off-label uses in various medical conditions treatment / Zhulai T., Otrishko I., Bezugla N., Almais S. // Клінічна фармація в Україні та світі : матеріали Всеукраїнської науково-практичної Internet-конференції з міжнародною участю, присвяченої 30-річчю заснування кафедри клінічної фармакології та клінічної фармації НФаУ (16-17 березня 2023 р., м. Харків). – Харків: НФаУ, 2023. – С. 137-139.

Structure and volume. The qualification work contains a summary in Ukrainian and English, an introduction, 3 chapters (literature review, materials and methods, 1 chapter of own research, discussion of the results, and practical recommendations), conclusions, and a list of used literature sources (50 references). The volume of the main text of the work is 51 pages. The dissertation is illustrated with 6 tables and 24 figures.

CHAPTER 1
MEDICAL CONDITIONS ASSOCIATED WITH DEPRESSION: THE CURRENT STATE OF THE PROBLEM (literature review)

1.1. Epidemiology and medico-social significance of medical conditions associated with depression

Depression is a state of mental illness. It is characterized by a deep, lasting feeling of sadness or despair. Depression can change a person's thinking/feeling and affect his/her social behavior and sense of physical well-being. It can affect people of any age group, including young children and teenagers. It can run in families and usually begins between the ages of 15 and 30. Women and elderly people get sick more often than men. There are several types of depression, for example, major depression is a change in mood that lasts for weeks or months. This is one of the most severe types of depression. Dysthymia (chronic depression) is a less severe form of depression but usually lasts for several years. Psychotic depression is a severe form of depression associated with hallucinations and delusions (false or unconfirmed feelings). Seasonal depression, which occurs only at a certain time of the year, usually in the winter, is also known as «winter boredom» [1-8].

Patients with chronic medical conditions have two to three times the severity of major depression compared with primary care patients of the same age and gender [1, 16-20]. Patten and colleagues found that 4% of patients with one or more diseases developed major depression over a 2-year period [1, 16-20]. Wells and colleagues found a 41% increase in the risk of any recent psychiatric disorder risk factors for the development of a range of medical disorders in adulthood [1, 16-20]. A meta-analysis of 13 studies found that depression predicted further development of diabetes, with a cumulative relative risk of 1.60 associated with major depression, during a 5-year follow-up in 3000 patients with diabetes mellitus, with baseline

minor and major depression, the number of symptoms of diabetes, and the presence of one or more cardiac procedures [2-8, 17-19]. A systematic review identified 8 studies investigating the risk of depression for further myocardial infarction (Fig. 1.1, 1.2.) [20].

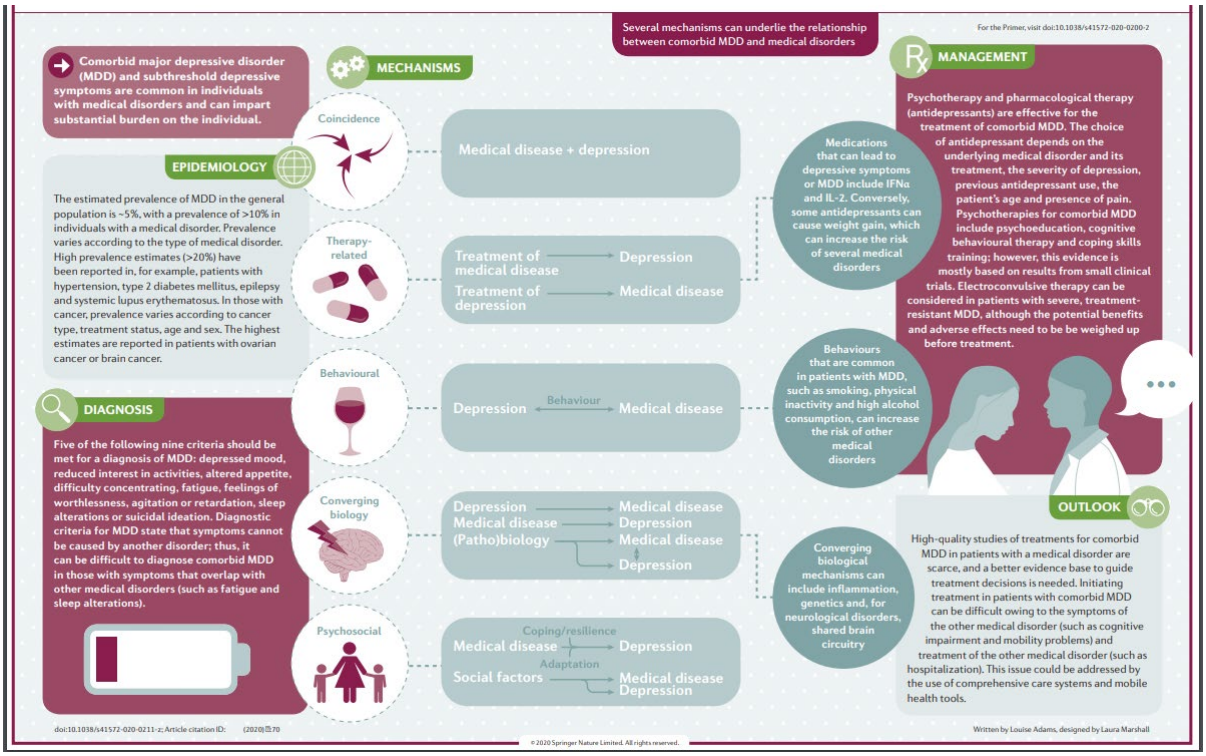

Fig. 1.1. Comorbid depression in medical diseases [20]

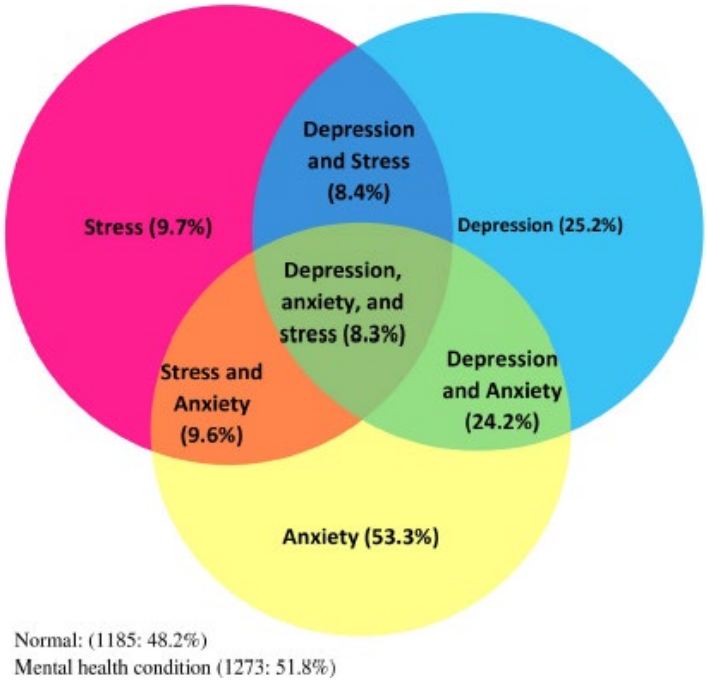

Fig. 1.2. Prevalence of depression, anxiety, and stress In Libanon [20]

What are the medical conditions associated with depression (Fig. 1.3.)? [1, 9, 10, 14-16, 21]

– depression of different etiology and different types;
– panic disorder;
– social anxiety disorder (social phobia);
– obsessive-compulsive disorder;
– major depressive episodes/disorders;
– generalized anxiety disorders;
– obsessive-manic disorder;
– post-traumatic stress disorder (PTSD).

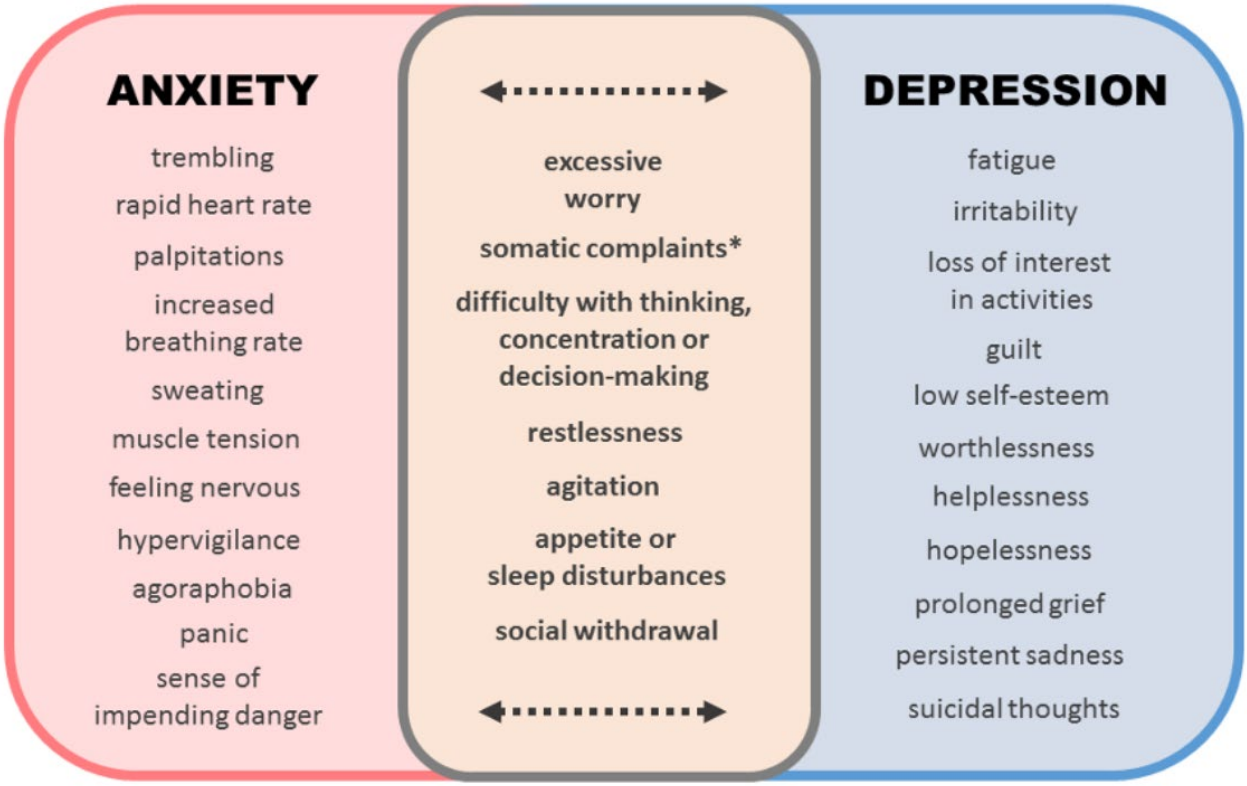

Fig. 1.3. Symptom overlaps between anxiety and depression [21]

Nowadays, there are many wars going on in the world, including in Ukraine. Therefore, there is an urgent need to increase public and professional concern for the mental health of veterans and military personnel. The mental health problems faced by this category of patients are post-traumatic stress disorder and depression. Some

studies have shown that approximately 14% to 16% of US military personnel serving in Afghanistan and Iraq have post-traumatic stress disorder or depression [22]. While these mental health issues are highlighted, other issues such as suicide, traumatic brain injury, substance abuse, and interpersonal violence may be equally harmful to this population. The consequences of these problems can be far-reaching and significantly affect military personnel and their families. Although combat is associated with an increased risk of mental illness, general military service can also cause difficulties. There is no specific term for presenting these mental health problems. However, there are particularly stressful times for individuals and families, such as in proximity to hostilities or discharge from active military service.

For example, more than 6% of the US population has served or is serving in the military [22]. However, these statistics do not take into account the number of family members affected by military service. Understanding military service and its relationship to a patient's physical and mental health can help providers improve the quality of care and potentially help save a patient's life (fig. 1.4) [22].

Post-traumatic stress disorder [1, 16, 21, 22]

PTSD as a medical term was first introduced in 1980 [22]. The criteria for PTSD remained largely unchanged until the most recent update in 2013, although its classification continues to be debated. PTSD is often studied among survivors of war and disaster, but it can affect anyone, including children. Many traumatized people experience temporary numbness or heightened emotions, nightmares, anxiety, and hypervigilance, but symptoms usually resolve within a month. In approximately 10-20% of cases, symptoms become persistent and debilitating. PTSD is characterized by intrusive thoughts, memories, and nightmares about past trauma, causing avoidance of reminders, hypervigilance, and trouble sleeping. Oftentimes, re-experiencing the event can feel just as threatening as inciting the trauma. Symptoms can interfere with interpersonal and occupational functioning and manifest in psychological, emotional, physical, behavioral, and cognitive aspects [22].

Depression [22]

Health care providers must consider not only bodily injury, but also less visible trauma such as post-traumatic stress disorder, acute stress disorder, and depression. Although the condition does not receive the attention that PTSD has, depression remains one of the major mental disorders in the military. The military environment can act as a catalyst for the development and progression of depression. Major depression has many symptoms, including depressed mood, loss of interest in activities, insomnia, weight loss or gain, mental retardation, fatigue, decreased concentration, useless thoughts, and suicidal thoughts. The combination of these symptoms has a significant impact on the ability of patients to function fully. Every second patient with depression is misdiagnosed by a general practitioner. Therefore, further examination, identification, and appropriate treatment are paramount, especially in the military and veterans.

