GREGO, Mateusz, GREGO, Katarzyna, STOJAK, Łukasz, POPIELA, Dariusz, URBAŃSKA, Karina, KWIATKOWSKI, Filip, BACZEWSKI, Mateusz and CZYŻ, Witold. Differences between SSRI and SNRI in depression treatment. Quality in Sport. 2025;37:57038. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.37.57038
https://apcz.umk.pl/QS/article/view/57038

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 15.12.2024. Revised: 03.01.2025. Accepted: 03.01.2025 Published: 07.01.2025.

Differences between SSRI and SNRI in depression treatment

GREGO Mateusz, GREGO Katarzyna, STOJAK Łukasz, POPIELA Dariusz, URBAŃSKA Karina, KWIATKOWSKI Filip, BACZEWSKI Mateusz, CZYŻ Witold

Authors:

lek. Mateusz Grego, 10th Military Clinical Hospital with Polyclinic ul. Powstańców Warszawy 5, 85-681 Bydgoszcz, Poland

e-mail: mateuszgrego@onet.eu

ORCID: https://orcid.org/0009-0008-4079-2168

lek. Katarzyna Grego, 10th Military Clinical Hospital with Polyclinic ul. Powstańców Warszawy 5, 85-681 Bydgoszcz, Poland

e-mail: k.grego521@gmail.com

ORCID: https://orcid.org/0009-0005-7388-8885

lek. Łukasz Stojak, 10th Military Clinical Hospital with Polyclinic ul. Powstańców Warszawy 5, 85-681 Bydgoszcz, Department of Normal Anatomy, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, ul. Łukasiewicza 1, 85-821 Bydgoszcz, Poland

e-mail: luk.stojak@gmail.com

ORCID: https://orcid.org/0009-0008-9910-0445

lek. Dariusz Popiela, Military Institute of Aviation Medicine, Krasińskiego 54/56 Street, 01-755 Warsaw, Poland,
e-mail: dariusz.popiela1@gmail.com
ORCID: https://orcid.org/0009-0009-8648-2365

lek. Karina Urbańska, Central Teaching Hospital of the Medical University of Lodz located at ul. Pomorska 251, 92-213 Lodz, Poland
e-mail: karina.urbanska2@gmail.com
ORCID: https://orcid.org/0000-0002-1981-9281

lek. Filip Kwiatkowski, Military Institute of Aviation Medicine, Krasińskiego 54/56 Street, 01-755 Warsaw, Poland
e-mail: filip.karol.kwiatkowski@gmail.com
ORCID: https://orcid.org/0009-0006-3873-1265

lek. Mateusz Baczewski, 10th Military Clinical Hospital with Polyclinic ul. Powstańców Warszawy 5, 85-681 Bydgoszcz, Poland
e-mail: mateuszxbaczewski@gmail.com
ORCID: https://orcid.org/0009-0007-2857-5219

dr n. med. Witold Czyż, Central Teaching Hospital of the Medical University of Lodz located at ul. Pomorska 251, 92-213 Lodz, Poland
e-mail: witoldczyz@googlemail.com
ORCID: https://orcid.org/0009-0006-4442-9900

ABSTRACT

Introduction

Depressive disorders represent a significant health problem worldwide. With the development of pharmacotherapy, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have become preferred therapeutic options. SSRIs are the most commonly used first-line medications, but there are controversies regarding their efficacy compared to SNRIs.

Aim of Study

The aim of this study is to analyze the differences between two groups of drugs – SSRIs and SNRIs – in the treatment of depression and to try to identify on this basis a group of drugs that should be used as first-line drugs in the treatment of depression.

Materials and Methods

This review was conducted by searching scientific publications on PubMed and Google Scholar. The analysis took into account a number of studies comparing individual drugs from both groups of drugs, and then concisely summarized their conclusions.

Conclusion

The review of the literature and clinical trial results shows that no single universal group of medications can be identified for depression therapy. The choice should be tailored individually to each patient, taking into account the symptoms of their illness and the side effects of previously used medications. At the same time, the review highlighted the need for further research into the types of treatment for depressive disorders.

