KNOWLEDGE BASED ON ANTIDEPRESSIVE DRUGS USE

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- Antidepressants are drugs used to treat major depressive disorders, anxiety disorders, chronic pain and help manage some addictions. [1]The use of antidepressants is increasing over the years. Antidepressants usually are used on doctor's recommendation to relieve the symptoms of various conditions emotional and mental to maintain health and well-being or to promote and improving emotional and mental health. Given the fact that use and misuse of antidepressants is not studied as well, aroused interest to accumulate data on their use and misuse, as important preparations for the best possible functioning of mental health. The purpose of this study is to analyze the use of antidepressants with or without a recommendation to the doctor and awareness about the use of antidepressants among the respondents in Tetovo and surroundings. A total of 223 patients of both sexes aged 25-65 years were surveyed. 75% of respondents have used antidepressant on doctor's recommendation, where most of the users of antidepressants were female, while 25% used antidepressants without the recommendation of doctor according to which awareness should be raised that their use is based on the recommendations of a doctor. Most have used benzodiazepines without a doctor's recommendation though benzodiazepines are most commonly prescribed to treat disorders of anxiety, insomnia, seizures and as a sedative before surgery. 63% are aware of the side effects while 37% do not. A small number of plant products have been used in these condtions due to the difficulty of finding and scant knowledge of them. To avoid misuse of antidepressants we recommend not to use without the specialist's recommendation and adhere to his instructions should also be raised awareness of the side effects of antidepressants and strictly prohibit their administration through the pharmacy without a perscription.

- Keywords: Andidepressants, Herbal products, Benzodiazepines, Mental conditions.

I.INTRODUCTION

Antidepressants are medications used to treat major depressive disorders, anxiety disorders, chronic pain, and to help manage some addictions. Common side effects of antidepressant medications include dry mouth, weight gain, dizziness, headaches, sexual dysfunction, [2] and emotional disorders. [3]

Pharmacology of antidepressants

The earliest and perhaps most widely accepted theory of antidepressant action is the monoamine hypothesis (which can be traced back to the 1950s), which states that depression is due to an imbalance (most often a deficiency) of monoamine neurotransmitters (respectively serotonin, norepinephrine and dopamine). [4] .All currently marketed antidepressants have the monoamine hypothesis as their theoretical basis, with the possible exception of agomelatine which acts in a melatonergic-serotonergic dual pathway. [5]

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors currently available include fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram. A large number of literatures supports the superiority of SSRIs over placebo in the treatment of major depressive disorder. In more than 10 systematic reviews and meta-analyzes, the effectiveness of SSRIs has been compared to that of other antidepressant drugs, mainly TCA. SSRIs have demonstrated comparable efficacy to TCAs [6], even when considering anxiety symptoms [7]. Although some analyzes suggest small advantages of SNRIs over SSRIs in relief rates [8], a data superiority finds no significant evidence of the superiority of any other class or agent over SSRIs [9].

Selective serotonin reuptake inhibitors (SSRIs) are believed to increase the extracellular level of neurotransmitter serotonin by limiting its reabsorption in the presynaptic cell, increasing the level of serotonin in the synaptic cleft available to bind to the postinaptic receptor. They have varying degrees of selectivity for other monoamine transporters, with pure SSRIs having poor affinity only for norepinephrine and dopamine transporters.

SSRIs are the most widely prescribed antidepressants in many countries. [10] The efficacy of SSRIs in mild or moderate cases of depression has been discussed. [11]

Norepinephrine reuptake inhibitors in serotonin

Currently available serotonin norepinephrine reuptake inhibitors are venlafaxine, desvenlafaxine (the major metabolite of venlafaxine), and duloxetine. An immediate release form of venlafaxine is available, but most clinics prefer the extended release formulation because it is approved for once daily dosing and may be associated less frequently with reported withdrawal symptoms.

Each of these drugs is effective (i.e., superior to placebo in controlled studies and meta-analyzes) [12] and venlafaxine (75–150 mg / day) and duloxetine (60 mg / day) have shown comparable efficacy in a pair of proofs [13]. For venlafaxine and possibly desvenlafaxine, clinically significant inhibition of norepinephrine intake may not be achieved for the average patient at lower therapeutic doses, although desvenlafaxine has a much greater bio-availability, resulting in a lower effective dose.

Serotonin-norepinephrine reuptake inhibitors (SNRIs) are potent inhibitors of serotonin and norepinephrine reuptake. These neurotransmitters are known to play an important role in mood. SNRIs can be contrasted with the most widely used selective serotonin reuptake inhibitors (SSRIs), which act primarily on serotonin alone.