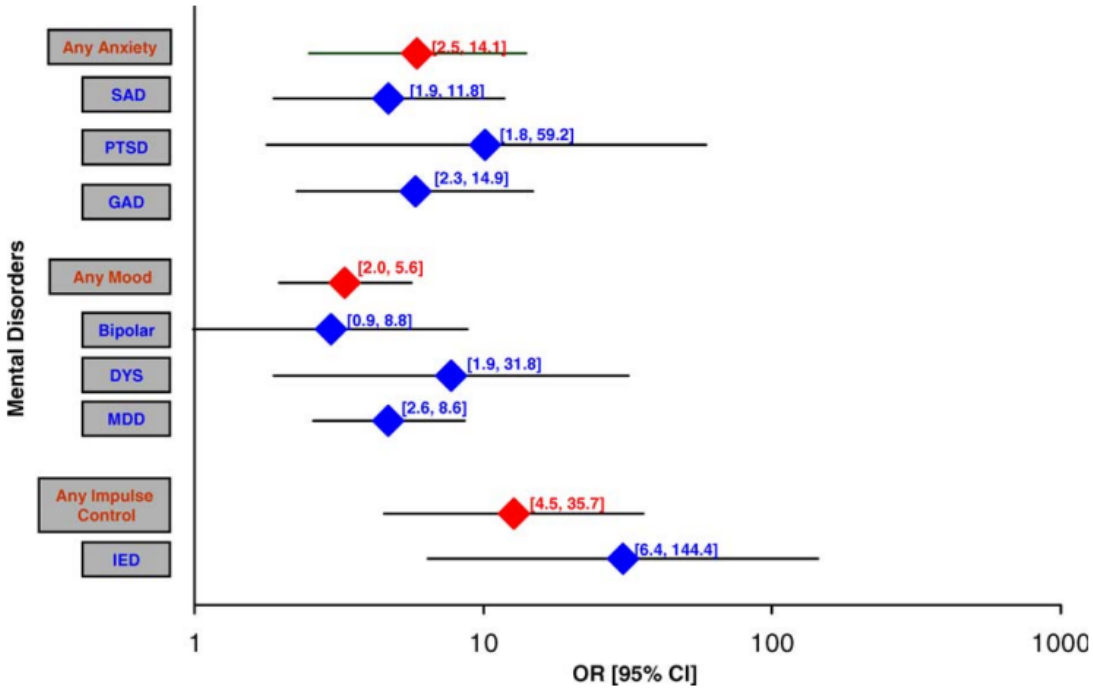

Fig. 1.4. The first manifestation of mental disorders as a result of military cumulative trauma [22]

Notes:

1) DYS – dysthymia;

2) GAD – generalized anxiety disorder;

3) IED – intermittent explosive disorder;
4) MDD – major depressive disorder;
5) SAD – separation anxiety disorder;
6) PTSD – post-traumatic stress disorder.

Suicide [22]

Veteran suicide rates are at an all-time high, with over 6,000 veterans committing suicide each year in the United States [22]. The overall suicide rate in the United States increased by 30% between 1999 and 2016, with 17.8% of reported suicides being committed by veterans [22]. Studies have shown that veterans have a significantly increased risk of suicide during their first year of non-military service.

Substance use disorders [22]

Despite the public attention of recent decades, substance use, including alcohol use, remains a problem among veterans and military personnel. In these populations, alcohol consumption is common and is often used for stress relief and socializing. This leads to significant medical, psychiatric, interpersonal, and professional consequences. A survey of military personnel in the United States found that about 30% of completed suicides and about 20% of risk behavior deaths were associated with alcohol or drug use [22]. Among the general US population, alcohol is the fourth preventable cause of death, and 31% of driving deaths are alcohol-related [22]. Addiction is a set of behavioral responses associated with compulsive drug seeking. This includes impaired control, days, and functional social functioning due to physiological changes caused by drug use. Drug addiction is the most severe stage, characterized by a loss of control over oneself, which leads to an obsessive search for drugs, despite the desire to quit. Substances include legal drugs such as caffeine, nicotine, and alcohol; prescription drugs such as opioids, sedatives/hypnotics, and stimulants; and illicit drugs such as marijuana, cocaine, methamphetamine, heroin, and hallucinogens.

Sleep disturbances [23]

The military lifestyle often involves continuous operations. These stressful conditions create problems for restful sleep in military personnel. Significant mental and physical impairments caused by metabolic, cardiovascular, musculoskeletal, and cognitive health disorders are often associated with insufficient sleep and/or circadian rhythm disturbances. Lack of sleep and the resulting fatigue pose a threat to personal and national security. In the long term, chronic sleep deprivation and circadian rhythm disturbances have been associated with other sleep disorders (e.g., insomnia, sleep apnea, and parasomnias). Other physiological and psychological diagnoses, such as post-traumatic stress disorder, cardiovascular disease, and dementia, are also associated with chronic sleep deprivation. Increased comorbidities and mortality are exacerbated by traumatic brain injury caused by blunt trauma, blast wave exposure, and performing complex tasks under stress.

Bipolar disorder [24]

Bipolar disorder is characterized by mood swings. Many physical complaints, such as mood disorders, movement problems, and sleep problems, are difficult to diagnose because manic and bipolar symptoms appear late in the illness. Treatment for bipolar depression depends on the different types recognized in unipolar depression. The effectiveness of treatment has increased in recent years due to the advent of new drugs and non-drug methods.

1.2. Modern approaches to the treatment of medical conditions associated with depression

Chronic disease management requires close collaboration between patients and physicians, as well as patients and their families. Primary care physicians find it more difficult to evaluate and treat patients with depression than patients without mood disorders. Patients with depression are almost twice as likely to seek medical attention, often because of vague physical symptoms, but also miss more appointments. Compared to non-depressed patients, depressed patients were less satisfied with their caregivers. Patients with depression may delay visits due to

important medical issues or fail to follow medical advice due to fear of becoming depressed and chronic medical illness (Fig. 1.5) [16]. Patients with an anxious attachment may be overly dependent on physicians, leading to increased use of medical services with minor physical symptoms, multiple phone calls, and subsequent frustration with physicians.

Depression is a serious illness that can lead to emotional and physical problems and requires long-term treatment with medication, psychotherapy, or both.

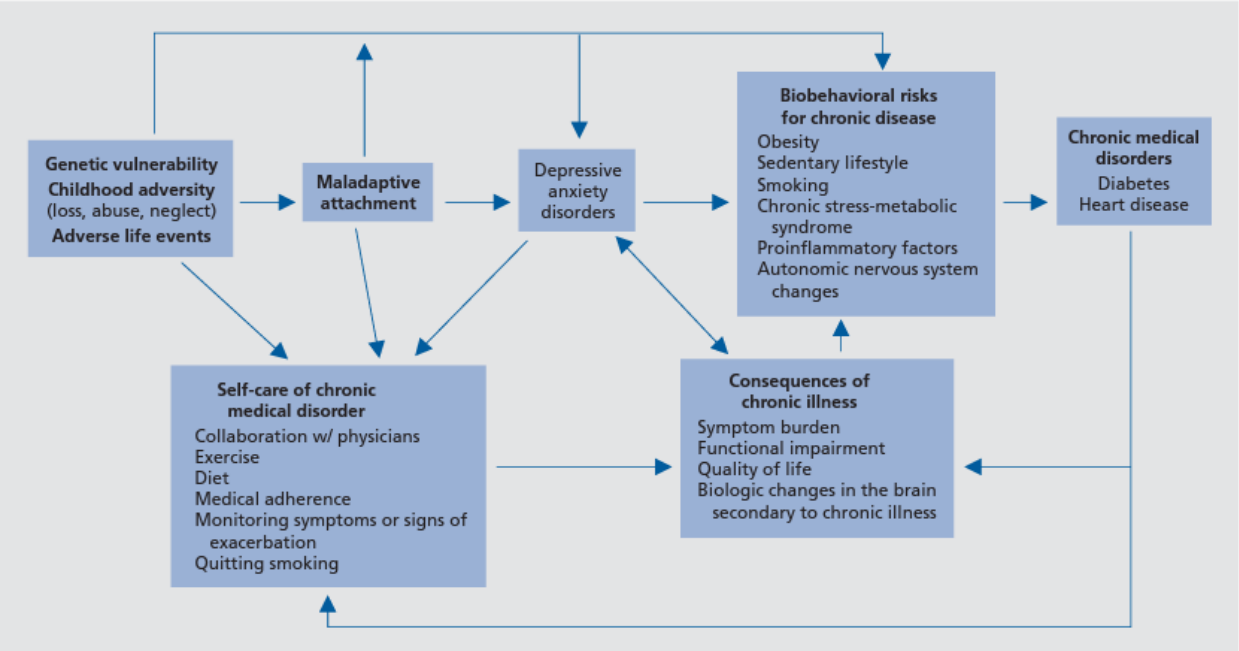

Fig. 1.5. Bidirectional interaction between depression and chronic medical disorders [16]

There are certain stages of getting patients out of depression [14-16, 22].

Recommendations for patients suffering from depression

✓ Plan your day and set clear goals for yourself. Depression can stop you from moving forward in life. Setting daily goals is easy and can help you get back on track.

✓ Focus on positive relationships. Don't get stuck alone when you're sad! Get out of the house and enjoy positive relationships: make plans with friends, join clubs, or participate in team sports. Communicate with people who have similar experiences and problems. Make a daily routine with others.

✓ Get enough sleep! Prepare your bedroom for a restful sleep. Set a relaxing sleep pattern without sitting in front of a screen. Go to bed at the same time every night and get up at the same time every morning. Get sunshine every day.

✓ Regular exercise reduces depression and anxiety by increasing endorphins and neurotransmitters.

✓ Get rid of negative thoughts by being aware of them first.

✓ Learn to think positively to feel good and calm.

✓ See a doctor for cognitive behavioral therapy.

1.2.1. Clinical and pharmacological characteristics of antidepressants

Teenagers, young people, and the elderly today suffer from depression, but often this problem is behind closed doors. Public awareness of the disease is long overdue. Talking openly about depression is critical to destigmatize the patient. Many people with depression find it difficult to explain the details of what they are experiencing. Depression is often described as a cloud hanging over you. But for some, it looks like anger and apathy. Some may experience very negative feelings. Stress can be a constant negative voice in your head that can trigger anything from mild anxiety to panic attacks [25].

The mind is a very complex dance of chemical and electrical signals that allows us to perceive and experience in different ways. Symptoms of depression can range from mild to severe and can be caused by many factors, and each person reacts differently to these conditions. Medications add another layer to the puzzle, as each person reacts differently to medications. That's why it's so important to stay in touch with your healthcare provider during your treatment [25].

But what medications are used to treat depression? How do they work?

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are a first-line treatment for depression.

- citalopram (Celexa)

- escitalopram (Lexapro)
- fluoxetine (Prozac, Sarafem)
- fluvoxamine (Luvox)
- paroxetine (Paxil)
- sertraline (Zoloft)

Serotonin and norepinephrine reuptake inhibitors (SNRIs)

SNRIs are a newer class of antidepressants compared with SSRIs. However, they work in a similar way.

Doctors may prescribe SNRIs for:

- ✓ attention deficit hyperactivity disorder (ADHD)
- ✓ obsessive-compulsive disorder (OCD)
- ✓ anxiety disorders
- ✓ menopausal symptoms
- ✓ fibromyalgia
- ✓ chronic neuropathic pain

Examples of SNRIs include:

- duloxetine (Cymbalta)
- venlafaxine (Effexor XR)
- desvenlafaxine (Pristiq)

Tricyclic antidepressants (TCAs)

Doctors may recommend TCAs for depression, fibromyalgia, some types of anxiety, and chronic pain.

Examples include:

- amitriptyline
- amoxapine
- clomipramine (Anafranil)
- desipramine (Norpramin)
- doxepin (Sinequan)
- imipramine (Tofranil)
- nortriptyline (Pamelor)

- protriptyline (Vivactil)
- trimipramine (Surmontil)

Monoamine oxidase inhibitors (MAOIs)

Due to their adverse side effects and drug-drug interactions, doctors do not typically suggest MAOIs as a first-line treatment option for depression. However, they may be an option if SSRIs do not work for depression.

Examples include:

- phenelzine (Nardil)
- tranylcypromine (Parnate)
- isocarboxazid (Marplan)
- selegiline (Emsam, Eldepryl)

Noradrenaline and specific serotoninergic antidepressants (NaSSAs)

Doctors use NaSSAs to treat anxiety disorders and depression. Examples include mianserin (Tolvon) and mirtazapine (Remeron, Avanza, Zispin). The main pharmacokinetic parameters of antidepressants are shown in figure 1.6 [26].