Keywords: depressive disorders, depression, SSRIs, SNRIs, mental health, depression treatment, serotonin, norepinephrine

Introduction

Depressive disorders are a serious illness widely prevalent around the globe, with a continuously increasing number of new cases. Consequently, the first antidepressants from the monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) groups emerged in the 1950s.(1, 2) However, these medications were characterized by numerous side effects, leading to their replacement by selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs).(1)

The medications most commonly utilized by primary care physicians in treating this condition are predominantly SSRIs.(3) This choice has been a topic of much controversy, as early hospital studies from 1987 highlighted the advantages of SNRIs over SSRIs.(4) Meanwhile, many other studies have presented two opposing views—one favoring SSRIs and the other indicating greater benefits of SNRIs in depression therapy.

This has created a platform for extensive academic discussion without a clear winner emerging, raising the question: Would changing the first-line medication for treating depression from SSRIs to SNRIs provide sufficient benefits to warrant such a switch?

Depression

Depression is the most common psychiatric disorder, affecting one in six individuals during their lifetime.(5) The accelerating pace of life, various social factors such as global unrest, armed conflicts, economic crises, and the recent COVID-19 pandemic contribute to a persistent increase in depression cases worldwide.(6) According to WHO projections, by 2030, depression will be the most prevalent disease globally.(7, 8)

It is essential to underscore the debilitating nature of this illness. It gradually wreaks havoc on the body, affecting multiple systems.

The most characteristic symptoms include low mood, anhedonia, apathy, and reduced psychomotor activity, which encompasses slowed thinking, hypomnesia, motor retardation or

inhibition, increased fatigue, anxiety, and cognitive impairments concerning oneself and one's environment.(9)

Symptoms also pertain to circadian rhythm disturbances—insomnia, excessive sleepiness, increased REM phase frequency, and decreased NREM phase duration—which further exacerbate the aforementioned symptoms.(10)

Depression can also manifest through less obvious symptoms that arise across various systems, creating a diverse array of somatic symptoms. Among these are gastrointestinal disturbances such as stomach pain, bloating, nausea, vomiting, heartburn, gastroesophageal reflux, constipation, and diarrhea.(7)

The mechanisms underlying depression are complex and multifactorial. To this day, numerous theories regarding its onset exist, necessitating further research aimed at fully elucidating this condition's etiology and developing optimal therapeutic agents. Currently accepted theories include neurotransmitter and receptor hypotheses, hypothalamic-pituitary-adrenal (HPA) axis hypothesis, cytokine hypothesis, neuroplasticity hypothesis, and systemic influence hypothesis.(8, 11)

The action of SNRIs, SSRIs, and TCAs

Drugs in the SNRI group, like TCAs, inhibit the reuptake of serotonin and norepinephrine; however, similar to SSRIs, they do not have clinically significant affinity for adrenergic, cholinergic, or histaminergic receptors. Consequently, they cause significantly fewer side effects, especially regarding cardiotoxic and cholinergic effects.(12) Additionally, they tend to act somewhat faster compared to TCAs.

Selective serotonin reuptake inhibitors (SSRIs), on the other hand, provide a highly selective blockade of the serotonin transporter responsible for the reuptake of this neurotransmitter from the synaptic cleft, having virtually no effect on norepinephrine transporters as seen with SNRIs. The therapeutic index of SSRIs is considerably broader than that of TCAs, and like SNRIs, they have a significantly narrower range of side effects.(11)

Discussion - Comparison of SSRIs and SNRIs

The comparison of SSRIs and SNRIs in the treatment of depression should be multifaceted and based on several key aspects such as efficacy, side effect profile, and onset of action.

Research shows that both drug groups are effective in treating depression. However, there are differences in their effectiveness. A substantial amount of literature and studies have compared specific medications from both groups.

As early as 1996, a comparison of these two drug groups was undertaken in a double-blind trial that evaluated the safety profile and efficacy of venlafaxine against fluoxetine. The results indicated that it is possible to equate these medications in both respects.(13)

Another double-blind, placebo-controlled trial from 1999 compared the efficacy and safety of extended-release venlafaxine (XR) and fluoxetine in outpatients with major depression and comorbid anxiety disorder, showing a significant advantage for the former. The response rate was 43% in the placebo group, 67% in the venlafaxine XR group, and 62% in the fluoxetine group. It is also important to note the discontinuation rates due to side effects: 5% for placebo, 10% for venlafaxine XR, and 7% for fluoxetine.(14)