The human serotonin transporter (SERT) and norepinephrine transporter (NET) are membrane proteins that are responsible for the recovery of serotonin and norepinephrine. Balanced dual monoamine reuptake inhibition may offer an advantage over other antidepressant medications by treating a wider range of symptoms. [14]

SNRIs are sometimes also used to treat anxiety disorders, obsessive-compulsive disorder (OCD), Attention Deficit Hyperactivity Disorder (ADHD), chronic neuropathic pain and fibromyalgia syndrome (FMS), and to relieve menopausal symptoms.

Monoamine oxidase inhibitors

MAOIs currently used as antidepressants include phenelzine, tranylcypromine, isocarboxazidine, moclobemide, and transdermally administered selegiline formulation. MAOIs are comparable in efficacy to other antidepressants for patients with major depressive disorder and may be appropriate for patients with major depressive disorder who have not responded to safer and easier-to-use treatments [15].

MAOIs have been shown to be particularly effective in treating depressed patients with atypical features, so psychiatrists should consider using these drugs for patients with symptoms such as reactive mood, opposite neurovegetative symptoms, and susceptibility to rejection [16].

Monoamine oxidase inhibitors (MAOIs) are chemicals that inhibit the activity of the monoamine oxidase family of enzymes. They have a long history of use as medications prescribed to treat depression. They are particularly effective in treating atypical depression. [17] They are also used to treat Parkinson's disease and some other disorders.

Because of potentially deadly dietary and drug interactions, monoamine oxidase inhibitors have historically been reserved as the last line of treatment, used only when other classes of antidepressant drugs (e.g. selective serotonin reuptake inhibitors and anticancer drugs) have failed. [18]

MAOIs have been found to be effective in treating panic disorder with agoraphobia, social phobia, atypical depression or anxiety and mixed depression, bulimia, and post-traumatic stress disorder, as well as borderline personality disorder. MAOIs appear to be particularly effective in managing bipolar depression, according to a retrospective analysis. [19] There are reports of MAOI efficacy in obsessive-compulsive disorder (OCD), trichotillomania, dysmorphophobia, and avoidant personality disorder, but these reports are from uncontrolled case reports. [20] .MAOI can also be used in the treatment of Parkinson's disease by targeting MAO-B in particular (thus affecting dopaminergic neurons), as and providing an alternative to migraine prophylaxis. Inhibition of both MAO-A and MAO-B is used in the treatment of clinical depression and anxiety disorders.

Serotonin moderators and stimulants

Serotonin modulators and stimulators (SMS), sometimes more simply referred to as "serotonin modulators", simultaneously modulate one or more serotonin receptors and inhibit serotonin uptake. The term was coined in connection with the mechanism of action of vortioxetine serotonergic antidepressant, which acts as a serotonin reuptake inhibitor (SRI), partial 5-HT1A receptor agonist and 5-HT3 and 5-HT7 receptor antagonist. [21] However, it can also technically be applied to vilazodone, which is also an antidepressant and acts as a partial agonist of SRI and 5-HT1A receptors. [22]

Serotonin antagonists and reuptake inhibitors

Antagonist and serotonin reuptake inhibitors (SARIs) while primarily used as antidepressants, are also anxiolytic and hypnotic. They act by antagonizing serotonin receptors such as 5-HT2A and inhibiting the retrieval of serotonin, norepinephrine and / or dopamine. Furthermore, most also act as α1-adrenergic receptor antagonists. Most of the SARIs currently marketed belong to the class of phenylpiperazine compounds. They include trazodone and nefazodone.

Norepinephrine reuptake inhibitors (NRI or NERI)

Norepinephrine reuptake inhibitors (NRIs or NERIs) are a type of drugs that act as a reuptake inhibitor for the neurotransmitter norepinephrine (noradrenaline) by blocking the action of the norepinephrine transporter (NET). This in turn leads to increased extracellular concentrations of norepinephrine.NRIs are commonly used in the treatment of conditions such as ADHD and narcolepsy due to their psychostimulatory effects and in overweight due to their suppressive effects on appetite. They are often used as antidepressants to treat major depressive disorder, anxiety and panic disorders. Moreover, many abuse drugs such as cocaine and methylphenidate possess NRI activity, although it is important to note that NRIs without combined dopamine inhibitor (DRI) properties are not significantly rewarding and are therefore considered to have a negligible potential for abuse. [23] However, norepinephrine has been implicated as a synergistic action with dopamine when combining actions on two neurotransmitters (e.g., in the case of NDRIs) to produce rewarding effects on psychostimulant abuse drugs. [24]