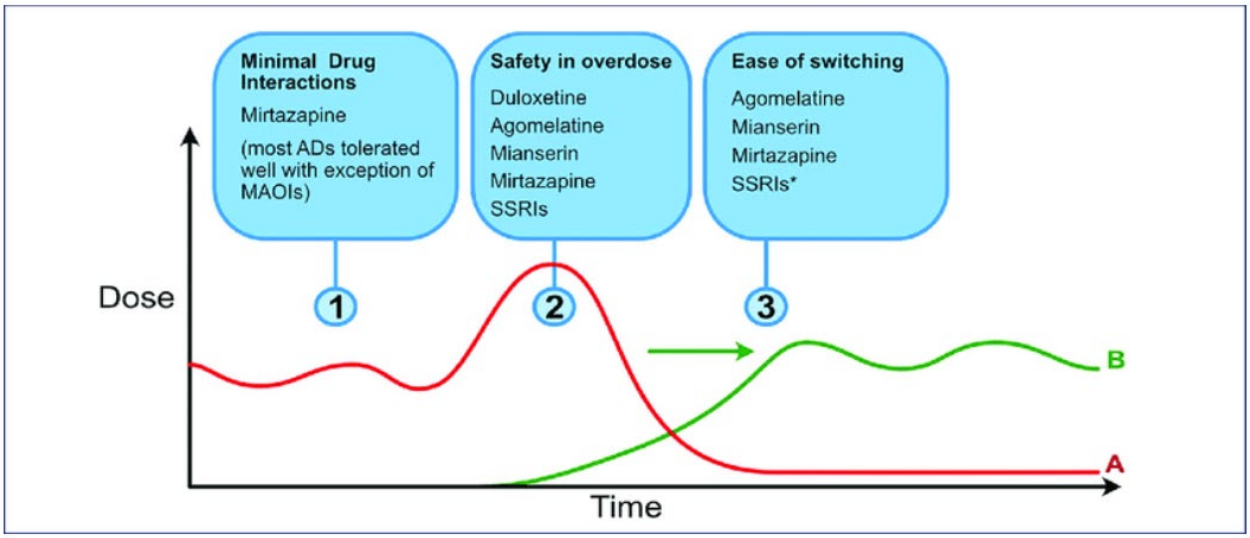

Fig. 1.6. Main pharmacokinetic parameters of antidepressants [26]

The pharmacodynamic effect is to reduce the main depressive symptoms such as depression, loss of interest, change in appetite, weight gain or drowsiness, anxiety or drowsiness, fatigue, feelings of helplessness, lack of concentration, and thoughts

of death. The goal of reducing depressive symptoms is to improve the overall quality of life. It is important to have the right professional, such as a psychiatrist (one who deals with mental health issues), to help decide which medication to use to achieve successful results. While there are many benefits to taking antidepressants, remember that it can take days or weeks for the medication to work.

Side effects (table 1.1) [26]

SSRIs and SNRIs:

✓ nausea and anxiety for the first couple of weeks;

✓ indigestion;

✓ headache;

✓ sexual dysfunction;

✓ increase in blood pressure (venlafaxine).

TCAs:

✓ dry mouth;

✓ tremor;

✓ fast heartbeat;

✓ constipation;

✓ insomnia;

✓ weight gain.

MAOIs:

✓ serotonin syndrome (combined MAOI with an SSRI) - a serious condition in which a person has too much serotonin in their body;

✓ dry mouth;

✓ diarrhea;

✓ nausea;

✓ drowsiness;

✓ constipation;

✓ dizziness;

✓ insomnia;

✓ lightheadedness;

✓ sexual dysfunction;

✓ hypertensive crisis, as a result of preventing the breakdown of tyramine by MAOIs (if a person consumes foods that contain tyramine, such as sausages, fish, and overripe fruit).

NaSSAs

These antidepressants can lead to side effects similar to SSRIs and SNRIs. They can also cause drowsiness and weight gain.

Rarer side effects:

✓ suicidal thoughts;

✓ withdrawal and rebound phenomena (table 1.2).

Table 1.1

Common side effects of antidepressants

Common Side-Effects	Management Tips
Nausea	Start at low dose, titrate slower, give after food, give dose at bedtime
Weight gain	Proactively educate about weight management, frequent weight measurement, refer to nutritionist if needed
Sexual dysfunction	Lower dose if possible, switch to more noradrenergic medication if appropriate, consider use of erectile dysfunction medications if appropriate, obtain urology/gynecology consult if appropriate
Sleep disturbances	If insomnia—consider AM dosing, and if it persists, consider adding trazodone (be watchful for serotonin syndrome) If somnolence—consider PM dosing, recommend against day time naps, offer sleep hygiene advise, consider switching to more noradrenergic medication
Agitation or worsening of anxiety	Consider lowering dose, offer reassurance, if difficulty is significant—consider offering a low dose, time limited course of benzodiazepines (we highly recommend only a 1-2 week course to avoid dependence development)

Pharmacologic characteristics of the ideal antidepressant [25]

Rapid onset of activity

All antidepressants are equally effective in treating depression. However, practitioners should be aware that antidepressant therapy induces mood-enhancing effects approximately 1 to 2 weeks after the start of treatment. However, synaptic effects occur within a few hours after the drug is taken by the patient. Because many side effects also have the same time course as the synaptic effects of these drugs, it is possible to link the synaptic effects of antidepressants to certain side effects and drug-drug interactions. Faced with a severely depressed patient, the clinician would like the remedy to take effect over time similar to synaptic effects. Such a rapid onset of action would be one of the characteristics of an ideal antidepressant. Some preliminary data suggest that venlafaxine may have a faster onset of action than other available antidepressants (Fig. 1.7) [25, 27-29].

Table 1.2

Antidepressant withdrawal and rebound phenomena

Syndrome	Characteristic
Withdrawal syndrome, ADS (antidepressant discontinuation syndrome), acute discontinuation syndrome	• Rapid onset following discontinuation • Transient, self-limiting • Rapid improvement following resumption of the medication • Symptoms may resemble (or differ from) primary disorder (depression) • Typically nonspecific symptoms ("FINISH," see text), possibly specific serotonergic/ cholinergic syndromes
Rebound	• Re-emergence of symptoms of the primary disorder to a greater extent than prior to medication and/or • Higher risk for relapse compared to patients not receiving antidepressants • Counter-regulatory mechanisms activated by treatment and excessive counter-regulation following drug discontinuations
Relapse	Re-emergence of the same disease episode due to loss of pharmacological effect
Recurrence	New episode of a recurring primary disorder following previous recovery (remission over 6–9 months) due to loss of pharmacological effect

Intermediate elimination half-life

Antidepressants can be ranked based on their half-life, the time it takes for half the drug to be eliminated from the body (Fig. 1.8). Information is not provided here on the active metabolites known to exist for most of these compounds. Ideally, the active metabolite should also have an intermediate half-life. This is an important issue for fluoxetine because its active metabolite norfluoxetine has a half-life ranging from 7 to 15 days [30-35]. From a theoretical point of view, compounds with a half-life of 17 to 36 hours (Fig. 1.8) can be administered once a day to

maintain adequate equilibrium levels. Drugs with a shorter half-life need to be given more frequently, while drugs with a longer half-life can be given less frequently than once a day. However, the introduction of the drug less than once a day, as a rule, is not carried out. An ideal antidepressant should have a half-life corresponding to a once-daily dosage, or a half-life of approximately 24 hours.

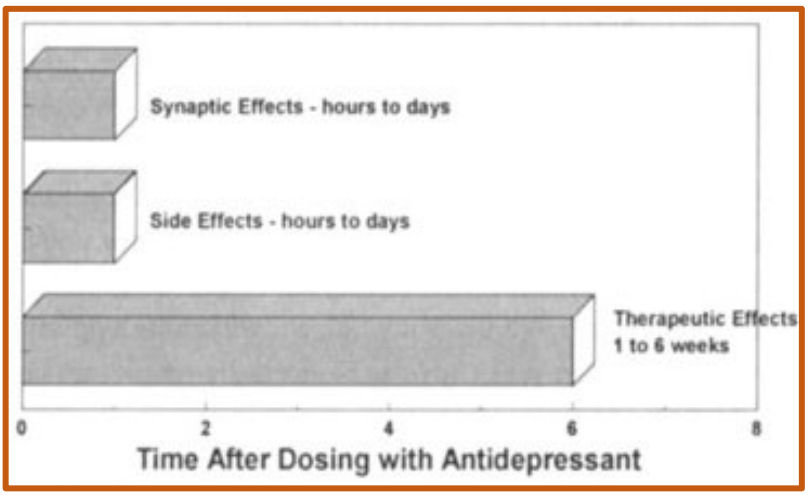

Fig. 1.7. Onset of action of antidepressants. Synaptic effects and side effects of antidepressants begin before therapeutic effects are observed [25]

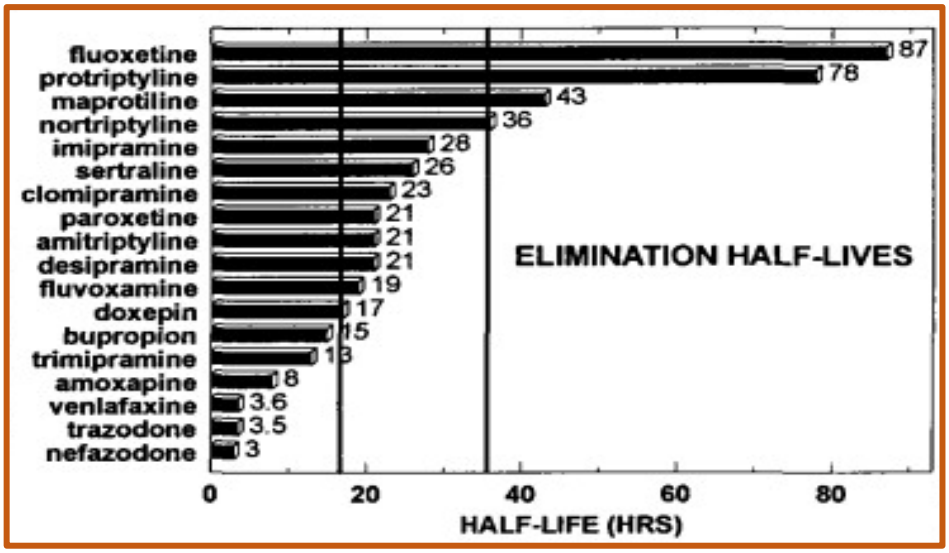

Fig. 1.8. Onset of action of antidepressants. Synaptic effects and side effects of antidepressants begin before therapeutic effects are observed [25]

Defined therapeutic blood level [25]

Individual variations in blood levels associated with the use of a given dose of an antidepressant can be significant. If the specific therapeutic blood level were

known, it would help clinicians to dose the drug for the patient to achieve therapeutic effects and avoid adverse effects. Measurement of plasma levels is clinically useful in certain situations for only three antidepressants (table 1.3). Optimal therapeutic ranges for other antidepressants remain to be established. Therefore, for the vast majority of antidepressants, this relationship is under study. However, for tricyclic antidepressants, therapeutic monitoring is currently the standard [25, 36].

Table 1.3

Therapeutic blood levels for antidepressants

Known
Imipramine
Desipramine
Nortriptyline
Possibly known
Amitriptyline
Under assessment
All other antidepressants

No side effects

Most of the side effects of antidepressants can be explained by their synaptic effects. In particular, the two most important synaptic effects of antidepressants are the blockade of the uptake or reuptake of neurotransmitters (norepinephrine, serotonin, and dopamine) and the blockade of certain neurotransmitter receptors. Their most clinically significant blockade is the blockade of histamine H_1, muscarinic, α-adrenergic, and dopamine D_2 receptors. It is possible that some of these synaptic effects are necessary for the therapeutic action of antidepressants. If so, then antidepressants can never be free from certain side effects caused by interactions with neurotransmitters and their receptors.

Blockade of neurotransmitter uptake by antidepressants [25]

The classic tricyclic antidepressants (desipramine and protriptyline) most effectively block norepinephrine uptake (Fig. 1.9), while paroxetine most effectively blocks serotonin uptake (Fig. 1.10). Most antidepressants block norepinephrine

uptake more than serotonin uptake (Fig. 1.11). However, newer antidepressants tend to be more potent and more selective (Fig. 1.11). In addition, some antidepressants (bupropion and trimipramine) weakly block the uptake of norepinephrine, serotonin, and dopamine. Sertraline is the most potent of antidepressant in blocking dopamine uptake, although it is much weaker than d-amphetamine (Fig. 1.12).

