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Experience using aripiprazole in the complex treatment of PTSD due to the war in Ukraine

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Relevance. Our country has fully experienced the incomprehensibility and fragility of the modern world with the beginning of the anti-terrorist operation in eastern Ukraine, later going through the COVID-19 pandemic with all its devastating consequences, and finally suffering a treacherous attack from a neighboring state that until recently positioned itself as “fraternal”.It is understandable that all of this has significantly influenced the overall anxiety, fear of the future, and lack of trust of the population as a whole, subjecting large segments of the population to an increased risk of developing post-traumatic stress disorder (PTSD) associated with being in a combat zone, among military personnel and war veterans, among forced migrants, and among those who have experienced violence and torture. Obtaining effective treatment is crucial for reducing disorder symptoms and improving functioning. Modern treatment options for PTSD include both psychological and pharmacological interventions. Since we currently have a large influx of patients with post-traumatic stress disorders, both as a result of combat stress and other mass stressors, it is necessary to review approaches to the treatment of such patients and choose the most effective and accessible ones for the majority of specialists. Of course, the effectiveness of trauma-focused psychotherapeutic methods is difficult to overestimate, and most of our professionals have undergone or are undergoing training in their application. However, one should not forget about the vast arsenal of available and effective medications that can effectively prepare a patient for psychotherapeutic treatment or serve as a complement to psychotherapy.

Objective. The objective of our study was to investigate the effectiveness of the atypical antipsychotic aripiprazole in the comprehensive treatment of PTSD and its mechanisms of influence on different clusters of PTSD, as well as comorbid disorders.

Materials and Methods. A literature analysis was conducted on the effectiveness of various PTSD therapy methods, including chronic complex PTSD and PTSD with comorbid psychiatric disorders and addictions. Our own clinical studies are being carried out on patients with PTSD undergoing inpatient and outpatient treatment at the “Prykarpatskyi Regional Clinical Mental Health Center of the Ivano-Frankivsk Regional Council” and the First Volunteer Surgical Hospital of the “BRASS” clinic. The group primarily consisted of males aged 21 to 45 with PTSD related to military actions and verified according to contemporary diagnostic criteria. Clinical-psychopathological examination and psychodiagnostic methods were used, including the Clinical-Administered PTSD Scale (CAPS) for clinical diagnosis of PTSD, the Hospital Anxiety and Depression Scale (HADS), the Dissociative Experiences Scale (DES), Richard Lazarus' Psychological Diagnosis of Coping Behavior Strategy, the Quality of Life Assessment

Scale (Chaban O.S., 2008), and others. A follow-up method was also employed to assess the results of the comprehensive treatment program. It should be noted that this article serves as a preliminary report, and the statistically analyzed results of the study will be reported in our future publications.

Results. Aripiprazole can be considered one of the most promising antipsychotic agents for the treatment of post-traumatic stress disorders in a comprehensive approach alongside psychotherapy, and in certain cases, as monotherapy, considering its broad spectrum of action and minimal side effects.

The key to successful treatment is the establishment of trusting and collaborative relationships with the patient when prescribing medication. Psychological preparation of patients regarding side effects, necessary dosages, treatment duration, and compliance can significantly improve outcomes. It is necessary to consider and discuss side effects, as well as weigh the risks and benefits of continued treatment. It is important to discuss treatment response and coordinate efforts. The doctor should engage in an ongoing dialogue with the patient regarding the effects of the medications and the presence of side effects. It is also crucial for the patient to actively participate in the treatment process rather than feeling like a passive recipient of medication to alleviate symptoms.

Conclusions. Trauma-focused psychotherapy is certainly the main method for treating PTSD, and in cases of recent uncomplicated PTSD, it may be the sole treatment method. However, considering the fact that we are increasingly encountering complex PTSD with psychotic dissociative symptoms, significant disruptions in the affective domain, and anticipating an increase in such cases in the future, we understand that psychotherapy may be ineffective or entirely unattainable in such situations. Currently, pharmacotherapy for post-traumatic stress disorders primarily focuses on SSRI/H antidepressants, adrenergic blockers, and short courses of benzodiazepines. Previous attempts at antipsychotic pharmacotherapy for post-traumatic stress disorders were mainly focused on the “dones” and “pines” groups, whose side effects (sedation, cardiometabolic effects, dyskinesia) hindered successful treatment. The new generation antipsychotic, “doublepipe-rip” aripiprazole, demonstrates effectiveness in influencing all clusters of PTSD: intrusive, avoidance, hyperarousal, and additionally shows efficacy in treating complex PTSD and comorbid disorders with PTSD, supported by numerous studies and practical experience. It makes sense to take a closer look at the role of antipsychotic medications in the treatment of PTSD, considering the specific characteristics of aripiprazole and possibly other newer antipsychotics, and consider them as effective agents for augmentation, and sometimes even monotherapy, in the treatment of PTSD and complex PTSD.

