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Assessment of the Antidepressant Side Effects Occurrence in Patients Treated in Primary Care

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ABSTRACT

Introduction: It is an undeniable fact that antidepressants can cause side effects. Antidepressants generally have a similar effect but they differ in their application safety, as well as their side effects. **Aim:** To determine differences in the frequency and intensity of antidepressant induced side effects in patients treated in primary care. **Methods:** The research was designed as a prospective, cross-sectional study, conducted on a voluntary and anonymous basis, and it included depression patients treated with antidepressant medications during 2013-2015 in Zenica-Doboj Canton using the Hamilton Depression Rating Scale and Toronto Side Effects Scale. **Results:** The total sample included 508 subjects. As a significant problem, abdominal pain was felt by 14% of subjects, indigestion by 19% of subjects, nausea by 15% of subjects, diarrhea by 9% of subjects, and constipation by 11% of subjects. 29% of subjects suffered from sweating, 20% suffered from a sudden heat stroke, 10% suffered from swelling, and 23% of them reported suffering from dry mouth as a significant problem. The prevalence of side effects in relation to how do they affect life and daily activities of subjects is statistically significant (P <0.000). Statistically significant side effects of SSRI antidepressants correlate with the duration of our subject's treatment: perception of increased sleep (0.039) as well as decreased sleep (P = 0.009), sweating (P <0.001), sudden heat stroke (P <0.001), being without orgasm (P = 0.004), decreased libido (P <0.001), weight loss (P = 0.045). **Conclusion:** It is necessary to educate the patients about the nature and features of the depressive disorder, and to notify the patients of the expected course of recovery, as well as the need to adhere to the recommended therapy and the possible side effects of the medication.

Keywords: depression, antidepressants, side effects of antidepressants.

1. INTRODUCTION

Depression is a disease of our modern age and it presents a great challenge not only for mental health professionals, but also for family medicine physicians (1). It is estimated that over 120 millions of people from all over the world suffer from depression, of which twice as many are women. Depression is expected to become the world's second significant health problem by 2020. Most of the patients who suffer from depression are between 35 and 55 years old (2).

The first step in the treatment of depression is to set a boundary between the domain of family medicine physicians and the domain of psychiatrists (3). According to the experiences of various authors, mild and moderate depression are in the domain of family medicine physicians. Their responsibility is not only the first contact with a patient, but also the monitoring of the patient treated by a psychiatrist.

Antidepressants generally have a similar effect, but they differ in their safety and side effects. A large number of antidepressants side effects is related to their effect on various neurotransmitter systems (4). The adverse reactions of antidepressants and the irrational use of these medicaments may be related to the low level of research in this domain and the lack of awareness among physicians about this problem (5).

In some patients antidepressants have an effective therapeutic effect, in some patients they cause a development of only mild, almost imperceptible side effects, while in some patients who suffer from mild depressive disorders they can cause a development of a severe chronic depression (6, 7). Individual hypersensitivity to the drug; age; sex; type of antidepressant based on its pharmacological effect; duration of the

therapy; polypragmasia; and other things are also important in the assessment of antidepressant side effects (2).

The main reason for discontinuing the treatment with antidepressants is a development of unwanted side effects. It is an undeniable fact that antidepressants can cause side effects (6). Depression and anxiety are very common symptoms that occur when discontinuing the treatment with antidepressants. In this case of adverse drug reactions the clinical manifestation is more severe. Unfortunately, these symptoms are usually misjudged as a recurrent episode of depression, so a patient continues to take an antidepressant, thereby creating a vicious circle. The group of antidepressants called Selective Serotonin Reuptake Inhibitors (SSRIS) are the most frequently prescribed ones nowadays. Known side effects of treatment with SSRIs that are common are: anxiety, restlessness, insomnia, dry mouth, overweight, nausea, diarrhea, sweating, headaches, dizziness, decreased libido, tremor and sexual difficulties (8, 9, 10) .

The most commonly noticed side effects of Venlafaxine are: nausea, insomnia, dry mouth, sleepiness, dizziness, constipation, sweating, anxiety, asthenia, sexual difficulties (ejaculation disorder), hypertension and palpitations (9, 10). Tricyclic antidepressants tend to cause more side effects than other antidepressants because of their broad mechanism of action. Drowsiness is a very common side effect, especially in the first few weeks after starting with the treatment. These antidepressants may cause cardiac arrhythmias, obesity, loss of libido, dizziness and nausea, dry mouth, blurred vision, constipation, impaired mycitis, and impaired mystic function with confusion (6, 8). Monoamine oxidase inhibitors (IMAOs) are the oldest group of antidepressants. Common side effects of these medications are dizziness, insomnia, weight gain, headaches, sexual problems, and daytime sleepiness (7, 11).