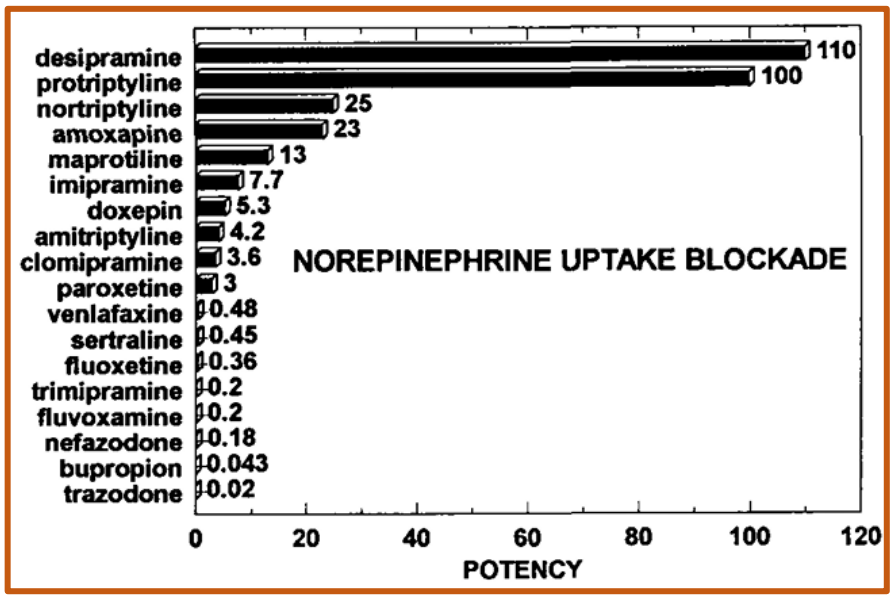

Fig. 1.9. Norepinephrine uptake blockade by antidepressants and related compounds [25]

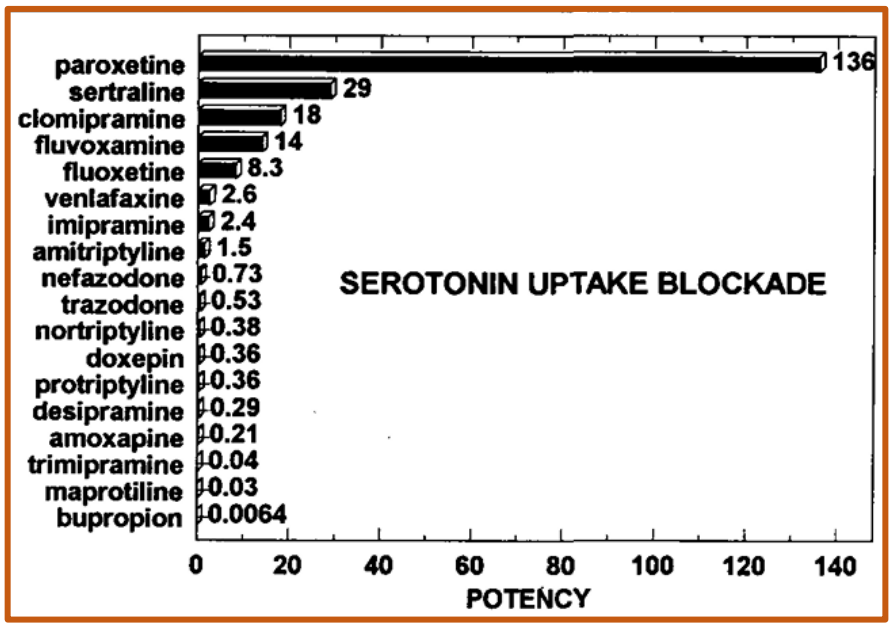

Fig. 1.10. Serotonin uptake blockade by antidepressants and related compounds [25]

Clinical consequences of neurotransmitter uptake blockade by antidepressants

Most of the possible clinical effects occur in the early stages of patient treatment. However, with long-term use of the drug, adaptive changes may occur, which can be expressed in adaptation to some side effects, the development of new side effects, and the appearance of therapeutic effects. The pharmacological properties and their possible clinical implications are listed in Table 1.4. Clinicians should be aware that the most potent drugs with these properties are more likely to cause possible effects than drugs that are weak in these properties.

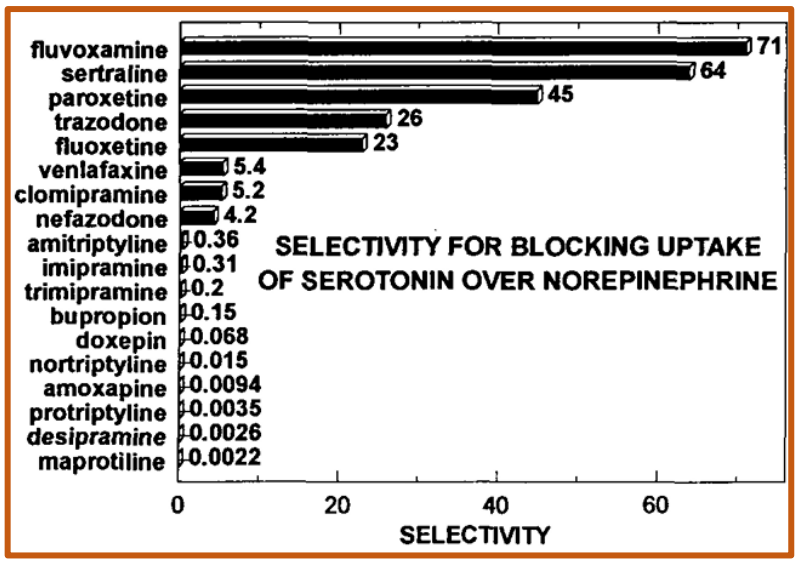

Fig. 1.11. Selectivity of antidepressants for blocking uptake of serotonin over norepinephrine [25]

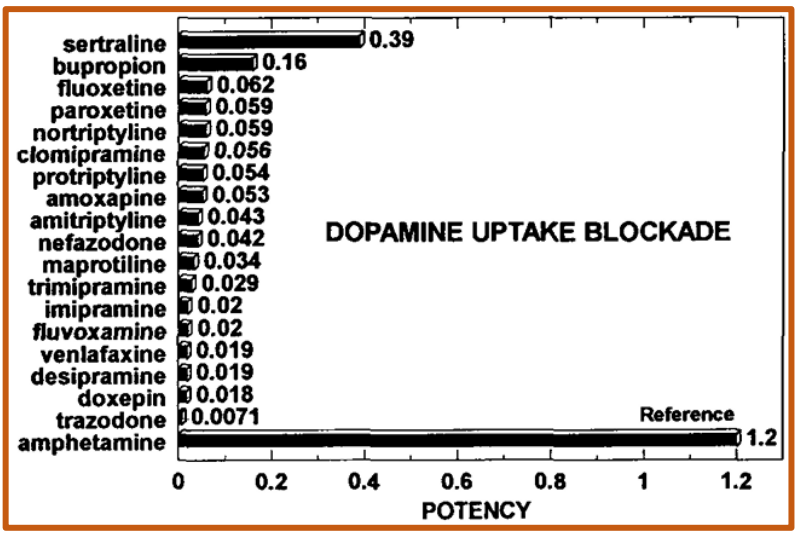

Fig. 1.12. Dopamine uptake blockade by antidepressants and related compounds [25]

Blockade of neurotransmitter receptors by antidepressants [25]

The new second-generation antidepressants are weaker than the older compounds in blocking neurotransmitter receptors. Thus, new drugs approach the ideal antidepressant without side effects. The weak blockade of receptors by newer drugs predicts that their side effect profile is better than, and different from, older drugs. In general, the strongest interaction of antidepressants, especially classic tricyclic drugs, occurs with the histamine H_1 receptor (Fig. 1.13) [25].

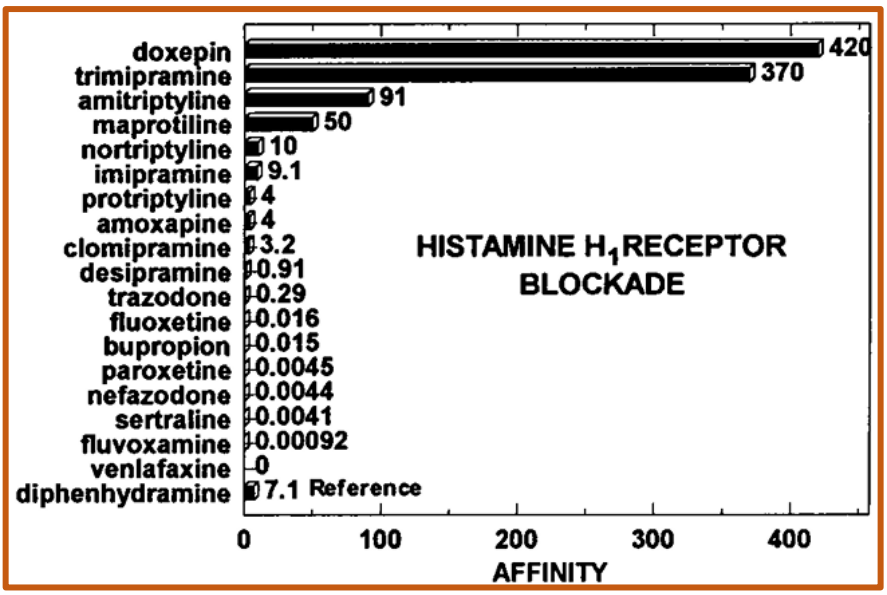

Fig. 1.13. Antidepressant blockade of histamine H_1 receptors [25]

The next most powerful effect of antidepressants is the muscarinic acetylcholine receptor. These receptors are the predominant type of cholinergic receptor in the brain, where they are associated with memory and learning, among other functions. Antidepressants have a wide spectrum of action and affinity for muscarinic receptors in the human brain (Fig. 1.14). The most potent is amitriptyline. Paroxetine is unique among the newer compounds because of its significant antimuscarinic activity, similar to that of imipramine (Fig. 1.14). In general, antidepressants differ little in their affinity for the five human muscarinic receptor subtypes [25].

Antidepressants are also weak competitive dopamine D_2 receptor antagonists (Fig. 1.15). The most potent compound is amoxapine. This activity may explain its

extrapyramidal side effects and its ability to increase prolactin levels. Because of this dopamine receptor-blocking property of amoxapine, some clinicians use it to treat psychotic depression [25, 37-40].

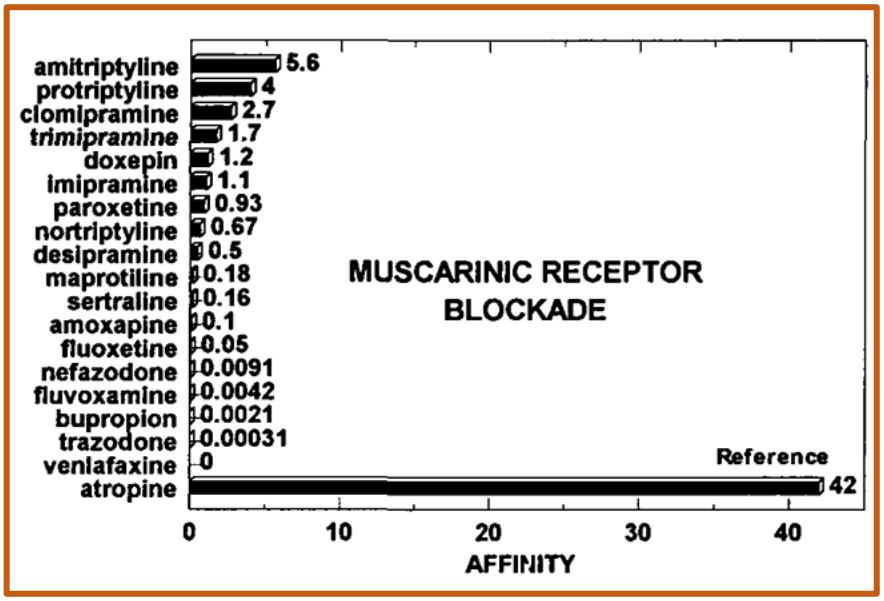

Fig. 1.14. Antidepressant blockade of muscarinic receptors [25]

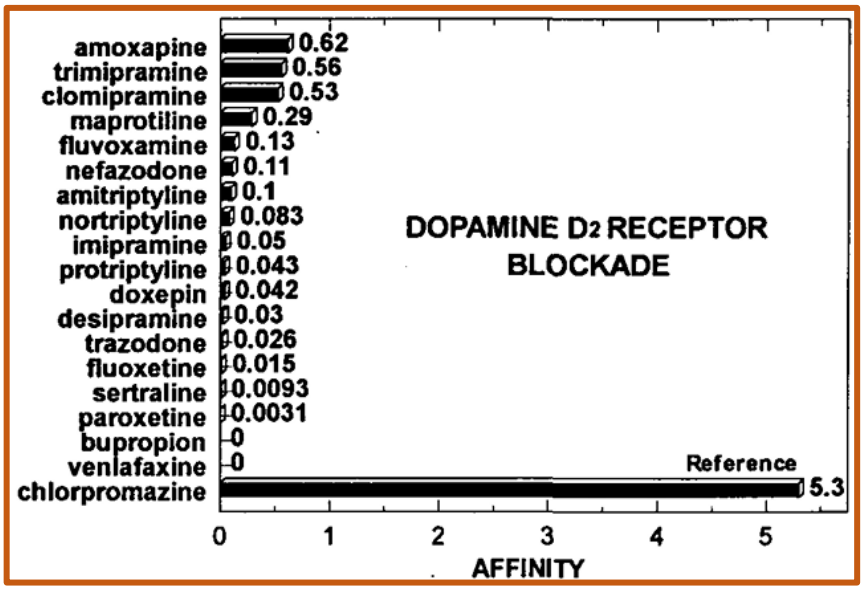

Fig. 1.15. Antidepressant blockade of dopamine D_2 receptor blockade [25]

Minimal drug interactions

Drug interactions of antidepressants can be divided into two groups - pharmacokinetic and pharmacodynamic. The levels of pharmacokinetic and pharmacodynamic interactions are shown in Table 1.5, respectively.

Low toxicity associated with overdose

Toxicity associated with antidepressant overdose is listed in Table 1.6.