Relevance.

At the end of the last century, the concept of transitioning from the familiar and stable world of SPOD (Steady; Predictable; Ordinary; Definite) to a new, uncertain and unstable world of VUCA (Volatility; Uncertainty; Complexity; Ambiguity) emerged in various spheres of social life. The 21st century has presented humanity with numerous challenges. It began with a period of violence and fear, where different segments of the population worldwide witnessed socio-political and armed

conflicts, civil wars, territorial disputes, and criminal activities. Over the past decade, there have been numerous unpredictable and often catastrophic events, leading to an increasing discussion about a new shift in the concept of the world towards an even more rapid, complex, and unpredictable world of BANI (Brittle; Anxious; Nonlinear; Incomprehensible). Our country has experienced the incomprehensibility and brittleness of the modern world fully, starting from the beginning of the Anti-Terrorist Operation (ATO) in eastern Ukraine, followed by the global experience of the COVID-19 pandemic with all its devastating consequences, and finally facing the treacherous attack of a neighboring state that had previously positioned itself as a “fraternal” one. It is clear that all of this has significantly impacted overall anxiety, fear of the future, and confidence in one's own abilities among the population of the country as a whole. This has put large segments of the population at increased risk of developing post-traumatic stress disorder associated with being in a war zone, affecting both military personnel, war veterans, internally displaced persons, and those who have experienced violence and torture.

The diagnosis of PTSD has appeared in clinical manuals relatively recently. In the United States, it was included in the DSM-III in 1980, and in the International Classification of Diseases in 1995. However, PTSD cannot be considered a new condition. It has existed as long as humans have existed, as long as wars have been fought, killings have occurred, and natural disasters have taken place. These events have caused stress disorders in individuals. In the medical history, several terms have been used to describe PTSD, such as “trench syndrome”, “soldier's heart”, “shell shock”, “Vietnam syndrome”, and “Afghan syndrome”. The term “post-traumatic stress disorder” emerged in the 1960s and 1970s in the United States. The attention surrounding this issue was triggered by the consequences of the wars in Korea and Vietnam. The large number of individuals experiencing common symptoms and sharing a common predisposition led to their classification under a single nosology [1].

Obtaining effective treatment is crucial for reducing the symptoms of the disorder and improving functioning. Currently, treatment options for PTSD include both psychological and pharmacological interventions. The choice of treatment depends on factors such as the patient's personal preference for a particular form of treatment, their motivation and adherence to therapy, clinical response to previous interventions, severity of symptoms, and the presence of comorbid somatic or mental disorders. It should be noted that PTSD has a high comorbidity with other mental disorders. It often co-occurs with depressive and anxiety disorders, as well as substance/alcohol use disorders, which can significantly complicate diagnosis and treatment interventions. According to a study in 2007 of 103,788 US veterans who served in Iraq and Afghanistan, among military personnel with PTSD, only 17% had this diagnosis without accompanying somatic or mental health issues. Another study found a more complex course of the illness (in terms of symptom severity) and less treatment effectiveness among individuals with comorbid PTSD and other disorders. Among other factors that may influence the choice of treatment method, it is worth mentioning the skills and experience of the doctor and the availability of well-trained clinical (medical) psychologists. Of course, the use of a particular psychotherapeutic method requires appropriate training of professionals, and the lack of such professionals (e.g., in small towns) significantly limits this choice.

In recent years, a number of clinical practice guidelines dedicated to the management of PTSD have been published in various parts of the world, including Europe, Australia, and North America. These guidelines are based on comprehensive analysis of scientific evidence regarding the diagnosis and effectiveness of relevant treatment methods. They share many commonalities but also have some differences in approaches to managing the disorder. According to D. Forbes et al. (2015), important shared recommendations include supporting the use of trauma-focused psychological treatment methods as first-line therapy and pharmacotherapy in specific clinical situations [2, 3].

The aim of our work was to study the effectiveness of the atypical antipsychotic aripiprazole in the comprehensive treatment of PTSD and its impact mechanisms on different clusters of PTSD, as well as its comorbid disorders.