A different double-blind trial conducted in the same year compared treatments for severe, treatment-resistant cases of depression using venlafaxine and paroxetine. The trial demonstrated that venlafaxine was more effective in treating such severe cases.(15)

A few years later, in 2001, a similar study compared the effects of venlafaxine (SNRI) and fluoxetine (SSRI) in patients suffering from depression with accompanying anxiety. A double-blind trial assessed the treatment outcomes of both medications. The final visits of patients participating in the study showed statistically significant efficacy of venlafaxine compared to fluoxetine, with overall treatment response rates of 75% for venlafaxine and 50.7% for fluoxetine. Sustained responses (lasting over two weeks) were observed at rates of 57.8% and 43.3%, respectively. At the final visit, remission rates were 59.4% for venlafaxine and 40.3% for fluoxetine.(16)

Between these studies, several others comparing the same medications were conducted, yielding comparable results to those presented. However, basing the analysis solely on one representative from each drug group would be a mistake.

Around the same time, in 1997, a study was conducted where patients suffering from depression with episodes of anger were treated with one of the following medications: norepinephrine reuptake inhibitor (desipramine), SSRI (sertraline or paroxetine), or SNRI (venlafaxine). The analysis conducted during this study indicated no differences in therapeutic effects.(17)

In 2000, a 24-week double-blind trial compared venlafaxine again, but this time with paroxetine. By week six, treatment response occurred in 55% of patients treated with venlafaxine and 29% with paroxetine. By week twelve, this result increased favorably for venlafaxine—59% to 31%. Notably, the rate of treatment discontinuation due to various reasons, including side effects, was reported at 39% for patients on venlafaxine and 26% for those on paroxetine.(18)

Two additional studies from 2004 and 2006 presented comparisons involving another SNRI—duloxetine—against paroxetine and placebo in double-blind trials. The results in both cases were very similar; significant improvements were observed in both duloxetine and paroxetine groups compared to the placebo group. However, duloxetine exhibited a higher efficacy rate than paroxetine. At the same time, the rate of treatment discontinuation due to side effects did not significantly differ between both drugs compared to placebo.(19, 20)

In 2004, another study utilized extended-release venlafaxine (XR), comparing it this time with escitalopram. Analyses indicated that treatment with both medications was equally effective; however, patients treated with escitalopram achieved sustained remission significantly faster than those treated with venlafaxine. Additionally, treatment with venlafaxine was associated with more frequent side effects such as nausea, constipation, increased sweating, and withdrawal symptoms after treatment cessation more often than with escitalopram.(21)

The same SNRI, namely extended-release venlafaxine (XR), was compared in 2005 and 2006 in two independent studies using a double-blind design against sertraline. Both studies demonstrated that treatment with either medication led to significant improvements in symptoms and, consequently, quality of life. The final therapeutic effects were comparable in both groups, although the percentage of individuals responding to treatment and achieving final remission was slightly higher with venlafaxine. According to the authors of the studies, this difference did not have a significant clinical impact. It is worth noting that the use of

sertraline may be associated with less severe withdrawal symptoms and a reduced risk of increased blood pressure.(22, 23)

The following year, in 2007, another study compared duloxetine with two SSRIs—fluoxetine and paroxetine. The remission rate for depression with all doses of duloxetine was 40.3% compared to 38.3% for the mentioned SSRIs. For patients with less severe depression, the remission rate was 46.5% for duloxetine and 51.7% for the two SSRIs. In both cases, the authors considered these differences statistically insignificant. The only exception was among patients suffering from more severe depression, where the remission rate was 35.9% for duloxetine and 28.6% for the two SSRIs. This difference was deemed statistically significant by the authors, which may indicate a greater efficacy of SNRIs in treating more severe forms of depression.(24)

In the same year, 2007, results from two independent double-blind studies comparing the effects of an SSRI (escitalopram) and an SNRI (duloxetine) were published, conducted over periods of 8 weeks and 8 months.(25, 26) In both the shorter and longer studies, the speed and efficacy of drug action were comparable, theoretically providing patients with similar therapeutic outcomes within the same timeframe.

A study comparing venlafaxine with one of the largest groups of SSRIs (fluoxetine, sertraline, paroxetine, fluvoxamine, and citalopram) was conducted a year later.(27) The double-blind trial using placebo showed that venlafaxine had superior efficacy in treating depression only compared to fluoxetine; no significant differences were found with other SSRIs.

