ORIGINAL ARTICLE

Antidepressant treatment outcomes in family medicine

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ABSTRACT

Aim To determine the prevalence of depressive episodes and recurrent depressive disorders despite of the length of therapy and type of antidepressants.

Methods The study was conducted among 508 patients aged 19-65 years who were treated for depression for at least 3 months (mild and moderate episodes were controlled and the effects of treatment monitored by family physicians, while severe episodes were controlled by a psychiatrist) during 2013- 2015 in Zenica-Doboj Canton using the Hamilton Depression Rating Scale (HDRS).

Results The average age of the patients was 48.98±11.585 years. Depressive disorder was most commonly represented in patients with high-level education, 22%, more frequently in non-productive workers (non-productive vs. manufacturing 58%:35%). A significant number of patients who were treated for depression were unemployed (57%). All respondents were suffering from the most serious episode of depression with an average depression rate at the Hamilton scale 18.49±8.603, with a very serious depression level of 32%, severe 17%, moderate 21%, and mild 20%. Most patients were treated with paroxetine, 27%, fluoxetine 22% and sertraline 17%. Efficacy of depression treatment with different types *of selective serotonin reuptake inhibitors* antidepressants (SSRIs) was not significantly different (p=0.502).

Conclusion Success of the treatment with the absence of symptoms of depression was achieved in 10% and the maintenance of depressive episodes occurred in 90% of cases. Adverse reactions with the most commonly prescribed SSRI in our country should be important in creating procedures and strategies for the future treatment of depression in family medicine.

Key words: depressive episodes, effects of medications, antidepressant side effects, general practitioners, recurrent depressive disorders

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INTRODUCTION

Depression can occur in any age. It is believed that over 120 million people worldwide suffer from depression, of which twice as many are women (1). The most frequently prescribed antidepressants are from serotonin reuptake inhibitors (SSRI) group. Family medicine physician should be familiar with the wider psychopharmacological choice, precisely to access chronic patients or patients on prolonged antidepressant therapy (2,3). Depression is a disease that represents a big challenge not only for mental health professionals, but also for family physicians (4).

Antidepressants generally have similar effects, but differ in their safety and side effects. A large number of side effects of antidepressants are related to the action on different neurotransmitter systems (5). To establish the diagnosis of depression with somatic symptoms, the presence of mild or moderately severe depressive episodes and four of the eight listed melancholic features need to be present. Common vegetative symptoms of depression include the reduction of interest in sexual activity (6).

According to the records of the Institute of Health Insurance of the Federation of Bosnia and Herzegovina (B&H), the most frequently prescribed antidepressants in 2009 were paroxetine 57.3%, sertraline 11%, fluoxetine 41.15%, amitriptyline 0.90% and maprotiline 0.59%. The most commonly used anxiolytics are: flurazepam (13%) and diazepam (6%). Large use of bromazepam, or rare combinations of antidepressants were prescribed if therapeutic goals were not achieved. The prevalence of depression with an upward trend in Bosnia and Herzegovina is 40% (7).

Antidepressants are the group of drugs that primarily improve depression mood, stimulate vital dynamics, and act anxiolytically. Their effect is based on the idea of a functional deficiency of "monoamine" in a depressive disorder. Thus, synthesized antidepressants increase the concentration of monoamines at receptor sites in the brain (8).

The aim of this study was to determine the prevalence of depressive episodes and recurrent depressive disorders as negative outcomes of the treatment by different types of antidepressants despite of the length of therapy. We expected the results of the study to provide an important degree of variability of side effects of prescribed antidepressants compared with the expected registrations in clinical studies that were conducted to monitor the effects of these drugs before their approval (placebo treatment). Results of the study may help optimise health care of patients and help family medicine physicians in their choice of antidepressants in practice.

PATIENTS AND METHODS

Patients and study design

The research was designed as a cross-sectional study, conducted on a voluntary basis and with anonymity. The study included patients treated from depressive mood disorder: mild and moderate episodes under the control and monitoring of treatment effects done by family medicine physician, while severe and serious episode was controlled by the psychiatrist, during 2013-2015 in the Family Medicine Teaching Centre, Primary Health Care Zenica, Bosnia and Herzegovina (B&H).