Norepinephrine-dopamine reuptake inhibitors

The only drug that is used in this class for depression is bupropion. [25]

Tricyclic antidepressants

Tricyclic antidepressants (amitriptyline, norttiptilin, protritiptine, imipramine, desipramine, doxepin, and trimipramine) are effective treatments for major depressive disorder and are comparable in efficacy to other classes of antidepressants, including SSRIs, SNRIs, and MAOs. The efficacy of tricyclic subclasses (e.g., secondary amines or tertiary amines) appears to be comparable. TCAs may be particularly effective in certain populations, such as in hospitalized patients [27]. Conventional knowledge is that this advantage is explained by the superiority of TCAs (versus SSRIs) among the subgroup of patients with more severe melancholy or depression, because such a specific advantage has not been consistently documented in the studies of more seriously ill outpatients [28].

Tetracyclic antidepressants

Tetracyclic antidepressants (TeCAs) are a class of antidepressants that were first introduced in the 1970s. They are named after their chemical structure, which contains four atom rings, and are closely related to tricyclic antidepressants (TCAs), which contain three rings of atoms.

NMDA receptor antagonists (N-methyl-D-aspartate)

NMDA (N-methyl-D-aspartate) receptor antagonists such as ketamine and esketamine are fast-acting antidepressants and function by blocking the NMDA ionotropic glutamate receptor. [29]

Other antidepressant medications

A number of other antidepressant drugs differ structurally or in their pharmacological action from the drugs in the categories described and included here. Although bupropion is classified as an inhibitor of norepinephrine and dopamine withdrawal, the latter effect is relatively weak and its mechanism of action remains unclear [30]. Bupropion differs from most antidepressant medications in the absence of an indication for treating any primary anxiety disorder, and it may be less tolerated than other antidepressant medications among patients with significant anxiety.

Patients usually experience minimal weight gain or even weight loss in bupropion [31], and may therefore be a suitable antidepressant for patients who are overweight. Mirtazapine is thought to function through noradrenergic and serotonergic mechanisms, although this tetracyclic compound is not a reuptake inhibitor [32]. Mirtazapine has comparable efficacy to SSRIs [33]. Trazodoni is the oldest drug from this group that is still widely used. Although trazodone is an effective antidepressant compared to placebo [34], in contemporary practice it is much more likely to be used in lower doses as a sedative-hypnotic than as an antidepressant. Despite the widespread use of trazodone as a hypnotic, little evidence supports its use for this indication. Nefazodone has a

structure analogous to trazodone, but somewhat different pharmacological properties. In comparative trials against SSRIs, nefazodone showed comparable efficacy and overall tolerance [35].

Benzodiazepines

Benzodiazepines are a class of psychoactive drugs whose essential chemical structure is the union of a benzene ring and a diazepine ring. They are in the family of drugs commonly known as minor sedatives. [36] Benzodiazepines are depressants that enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) on the GABAA receptor, resulting in sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant, and relaxant. High doses of many short-acting benzodiazepines can also cause anterograde amnesia and detachment. [37] These properties make benzodiazepines useful in treating anxiety, insomnia, agitation, seizures, muscle spasms, alcohol withdrawal, and as a preparation for medical or dental procedures. [38] Benzodiazepines are categorized as short, intermediate, or long-acting. Short-acting and intermediate-acting benzodiazepines are preferred for the treatment of insomnia; Long-acting benzodiazepines are recommended for the treatment of anxiety. [39]

Benzodiazepines are generally seen as safe and effective for short-term use, which is considered two to four weeks, [40] although cognitive impairments and paradoxical effects such as aggression or behavioral disinhibition occasionally occur. A minority of people may have paradoxical reactions such as aggravated agitation or panic when they stop taking benzodiazepines. [41] Benzodiazepines are also associated with an increased risk of suicide because all depressions change perception and when depression stops patients experience collapse (a decrease) and this creates extreme fear. Long-term use is controversial due to concerns about reduced effectiveness, physical dependence, benzodiazepine withdrawal syndrome, and an increased risk of dementia and cancer. [42] In the long run, stopping benzodiazepines often leads to improved physical and mental health. The elderly are at an increased risk of short-term and long-term side effects, and as a result, all benzodiazepines are listed in the list of unsuitable drugs for older adults. [43] There is controversy regarding the safety of benzodiazepines in pregnancy. While they are not major teratogens, uncertainty remains as to whether they cause palate rupture in a small number of infants and whether neurobehavioral effects occur as a result of prenatal exposure; [44] they are known to cause withdrawal symptoms in the newborn. Benzodiazepines can be taken in overdose and can cause profoundly dangerous unconsciousness. However, they are less toxic than their predecessors, barbiturates, and death rarely results when a benzodiazepine is the only drug taken. When combined with other central nervous system (CNS) depressants such as alcohol and opioids, the potential for toxicity and fatal overdose increases. [45] Benzodiazepines are commonly misused when taken in combination with other addictive substances.

