# SELECTIVE SEROTONIN REUPTAKE INHIBITORS USED TO TREAT DEPRESSIVE DISORDERS

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***Abstract***

*Depression is a very serious mental disorder with a high prevalence worldwide in both developed and developing countries. Nowadays, it is estimated that depression affects 350 million people in all communities across the world. Treatment of depression is complex comprising both the drug approach and psychotherapy. Among the antidepressant drugs, selective serotonin reuptake inhibitors (SSRI) have become the most common antidepressant drugs prescribed by doctors.*

*We have studied six SSRI drugs (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) which have been issued between 2008-2013 as 13 pharmaceuticals in a community pharmacy in Oradea city. Because of the higher incidence of side effects the old generation of SSRI, such as fluoxetine and fluvoxamine, are currently less prescribed by doctors. The new generation of SSRI (paroxetine, sertraline, escitalopram and citalopram) are considered safer agents for the treatment of depression. Pharmacological studies classified escitalopram as a very active SSRI with low probability of side effects. The pharmaceuticals containing escitalopram recommended to patients exceeded paroxetine and sertraline in 2013.*

**Key words:** depression, selective serotonin reuptake inhibitors, neurotransmitters, anxiety, tolerability, side effects.

## INTRODUCTION

According to the World Health Organization (WHO), ”depression is a common mental disorder characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration” (http://www.euro.who.int; http://www.who.int/topics).

Depression is a serious illness, varied as a means of expression, origin and severity, that can cause significant problems in mood, thinking and behavior at home and also at work (http://www.nimh.nih.gov/health). Depression has a high prevalence worldwide in both developed and developing countries being a leading cause of illness and disability among young people aged between 10 and 19 years (Marcus M. et al., 2012; http://www.agerpres.ro). Nowadays, it is estimated that depression affects 350 million people in all communities across the world and is a leading cause of disability in terms of total years lost due to disability, according to the WHO (WHO, 2012; Marcus M. et al., 2012). Moreover, depression not only affects the patient’s quality of life but increases the risk of mortality by suicide and cardiovascular diseases (Lepine J.P., Briley M., 2011; Reddy M.S., 2010).

Treatment of depression is complex comprising both the drug approach and psychotherapy. These two treatment ways do not exclude, but complete each other. The neurotransmitters (serotonin, norepinephrine and dopamine) are involved in regulating a person's mood. Research has shown that depression is associated with a deficiency of serotonin (5-HT) and norepinephrine (NE) in brain and antidepressant therapy aims to correct this deficiency by normalizing the chemicals levels in the brain. There are different classes of antidepressants: tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), serotonin and norepinephrine reuptake inhibitors (SNRI), monoamine oxidase inhibitors (MAOI), every class affecting different neurotransmitters in particular ways (Lemke L.T. et al., 2013; http://www.mayoclinic.org; http://www.fda.gov).

**MATERIAL AND METHOD**

SSRI drugs have shown to alleviate depression and have become the most common antidepressant drugs prescribed by doctors. Due to their high effectiveness and tolerability, decreased adverse effects and less toxicity in overdose, SSRI are considered first-line agents in the treatment of depression. SSRI are very effective drugs not only in the depression treatment but also in panic disorder, obsessive-compulsive disorder, dysthymia and post-traumatic stress disorder. The great advantage of these compounds is their low/absence of affinity to some receptors (alpha adrenergic, histamine $H_1$ or cholinergic M) known to be responsible for many adverse effects of TCA. SSRI may have an increased risk of suicide among children and teenagers (Lemke L.T. et al., 2013; Cristea A.N., 2005; http://www.nimh.nih.gov/health; March J. et al., 2004; Olfson M. et al., 2006; Simon G.E. et al., 2006; Gibbons R.D. et al., 2006).

The purpose of this paper was the study of some SSRI drugs issued by medical prescriptions between 2008-2013 in a community pharmacy in Oradea city. Following the turnover of these products, we tried to make a determination of growth or decline of these drugs' use by patients for a period of six years. Because these products are released by medical prescriptions which remains at the pharmacy, we could determine exactly the quantity of drugs necessary to accomplish the pharmacological effect and not the marketing of these pharmaceutical products.