Materials and Methods:

A brief literature review was conducted on the effectiveness of different methods of therapy for PTSD, including chronic complex PTSD and PTSD with comorbid mental disorders and addictions. Our own clinical studies are being carried out on patients with PTSD undergoing inpatient and outpatient treatment at the Regional Clinical Mental Health Center of the Ivano-Frankivsk Regional Council and the First Volunteer Surgical Hospital of the “BRASS” Clinic. The group consisted primarily of men aged 21 to 45 with PTSD related to military actions and verified according to contemporary diagnostic criteria. Clinical-psychopathological examination and psychodiagnostic methods were used, including the Clinical-administered PTSD Scale (CAPS) for clinical diagnosis of PTSD, the Impact of Event Scale Revised (IES-R) for assessing the impact of traumatic events, the Hospital Anxiety and Depression Scale (HADS) for anxiety and depression assessment, the Dissociative Experiences Scale (DES) for measuring dissociative experiences, the Symptom Checklist-90 (SCL-90) for self-assessment of mental status, and the Narcissistic Inventory (F.-W. Deneke & B. Hilgenstock) for self-esteem regulation assessment. The results of the comprehensive treatment program were also evaluated using the follow-up method. It should be noted that this article is a preliminary report, and the statistically analyzed results of the study will be reported in our future publications. This publication will provide a series of brief clinical examples.

Results:

Undoubtedly, according to the main standards of psychiatric care, psychotherapy, specifically trauma-focused and cognitive-behavioral therapy, is the priority method in treating PTSD. However, we are increasingly encountering complicated variants of PTSD, complex PTSD with a significant tendency to chronification. In the clinical presentation of patients with PTSD, we often observe dissociative symptoms at a psychotic level, depressive states with psychotic symptoms, and other manifestations that greatly complicate, and sometimes make it impossible to engage the patient in psychotherapy. That is why the combined use of psychotherapy and psychopharmacotherapy is recognized by the majority of clinical guidelines for PTSD treatment (WHO, NICE, APA, ISTSS, Va/DoD), with some of them (APA, ISTSS, Va/DoD) considering the effectiveness of psychotherapy and medication therapy in treating PTSD as equivalent [5, 6, 7]. A systematic review and meta-analysis were published in the journal Psychiatry Research. Researchers demonstrated that the prioritization of psychotherapy over medication therapy in treating PTSD was based on comparing the treatment effects of methodologically incomparable studies of psychotherapy and pharmacological interventions. Therefore, a meta-analysis consisting exclusively of randomized trials was conducted by the researchers. This analysis yielded ambiguous results regarding the differences in the effects of psychotherapy and pharmacotherapy. Therefore, the study authors believe that in the absence of clear evidence of the superiority of one method over the other, physicians should make joint decisions with patients regarding which method to use [8].

According to the majority of clinicians, the combination of psychotherapy and psychopharmacotherapy is considered the most effective [9, 10]. The most commonly used groups of psychotropic medications in the treatment of PTSD, as stated in most clinical guidelines, are selective serotonin/norepinephrine reuptake inhibitors (SSRIs/SNRIs) and adrenergic blockers, while less attention has been given to antipsychotic agents mainly due to their significant side effects. In the domestic literature, second-generation antipsychotics such as risperidone, olanzapine, and quetiapine were considered as examples of antipsychotic agents for PTSD [11, 12, 13], with their use being suggested for psychotic variants of PTSD when SSRI/SNRI treatment is ineffective.

As we are currently facing a significant influx of patients with post-traumatic stress disorders, both as a result of combat stress and other major stressors, we need to review the approaches to treating such patients and choose the most effective and accessible ones for the majority of

specialists. Undoubtedly, the effectiveness of trauma-focused psychotherapy methods is invaluable, and most of our professionals have received or are undergoing training in their implementation. However, we should not overlook the extensive arsenal of available and effective psychotropic medications that can effectively prepare patients for psychotherapeutic treatment or serve as an augmentation to psychotherapy.

In this regard, it is worth considering the atypical antipsychotic of the third generation, aripiprazole.

Aripiprazole is a medication belonging to the class of atypical antipsychotics, and it is available on our pharmaceutical market, in particular under the brand name Aripiprazole Acino.

Aripiprazole exhibits typical antipsychotic antagonism towards dopamine D2 receptors in the mesolimbic pathway, while possessing a unique property of partial agonism towards the same receptors in the mesocortical pathway. Similar to other “atypical antipsychotics”, aripiprazole shows strong antagonism towards serotonin 5-HT2A receptors and, similar to ziprasidone, agonism towards 5-HT1A receptors. Simply put, aripiprazole is a partial agonist (mixed agonist-antagonist) of 5-HT1 and D2 receptors, meaning it stimulates the receptor in the absence of neurotransmitter and blocks it in excess. The medication has the lowest affinity among all atypical antipsychotics for adrenergic (α1), histaminic (H1), and muscarinic (m1) receptors. This pharmacodynamic profile explains the high therapeutic effectiveness of aripiprazole and, at the same time, the low frequency and severity of side effects observed with most antipsychotics, including weight gain, movement disorders, prolactin elevation, cardiac issues, and others. In fact, the presence of side effects led patients with PTSD to refuse antipsychotic treatment, as indicated by data from many studies [12, 13, 14]. The absence or minimal expression of side effects when taking aripiprazole allows it to be considered as a promising alternative to the commonly used “dones” (risperidone, lurasidone, ziprasidone) and “pines” (quetiapine, olanzapine, clozapine) in our practice. Considering the fact that aripiprazole is effective in treating various manifestations of PTSD and comorbid psychopathological disorders, it is worth exploring this medication in more detail, referring to numerous publications in professional journals and relying on our own clinical observations.