Side effects of antidepressants

Antidepressants can cause various adverse effects, depending on the individual and the drug in question. [46] Almost every drug involved in serotonin regulation has the potential to cause serotonin toxicity (also known as serotonin syndrome) - an excess of serotonin that can cause mania, anxiety, agitation, emotional distress, insomnia, and confusion. as its main symptoms. [47] Although the condition is serious, it is not particularly common, usually occurring only in high doses or during other medications. Assuming proper medical intervention is obtained (within about 24 hours) is rarely fatal. [48] Antidepressants appear to increase the risk of diabetes by about 1.3-fold. [49]

MAOIs (monoamine oxidase inhibitors) tend to have pronounced (sometimes fatal) interactions with a wide variety of drugs and over-the-counter drugs. If dealt with foods that contain very high levels of tyramine (e.g., baked cheese, cooked meats or yeast extracts), they can cause a potentially deadly hypertension crisis. At lower doses, the person may experience only one headache due to an increase in blood pressure. [50] In response to these side effects, another type of MAOI has been developed: reversible monoamine oxidase A class of drugs (RIMA-reversible monoamine oxidase inhibitors). Their main advantage is that they do not require the person to follow a special diet, while being seemingly effective as SSRIs and tricyclics in treating depressive disorders. [51] .Tricyclics and SSRIs can cause so-called drug-induced QT prolongation, especially in older adults; [52] this condition can degenerate into a specific type of abnormal heart rhythm called torsades de point which can lead to sudden cardiac arrest. [53]

II. PURPOSE OF THE WORK

Given the fact that the use of antidepressants is little studied, aroused interest to accumulate data on their use and misuse, as important preparations for the better functioning of mental health. Thus, the main purpose of this study is the analysis and evaluation of attitudes and practices of using antidepressants with or without a doctor's recommendation, the use of herbal products for the treatment of depression and the reason for use, types of antidepressants used and awareness about the use of antidepressants among respondents in Tetovo and surroundings

III.MATERIAL AND METHODS

The target population randomly selected for the study were females and males aged 25 to 65 years.

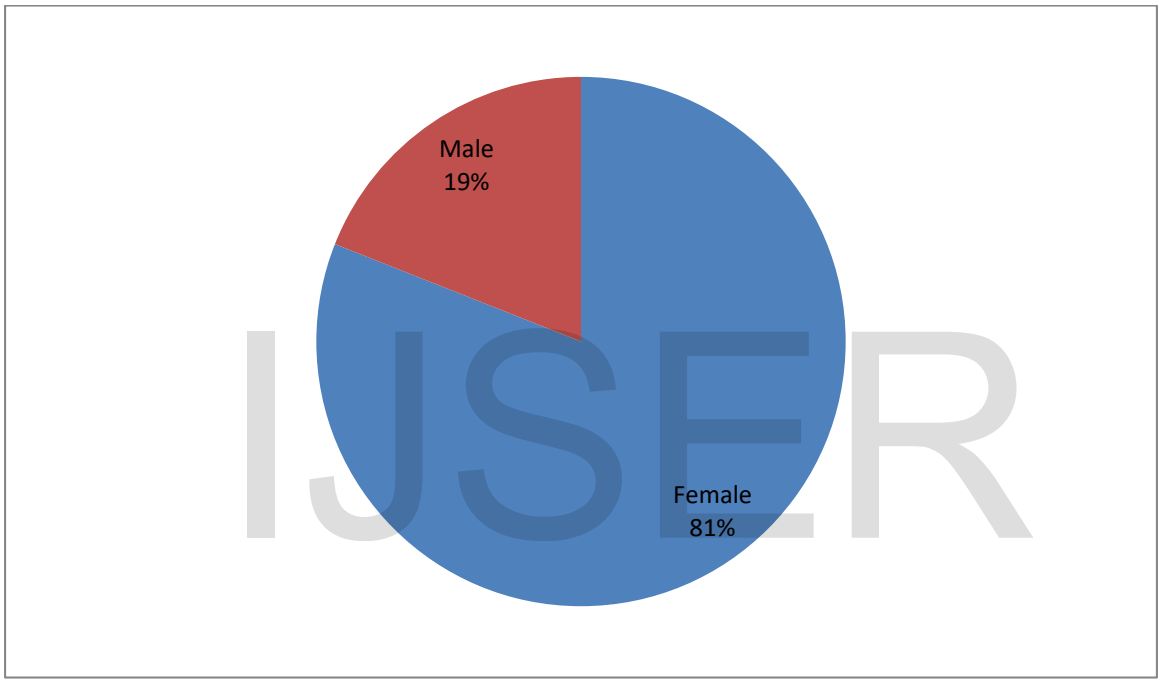
The study was conducted through the survey process with the Google Questionnaire platform. For the design of the self-administered questionnaire, literature and questionnaires similar to our research were consulted. The questionnaire was formulated to identify the prevalence of antidepressant use, with or without recommendation. of the doctor, taking them according to the recommendation or needs, the period of use and the attitude of individuals to the effectiveness of use. In this section the questions are formulated to identify the prevalence and reason for using herbal products. Individual attitudes and awareness of the side effects of antidepressants