We have studied six SSRI drugs (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) which have been issued from the pharmacy as 13 pharmaceuticals as can be seen in table 1 (Vastag A.M., 2014).

*Table 1*

SSRI drugs used to treat depression

| Item No. | International common name | Proprietary name | Dose | Pharmaceutical presentation |
|---|---|---|---|---|
| **1.** | **FLUVOXAMINE** | FEVARIN | 50 mg<br>100 mg | tablets |
| **2.** | **FLUOXETINE** | FLUOXIN | 20 mg | capsules |
| | | FLUOXETIN | | |
| | | PROZAC | | |
| **3.** | **PAROXETINE** | SEROXAT | 20 mg<br>40 mg | tablets |
| | | ARKETIS | | |
| **4.** | **SERTRALINE** | ZOLOFT | 50 mg<br>100 mg | tablets |
| | | SERLIFT | | |
| | | STIMULOTON | | |
| | | ASENTRA | | |
| **5.** | **CITALOPRAM** | CITALOPRAM | 5 mg, 10 mg | tablets |
| **6.** | **ESCITALOPRAM** | CIPRALEX | 5 mg, 10 mg,<br>15 mg, 20 mg | tablets |
| | | ESCITALOPRAM | | |

**RESULTS AND DISCUSSION**

In order to avoid a study based on a particular pharmaceutical product, we used the international common name instead of the commercial name of drugs.

*Table 2*

The amount of pharmaceuticals containing SSRI drugs issued during the years 2008-2013

| Item No. | International common name | Dose | 2008/ boxes | 2009/ boxes | 2010/ boxes | 2011/ boxes | 2012/ boxes | 2013/ boxes |
|---|---|---|---|---|---|---|---|---|
| **1.** | **FLUVOXAMINE** | 50 mg | 1 | 3 | 2 | 0 | 0 | 0 |
| | | 100 mg | 11 | 2 | 1 | 1 | 2 | 0 |
| **2.** | **FLUOXETINE** | 20 mg | 2 | 1 | 0 | 0 | 0 | 0 |
| **3.** | **PAROXETINE** | 20 mg | 55 | 53 | 57 | 49 | 89 | 45 |
| **4.** | **SERTRALINE** | 50 mg | 52 | 52 | 35 | 26 | 65 | 43 |
| | | 100 mg | 7 | 6 | 9 | 5 | 5 | 4 |
| **5.** | **CITALOPRAM** | 10 mg | 1 | 3 | 2 | 2 | 1 | 0 |
| **6.** | **ESCITALOPRAM** | 10 mg | 37 | 34 | 30 | 31 | 48 | 71 |

A previous study which followed the release rate of antidepressant drugs in the same pharmacy showed that the SSRI such as fluoxetine and fluvoxamine were among the most prescribed drugs for depression for the period 2005-2007 (Horvath T., Şerban G., 2009).

As shown in table 2 and figure 1, fluoxetine and fluvoxamine, the first SSRI used in the therapy of depression were less prescribed by doctors in the last years. There were not any fluoxetine prescriptions since 2010 and new drugs such as paroxetine and sertraline were prescribed more frequently.