What is particularly important is that aripiprazole has a definite impact on all three clusters of PTSD symptoms: re-experiencing traumatic events (intrusive, dissociative symptoms), avoidance (“numbing”, social isolation), and hyperarousal (anxiety, heightened vigilance). Furthermore, if we consider additional criteria of complex PTSD, such as depressive symptoms and affect dysregulation, the relevance of aripiprazole in the treatment of PTSD becomes even greater.

Let us examine sequentially how aripiprazole affects different clusters of PTSD symptoms, complex PTSD, and the most common comorbid psychopathological conditions associated with PTSD. To illuminate this issue, we have utilized published data from contemporary cohort studies as well as the results of our own clinical experience with combat veteran patients.

People with PTSD often suffer from intrusions of traumatic memories, which can range from relatively mild (with a sense of absence or temporary feeling that the frightening event is happening here and now) to severe (with complete loss of awareness of current reality and massive dissociative production). This also includes recurring horrifying dreams or nightmares. Several studies have shown that the mechanism underlying post-traumatic stress disorder primarily involves a disruption in fear extinction processes and functional imbalance in the “fear” regions associated with the amygdala. Previous evidence suggested that central dopamine plays a key role in regulating fear memory processes, but it remained unclear whether modulating dopamine modulators would be beneficial in correcting abnormalities in fear extinction processes. Animal studies demonstrated that a subchronic 14-day treatment regimen of aripiprazole at a dose of 5.0 mg/kg alleviates fear memory dysfunction, restores the ability to extinguish conditioned fear reflexes induced by trauma, and normalizes the reduced amygdala dopamine release caused by trauma. This study demonstrated the therapeutic potential of subchronic treatment with

aripiprazole in patients suffering from intrusive fear [15]. Dissociative disorders in chronic complex PTSD often take the form of auditory hallucinations, frequently of a hostile nature, which can lead to complications such as substance abuse, impulsive aggression, and, notably, suicidal tendencies. Trauma-focused therapy alone is often ineffective in such conditions, and at times, hallucinations hinder the effective delivery of psychotherapy. Several studies have demonstrated the efficacy of adjunctive antipsychotic treatment with aripiprazole in patients with auditory hallucinations within the framework of chronic PTSD [16].

A soldier who is undergoing rehabilitation in one of the hospitals in the region after being released from captivity experiences panic attacks at night following the onset of a new wave of shelling. After falling asleep, he has military-themed nightmares with flashbacks to his combat experience. He wakes up in a state of panic and can no longer fall back asleep. He has an urge to run out of the hospital onto the streets, dig a trench, and sleep there, stating that he knows how to protect himself from incoming attacks. Each “falling asleep” ends with a similar episode, so he has been unable to sleep at night for several consecutive days. He walks around the department, smokes, and then falls asleep again in the morning. He says that the prescribed trazodone has a more stimulating effect on him rather than a sedative one, and lorazepam is too weak to alleviate the intensity of his anxiety attacks.

In the conversation with him, it becomes clear that all three of his injuries - two in the legs and one in the head - occurred at night when he didn't sense any danger and was confident that there were no enemies nearby. He says that among military personnel worldwide, there is a belief that God saves a person from death twice, and then the individual is responsible for themselves - no one holds a “protective shield” over them anymore. And furthermore, it's not true that one cannot experience two deaths - he has already undergone clinical death once when a structure he was sleeping in was blown up. His comrades simply pulled him out from under the debris and revived him. So he considers himself a special lucky person, as even his third rescue came from his comrades. But one cannot abuse their luck... Moreover, he has already used up all his fortunate chances. Therefore, from now on, he is facing death alone and cannot just sleep and “wait for it to come”...

After spending several weeks in safety, he begins to complain that his “psyche exists on its own, independently of him”. He constantly experiences déjà vu, and while during his time in captivity, it somehow helped him endure all the torture and “other misfortunes”, now this “intrusive state” is experienced by him as quite painful and tense, giving him a feeling that he is slowly “going insane”. He doesn't have much faith in medication as a treatment because it seems “naïve” to believe that drugs can “cure him of the war experience”.

In the conversation, we managed to calm him down with the reasoning that experiencing similar things in captivity, which “he has already been through before”, was a survival strategy. If it happened once and passed, then it can happen again and again, and therefore survival is possible. He agrees with this, as during captivity, he was convinced that he would be executed according to the laws of the Donetsk People's Republic (DPR).