The following year, a comparison was made between escitalopram—introduced into global treatment in the 21st century—and two leading SNRIs: duloxetine and venlafaxine. The analysis revealed better efficacy and tolerability for escitalopram compared to the SNRIs being compared. Additionally, the group of patients taking escitalopram had a significantly higher clinical response rate (73% vs. 44%) and remission rate (62% vs. 41%).(28)

A broad analysis of side effects among TCAs, SSRIs, and SNRIs(29) indicated that while side effects are less frequent and less severe than with TCAs, they are still present with both drug groups. There is a cardiovascular risk associated with both groups; SSRIs, particularly citalopram, are associated with a risk of QTc interval prolongation.(30) In contrast, SNRIs carry a risk of hypertension that is minimal with SSRIs.(31) Both SSRIs and SNRIs are

associated with dry mouth symptoms, however, this risk is significantly higher with SNRIs.(32) Gastrointestinal symptoms such as nausea, vomiting, diarrhea, or constipation are present in both groups but are reported more frequently with SNRIs, particularly venlafaxine.(13) Up to 80% of patients undergoing depression therapy report issues related to sexual dysfunction.(33) Studies have shown that highly selective serotonin antidepressants such as citalopram, fluoxetine, paroxetine, sertraline, and venlafaxine exhibit the highest rates of overall sexual dysfunction.(4, 34, 35)

An important consideration is also the treatment of additional symptoms often co-occurring with depression. Studies have shown that both groups have additional therapeutic possibilities; both have anti-inflammatory properties as well.(36) However, there is a lack of reports regarding the effectiveness of SSRIs in treating pain. Such reports are widely documented for SNRIs.(37)

Lastly, yet often overlooked aspect is the financial issue and broad availability of medications. An analysis considering drug prices, treatment for side effects, and long-term effectiveness conducted in Sweden shows that escitalopram is the most cost-effective option for treating depression in over 85% of cases compared to both venlafaxine and duloxetine.(38) It should be noted that the prices of these medications do not significantly differ from one another.

Conclusions

Both drug groups have a significant number of advantages that can be utilized in everyday medical practice. Selective serotonin and norepinephrine reuptake inhibitors (SNRIs) demonstrate therapeutic potentials similar to those of selective serotonin reuptake inhibitors (SSRIs). However, there are some differences in their effectiveness. SNRIs may have an advantage over certain SSRIs as a first-line treatment for mild to moderate depression, although some SSRIs, including escitalopram, may prove to be more effective. Many studies have shown that higher rates of therapeutic efficacy in treating severe and treatment-resistant depression can be achieved with SNRIs.

SSRIs, as demonstrated in numerous studies, are generally better tolerated than SNRIs, making them the preferred choice in depression therapy. Research has indicated that patients taking SNRIs often report more side effects compared to those on SSRIs, which could lead to

a higher rate of treatment discontinuation. Nevertheless, SNRIs may be more beneficial for patients with comorbid anxiety disorders or chronic pain conditions. This does not imply that SSRIs are entirely free from side effects, such as sexual dysfunction.

Additionally, studies show that the onset of action is comparable for both drug groups, allowing patients to expect similar therapeutic effects within a similar timeframe. Cost remains a separate issue, with both options currently being optimally accessible for patients with average incomes.

In summary, the choice between SSRIs and SNRIs should be tailored to the individual needs of the patient, considering the side effect profiles. Therefore, it is not possible to unequivocally identify a superior drug group. This should serve as guidance for primary care physicians to thoroughly analyze the symptoms of depression presented by each patient, which can vary widely. Only based on this assessment, taking symptoms into account, should both the efficacy of the medication and its side effect profile be considered.

At the same time, attention should be drawn to the need for further research on optimizing depression therapy.

Author's contributions:

Conceptualization, Mateusz Grego, Katarzyna Grego, and Łukasz Stojak; Methodology, Dariusz Popiela and Karina Urbańska; software, Mateusz Baczewski and Filip Kwiatkowski; check, Mateusz Grego, Katarzyna Grego and Łukasz Stojak; formal analysis, Witold Czyż; investigation, Karina Urbańska; resources, Dariusz Popiela; data curation, Witold Czyż; writing - rough preparation, Mateusz Grego; writing - review and editing, Katarzyna Grego; visualization, Łukasz Stojak; supervision, Mateusz Grego; project administration, Dariusz Popiela and Filip Kwiatkowski; receiving funding, not-applicable.