IV. RESULTS

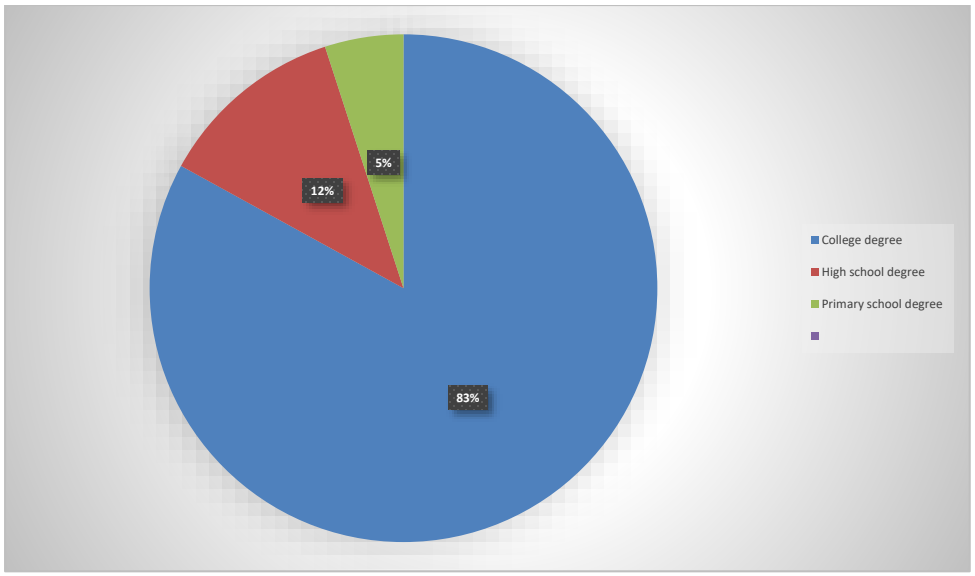
Socio-demographic characteristics

The first part of the questionnaire included the socio-demographic characteristics of the individuals who participated in the study. The questionnaire starts with the age of the respondents and the frequency and percentages of the answers will be presented below.

The age of the individuals was 25 to 65 years.