He was further reassured by the second comment about how he had been in captivity for too long, so his psyche had already become accustomed to protecting him from danger and couldn't simply switch off, continuing to protect him “out of inertia” even when he was safe. His psyche just needs time to understand that the situation has changed and that he no longer requires such intense protection. He complements my comment with his metaphor, saying: “It's like my psyche has grown a protective layer of fat, and now this fat is preventing me from connecting with myself... it takes time for this protective fat to dissolve”.

I suggest to him to facilitate this process of “weaning the psyche off the sense of mortal danger” through medication. He agrees. Taking 15 mg of aripiprazole (starting with 5 mg) over the course of a week improved his sleep, alleviated panic states and the experience of déjà vu, and made him

more open to further psychotherapy.

PTSD is also closely associated with an increased risk of suicide. Sarin et al. [17] used data from the National Comorbidity Survey (NCS) to examine the relationship between anxiety disorders, suicidal thoughts, and suicide attempts. Only PTSD, unlike other anxiety disorders, could significantly predict suicidal thoughts and suicide attempts. Overall, among U.S. Army veterans, PTSD is strongly linked to mortality from external causes, including homicides, suicides, drug overdoses, and accidental injuries. Therefore, professionals treating PTSD should regularly assess the patient's suicide proneness and take suicidal thoughts into account to implement preventive measures in a timely manner. Often, in such situations, psychotherapy alone proves ineffective, and there is a need for pharmacological treatment. Considering the prolonged latent period for the antidepressant effects of SSRIs/SNRIs and the risk of exacerbating suicidal behavior during their use, it is more appropriate for patients with PTSD and high suicide risk to use second-generation antipsychotics, which have a significant anxiolytic and antidepressant component in their mechanism of action. This is precisely the characteristic of aripiprazole. Additionally, a significant reduction in the risk of suicidal events in PTSD through the administration of antipsychotics, including aripiprazole, was demonstrated in a study conducted in 2021 [18].

The symptoms of the avoidance cluster, in addition to significantly complicating the patient's life to the point of practical disability, often pose a significant obstacle to any psychotherapeutic interventions. In such cases, pharmacotherapy is appropriate, in which aripiprazole holds a worthy place alongside SSRIs/SNRIs and adrenergic blockers. In the structure of chronic PTSD, the avoidance cluster is often accompanied by symptoms of obsessive-compulsive disorder. There is clinical evidence that augmentation of sertraline with aripiprazole is much more effective than sertraline monotherapy in the treatment of post-traumatic OCD [19].

The hyperarousal cluster is characterized by symptoms of anxiety and hyper-vigilance. In complex PTSD cases, the symptomatology is complemented by severe and pervasive affect dysregulation, with anger, loss of impulse control, and persistent self-beliefs of being humiliated, defeated, or worthless, accompanied by deep and pervasive feelings of shame and guilt. Such symptomatology brings the clinical picture of chronic PTSD closer to borderline personality disorder. Some neurophysiological features in borderline personality disorder significantly overlap with those in PTSD. In the top-down control system, the amygdala is connected to several cortical structures that are crucial for the cognitive processing of stimuli, especially social stimuli. Ventral parts of the prefrontal cortex, as well as the rostral areas of the anterior cingulate cortex, control and modulate amygdala activity, leading to its “extinction”. Furthermore, cognitive regulatory strategies are complicated by the dorsal sections of the medial prefrontal cortex, which overall influence the activity of the limbic system. Numerous studies [20, 22] indicate that modulating amygdala activity originating from the anterior cingulate cortex is also related to the appraisal/detection of danger. In individuals with borderline personality disorder, this part of the cortex functions less effectively. Avoidance of danger is considered one of the fundamental temperament factors in Cloninger's personality model and is believed to have a genetic determinant [23]. Other studies have also shown that patients with borderline personality disorder exhibit heightened amygdala readiness for activation in response to any stimulus [22].

Anger and irritability are common symptoms of PTSD. Intense anger often becomes a problem for patients with PTSD, especially those who have experienced trauma during combat. Vietnam veterans with PTSD have higher levels of anger compared to veterans without PTSD, and the level of anger among Afghanistan and Iraq veterans is also higher than average. Veterans with PTSD take less time to become angry compared to those without PTSD. Additionally, they experience higher blood pressure and increased heart rate during episodes of anger. Veterans with PTSD also exhibit greater anxiety during laboratory tasks when asked to recall something that provokes anger. Anger outbursts in patients can present a challenge for professionals due to the difficulty of establishing rapport and initiating treatment. Research on Australian veterans found that anger outbursts hinder symptom identification. Anger can interfere with important treatment stages such

as activation and processing of traumatic memories. A high level of anger at the beginning of treatment hampers methods such as prolonged exposure therapy. Therefore, reducing anger should be a primary goal in the initial stages of treatment. Patients should learn anger management skills (such as using time to cool down, self-control of anger, identifying anger triggers, relaxation/breathing techniques, anger discrimination, self-talk, and acceptance of learning) to decrease their anger or modify its expression. Alongside psychotherapeutic techniques for anger reduction, medication therapy is actively utilized and, in some cases, becomes the only viable option in the early stages of treatment.