For the sake of safety and achievement of the desired sample, 600 respondents were surveyed. Inclusion criteria were: diagnosed depressive disorder without psychotic symptoms, respondents aged 19-65, treatment with antidepressants for at least three months. The diagnosis was based on two typical and two other common symptoms (DSM-IV) (10). Typical symptoms included: depressive mood, loss of interest and satisfaction, decreased energy and increased tiredness. Other common symptoms were: disturbed sleep, reduced appetite, reduced concentration and attention, decreased self-esteem and self-confidence, guilt and worthlessness, pessimistic view of the future, ideas of self-injury and injury.

This study was approved by the Ethics Committee of the Primary Health Care Zenica.

Methods

Self-response questionnaire survey on a voluntary basis with adherence to ethical terms of anonymity was done. Prior to access to the survey, patients were provided with relevant information to clarify the purpose, objectives and importance of the research.

Prevalence rates of the treatment or negative outcome of the treatment and maintenance of depressive episodes and recurrent depression

episode despite the treatment of antidepressants, were determined by a screening method using the Hamilton Depression Scales translated into the B&H language. Intervals of the Hamilton scale represent and categorize depression. It contains 17 numbered graduated doors (symptoms of depression) whose sum is added: 0 -7 normal mental status, 8-13 mild depression, 14-18 moderate depression, 19-22 serious depression, and > 22 very serious-depression (9).

Statistical analysis

Standard methods of descriptive statistics were applied. The $\chi 2$-test and t-test ($p < 0.05$) were used to test statistical significance of the difference of the selected variables. For non-parametric Spearman correlation test and multivariate regression analysis of ANOVA variance, multivariate correlation analysis were used.

RESULTS

The study included 508 patients. Response rate was very satisfactory, 85% (out of 600). The mean age of the respondents was 48.98±11.585 years. The age ranged from 18 to 78 years. The majority of respondents who were treated for depression were women, 320 (63%), and they were mostly 41-60 years old, 302 (59%). Only 33 (11%) patients were younger than 30 years of age. Depressive disorder was most commonly reported in persons with secondary school education, 189 (37%), and those with a university degree, 66 (13%). A total of 219 (43%) patients were unemployed; 165 (33%) were employees of services and administration, 116 (22%) were pensioners.

The mean value of depression 18.49 ± 8,603 SD reveals that all respondents were approaching or mostly suffering from a serious episode of depression.

The first life episode of depressive disorder, which had never occurred before, was noticed in 182 (36%) patients; 326 (64%) recovered from depressive disorder. Backward disorder that occurred one more time was noticed in 141 (28%), twice in 45 (9%), three times in 66 (13%), and more than three times in 74 (14%) patients.

Only 53 (10%) patients achieved remission and absence of the depressive disorder as a successful treatment outcome. 101 (20%) patients suffered from mild depressive disorder, and 103 (21%) patients from moderately severe depression. Serious depression was recorded in 87 (17%), and very serious with treatment in 164 (32%) patients. Failure to treat and maintain depression was found in 457 (90%) and serious depressive level in 248 (49%) patients.

The patients were mostly treated with paroxetine, 141 (27%), 90 (17%) with sertraline, 116 (22%) fluoxetine, 107 (21%) with escitalopram or another antidepressant, and 65 (13%) with flurazepam ($p<0.000$). Differences in achieving the success/failure of treating depression according to the chosen first antidepressant were not statistically significant ($p=0.502$). (Table 1). A total of 296 (59%) respondents did not show any suicidal thoughts or suicidality. Suicidality was manifested in 212 (41%) respondents.

Table 1. Comparative distribution of choice of the first antidepressant in the treatment and the outcome of treatment success according to the reported level of depression

	Antidepressant (No of patients)				
The level of depression	**Paroxetine (130)**	**Sertaline (90)**	**Fluoxetine (116)**	**Flurazepam (65)**	**Other (107)**
Normal mental status	17 (13)	7 (8)	8 (7)	6 (9)	15 (14)
Mild depression	31(24)	18 (20)	20 (17)	12 (19)	20 (19)
Moderate depression,	21 (16)	17 (19)	22 (19)	19 (29)	24 (22)
Severe depression	21 (16)	16 (18)	22 (19)	10 (15)	18 (17)
Very severe	40 (31)	32 (35)	44 (38)	18 (28)	30 (28)

p=0.502

DISCUSSION

In stationary psychiatric institutions, about 3000 depressed persons are treated annually, of whom 69% are females (10), which is similar to the results of our study, e. g. 63% of women-being treated for depressive episodes. Our patients mostly suffered from serious, most recurrent episode of depression; 36% of patients had the first life episode of depressive disorder. The prevalence of recurrent depression with recurrent episodes was 64%; a serious level of depression was found in 32% of patients.