Table 1.4

Pharmacologie properties of antidepressants and their possible clinical consequences [25]

Property	Possible clinical consequences
Blockade of norepinephrine uptake at nerve endings	Tremors Tachycardia Erectile and ejaculatory dysfunction Blockade of the antihypertensive effects of guanethidine and guanadrel Augmentation of pressor effects of sympathomimetic amines
Blockade of serotonin uptake at nerve endings	Gastrointestinal disturbances Increase or decrease in anxiety (dose-dependent) Sexual dysfunction Extrapyramidal side effects Interactions with L-tryptophan, monoamine oxidase inhibitors, and fenfluramine
Blockade of dopamine uptake at nerve endings	Psychomotor activation Antiparkinsonian effect Aggravation of psychosis
Blockade of histamine H_1 receptors	Potentiation of central depressant drugs Sedation, drowsiness Weight gain Hypotension
Blockade of muscarinic receptors	Blurred vision Dry mouth Sinus tachycardia Constipation Urinary retention Memory dysfunction
Blockade of α_1-adrenergic receptors	Potentiation of the antihypertensive effect of prazosin, terazosin, doxazosin, and labetalol Postural hypotension, dizziness Reflex tachycardia
Blockade of dopamine D_2 receptors	Extrapyramidal movement disorders Endocrine changes Sexual dysfunction (males)

Table 1.5

Potential for serious pharmacokinetic and pharmacodynamic drug-drug interactions among antidepressants [25]

Antidepressant	Severity of interactions
Monoamine oxidase inhibitors	Low
Classic tricyclic antidepressants	Intermediate
Amoxapine	Intermediate
Maprotiline	Intermediate
Trazodone	Low
Bupropion	Low
Fluoxetine	High
Sertraline	Intermediate-low
Paroxetine	High
Venlafaxine	Low
Nefazodone	?

Antidepressant	Severity of interactions
MAOIs	Lethal with serotonin selective reuptake inhibitors
Classic tricyclic antidepressants	Intermediate
Amoxapine	Intermediate
Maprotiline	Intermediate
Trazodone	Low
Bupropion	Low
Fluoxetine	Lethal with MAOIs
Sertraline	Lethal with MAOIs
Paroxetine	Lethal with MAOIs
Venlafaxine	Lethal with MAOIs
Nefazodone	?

Table 1.6

Potential for serious pharmacodynamic drug-drug interactions among antidepressants [25]

Table 5.—**Potential for Serious Pharmacodynamic Drug-Drug Interactions Among Antidepressants***

Antidepressant	Severity of interactions
MAOIs	Lethal with serotonin selective reuptake inhibitors
Classic tricyclic antidepressants	Intermediate
Amoxapine	Intermediate
Maprotiline	Intermediate
Trazodone	Low
Bupropion	Low
Fluoxetine	Lethal with MAOIs
Sertraline	Lethal with MAOIs
Paroxetine	Lethal with MAOIs
Venlafaxine	Lethal with MAOIs
Nefazodone	?

*MAOIs = monoamine oxidase inhibitors.

Broad spectrum of efficacy [25]

A final criterion for a pharmacologically ideal antidepressant is broad efficacy in the treatment of various types of depressive disorders, including mild to severe major depression, major depression with or without melancholia, bipolar depression,

dysthymia, and atypical depression. Recent reviews and clinical studies involving various types of depression show that newer antidepressants have a broader spectrum of efficacy than older drugs [25, 41-45].

1.2.2. Off-label uses of selective serotonin reuptake inhibitors

Antipsychotics are one of the leading off-label prescriptions [46, 47]. Among them, selective serotonin reuptake inhibitors (SSRIs) are very versatile and therefore widely prescribed. Moreover, SSRIs generally have a better safety profile than other antidepressants. Physicians are certainly allowed to prescribe off-label drugs according to the latest literature date and their knowledge and beliefs. For this reason, the absence of specific (direct) indications should not be considered an obstacle to specific therapy prescribing. The decision on which medicine to give is a process that has to be done taking into account all the potential risks and benefits for the patient and has to be supported by the best available evidence. Thus, when it comes to off-label prescriptions, SSRIs are at the top of the list. It seemed interesting to us the current state of selective serotonin reuptake inhibitors off-label use [46, 47]. We have conducted a review of SSRIs off-label prescribing and identified the most common medical conditions and SSRI evidence base for conditions treatment [46, 47]. We have reviewed the evidence base for SSRIs off-label prescribing using data from The National Center for Biotechnology Information (pubmed.ncbi.nlm.nih.gov). The search was carried out using the keywords: selective serotonin reuptake inhibitors, off-label uses, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, evidence base, and FDA approval. The following filters were included in the search: free full text, all article types (books and documents, clinical trial, meta-analysis, randomized controlled trial, review, and systematic review), and publication date of 10 years [46, 47].

One of the off-label SSRI indications is migraine prophylaxis. SSRIs have not shown promising results compared to other antidepressants such as tricyclic

antidepressants (TCAs). Fluoxetine was the most commonly used SSRI in randomized controlled trials. The American Academy of Neurology/American Headache Society recommends fluoxetine with evidence base level U (there is inadequate or conflicting evidence to support or refute drug use) [46, 47].

Very little evidence has been provided that SSRIs are the best treatment for body dysmorphic disorder, probably because they act on the obsessive signs of body dysmorphic disorder (fluoxetine, escitalopram, and citalopram). However, further randomized, placebo-controlled trials will be required for more consistent conclusions [46, 47].

Despite encouraging results, little evidence remains to date on SSRI effectiveness in impulse-control disorder (fluoxetine, citalopram, escitalopram, and paroxetine). More trials with larger populations are needed to shed more light on this topic [46, 47].

Although TCAs have proven to be the most effective, SSRIs have shown promising results in the treatment of irritable bowel syndrome with significant improvement in gastrointestinal symptoms and associated psychiatric symptoms (paroxetine and fluoxetine). Despite encouraging results, data are still scarce and require further clinical trials [46, 47]. A number of authors have presented important data on the use of SSRIs for the treatment of both paraphilias and hypersexuality with level E evidence (fluoxetine, sertraline, and citalopram). Numerous convincing shreds of evidence for long-acting SSRIs (paroxetine, fluoxetine, sertraline, citalopram, and escitalopram) in the treatment of premature ejaculation have been presented in the literature [46, 47].

The arrival of the first and unique approved short-acting, sexually-sparing SSRI called dapoxetine is to be welcomed. Based on the fact that randomized clinical trials of dapoxetine are the largest, with up to 6,000 participants, dapoxetine should be considered the best choice compared to other long-acting SSRIs such as paroxetine [46, 47].

Off-label SSRIs uses list is not limited to those mentioned above. Numerous

literature data highlight the importance of SSRIs in the treatment of menopause hot flashes, with the best evidence being for paroxetine, escitalopram, and citalopram. Trials on the use of SSRIs in the treatment of autism spectrum disorders have been inconclusive. The results of using SSRIs for the treatment of chronic pain open up promising new scenarios (escitalopram and fluoxetine). SSRIs are considered first-line treatments for the main symptoms of post-traumatic stress disorder [46, 47].

For these reasons, SSRIs have been proposed for the treatment of recurrent nightmares in patients after a traumatic event (paroxetine and citalopram). Negative findings have also been reported on the use of paroxetine in the treatment of obstructive sleep apnea. Although preliminary evidence for the use of SSRIs for stroke recovery has been encouraging, recent results have not reported strong evidence. There is still no consensus on the effectiveness of SSRIs in neuro-cardiogenic syncope (fluoxetine and citalopram) [46, 47].

SSRIs have been proposed as a potential treatment strategy for eating disorders such as food addiction, compulsive overeating, and nighttime eating syndrome in the context of the obesity epidemic, especially when combined with psychotherapy [46, 47]. SSRIs may play an important role in SARS-CoV-2 treatment (fluoxetine). However, to date, evidence has only come from in vitro studies or model systems studies, and thus there is still no clinical data available to support such an effect [46, 47].

SSRIs are widely prescribed drugs, mainly due to their off-label use. Evidence for SSRIs ranges from migraine prevention to hypersexuality. These results suggest that SSRIs are extremely versatile and non-addictive, are considered easy to administer, and are commonly prescribed by a general physician, often without conclusive scientific evidence and underestimating the risk of side effects in routine clinical practice. SSRIs are antidepressants and therefore psychiatric drugs, it would be extremely important to consult a psychiatrist before prescribing these drugs to off-label indications [46, 47].

Conclusions for Chapter 1

Depression is a state of mental illness. Depression can change a person's thinking/feeling and affect his/her social behavior and sense of physical well-being. Women and elderly people get sick more often than men. Nowadays, there are many wars going on in the world, including in Ukraine. The mental health problems faced by this category of patients are post-traumatic stress disorder and depression. Some studies have shown that approximately 14% to 16% of US military personnel serving in Afghanistan and Iraq have post-traumatic stress disorder or depression.

Chronic disease management requires close collaboration between patients and physicians, as well as patients and their families. SSRIs are a first-line treatment for depression.

SSRIs are widely prescribed drugs, mainly due to their off-label use. Evidence for SSRIs ranges from migraine prevention to hypersexuality. These results suggest that SSRIs are extremely versatile and non-addictive, are considered easy to administer, and are commonly prescribed by a general physician, often without conclusive scientific evidence and underestimating the risk of side effects in routine clinical practice. SSRIs are antidepressants and therefore psychiatric drugs, it would be extremely important to consult a psychiatrist before prescribing these drugs to off-label indications.

CHAPTER 2

MATERIALS AND METHODS

The practical part of the study was conducted in cooperation with Royal Pharmacy, Salmiya, Kuwait. We have developed two versions of the Questionnaires, which are presented in Figures 2.1 and 2.2:

1) Questionnaire for pharmacists on their awareness of the rational use of Cipralex to treat depression;

2) Questionnaire for pharmacy visitors on their awareness of the rational use of Cipralex in the treatment of depression.

We analyzed questionnaires from 40 pharmacists and 73 questionnaires from pharmacy visitors on their awareness of escitalopram's rational use for depression on the criteria of effectiveness and safety of treatment.

Statistical analysis of the results was performed using a one-way Kruskal-Wallis analysis of variance and the Mann-Whitney test for posterior pairwise comparisons [48, 49]. The computer software used included IBM SPSS STATISTICS V. 22 (IBM Corp., USA) and ms EXCEL 2016 (Microsoft Corp., USA). The level of statistical significance was considered $p < 0.05$ [50].

QUESTIONNAIRE FOR PHARMACISTS

about awareness of escitalopram's rational use in depression treatment

To fill in the questionnaire, circle the correct answers or write the necessary information by hand.
Thank you for your cooperation!

Do you know the clinical forms of depression? If yes, name them.

☐ Yes ☐ No ☐ I do not have precise information

1)
2)
3)

Do you know the pharmacological groups of drugs used to treat depression? If yes, name them.

☐ Yes ☐ No ☐ I do not have precise information

1)
2)
3)

Write some general rules for escitalopram using

1)
2)

What are the advantages/disadvantages of escitalopram? If you know, enter the trade name

1)
2)

What side effects of escitalopram do you know and have you informed the consumer about these risks

1)
2)

Fig. 2.1. Version of the questionnaire for pharmacists about their awareness of escitalopram's rational use in depression treatment

QUESTIONNAIRE FOR PHARMACY VISITORS

about awareness of escitalopram's rational use in depression treatment

To fill in the questionnaire, circle the correct answers or write the necessary information by hand.

Thank you for your cooperation!

Write some general rules for using escitalopram

1)

2)

3)

Has your doctor and/or your pharmacist told you about the potential side effects of antidepressants? If so, name these side effects.

☐ Yes ☐ No ☐ I do not have precise information

1)

2)

3)

Have you been informed by your doctor and/or pharmacist about the rules for the use of escitalopram? If so, provide this information.

☐ Yes ☐ No ☐ I do not have precise information

1)

2)

3)

Give an example of the different demands on escitalopram before the revolution until now.

1)

2)

3)

Fig. 2.2. Version of the questionnaire for pharmacy visitors about their awareness of escitalopram's rational use in depression treatment

Conclusion for Chapter 2

The questions concerning the criteria of efficiency of treatment and about the factors, that from the point of the patient are the most important for the effectiveness of the treatment were in both questionnaires same. In the questionnaire for patients, the questions and answers were adapted for better understanding by patients. For the purposes of the survey were pooled 40 pharmacists. For the purposes of the survey were pooled 73 pharmacy visitors.

CHAPTER 3

STUDY RESULTS AND PRACTICAL RECOMMENDATIONS

3.1. Survey of pharmacists about awareness of escitalopram's rational use in depression treatment

We analyzed questionnaires from 40 pharmacists about their awareness of escitalopram's rational use for depression on the criteria of effectiveness and safety of treatment.

The results of pharmacists' survey on their awareness of escitalopram's rational use in depression treatment are presented below.

In response to the question «Do you know the clinical forms of depression? Name them» 80% of respondents answered «Yes», 10% answered «No» and 10% of all respondents considered this information irrelevant (fig. 3.1).