All authors have read and agreed with the published version of the manuscript.

Funding Statement:

Not applicable.

Institutional Review Board Statement:

Not applicable.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

Not applicable.

Acknowledgments:

Not applicable.

Conflict of interest statement:

Authors have declared no conflict of interests.

References:

1. Ferguson JM. SSRI Antidepressant Medications: Adverse Effects and Tolerability. Prim Care Companion J Clin Psychiatry. 2001;3(1):22-7.
2. Brigitta B. Pathophysiology of depression and mechanisms of treatment. Dialogues Clin Neurosci. 2002;4(1):7-20.
3. Montes JM, Ferrando L, Saiz-Ruiz J. Remission in major depression with two antidepressant mechanisms: results from a naturalistic study. J Affect Disord. 2004;79(1-3):229-34.
4. Thase ME. Are SNRIs more effective than SSRIs? A review of the current state of the controversy. Psychopharmacol Bull. 2008;41(2):58-85.
5. Liu Q, He H, Yang J, Feng X, Zhao F, Lyu J. Changes in the global burden of depression from 1990 to 2017: Findings from the Global Burden of Disease study. J Psychiatr Res. 2020;126:134-40.
6. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet. 2021;398(10312):1700-12.
7. Yan M, Chen J, Liu F, Li H, Huang R, Tang Y, et al. Disrupted Regional Homogeneity in Major Depressive Disorder With Gastrointestinal Symptoms at Rest. Front Psychiatry. 2021;12:636820.
8. Cui L, Li S, Wang S, Wu X, Liu Y, Yu W, et al. Major depressive disorder: hypothesis, mechanism, prevention and treatment. Signal Transduct Target Ther. 2024;9(1):30.