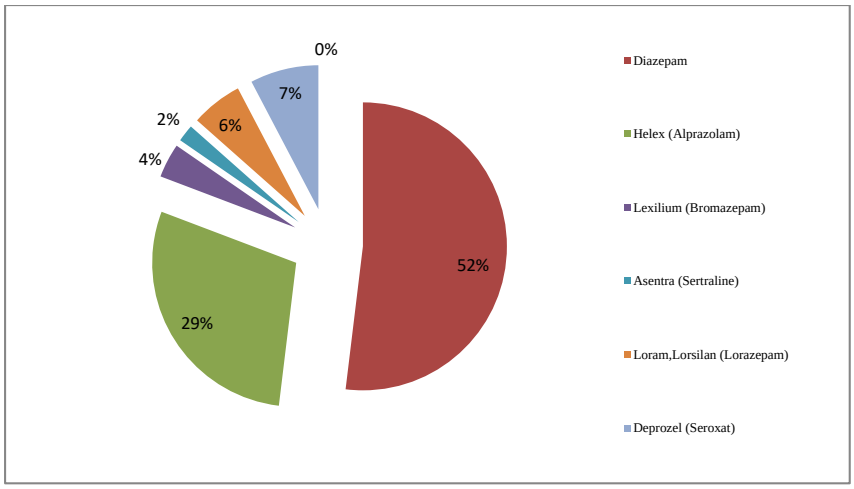


Graph.1. Gender of respondents divided by percentage

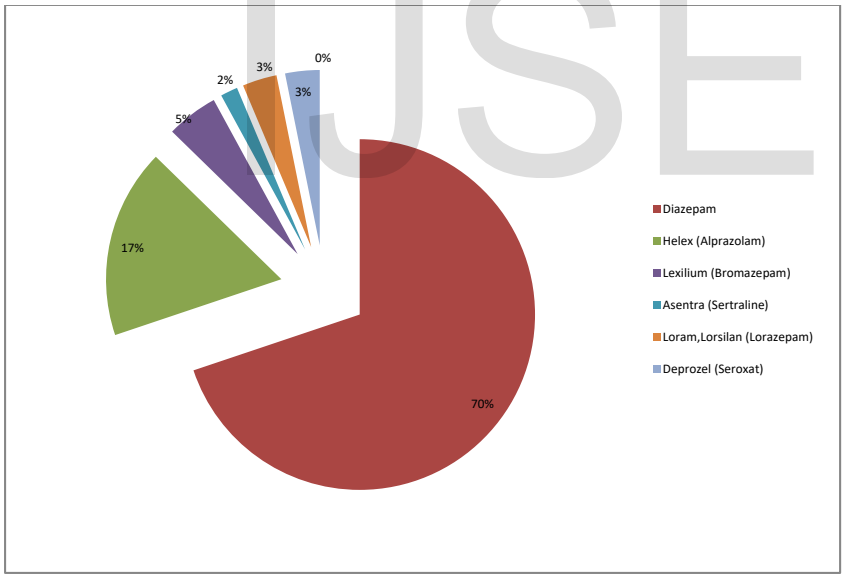


Graph.2.The level of education of the respondents

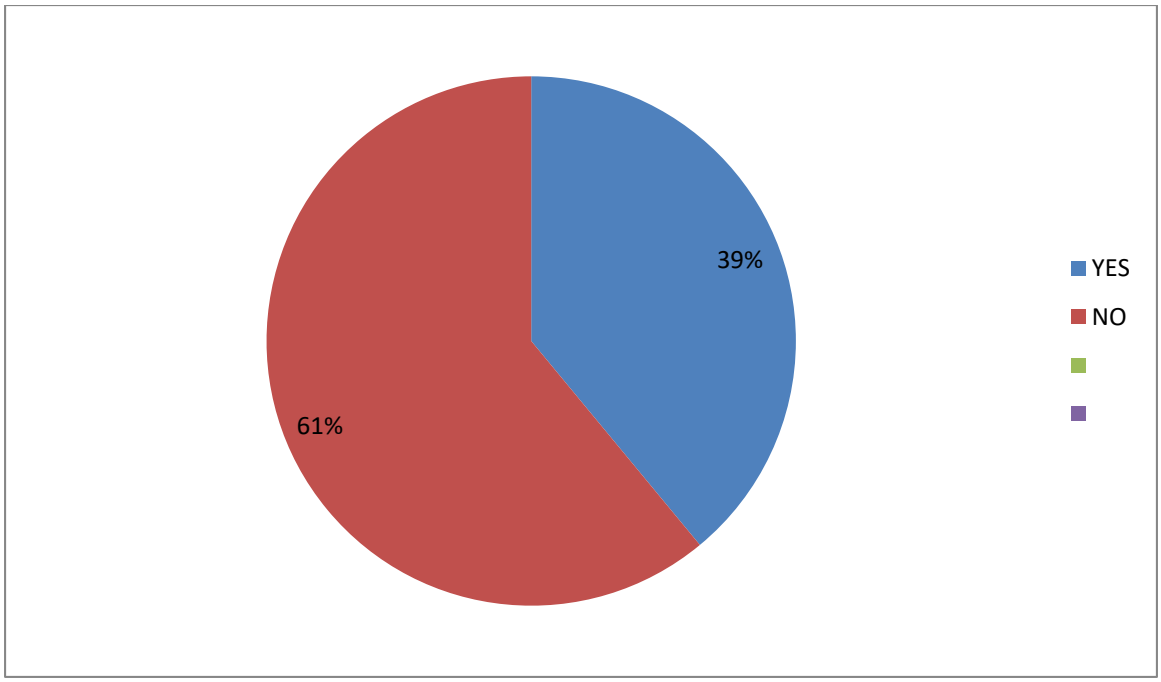
Graph.3. Prevalence of use of antidepressants recommended by the doctor