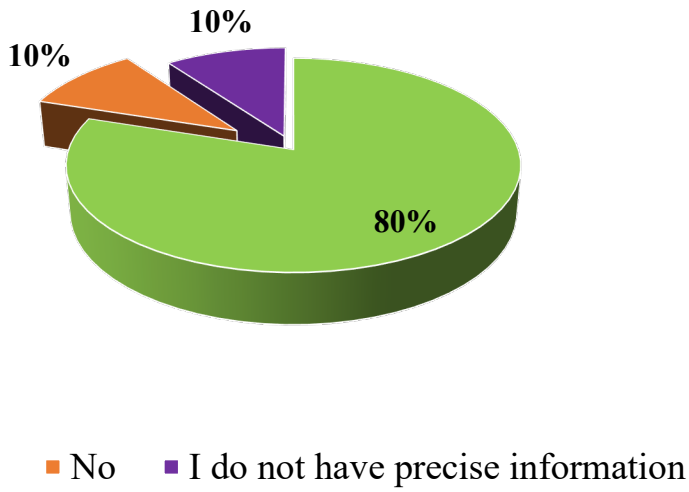

Fig. 3.1. «Do you know the clinical forms of depression? Name them»

When answering the question «Do you know the pharmacological groups of drugs used to treat depression? If yes, name them» answers were distributed as follows (fig. 3.2):

- Yes – 84%

1. Selective serotonin reuptake inhibitors (SSRIs) – 7%;
2. Serotonin/norepinephrine reuptake inhibitors (SNRIs) – 6%;
3. Tricyclic antidepressants (TCAs) – 37%;
4. Atypical antidepressants – 41%;
5. Serotonin modulators – 4%;
6. Monoamine oxidase inhibitors (MAOIs) – 5%;

- No – 7%;
- I do not have precise information – 9%.

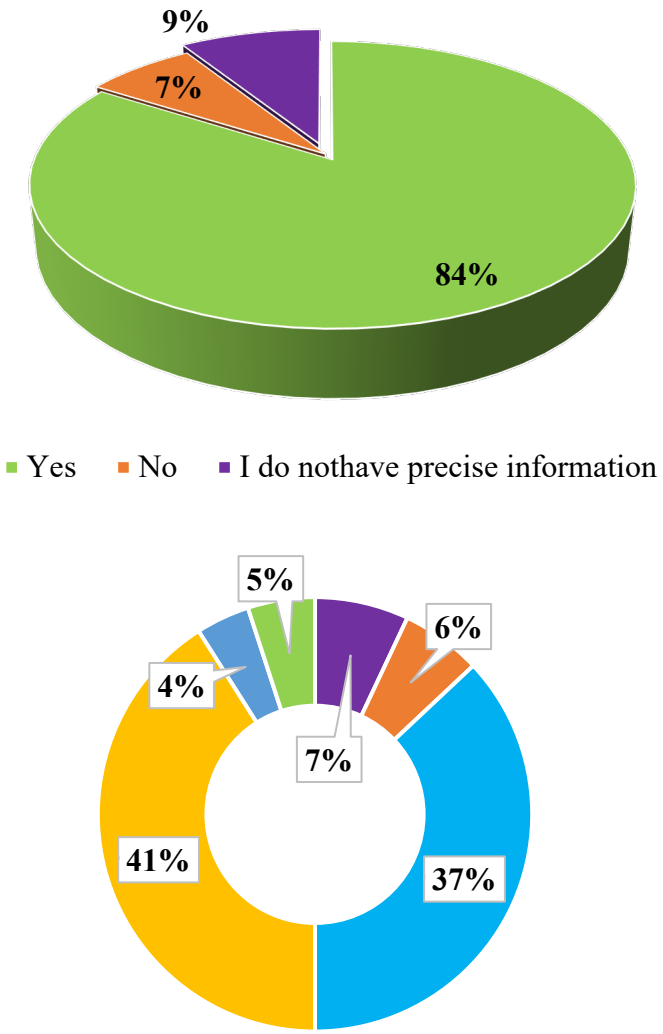

Fig. 3.2. «Do you know the pharmacological groups of drugs used to treat depression? If yes, name them»

Answering the question, «Write some general rules for escitalopram use»

respondents' answers were distributed as follows (by frequency of recommendations) (Fig. 3.3.):

1) Follow the recommendations specified in the instructions (50%)

2) Use on demand (30%)

3) Do not use longer than 6 months (20%)

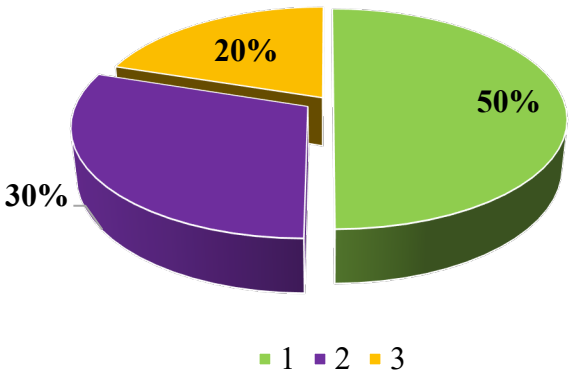

Fig. 3.3. «Write some general rules for escitalopram use»

Answering the question «What are the advantages/disadvantages of escitalopram? If you know, enter the trade name» respondents' answers were distributed as follows (Fig. 3.4.):

1) <50%>answer advantage that removes stress and makes the patient feel good;

2) <30%> answer that escitalopram it’s not good that makes your body need it all the time if we take it for a long time it will make you addicted to this drug;

3) <20%> answer not knowing anything about it.

Answering the question «What side effects of escitalopram do you know and have you informed the consumer about these risks» respondents' answers were distributed as follows (Fig. 3.5.):

1 Feeling sick (nausea) try taking escitalopram with or after food – 21%;

2 Headaches. Make sure you rest and drink plenty of fluids – 19%;

3 A dry mouth. Chew sugar-free gum or suck sugar-free sweets – 16%;

4 Sweating a lot – 8%;

5 Being unable to sleep – 13%;

6 Feeling sleepy – 12%;

7 Feeling tired or weak – 11%.

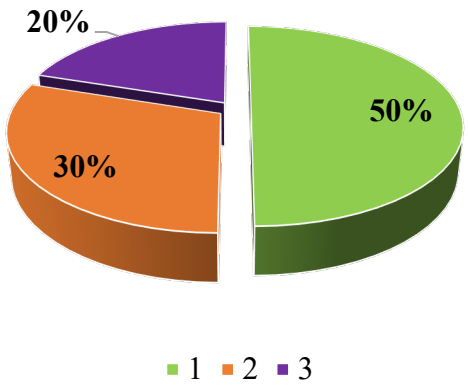

Fig. 3.4. «What are the advantages/disadvantages of escitalopram? If you know, enter the trade name»

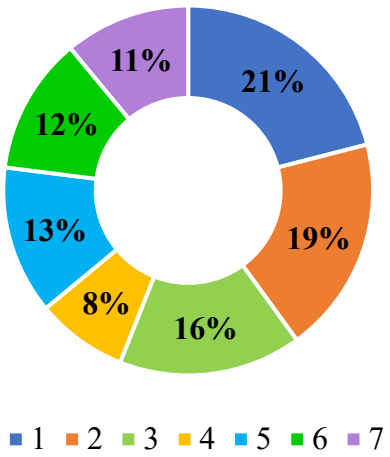

Fig. 3.5. «What side effects of escitalopram do you know and have you informed the consumer about these risks»

3.2. Survey of pharmacy visitors about awareness of escitalopram's rational use in depression treatment

We analyzed 73 questionnaires from pharmacy visitors. The results of the pharmacy visitors' survey on their awareness of escitalopram's rational use in

depression treatment are presented below.

In response to the question «Has your doctor and/or your pharmacist told you about the potential side effects of antidepressants? If so, name these side effects» respondents' answers were distributed as follows (fig. 3.6):

1) 77% of respondents answered «Yes»:
   - informed by the doctor – 41%;
   - informed by the pharmacist – 38%;
   - both experts provided information – 21%.
2) 14% of respondents answered «No»;
3) 9% of all respondents considered this information irrelevant.

The distribution of responses by side effects was about the same as in the survey of pharmacists:

1 Feeling sick (nausea) try taking escitalopram with or after food – 22%;

2 Headaches. Make sure you rest and drink plenty of fluids – 17%;

3 A dry mouth. Chew sugar-free gum or suck sugar-free sweets – 11%;

4 Sweating a lot – 7%;

5 Being unable to sleep – 15%;

6 Feeling sleepy – 14%;

7 Feeling tired or weak – 14%.

The answers of the respondents to the question «Have you been informed by your doctor and/or pharmacist about the rules for the use of escitalopram? If so, provide this information» were distributed as follows:

4) 69% of respondents answered «Yes»:
   - informed by the doctor – 39%;
   - informed by the pharmacist – 36%;
   - both experts provided information – 25%.
5) 16% of respondents answered «No»;
6) 15% of all respondents considered this information irrelevant.

The answers of the respondents to the question «Give an example of the different demands on escitalopram before the revolution until now» were distributed as follows:

1) increased need for regular intake – 69%;
2) increase in demand as required – 12%;
3) not changed – 19%.

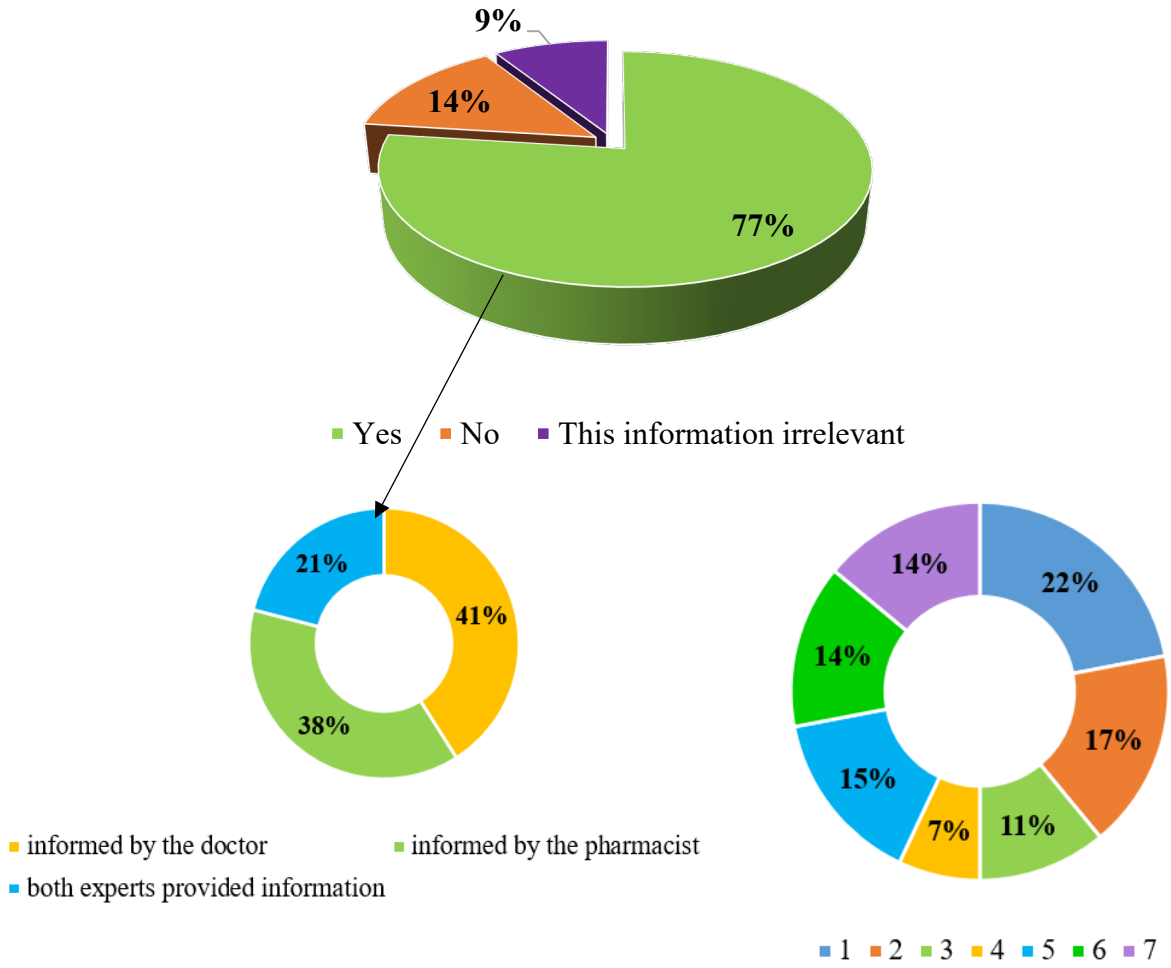

Fig. 3.6. «Has your doctor and/or your pharmacist told you about the potential side effects of antidepressants? If so, name these side effects»

«The economic situation continues to deteriorate in Lebanon, aid organizations face daunting challenges to meet the immense needs of the population», CARE International warned today. On Monday, Lebanese banks ended a three-week strike. Public sector employees also observe strikes intermittently. This has been the case since January, including for teachers in public schools. Public

schools have been closed for over a month and a half, heavily weighing on the education sector.

The Lebanese Lira continues its vertiginous fall against the dollar. Its fixed value in September 2019 was 1,500 Liras per dollar; now, 1 USD is equivalent to 80,000 Liras. Otherwise put, in 2019, 100,000 Lebanese Liras had a value of 66 USD; today they are worth less than 1.5 USD. Adding to that, the Lebanese people have seen their life savings evaporate, with banks freezing the withdrawal of all deposits. Pierre Valiquette, CARE Lebanon Country Director, said, «With the current acute economic crisis that Lebanon is facing, prices are rising every day and the populations living in the country are confronted with a tremendous challenge», Pierre.