2. AIM

To determine differences in the frequency and intensity of antidepressant induced side effects in patients treated in primary care. Including factors were diagnosis of depressive dissorder without phsyhotic simptoms or other comorbidities and treatment with antidepressive drugs in duration of minimaly three months.

3. PATIENTS AND METHODS

The research was designed as a prospective, cross-sectional study, conducted on a voluntary and anonymous basis, and it included depression patients treated with antidepressant medications during 2013-2015 in Zenica-Doboj Canton using the Hamilton Depression Rating Scale and Toronto Side Effects Scale .

Questionnaires

Objective screening tests were used in the research: Hamilton Depression Rating Scale (12). The Toronto Side Effects Scale (TSES) which contains 32 items was also used in this research (13). It has been created for a direct evaluation of antidepressants side effects on the central nervous system, gastrointestinal tract and it also relates to sexual difficulties, their frequency and intensity (14, 15). Answers were based on intensity and severity of symptoms.

Statistical Data Analysis

The analysis of results was performed by using the standard Statistical Package for the Social Sciences (SPSS) version 19.0. Standard methods of descriptive statistics were applied in the statistical analysis of results. The ⊠2-test and the t-test ($p < 0.05$) were used in order to test the statistical significance of the difference of the selected variables. A non-parametric Spearman's rank correlation test and multivariate regression analysis of variance ANOVA were helpful in multivariate correlation analyzes.

4. RESULTS

A total sample included n = 508 subjects. The average age of the subjects (n = 508) was 48.98 years ± 11.585 years (standard deviation, SD). The highest number of subjects treating an episode of depression were women, 320 out of 508 (63%), and between 41 and 60 years of age (59%). Only 10% patients achieved remission and absence of the depressive disorder as a successful treatment outcome. 20% patients suffered from mild depressive disorder, and 21% patients from moderately severe depression. Serious depression was recorded in 17%, and very serious with treatment in 32% patients.

Frequency of the symptom	No (%)	Intensity of the problem	No (%)	P
Nervousness				X^2=623.387
never	43 (9)	not a problem	79 (16)	
rarely	99 (19)	insignificant	109 (20)	
sometimes	168 (33)	moderate	139 (27)	**0.001**
often	143 (28)	significant	112 (22)	
daily	55 (10)	severe	76 (15)	
Anxiety, fear				X^2=155.790
never	47 (9)	not a problem	80 (16)	
rarely	102 (20)	insignificant	111 (22)	
sometimes	172 (34)	moderate	147 (29)	0.001
often	131 (26)	significant	112 (22)	
daily	56 (11)	severe	58 (11)	
Shaky hands				X^2=902. 868
never	161 (32)	not a problem	203 (40)	
rarely	140 (28)	insignificant	121 (24)	
sometimes	110 (22)	moderate	87 (17)	0.001
often	61 (12)	significant	42 (8)	
daily	36 (7)	severe	55 (11)	
Muscle spasm				X^2=887. 215
never	179 (35)	not a problem	230 (45)	
rarely	148 (30)	insignificant	123 (24)	
sometimes	103 (20)	moderate	85 (17)	0.001
often	62 (12)	significant	42 (8)	
daily	16 (3)	severe	28 (6)	

Table 1. Comparative representation of differences in the incidence of undesirable symptoms of nervousness and anxiety in a relation to the intensity of a problems that these undesirable symptoms present in all subjects, according to the Toronto scale (n = 508)

Frequency of the symptom	No (%)	Intensity of the problem	No (%)	P
Decreased appetite				X^2=643.637
never	185 (36)	not a problem	256 (50)	
rarely	91 (18)	insignificant	84 (17)	
sometimes	120 (24)	moderate	77 (15)	**0.001**
often	63 (12)	significant	46 (9)	
daily	49 (10)	severe	45 (9)	
Increased appetite				X^2=1047.579
never	221 (44)	not a problem	274 (54)	
rarely	129 (25)	insignificant	105 (20)	
sometimes	90 (18)	moderate	65 (13)	0.001
often	49 (10)	significant	40 (8)	
daily	19 (4)	severe	24 (5)	

Table 2. Comparative representation of differences in the incidence of increased or decreased appetite as a side effect of antidepressants in relation to the intensity of the problems which these side effects present in all subjects according to the Toronto Side Effects Scale (n= 508)

In the total sample, the highest number of subjects (141 = 27%) were treated with Paroxetine; with Sertaline 90 (17%); with Flusetin 116 (22%), with Escitalopram or with an other antidepressant 107 (21%); and with Fluzepam 65 (13%) of subjects.X2 = 828,905 P <0.000. Previously, subjects were treated with Paroxetine (32%: 37% vs. 169: 141) significantly more frequently, and they were significantly less frequently treated with Sertalin (9%: 17% vs. 48:90) and Flusetin 17%: 22% (P = 0.001).