The results of studies that have demonstrated the effectiveness of aripiprazole in reducing anger, impulsivity, depression, and anxiety in patients with borderline personality disorder [23, 24, 25, 26] can be extrapolated to the treatment of such symptoms in patients with PTSD.

Since practically all patients in our study had PTSD, which was somehow related to war (combatants, forced migrants), the aspect of traumatic loss was present in almost all participants. This includes the loss of comrades, friends, and family members, as well as property, jobs, and the familiar way of life. Traumatic loss can lead to anhedonia and depression, as grief over what has been lost can make everyday life and activities seem meaningless. In veterans with PTSD, the loss of comrades and friends in combat often triggers post-war mourning and social phobia. Piver and Field [27] found that the average grief score among those who lost comrades 30 years ago was higher than among those who lost a spouse in the last six months. The authors claim that without clinical intervention, grief over the deceased can trouble a person for a very long time. Treating the symptoms of unresolved grief and mourning can be just as important as treating the symptoms of the core clusters of PTSD. Unfortunately, the treatment of complications resulting from significant loss is often neglected. PTSD treatment should be adapted to address the complications arising from significant loss, including education on grief, restructuring cognitive distortions about the events, restoring positive memories of the deceased, and providing reassurance and support for the grieving process).

The soldier was involved in military operations since 2014 and then in the most intense combat zones from February 2022. After some time, due to deteriorating eyesight, he was relieved of his demanding combat duties and assigned to be responsible for military training and fostering the fighting spirit of new recruits. He had to teach young soldiers to “rush into battle like an exciting adventure” on one hand, while not being afraid of real combat on the other. He instilled a sense of camaraderie among them so that they could function as one team on the battlefield.

He takes pride in having raised not one good soldier and becoming involved in the fight of the Ukrainian people against the “otherworldly darkness” brought by the Russian army.

He recalls witnessing firsthand “apocalyptic scenes” as they are described in the Bible. He mentions that he will never forget how nursing mothers in the city, due to constant shelling, lost their breast milk. They emerged from basements with starving infants, pleading with the soldiers to provide them with cow's milk before their children died. “It's exactly as it's written in the Bible: “War and death will take away the mother's milk, so that life shall no longer endure...”

He says that this darkness of cruelty and indifference from the enemy has “infiltrated from within”, and in order to protect himself, he has “encapsulated himself” from it. Now, most of the time, he feels nothing at all, perhaps only the pain of this “emotional emptiness”. But sometimes, he sees the faces of his trained recruits who died while carrying out their missions. Then he feels that it is his fault, that he didn't prepare them enough, didn't teach them well enough to fight. He says that along with them, their parents and grandparents perished, their unborn children and grandchildren, whole families ceased to exist... And he feels that he “also had a hand in this loss”, the loss of entire generations of brave warriors.

He refused to communicate with his comrades and his own family, “so that the darkness wouldn't

spread to them”...

He refused to communicate with psychologists and psychotherapists until our meeting. He also refused to take most medications, except those that “helped him sleep”. However, antidepressant therapy with mirtazapine did not yield results for four weeks. After two conversations, he agreed to additional prescriptions. He personally wrote down the dosage schedule in his diary and started monitoring the regularity of intake. After two weeks of treatment with a combination of escitalopram at a dose of 20 mg and aripiprazole at a dose of 7.5 mg, his depressive state began to recede, and he agreed to meet with his family.

Regarding depressive symptoms in PTSD, several authors consider major depressive disorder as comorbid with PTSD, while others see it as one of the manifestations of chronic PTSD. PTSD often co-occurs with depression. For example, Vietnam veterans with PTSD are more likely to suffer from depression compared to veterans without PTSD. Retrospective studies have shown that most patients with both disorders reported that PTSD appeared first. A two-year study investigating the temporal relationship between PTSD and depression symptoms in Persian Gulf War veterans revealed a certain interdependence. Initial PTSD symptoms predicted worsening of depression symptoms, and initial depression symptoms predicted the development of PTSD. Breslau [28] identified an increased risk of severe depression in individuals with PTSD in her study. Several publications demonstrate the results of studies on the efficacy of aripiprazole in treating depressive disorders within the framework of bipolar affective disorder and major depressive disorder, as well as within the framework of PTSD [29, 30]. One of the earliest such studies conducted at the University of São Paulo in 2007 showed significant improvement in patients with PTSD and depression based on the overall PTSD scale, Beck's anxiety and depression inventories, and the social functioning scale after 16 weeks of flexible-dose monotherapy with aripiprazole (mean dosage of 9.6 mg/day) [31].