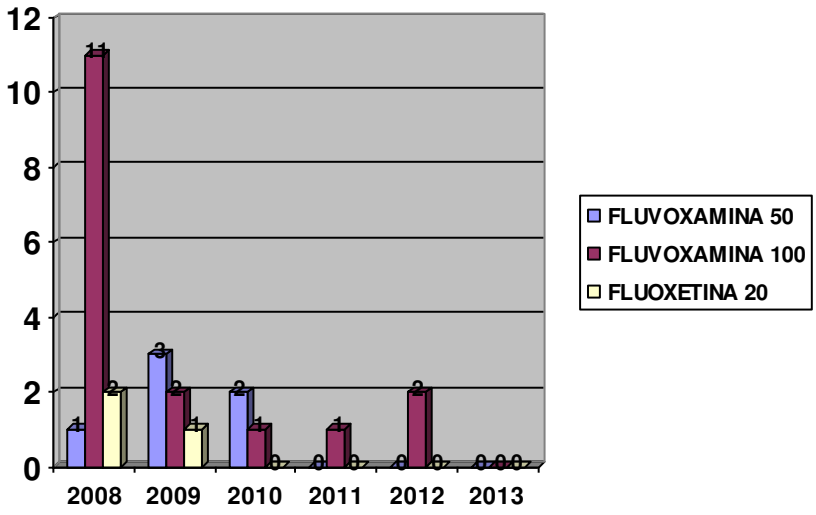


Fig. 1. The pharmaceuticals containing fluoxetine and fluvoxamine issued during the years 2008-2013

Even if the clinical studies have not been shown that paroxetine and sertraline are more effective than fluoxetine in treating major depression, these new drugs (paroxetine, sertraline) are characterized by selective antidepressant and anxiolytic effects, less side effects and higher tolerability and thus they are considered safer agents for the treatment of depression (Fava M. et al., 2000; Feiger A.D. et al., 2003). Treatment with fluoxetine is associated with a higher incidence of symptoms such as anxiety, agitation and insomnia. It may be noted the use of pharmaceuticals containing paroxetine 20 mg and sertraline 50 mg with a comparable frequency in 2008, 2009 and 2013 and some changes in their use in 2010-2011. Overall, there is higher use of paroxetine for the entire period analyzed.

Citalopram was introduced in the therapy of depression in USA in 1996 as the most selective SSRI with the lowest side effects. It is often used as the S-enantiomer, escitalopram, which is 27 times more active than the

R-enantiomer. Even if the level of citalopram (racemic and S-enantiomer) sold in pharmacy was below paroxetine and sertraline in 2008-2012, the advantages of this new product were noted and the use of pharmaceuticals containing escitalopram exceeded paroxetine and sertraline in 2013 (fig. 2).

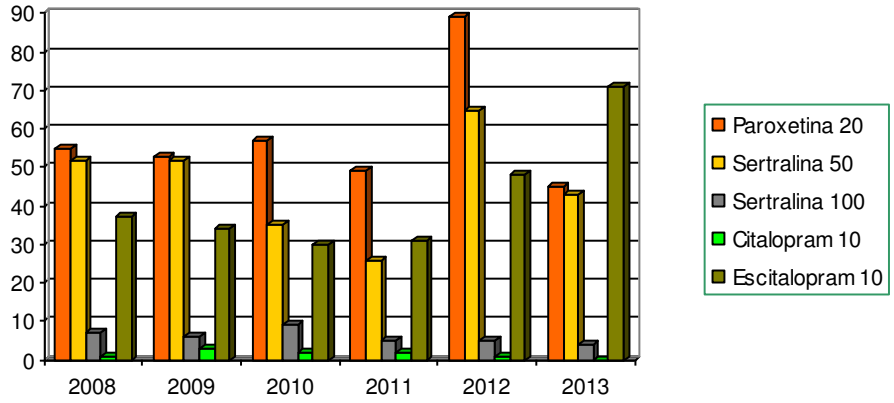


Fig. 2. The pharmaceuticals containing ISRS issued during the years 2008-2013

**CONCLUSIONS**

The study of six SSRI drugs: fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram and escitalopram showed that the old generation of SSRI, such as fluoxetine and fluvoxamine, are currently less prescribed by doctors. Even if the clinical studies have not been shown significant differences in efficacy of fluoxetine, paroxetine and sertraline, treatment with fluoxetine is associated with a higher incidence of side effects making the new generation of SSRI (paroxetine, sertraline, escitalopram and citalopram) to be considered safer and more effective agents for the treatment of depression.

Pharmacological studies classified escitalopram as a very active SSRI with low probability of side effects. Currently, the pharmaceuticals containing escitalopram are prescribed by doctors in Oradea and thus esitalopram surpassed paroxetine and sertraline' use in 2013.

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