Today, 82% of the Lebanese population lives in multidimensional poverty. While social assistance programs are almost non-existent. Many households in the country's poorest areas survive without electricity or heating; families lack food, forcing them to reduce their meals to two a day. The World Bank has classified the Lebanese crisis as one of the 10 worst. Economic crises globally since the 19th century – and possibly even as one of the top three. The price of bread, which is the staple food, is revised upwards several times. Month, and the price of fuel, twice a day. Supermarkets no longer display the prices of goods because of the fluctuating Lira rate.

«The war in Ukraine and the rocketing fuel prices have also made things worse, even more so, the Lebanese have lived almost without government-produced electricity for the past two years and have had to rely on private generators for lighting. The increase in the price of fuel is also a problem for hospitals and motorists in a country where a public transport network is non-existent», added Pierre Valiquette.

The study showed that around three weeks post-war, 25.9% of Lebanese young persons had major depressive disorder, 16.1% had a separation anxiety disorder, 28% had an overanxious disorder, 26% had PTSD, and 44.1% had any disorder.

In general, the demand for escitalopram before the revolution and until now is too much since before that people that has depression disease came to the pharmacy with a prescription from a doctor but now since life in Lebanon is too hard since the minimum wage is too small and all product that you need to buy it from any shops like if you go to the supermarket the price of the piece has become 10 times from before.

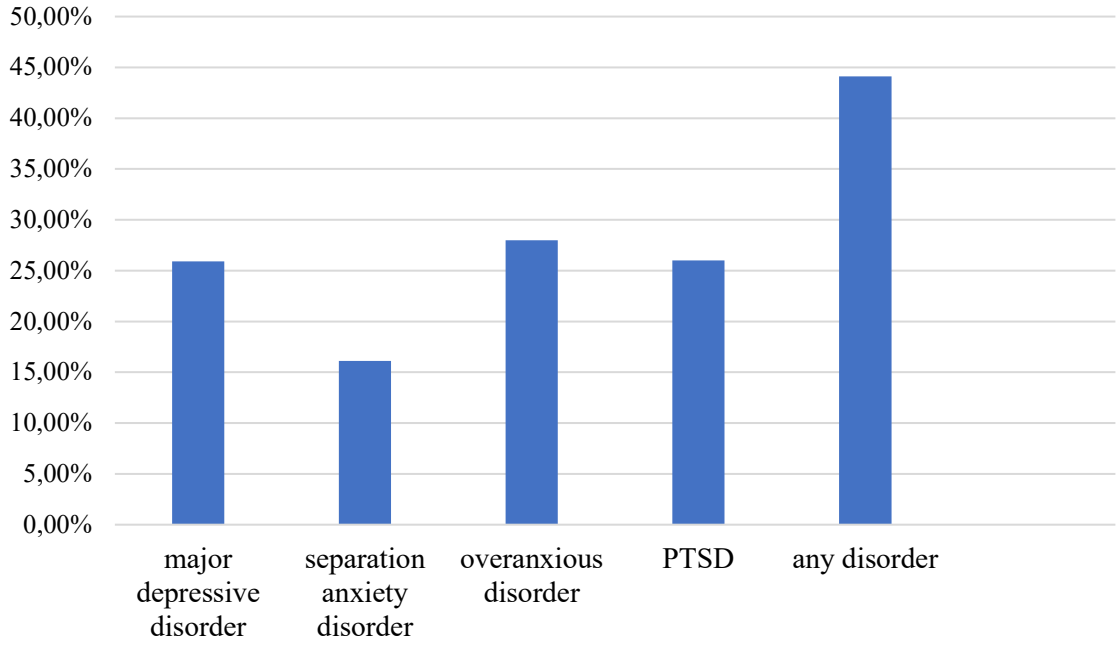

Fig. 3.7. Prevalence of depression in Lebanese young persons

3.3. Discussion of the results and practical recommendations for all participants of the treatment process about escitalopram's rational use in depression treatment

Now makes the demand for depression medication is 40% while before this crisis maximum the percentage of demand for escitalopram is between 7% to 10 % in all of Lebanon also there is another depression problem the price of escitalopram before the crisis is 22000 Lebanese lira is like 10 dollar It is the rise of the dollar from 1,500 to 100,000 Lebanese pounds. This is also a reason for the rise in drug prices. For example, in 2019 and before the crisis, the price of a box of escitalopram was 20,000, equivalent to 12 US dollars, but now the price of one box is 170,000

Lebanese pounds, equivalent to 17 dollars. It also negatively affected the demand, as it became precious, so suicides increased due to depression and the inability to buy the box, as half of the people became depressed because of their inability to live and their inability to buy antidepressant treatment, but with the occurrence of the earthquake in Turkey and Syria, the demand for escitalopram increased, and here I am talking about The rich and middle-income class who are able to buy medicine because most people have fear and obsession, that is, when the lights flicker in the house or at work, they think that it is an earthquake.

The focus was to analyze the psychopharmacological treatment of psychiatric inpatients in relation to the severity of MDD according to the ICD-10 in a naturalistic setting. To the best of our knowledge, this is the first study to provide a detailed analysis of utilization rates of psychotropic drugs in psychiatric inpatients depending on the severity degree of MDD. Most patients in the present study were treated with at least one psychotropic drug, of which ADDs were the most used psychotropic drug group. ADD use differed only slightly between severity levels. The utilization of APDs showed greater differences in association with the severity of MDD. While the rates of lp FGA utilization were relatively equal among all three degrees of severity, SGAs were used significantly more often in patients with psychotic MDD. ADD monotherapy was observed in only a small proportion of patients, whereas the use of two or more psychotropic drugs was common even among moderate MDD and was highest among patients with psychotic MDD. The number of psychotropic drugs used per patient also increased with the severity of MDD. Patients with psychotic MDD showed the highest utilization of psychotropic drugs and monotherapy was least common among these patients. The combination of two ADDs was observed in almost one-fourth of patients irrespectively of severity degree. The use of an ADD combined with an APD varied significantly according to severity of MDD and was lowest among patients with moderate MDD (32.8%) and highest in psychotic MDD (74.4%).It is important to note that guidelines are merely able to make recommendations for the treatment that should be offered to the affected individuals. Unless appointed by court order, treatment cannot be forced

upon the patient regardless of guideline suggestions. This should be considered whenever the implementation of guideline recommendations is discussed in the following.

Based on that this shows us the drug that takes it to treat depression:

- sertraline (Zoloft)
- fluoxetine (Prozac, Sarafem)
- citalopram (Celexa)
- escitalopram (Lexapro)
- paroxetine (Paxil, Pexeva, Brisdelle)
- fluvoxamine (Luvox)

As a result of our work, we have developed practical recommendations for all participants of the treatment process about escitalopram's rational use in depression treatment.

Practical recommendations for pharmacists and patients:

1) By oral can be used as a starting or adjunctive therapy for many depression conditions.

2) Escitalopram affects both the early and late stages of depression. It works by increasing levels of a neurotransmitter called serotonin in the brain. Increased serotonin levels can lead to an improved mood. The medication usually begins to work within 2 to 4 weeks. However, it may take several weeks of treatment before the full effects are seen.

3) Escitalopram is safe, but some side effects are common. Patients experience local side effects, including headache, dryness in the mouth, being unable to sleep, feeling sleepy, feeling tired, or weak.

4) Proper administration of escitalopram is crucial for the desired therapeutic effect. Healthcare professionals should show patients how to reduce side effects and increase adherence to treatment. Daily use is often required for full therapeutic effect for 8–12 weeks, but adherence to treatment may be affected by cost.

Conclusion for Chapter 3

According to the results of the pharmacists' survey, this should be noted the following.

Pharmacists' awareness of the rules for using escitalopram is insufficient, and some of the respondents (50%) do not consider this information important at all. This can adversely affect the effectiveness of treatment.

It should also be noted that there was no opposition (30%) to the selection criteria for escitalopram.

According to a survey of pharmacy visitors, it is indicated that it is a very small number of respondents (10%) were able to indicate at least one rule to use escitalopram. The most common response was, «Follow the instructions for use» (50%).

On the positive side, almost half of the respondents (40%) were to inform their doctor and pharmacist of possible side effects.

Based on the results of the work, practical recommendations for the rules of escitalopram use in the treatment of depression have been developed. In view of all the above, the issue of pharmaceutical care of escitalopram in the treatment of depression remains a pressing issue and needs further study and improvement

CONCLUSIONS

1) Depression is one of the most common conditions in primary health care but is often not recognized, diagnosed or treated. Depression has a high morbidity and mortality rate if left untreated. All physicians must remain vigilant to effectively screen for depression in their patients. Primary care physicians should carefully evaluate patients with depression for suicide. Depression in the elderly is not part of the normal aging process. The prognosis for recovery is similar in younger and older patients, although older patients may take longer to achieve remission.

2) The efficacy of antidepressants is generally comparable between and within drug classes. Most psychiatrists agree that SSRIs should be the first line of choice. The dual-acting reuptake inhibitors venlafaxine and bupropion are usually considered second-line agents. Tricyclic drugs and other mixed- or dual-acting inhibitors are third-line, and MAOIs are usually the drugs of last resort for patients who have not responded to other drugs due to poor tolerability, dietary restrictions, and drug interactions. SSRIs are the most widely prescribed antidepressants, mainly due to their off-label use. SSRIs are extremely versatile and non-addictive, considered easy to administer, and commonly prescribed by a general practitioner, often without conclusive scientific evidence and underestimating the risk of side effects in routine clinical practice. SSRIs are antidepressants and therefore psychiatric drugs, it would be extremely important to consult a psychiatrist before prescribing these drugs off-label.

3) We developed a questionnaire to survey pharmacists about their awareness of the rational use of escitalopram in the treatment of depression. Based on the results of the survey, it can be concluded that pharmacists are sufficiently aware of the clinical forms of depression (80% of positive responses) and the pharmacological groups of drugs used to treat it (84% of positive responses), but are not sufficiently aware of the rationality of use and side effects of escitalopram.

4) We developed a questionnaire to survey pharmacy customers about their awareness of the rational use of escitalopram in the treatment of depression. Based

on the results of the survey, it can be concluded that pharmacy visitors were not sufficiently aware of both doctors and pharmacists about the rational use and side effects of escitalopram.

5) We developed practical recommendations for all participants of the treatment process about escitalopram's rational use in depression treatment.

6) Taking into account the results obtained, we can conclude that depression in any of its manifestations is a big problem in the modern world, with a tendency to increase. Therefore, aspects of the rational use of new antidepressants from the group of serotonin reuptake inhibitors, as the most effective and safe drugs, acquire new relevance and require further study and improvement.

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APPENDIX

Appendix A

КЛІНІЧНА ФАРМАЦІЯ В УКРАЇНІ ТА СВІТІ

2023

Міністерство охорони здоров'я України
Національний фармацевтичний університет
Кафедра клінічної фармакології
та клінічної фармації

The Ministry of HealthCare of Ukraine
National University of Pharmacy
Department of Clinical Pharmacology
and Clinical Pharmacy

СЕРТИФІКАТ
CERTIFICATE

№ 271

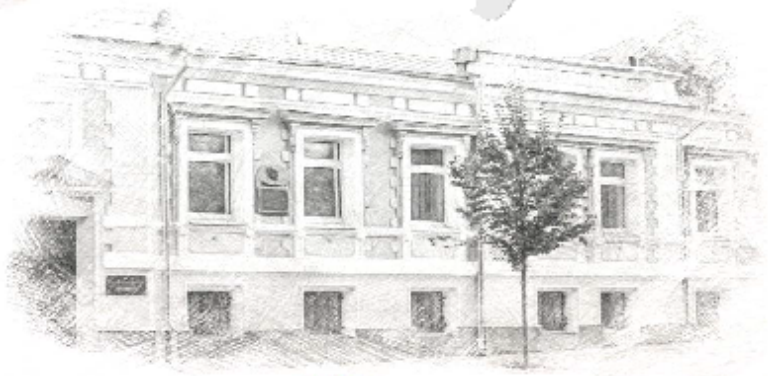
Цим засвідчується, що

This is to certify that

Almais Sobhi

брав(ла) участь у роботі Всеукраїнської науково-практичної Internet-конференції з міжнародною участю "Клінічна фармація в Україні та світі", присвяченої 30-річчю заснування кафедри клінічної фармакології та клінічної фармації Національного фармацевтичного університету
16-17 березня 2023 р., м. Харків

participated in the All-Ukrainian scientific and practical Internet-conference with international participation "Clinical pharmacy in Ukraine and the World", dedicated to the 30th anniversary of the Department of Clinical Pharmacology and Clinical Pharmacy of the National University of Pharmacy founding
March 16-17, 2023, Kharkiv



В.о. ректора НФаУ, проф. Алла КОТВІЦЬКА

Проректор з науково-педагогічної роботи НФаУ, проф. Інна ВЛАДИМИРОВА

Завідувачка кафедри клінічної фармакології та клінічної фармації, проф. Катерина ЗУПАНЕЦЬ

Continuation of Appendix A

THE MINISTRY OF HEALTHCARE OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF CLINICAL PHARMACOLOGY
AND CLINICAL PHARMACY

CLINICAL PHARMACY IN UKRAINE AND THE WORLD

MATERIALS
of the All-Ukrainian scientific and practical Internet-conference
with international participation, dedicated to the 30th anniversary
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of the National University of Pharmacy founding

March 16-17, 2023
Kharkiv

Registration certificate UkrISTEI
No. 543 dated December 19, 2022

Kharkiv
NUPh
2023

PERSPECTIVES OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS OFF-LABEL USES IN VARIOUS MEDICAL CONDITIONS TREATMENT

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Introduction. Antipsychotics are one of the leading off-label prescriptions. Among them, selective serotonin reuptake inhibitors (SSRIs) are very versatile and therefore widely prescribed. Moreover, SSRIs generally have a better safety profile than other antidepressants. Physicians are certainly allowed to prescribe off-label drugs according to the latest literature date and their knowledge and beliefs. For this reason, the absence of specific (direct) indications should not be considered an obstacle to specific therapy prescribing. The decision on which medicine to give is a process that has to be done taking into account all the potential risks and benefits for the patient and has to be supported by the best available evidence. Thus, when it comes to off-label prescriptions, SSRIs are at the top of the list. It seemed interesting to us the current state of selective serotonin reuptake inhibitors off-label use.