Side effects of antidepressants that occur often and on daily basis are: gastrointestinal problems (in 17% of subjects), indigestion (22%), nausea (18%), diarrhea (9%) and constipation (11%). As a significant problem, abdominal pain is felt by 14% of subjects, indigestion by 19% of subjects, nausea by 15% of subjects, diarrhea by 9% of subjects, and constipation by 11% of subjects.

Somatic side effects of antidepressants with often and daily occurrence are: tiredness in 45% of subjects (a high frequency); dizziness (24%); hypotension (15%); headache (34%); and blurred vision (22% of subjects). As a significant problem 40% of subjects feel tiredness; dizziness (25%); hypotension (15%); headache (34%); and blurred vision (22%).

Somatic side effects of antidepressants related to hormone dysregulation that occur often and on daily basis are: sweating in 34%; a sudden heat stroke in 22%; swelling in 8%; and dry mouth in 25% of subjects. As a significant problem in 29% of subjects occur sweating; in 20% a sudden heat stroke; in 10% swelling; and in 23% of them dry mouth. The frequency of side effects in relation to how do they present a problem to subjects in their daily life and activities is statistically significant (P<0.000).

Occurrence of tiredness is most frequent in treatment with Paroxetine (50%) and Flusetin (48%), but differences in the incidence of this side effect among the 5 most prescribed antidepressants are not significant. This side effect is most common in a treatment of a first recurrent episode of depression. It is significantly related to the duration of the treatment statistically (P=0.008) and it has a growing trend over time (P <0.001).

5.DISCUSSION

A treatment with antidepressants has often a potential risk of side effects and suicidal thoughts (16, 17). Although Selective Serotonin Reuptake Inhibitors (SSRIs) do have better overall safety and tolerability comparing to older antidepressants, experience and clinical trials have shown a significant incidence of their side effects.

Ferguson has investigated the causes of various side effects profiles, especially the causes of sexual dysfunction, weight gain, and sleep disorders. An occurence of side effects in long-term SSRI therapy is most concerning. Ferguson's results comply with ours. The statistically significant side effects of SSRI antidepressants in correlation with the duration of the treatment in our subjects are: perception of increased sleep (0.039) as well as decreased sleep (P = 0.009), sweating (P <0.001), sudden heat stroke (P <0.001), being without orgasm (P = 0.004), decreased libido (P <0.001), weight loss (P = 0.045).

In clinical studies it has been confirmed that SSRIs have significantly less side effects compared to Tricyclic Antidepressants (TCA) (19). They do not cause irregularities in cardiac conduction or rhythm disturbances in case of an overdose (20). As confirmed in our study, Selective Serotonin Reuptake Inhibitors (SSRIs) are currently the first choice of therapy for depression (17).

In a prospective control study which included 1251 patients, in the treatment of depression 659 of them have used sertraline and 592 of others have used SSRIs (paroxetine, fluoxetine, or fluvoxamine) for at least 12 months. A significant side effect in patients treated with Sertraline compared to patients treated with other SSRI antidepressants is diarrhea (14% vs.. 6.8%), P <0.05 (21). Our results are contradictory. In our study, tiredness occurred most commonly in treatment with Paroxetine (50%) and Flusetin (48%), but differences in the prevalence of this side effect among the five most prescribed antidepressants were not significant. Headache most frequently occurs in treatment with Flusetin (39%), just as well as dizziness (30%); blurred vision (26%), and dry mouth occur in treatment with Paroxetin. However, the differences for all known SSRI side effects are not significant.

6. CONCLUSION

It is necessary to educate the patient about the nature and properties of the depressive disorder, and to introduce him to the expected course of recovery, as well as the need to adhere to the recommended therapy and the possible side effects of the drug. The results of our research have shown an important degree of variability in side effects of the most commonly prescribed SSRI antidepressants compared to those reported in clinical trials, which had been monitored before they were approved.

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