Окрім опублікованих результатів досліджень щодо ефективності арипіпразолу в лікуванні ПТСР та коморбідних з ним станів, існує великий клінічний досвід зокрема наших фахівців, які працюють з наслідками бойового та небойового екстремального стресу. In addition to published research results on the effectiveness of aripiprazole in the treatment of PTSD and its comorbid conditions, there is extensive clinical experience, particularly among our specialists, who work with the consequences of combat and non-combat extreme stress.

In addition to the aforementioned effects, several reports indicate the high efficacy of low doses of aripiprazole in the initial treatment of comorbid conditions with PTSD, particularly in addressing substance abuse issues, primarily alcohol, by alleviating excessive anxiety and sleep disturbances, thus facilitating substance discontinuation. The co-occurrence of substance abuse and PTSD symptoms is well-known among both civilian individuals and military veterans. R. Kulka et al. [32] note that 73% of Vietnam veterans have a history of alcohol abuse or alcohol dependency problems. It is highly likely that alcohol and drug dependency hinder treatment, perpetuating PTSD symptoms, impeding successful psychotherapy, and negatively impacting the patient's quality of life. Some studies suggest that treatment for veterans suffering from PTSD and substance abuse will be more successful if they address their substance dependency alongside PTSD symptoms. Patients who undergo additional PTSD treatment within the first three months after addressing substance dependency have a greater chance of recovery. The association between these diagnoses has led to the development of integrated treatment approaches for PTSD and substance dependency. There is also evidence that PTSD is often associated with smoking, and the onset of PTSD symptoms is frequently accompanied by the acquisition of this harmful habit. Clinical studies conducted by McFall et al. [33] have shown that smoking cessation assistance is more effective when integrated into PTSD treatment.

Therefore, summarizing all of the above, aripiprazole can be considered one of the most promising antipsychotic agents for the treatment of PTSD in a comprehensive approach, alongside psychotherapy, and in some cases as monotherapy, considering its broad spectrum of action and

minimal side effects.

It should also be noted that the key to successful treatment lies in establishing trusting partnerships with patients when prescribing medication. Patient psychoeducation regarding side effects, necessary dosages, treatment duration, and adherence to the regimen can significantly improve outcomes. Side effects should be discussed and weighed against the risks and benefits of continued treatment.

It is important to discuss treatment response and coordinate efforts. This is important for the doctor to maintain an ongoing dialogue with the patient regarding the effects of the medication and the presence of any side effects. It is also important for the patient to actively participate in the treatment process rather than feeling like a passive recipient of medication aimed at alleviating symptoms.

A 28-year-old soldier was admitted to the hospital for inpatient treatment after suffering from a blast injury due to an artillery shell hitting his cannon. He miraculously survived but remained unconscious for some time after the explosion. When he regained consciousness, he experienced ringing in his ears, was agitated, and joked about being like an “indestructible terminator”. After two days, he started feeling nauseous, refused to eat, began stuttering, and sometimes would “disconnect” – he was unable to understand what others were saying to him or provide coherent responses to questions. From his medical history, it is known that he was an activist in civic movements from a young age. During his mandatory military service, he participated in combat actions in the ATO zone. In civilian life, he worked at a construction site in Germany. He returned to Ukraine at the start of the war to join the ranks of the Armed Forces and fulfill his patriotic duty.

With a gleam in his eyes, he recounts that in the first days of his service as an artilleryman, he found himself under intense shelling. He felt a primal survival instinct kick in, as if he could “sense” the danger deep within him and skillfully avoid it. He says he was able to escape the artillery barrage with his comrades because he could feel where the shells would land and where they wouldn't. He felt as though his brain had transformed into a powerful cyborg computer, functioning flawlessly and swiftly, reacting precisely to the changes on the battlefield. From that moment on, he fought with great effectiveness, fueled by adrenaline, fearing neither shelling nor death, for to die a hero's death for his Motherland was a worthy end for a true man! (As he tells this, he doesn't stutter or hesitate.)

He takes pride in his ability to fight. He believes that the enemy's precise hit on his cannon was a result of his and his partner's accurate shooting, which is why the enemy tried to eliminate them. And once again, it's just a miracle that at that moment, he and his partner decided to take a rest in the trench, which is why both of them survived. However, his partner left the unit after these events and is considered a deserter.