Aim of the study. Conduct a review of SSRIs off-label prescribing, identify the most common medical conditions and SSRI evidence base for conditions treatment. This analysis is one of the qualification work chapters on the topic «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors».

Materials and methods. To review the evidence base for SSRIs off-label prescribing using data from The National Center for Biotechnology Information (pubmed.ncbi.nlm.nih.gov). The search was carried out using the keywords: selective serotonin reuptake inhibitors, off-label uses, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, evidence base, and FDA approval. The following filters were

included in the search: free full text, all article types (books and documents, clinical trial, meta-analysis, randomized controlled trial, review, and systematic review), and publication date of 10 years.

Results and discussion. One of the off-label SSRI indications is migraine prophylaxis. SSRIs have not shown promising results compared to other antidepressants such as tricyclic antidepressants (TCAs). Fluoxetine was the most commonly used SSRI in randomized controlled trials. The American Academy of Neurology/American Headache Society recommends fluoxetine with evidence base level U (there is inadequate or conflicting evidence to support or refute drug use).

Very little evidence has been provided that SSRIs are the best treatment for body dysmorphic disorder, probably because they act on the obsessive signs of body dysmorphic disorder (fluoxetine, escitalopram, and citalopram). However, further randomized, placebo-controlled trials will be required for more consistent conclusions.

Despite encouraging results, little evidence remains to date on SSRI effectiveness in impulse-control disorder (fluoxetine, citalopram, escitalopram, and paroxetine). More trials with larger populations are needed to shed more light on this topic.

Although TCAs have proven to be the most effective, SSRIs have shown promising results in the treatment of irritable bowel syndrome with significant improvement in gastrointestinal symptoms and associated psychiatric symptoms (paroxetine and fluoxetine). Despite encouraging results, data are still scarce and require further clinical trials.

A number of authors have presented important data on the use of SSRIs for the treatment of both paraphilias and hypersexuality with level E evidence (fluoxetine, sertraline, and citalopram). Numerous convincing shreds of evidence for long-acting SSRIs (paroxetine, fluoxetine, sertraline, citalopram, and escitalopram) in the treatment of premature ejaculation have been presented in the literature.

The arrival of the first and unique approved short-acting, sexually-sparing SSRI called dapoxetine is to be welcomed. Based on the fact that randomized clinical trials of dapoxetine are the largest, with up to 6,000 participants, dapoxetine should be considered the best choice compared to other long-acting SSRIs such as paroxetine.

Off-label SSRI uses list is not limited to those mentioned above. Numerous literature data highlight the importance of SSRIs in the treatment of menopause hot flashes, with the best evidence being for paroxetine, escitalopram, and citalopram. Trials on the use of SSRIs in the treatment of autism spectrum disorders have been inconclusive. The results of using SSRIs for the treatment of chronic pain open up promising new scenarios (escitalopram and fluoxetine). SSRIs are considered first-line treatments for the main symptoms of post-traumatic stress disorder.

For these reasons, SSRIs have been proposed for the treatment of recurrent nightmares in patients after a traumatic event (paroxetine and citalopram). Negative findings have also been reported on the use of paroxetine in the treatment of obstructive sleep apnea. Although preliminary evidence for the use of SSRIs for stroke recovery has been encouraging, recent results have not reported strong evidence. There is still no consensus on the effectiveness of SSRIs in neuro-

cardiogenic syncope (fluoxetine and citalopram).

SSRIs have been proposed as a potential treatment strategy for eating disorders such as food addiction, compulsive overeating, and nighttime eating syndrome in the context of the obesity epidemic, especially when combined with psychotherapy.

SSRIs may play an important role in SARS-CoV-2 treatment (fluoxetine). However, to date, evidence has only come from in vitro studies or model systems studies, and thus there is still no clinical data available to support such an effect.

Conclusions. SSRIs are widely prescribed drugs, mainly due to their off-label use. Evidence for SSRIs ranges from migraine prevention to hypersexuality. These results suggest that SSRIs are extremely versatile and non-addictive, are considered easy to administer, and are commonly prescribed by a general physician, often without conclusive scientific evidence and underestimating the risk of side effects in routine clinical practice. SSRIs are antidepressants and therefore psychiatric drugs, it would be extremely important to consult a psychiatrist before prescribing these drugs to off-label indications.

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of clinical pharmacology and clinical pharmacy

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
Acting Head
of Department
of Clinical Pharmacology
and Clinical Pharmacy

Tetiana SAKHAROVA
«02» of September 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Sobhi AL MAIS

1. Topic of qualification work: « Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors»,
supervisor of qualification work: Tetiana ZHULAY, PhD, assistant.

approved by order of NUPh from «06th» of February 2023 № 35

2. Deadline for submission of qualification work by the applicant for higher education: April 2023.

3. Outgoing data for qualification work: depression, antidepressants, selective serotonin reuptake inhibitors, efficacy criteria, and safety criteria.

4. Contents of the settlement and explanatory note (list of questions that need to be developed):
to review the literature on the treatment of medical conditions associated with depression; to analyze the issues of adherence to therapy with selective serotonin reuptake inhibitors; to develop a questionnaire for pharmacists and patients; to conduct surveys and process experimental data; to develop practical recommendations for the rational use of serotonin reuptake inhibitors.

5. List of graphic material (with exact indication of the required drawings):
tables – 6, figures – 24

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022
2.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022
3.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022

7. Date of issue of the assignment: «02» September 2022

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Conducting a literature review on the issues of the work.	September-November 2022	**done**
2.	Conducting a survey of pharmacists and patients.	December 2022	**done**
3.	Experimental data processing.	January-February 2023	**done**
4.	Writing the qualification work.	March-April 2023	**done**
5.	Registration of the work and accompanying documents and submission to the Examination Committee of the NUPh.	April 2023	**done**

An applicant of higher education _____ Sobhi AL MAIS

Supervisor of qualification work _____ Tetiana ZHULAI

ВИТЯГ З НАКАЗУ № 35
По Національному фармацевтичному університету
від 06 лютого 2023 року

нижченаведеним студентам 5-го курсу 2022-2023 навчального року, навчання за освітнім ступенем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація, освітня програма – фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців та 3 роки 10 місяців), які навчаються за контрактом, затвердити теми кваліфікаційних робіт:

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **кафедри клінічної фармакології та клінічної фармації**				
Аль Маіс Собхі	Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors	Клініко-фармакологічний аналіз застосування антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну	асистент Жулай Т.С.	професор Оклей Д. В.

Підстава: подання декана, згода ректора

Ректор

Вірно. Секретар

Національний фармацевтичний університет
Факультет з підготовки іноземних громадян
№02010936
місто Харків

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 114216 від «29 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Аль Маіс Собхі, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Клініко-фармакологічний аналіз застосування антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну / Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
професор **Інна ВЛАДИМИРОВА**

1%
27%

Ф А 2.2.1-32-356

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Sobhi AL MAIS

on the topic: «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors»

Relevance of the topic. According to statistics from the WHO, hundreds of millions of people worldwide suffer from various manifestations of depression. In Lebanon, according to official data, somatic diseases associated with depression affect about 13% of the population (unofficial data is 20-30%). Depression significantly worsens the quality of life and negatively affects socioeconomic well-being. Although depression usually requires long-term treatment, poor adherence to depression therapy has been documented.

The practical value of conclusions, recommendations, and their validity. The research conducted in this qualification work is the basis for further clinical and pharmaceutical research, development, and implementation of principles for optimizing the rational use of serotonin reuptake inhibitors for the long-term treatment of various clinical forms of depression. The implementation of these principles and provisions into practical medicine and pharmacy will increase the effectiveness and safety of depression treatment.

Assessment of work. The work is performed at a sufficient scientific and methodological level. In terms of relevance, scientific novelty, and practical significance, it fully meets the requirements for qualification works.

General conclusion and recommendations on admission to defend. The work is performed in full, designed in accordance with the current requirements for the qualification works at the National University of Pharmacy, and can be recommended for submission to the EC for further defense.

Scientific supervisor _____ Tetiana ZHULAI

«11» April 2023

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Sobhi AL MAIS

on the topic: «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors»

Relevance of the topic. Depression can change a person's thinking/feeling and affect their sense of physical well-being. Now there are many wars in the world, including in Ukraine. Therefore, there is a need to increase public and professional care for veterans' and military personnel's mental health. Chronic disease management requires close collaboration between patients and physicians, as well as patients and their families. Selective serotonin reuptake inhibitors are first-line drugs for the long-term treatment of depression. Therefore, the issues of their rational and safe use are of particular relevance.

The theoretical level of work. The literature review conducted subject of the study illustrates the lack of patients' adherence to depression long-term treatment with serotonin reuptake inhibitors to date and outlines the prospects for research.

Author's suggestions on the research topic. The provisions of the author of the work on medication adherence are of practical importance for the modern healthcare system.

The practical value of conclusions, recommendations, and their validity. Based on the research results, approaches to the rational use of serotonin reverse inhibitors have been developed using the example of escitalopram. The author discusses the main approaches to increasing patients' adherence to long-term treatment of depression. Practical recommendations for all healthcare providers are proposed.

Disadvantages of work. Single grammatical and spelling errors do not affect the overall positive assessment of the work.

General conclusion and assessment of the work. The work meets the requirements for qualification work in NUPh and can be recommended for defense.

Reviewer _____ ass. prof. Denys OKLEI

«15» April 2023

МОЗ України
Національний фармацевтичний університет

ВИТЯГ З ПРОТОКОЛУ №10

Засідання кафедри клінічної фармакології та клінічної фармації

м. Харків «19» квітня 2023 р.

СЛУХАЛИ: Про представлення до захисту в Екзаменаційній комісії випускної кваліфікаційної роботи на тему: **«Клініко-фармакологічний аналіз застосування антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну» / «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors»**
здобувача вищої освіти 5 курсу, спеціальність – 226 Фармація, промислова фармація, освітня програма – Фармація, ступінь вищої освіти – магістр, термін навчання – 4 р. 10 міс., денна форма навчання, НФаУ 2023 року випуску

Собхі Аль Маіс
прізвище, ім'я та по батькові

Керівник: асистент кафедри клінічної фармакології та клінічної фармації, к.мед.н. Жулай Т.С.

Рецензент: професор закладу вищої освіти кафедри хірургічних хвороб Харківського національного університету імені В. Н. Каразіна, д.мед.н., доцент Оклей Д.В.

В обговоренні кваліфікаційної роботи брали участь:
В.о. зав. кафедри, професор Т.С. Сахарова; професор В.А. Мороз; професор С.К. Шебеко; доцент О.О. Андрєєва; доцент Н.П. Безугла; доцент В.В. Пропіснова; доцент С.В. Місюрьова; доцент І.А. Отрішко; доцент О.О. Тарасенко; доцент К.М. Ткаченко; асистент С.М. Зімін; асистент Т.С. Жулай; асистент Н.В. Давішня; асистент Т.Ю. Колодєзна; асистент К.В. Вєтрова; асистент Ю.В. Тимченко

ПОСТАНОВИЛИ: Рекомендувати до захисту в ЕК кваліфікаційну роботу здобувача вищої освіти

Собхі Аль Маіс
прізвище, ім'я та по батькові

На тему: **«Клініко-фармакологічний аналіз застосування антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну» / «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors»**

В.о. завідувачки кафедри _____ Тетяна САХАРОВА
(підпис)

Секретар _____ Катерина ТКАЧЕНКО
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Собхі АЛЬ МАІС до захисту кваліфікаційної роботи

за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Клініко-фармакологічний аналіз застосування антидепресантів з групи селективних інгібіторів зворотного захвату серотоніну» / «Clinical and pharmacological analysis of antidepressant use from the group of selective serotonin reuptake inhibitors».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Собхі АЛЬ МАІС виконав весь необхідний обсяг робіт. Кваліфікаційна робота може бути рекомендована до подачі в ЕК НФаУ для подальшого її захисту.

Керівник кваліфікаційної роботи

_____ Тетяна ЖУЛАЙ

«11» квітня 2023 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Собхі АЛЬ МАІС допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

В.о. завідувачки кафедри
клінічної фармакології та клінічної фармації

_____ Тетяна САХАРОВА

«19» квітня 2023 року

Qualification work was defended
of Examination Commission on
«___» June 2023
with the grade _____

Head of the State Examination Commission,
DPharmSc, Professor
_____ / Oleh SHPYCHAK /