The diagnosis of depression is associated with high suicidal risk. The assessment of suicidal risk is an integral part of clinical practice. Suicide is manifested by the following perceptions: life is not worth living; desires death or shows suicidal intentions (10). Authors of a systematic meta-analysis in 2005 concluded that increased

risks of suicide and suicidal attempts caused by SSRIs could not be ruled out (11). Some authors fail to support either an overall difference in suicide risk between antidepressant and placebo-treated depressed patients in controlled trials, or a difference between SSRIs and either other types of antidepressants or placebo (12,13). Our results are worrying because of a very high prevalence rate of suicide related to the treatment of SSRIs.

Social theories assume that a number of stress situations predispose a person to the development of depression (14). Our results support social theory and the role of stress in the development of depression. Today's environment lifts the spiritual sphere and makes life difficult. How much a social moment is associated with depression speaks in favour of the incidence rate of depressive disorder in work-active respondents in our study; non-productive workers were represented with 65% compared to the workers with professional education in production with 35%. In our study, health workers have a high prevalence of depression (13%) compared to educators (3%). In addition, production workers suffer from depression with the prevalence of 35%, and most often due to the lack of respect for their employment rights. Unfortunately, there is an impression that the most important of all sociodemographic factors is unemployment. In our study depression affected 43% of the unemployed. The guidelines for treating depression are based on a review of literature and guides by various psychiatric societies and organizations dealing with the treatment organization of mental disorders (15,16).

It is very important to evaluate well all of the conditions associated with a depressive disorder, then select an antidepressant (17). Most patients should be trained to continue the treatment after remission of the disease or to achieve significant improvement (18). Selective serotonin reuptake inhibitors (SSRIs) (sertraline, paroxetine, fluoxetine, escitalopram), selective serotonin inhibitors (noreprinephrine-venlafaxine), bupropion and mitrazapine are often the first choice drugs for depression (19), which was confirmed in our research. Fluoxetine is an atypical SSRI that is the only one to acutely increase the extracellular concentration of dopamine and norepinephrine amongst the SSRIs examined (20).

Symptoms such as fear and concern should be treated with tricyclic antidepressants (TCA) (amitriptyline, imipramine). They make the second line of treatment for depressive disorder (21).

Unfortunately, the treatment with antidepressants often has a potential risk of side effects and suicidal ideals (22).

Previous clinical studies and experience have shown the frequency of side effects of SSRI with long-term use, especially sexual dysfunction, sleep disorders and weight gain (23).

Patients suffering from depression require a multidisciplinary approach to treatment. Early recognition and effective, time-long enough treatment are important to avoid the consequences and chronic disease course (24,25). Depression treatment is performed with psychopharmaceuticals, psychotherapy and psycho-education of the affected patient and family members. Depressive episodes can be treated in 70 to 80% of cases (26).

Patients requiring depressive episodes to repeat maintenance therapy should take it for at least five years and a certain number of patients for a lifetime (27-30).

In conclusion, the management of depression requires a family physician to have good knowledge and diagnostic skills on the use of appropriate antidepressants.

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REFERENCES

1. Kessler RC, Ormel J, Petukhova M, McLaughlin KA, Green JG, Russo LJ, Stein DJ, Zaslavsky AM. Development of lifetime comorbidity in the World Health Organization world mental health surveys. Arch Gen Psychiatry 2011; 68:90.
2. Sutherland JE, Sutherland AJ, Hoehns D. Achieving the best outcome in treatment of depression. J Fam Pract 2003; 59:203-10.