Our first session begins with him expressing frustration about his poor sleep, constant headaches, unrelenting anxiety that is always there, he says that his body is in the terrible condition and that no one seems to address these problems. I spontaneously intervene, pointing out that something is clearly troubling him, and he cannot understand “what it is” or find a solution. Surprisingly, he responds that he can't sleep because he has horrifying nightmares. My assumption that these nightmares might be related to his combat experiences is firmly rejected by him. So, I ask him to share any of his terrifying dreams. He agrees and tells me: “He and his comrades go to a nightclub to relax. They have a great time, eating, drinking beer, playing billiards. Then a beautiful woman appears in the club, catching his eye. He starts gazing at her, and she winks at him in response. He invites her to his table with a glance, she agrees, approaches, and immediately sits on his lap, embracing him. Filled with a sense of “easy victory”, he leans closer to her cleavage and suddenly sees that her skin is torn apart in pieces and hanging, like the tattered bandages of an Egyptian mummy. Then he looks at her hands, neck, and sees the same thing. Overwhelmed by horror, he starts screaming to his comrades to take her away from him and desperately pushes her away. A

fear takes hold in his soul that he has contracted an incurable disease from her... In a panic, he wakes up...” (he stutters more now). After a few introductory sentences, I dare to offer him an interpretation that this dream contains the thought that there might not be an “easy victory” and that his involvement in the war might end with some form of mutilation... Surprisingly, he agrees with my interpretation, saying that he had imagined his death as a hero, with his body torn to pieces, and he would die instantly. He is not afraid of that at all! However, after the recent incident, he realized that things could turn out differently... He says he doesn't want to live out his life as a cripple, helpless, with someone - whether it be his mother, future wife, or some nurse - taking care of him.

We agree on the next meeting, and he emotionally thanks me for the conversation... But the next meeting starts again with dissatisfaction because his sleep is still not going well! Now he falls asleep easily but wakes up in the middle of the night and can't fall back asleep. He keeps having some meaningless nonsense dream that he can't get rid of... I ask him to try to tell me about this meaningless nonsense if he can. He vividly describes the following images: “Whether it's a train station, a wide entrance, or a long corridor of some government institution, various people are wandering around: gypsies, homeless people, large families, elderly people, upset women, so you can't understand where they are going or if they are going anywhere at all... I'm sitting on the floor, aimlessly observing all of this...”

Considering that the disruption of his sleep caused noticeable irritability, anxiety, and emotional instability, which hindered productive psychotherapeutic work, the patient was offered a combination of stress-reducing psychological exercises and pharmacological treatment, specifically aripiprazole at a nightly dose of 10 mg. The subsequent psychotherapy sessions were more fruitful, with a significant reduction in anxiety (and consequently, interruptions) and improved overall well-being.

There are several common fears and misconceptions that patients have, which act as barriers to effective pharmacological treatment of PTSD. They should be addressed through ongoing dialogue between the patient and the physician:

- Fear of possible side effects in the sexual sphere.
- Concern that medication implies weakness and dependence.
- Fear of becoming dependent on the medication.
- Desire to take medication only occasionally when symptoms become severe.
- Inaccurate understanding of how to take the medication properly.
- Overdosing, taking multiple pills, or forgetting whether the medication was already taken and repeating the dose.
- Self-medicating with alcohol or drugs concurrently with the prescribed medication.

Family and close relatives play a crucial role in supporting patients with PTSD. Depending on the nature of the traumatic event and its consequences, the family itself may require assistance from professionals. In all cases, the impact of trauma and the presence of PTSD in the patient should be taken into account for all other family members. With the patient's consent, family members should be provided with comprehensive information about the condition, symptoms, their course, and treatment in an accessible format. In addition to the information obtained from professionals, family members and close relatives should be informed about support groups and mutual aid organizations available in their area and encouraged to participate in them. If the entire family is affected by the traumatic circumstances, PTSD may develop in multiple family members. In such cases, their treatment should be well-coordinated.

Conclusions

Undoubtedly, trauma-focused psychotherapy is the main method for treating PTSD and can be the sole treatment method in cases of recent uncomplicated PTSD. However, considering the fact that

we are increasingly encountering complex PTSD with psychotic dissociative symptoms, significant disturbances in the affective sphere, and anticipating an unfortunate increase in such cases in the future, we understand that psychotherapy may be ineffective or inaccessible in such situations.

Currently, pharmacotherapy for PTSD primarily focuses on SSRIs/SNRIs antidepressants, adrenergic blockers, and short courses of benzodiazepines. Previous attempts at antipsychotic pharmacotherapy for PTSD primarily focused on the “dones” and “pines” groups, but their side effects (sedation, cardio-metabolic, dyskinetic) hindered successful treatment.

Aripiprazole, a novel antipsychotic, demonstrates effectiveness in influencing all clusters of PTSD: intrusive, avoidance, hyperarousal, and also proves its effectiveness in treating complex PTSD and comorbid disorders with PTSD, supported by numerous studies and practical experience.

It is worth carefully reconsidering the role of antipsychotic pharmacotherapy in the treatment of PTSD, taking into account the characteristics of aripiprazole and possibly other newer antipsychotics, and considering them as effective means for augmentation and sometimes monotherapy in the treatment of PTSD and complex PTSD.

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