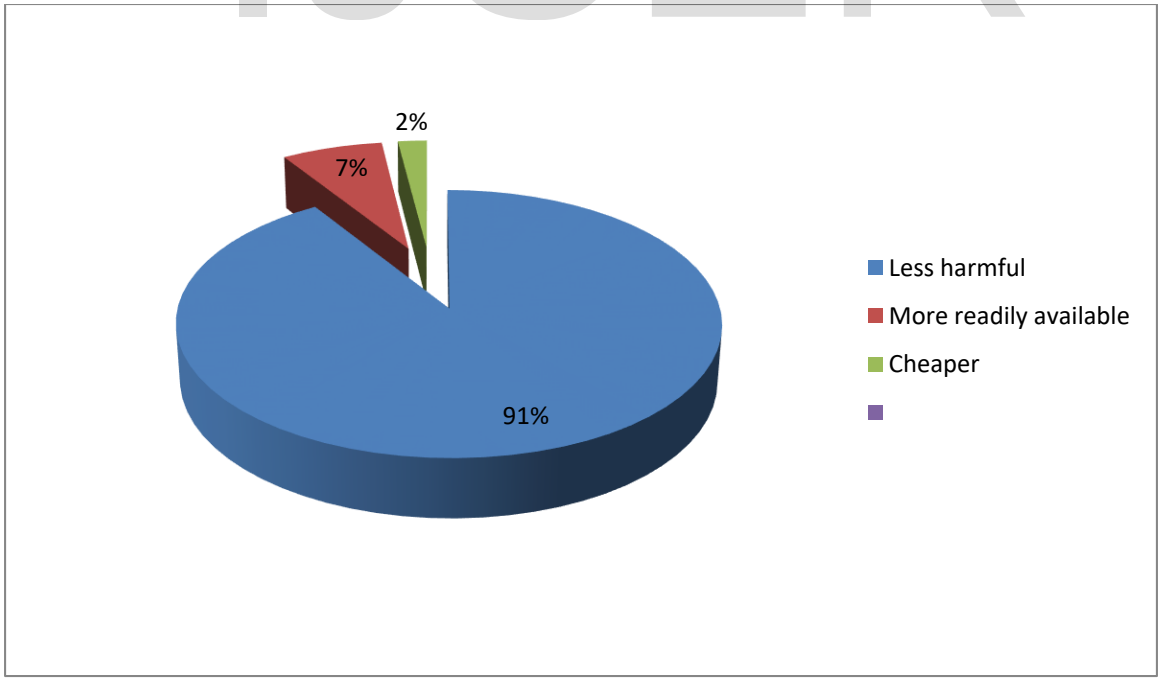
Graph.4. Type of antidepressant used on doctor's recommendation



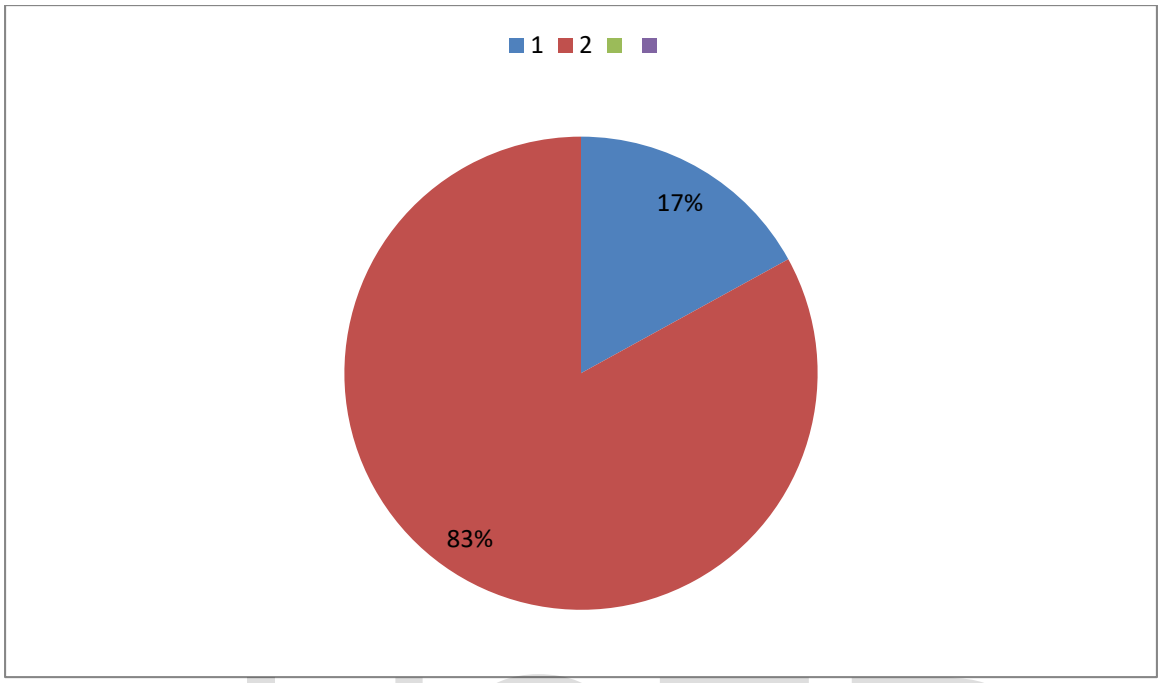
Graph.5.Type of antidepressant used without a doctor's recommendation