3. 3.Turner EH, Matthews AM, Linardatos E, Tell A, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. N Engl J Med 2008; 358:252-60.
4. Nelson JC, Devanand DP. A systematic review and meta-analysis of placebo controlled antidepressant studies in people with depression and dementia. J Am Geriatr Soc 2011; 59:203-10.
5. Gilbody S. Whitty P, Grimshaw J, Thomas R. Educational and organisational interventions to improve the management of depression in primary care: a systematic review. JAMA 2003; 289:3145-51.
6. Trumić E, Pranjić N, Begić L, Bečić F. Prevalence of polypharmacy and drug interaction among hospitalized patients: Opportunities and responsibilities in pharmaceutical care. Mat Soc Med 2012; 24:68-72.
7. Zavod za javno zdravstvo Federacije Bosne i Hercegovine, Sarajevo. Zdravstveno stanje stanovništva 2009. https://www.zzjzfbih.ba/zdravstvena-stanja-stanovnistva/ (16 April 2019)
8. Jašović Gašić M, Marić Bojović N, Jovanović A, Pejović Nikolić S. Antidepresivi. Beograd: Glaxo Smith Kline, 2012.
9. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56-62.
10. Bertolote JM, Fleischmann A, De Leo D, Wasserman D. Psychiatric diagnoses and suicide: revisiting the evidence. Crisis 2004; 25:147-55.
11. Gunnel D, Saperia J, Ashby D. Selective serotonin reuptake inhibitors (SSRIs) and suicide in adults; meta-analysis of drug company data from placebo controlled, randomised controlled trials submitted to the MHRA's safety review. BMJ.2005; 330:385.
12. Khan A, Khan S, Russell LK, Brown W. Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: analysis of FDA reports. Am J Psychiatry 2003; 160:790-2.
13. Bostwick JM, Pankratz VS. Affective disorders and suicide risk: a re-examination. Am J Psychiatry 2000; 157:1925-32.
14. Pranjić N, Bajraktarević A. Depression and suicide ideation among secondary school adolescents involved in school bullyng. Prim Health Care Res Dev 2010; 11:349-62.
15. National Institute for Health Care Excellence-NICE. Depression in adults: recognition and management, 2009. https://www.nice.org.uk/guidance/cg90 (16 April 2019)
16. Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry 2009; 70:1219-24.
17. Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G, Thase ME, Lavori PW, Lebowitz BD, McGrath PJ, Rosenbaum JF, Sackeim HA, Kupfer DJ, Luther J, Fava M. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiatry 2006; 163:1905-17.
18. Goodnick PJ, Goldstein BJ Selective sertonin reuptake inhibitors in affective disorders. J Pharmacol 1998; 12:S5-20.
19. Anderson IM. SSRIs versus tricyclic antidepressants in depressed patients: meta-analysis of efficacy and tolerability. Depress Anxiety 1998; 7:11-7.
20. Bymaster FP, Zhang W, Carter PA, Shaw J, Chernet E, Phebus L, Wong DT, Perry KW. Fluoxetine, but not other selective serotonin uptake inhibitors, increases norepinephrine and dopamine extracellular levels in prefrontal cortex. Psychopharmacology 2002; 160:353-61.
21. Edvrds JG, Anderson I. Systematic review and guide to selection of selective serotonin reuptake inhibitors. Drags 1999; 58:1207-58.
22. Kupfer DJ, Frank E, Phillips ML. Major depressive disorder: new clinical, neurobiological, and treatment perspectives. Lancet 2012; 379:1045-9.
23. Ferguson JM. Antidepressant medications: adverse effects and tolerability. Prim Care Companion J Clin Psych 2001; 3:22-7.
24. Cuijpers P, van Straten A, Warmerdam L, Andersson G. Psychotherapy versus the combination of psychotherapy and pharmacotherapy in the treatment of depression: a meta-analysis. Depress Anxiety 2009; 26:279-88.
25. Jašović-Gašić M, Damjanović A, Miljević Č, Marić N. Antidepresivi. Beograd: Hemofarm, 2006.
26. Jašović-Gašić M, Damjanović A, Miljević Č, Marić N. Antidepresivi. Niš: SKC, 2000.
27. Sussman N, Ginsber D. Rethinking side effects of the selective serotonin reuptake inhibitors: sexual dysfunction and weight gain. Psychiatr Ann 1998; 28:89-97.
28. Eitan R. Nonpharmacological, somatic treatmens of depression: electroconvulsive therapy and novel brain stimulation modalities. Dialogus Clin Neurose 2006; 8:235-43.
29. Sotsky SM, Glass DR, Shea MT, Pilkonis PA, Collins JF, Elkin I, Watkins JT, Imber SD, Leber WR, Moyer J. Patient predictors of response to psychotherapy and pharmacotherapy: findings in the NIMH Treatment of Depression Collaborative Research Program. Am J Psychiatry1991; 148:997-1008.
30. Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, Frank E, Goodwin GM. Relapse prevention with antidepressant drug treatment in depressive disorders. Lancet 2003; 361:653-61.