9. Otte C, Gold SM, Penninx BW, Pariante CM, Etkin A, Fava M, et al. Major depressive disorder. Nat Rev Dis Primers. 2016;2:16065.
10. Murphy MJ, Peterson MJ. Sleep Disturbances in Depression. Sleep Med Clin. 2015;10(1):17-23.
11. Tran PV, Bymaster FP, McNamara RK, Potter WZ. Dual monoamine modulation for improved treatment of major depressive disorder. J Clin Psychopharmacol. 2003;23(1):78-86.
12. Wasielewska M. Comparison of the mechanisms of action of antidepressants and their side effects. Journal of Education, Health and Sport. 2020;10:260.
13. Dierick M, Ravizza L, Realini R, Martin A. A double-blind comparison of venlafaxine and fluoxetine for treatment of major depression in outpatients. Prog Neuropsychopharmacol Biol Psychiatry. 1996;20(1):57-71.
14. Silverstone PH, Ravindran A. Once-daily venlafaxine extended release (XR) compared with fluoxetine in outpatients with depression and anxiety. Venlafaxine XR 360 Study Group. J Clin Psychiatry. 1999;60(1):22-8.
15. Poirier MF, Boyer P. Venlafaxine and paroxetine in treatment-resistant depression. Double-blind, randomised comparison. Br J Psychiatry. 1999;175:12-6.
16. De Nayer A, Geerts S, Ruelens L, Schittecatte M, De Bleeker E, Van Eeckhoutte I, et al. Venlafaxine compared with fluoxetine in outpatients with depression and concomitant anxiety. Int J Neuropsychopharmacol. 2002;5(2):115-20.
17. Bagby RM, Kennedy SH, Schuller DR, Dickens SE, Minifie CE, Levitt A, et al. Differential pharmacological treatment response in high angry hostile and low angry hostile depressed patients: a retrospective analysis. J Affect Disord. 1997;45(3):161-6.
18. Ballús C, Quiros G, De Flores T, de la Torre J, Palao D, Rojo L, et al. The efficacy and tolerability of venlafaxine and paroxetine in outpatients with depressive disorder or dysthymia. Int Clin Psychopharmacol. 2000;15(1):43-8.
19. Perahia DG, Wang F, Mallinckrodt CH, Walker DJ, Detke MJ. Duloxetine in the treatment of major depressive disorder: a placebo- and paroxetine-controlled trial. Eur Psychiatry. 2006;21(6):367-78.
20. Detke MJ, Wiltse CG, Mallinckrodt CH, McNamara RK, Demitrack MA, Bitter I. Duloxetine in the acute and long-term treatment of major depressive disorder: a placebo- and paroxetine-controlled trial. Eur Neuropsychopharmacol. 2004;14(6):457-70.
21. Montgomery SA, Huusom AK, Bothmer J. A randomised study comparing escitalopram with venlafaxine XR in primary care patients with major depressive disorder. Neuropsychobiology. 2004;50(1):57-64.
22. Sir A, D'Souza RF, Uguz S, George T, Vahip S, Hopwood M, et al. Randomized trial of sertraline versus venlafaxine XR in major depression: efficacy and discontinuation symptoms. J Clin Psychiatry. 2005;66(10):1312-20.
23. Shelton RC, Haman KL, Rapaport MH, Kiev A, Smith WT, Hirschfeld RM, et al. A randomized, double-blind, active-control study of sertraline versus venlafaxine XR in major depressive disorder. J Clin Psychiatry. 2006;67(11):1674-81.
24. Thase ME, Pritchett YL, Ossanna MJ, Swindle RW, Xu J, Detke MJ. Efficacy of duloxetine and selective serotonin reuptake inhibitors: comparisons as assessed by remission rates in patients with major depressive disorder. J Clin Psychopharmacol. 2007;27(6):672-6.
25. Khan A, Bose A, Alexopoulos GS, Gommoll C, Li D, Gandhi C. Double-blind comparison of escitalopram and duloxetine in the acute treatment of major depressive disorder. Clin Drug Investig. 2007;27(7):481-92.
26. Pigott TA, Prakash A, Arnold LM, Aaronson ST, Mallinckrodt CH, Wohlreich MM. Duloxetine versus escitalopram and placebo: an 8-month, double-blind trial in patients with major depressive disorder. Curr Med Res Opin. 2007;23(6):1303-18.
27. Nemeroff CB, Entsuah R, Benattia I, Demitrack M, Sloan DM, Thase ME. Comprehensive analysis of remission (COMPARE) with venlafaxine versus SSRIs. Biol Psychiatry. 2008;63(4):424-34.
28. Lam RW, Lönn SL, Despiégel N. Escitalopram versus serotonin noradrenaline reuptake inhibitors as second step treatment for patients with major depressive disorder: a pooled analysis. Int Clin Psychopharmacol. 2010;25(4):199-203.
29. Wang SM, Han C, Bahk WM, Lee SJ, Patkar AA, Masand PS, et al. Addressing the Side Effects of Contemporary Antidepressant Drugs: A Comprehensive Review. Chonnam Med J. 2018;54(2):101-12.
30. Rao P, Kowey PR. Drug-induced long-QT syndrome and torsade de pointes: an underrated problem? Europace. 16. England2014. p. 4-5.
31. Mago R, Tripathi N, Andrade C. Cardiovascular adverse effects of newer antidepressants. Expert Rev Neurother. 2014;14(5):539-51.
32. Cappetta K, Beyer C, Johnson JA, Bloch MH. Meta-analysis: Risk of dry mouth with second generation antidepressants. Prog Neuropsychopharmacol Biol Psychiatry. 2018;84(Pt A):282-93.

33. Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. Ann Intern Med. 2011;155(11):772-85.
34. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. J Clin Psychopharmacol. 2009;29(3):259-66.
35. Koenig AM, Thase ME. First-line pharmacotherapies for depression - what is the best choice? Pol Arch Med Wewn. 2009;119(7-8):478-86.
36. Dionisie V, Filip GA, Manea MC, Manea M, Riga S. The anti-inflammatory role of SSRI and SNRI in the treatment of depression: a review of human and rodent research studies. Inflammopharmacology. 2021;29(1):75-90.
37. Wohlreich MM, Watkin JG. The Role of Duloxetine in the Treatment of Depression and Associated Painful Physical Symptoms. Prim Care Companion J Clin Psychiatry. 2003;5(6):286-7.
38. Nordström G, Despiegel N, Marteau F, Danchenko N, Maman K. Cost effectiveness of escitalopram versus SNRIs in second-step treatment of major depressive disorder in Sweden. J Med Econ. 2010;13(3):516-26.