Graph.6.Prevalence of use of herbal products for the treatment of depression



Graph.7. The reason for using herbal products to treat depression



Graph.8. Respondents attitudes regarding awareness of the side effects of antidepressant use

V.DISCUSSION

Our prevalence estimates for new concomitant use are similar to those reported in another US population-based study [54] examining this question in a group of depressed veterans. Perhaps the 2001 Cochrane publication (and the 2009 update) played a role because it summarized evidence of combined use of antidepressants and benzodiazepines and reported increased short-term response and decreased abandonment attributed to adverse effects in casual patients on combined versus an antidepressant alone (although only 1 trial lasted> 8 weeks). [55] Another possible factor is the increased recognition of concomitant anxiety in patients with depression. [56,57] The plateau we observed in the new concomitant use may be related to increased caution in prescribing benzodiazepines that may have followed publications [58,59] enumerating the potential harms of benzodiazepines when used concomitantly with opioids. In addition, changes in the use of drugs used for similar indications but distinct from benzodiazepines (i.e. z drugs) may have influenced the trends observed in the new concomitant use of benzodiazepines. When prescribed with caution to appropriate patients, benzodiazepines are considered to be beneficial drugs. [60] , visits to the emergency department. and the increased risk of fractures, car crashes and overdose. [58,61]. So our study corresponds to those of other authors where we note that all patients have used benzodiazepines together with antidepressants and have been effective in improving symptoms. .

VI.CONCLUSION

Regarding the results obtained we note that 75% of respondents used antidepressants recommended by the doctor, while 25% used antidepressants without a doctor's recommendation.

From the accumulated results, in the level of education of the respondents we notice that most of the respondents had high professional training represented with 83% of the total. 12% of the respondents had secondary education and only 5% had primary education.

From the accumulated results for the types of antidepressants used with a doctor's recommendation we can see 52% of individuals have used Diazepam to treat depression, 29% have used Alprazolam (Helex), 7% Paroxetine (Deprozel, Seroxat), 6% Lorazepam (Loram, Lorsilan), 4% Bromazepam (Lexilium) and 2% Sertraline (Asentra).

Of the accumulated results for the types of antidepressants used without a doctor's recommendation is Diazepam for the treatment of depression, 17% used Alprazolam (Helex), 5% Bromazepam (Lexilium), 3% Paroxetine (Deprozel, Seroxat), 3% Lorazepam (Loram, Lorsilan) and 2% Sertraline (Asentra). From these results as a recommendation should be taken measures towards the awareness of the population for the treatment of depression and not only for its simultaneous treatment as well as the best antidepressants only with the recommendation of the doctor and to follow the instructions given by the doctor.

Regarding the knowledge on the side effects, the respondents answered that 83% have knowledge on the side effects and 17% are not aware of the side effects of antidepressants.

Regarding the use of herbal products for the treatment of depression 61% did not use while 39% of respondents used herbal products for the treatment of depression.

The reason for using herbal products to treat depression has also been researched. The results show that 91% of individuals are aware that plant products are less harmful to use, 7% have used plant products because they are more readily available and 2% have used plant products because they are cheaper. .

The use of herbal products for the treatment of depression is a common phenomenon but our study showed that very few patients use herbal products for the treatment of depression The number of users of herbal products is very small and disturbing as most individuals choose to use benzodiazepines for management of their disturbing symptoms and from this we can recommend raising awareness by pharmacists to patients when purchasing products and make a clarification on the use of herbal products as an alternative.

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