International Journal of Scholarly Research in
Multidisciplinary Studies
Journal homepage: https://srrjournals.com/ijsrms/
ISSN: 2961-3329 (Online)

(REVIEW ARTICLE)

Check for updates

A comparative overview of SSRI-sertraline and SNRI-desvenlafaxine

Sree Sudha T Y [1,*] and Hemasri Velmurugan [2]

[1] *Department of Pharmacology, All India Institute of Medical Sciences, Deoghar, Jharkhand, India.*
[2] *Department of Pharmacology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India.*

International Journal of Scholarly Research in Multidisciplinary Studies, 2023, 03(01), 016–021

Publication history: Received on 27 May 2023; revised on 04 July 2023; accepted on 07 July 2023

Article DOI: https://doi.org/10.56781/ijsrms.2023.3.1.0072

Abstract

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. The common features of all the depressive disorders are sadness, emptiness, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function. Depression is commonly treated in primary care, and SSRI drugs are frequently used as the first line of treatment. Selective Serotonin Reuptake Inhibitors (SSRIs) have the advantage of the ease of dosing and low toxicity in overdose. They are also the first-line medications for late-onset depression. Selective Serotonin and Norepinephrine Reuptake Inhibitors **(**SNRIs), which include venlafaxine, desvenlafaxine, duloxetine, and levomilnacipran can be used as first-line agents, particularly in patients with significant fatigue or pain syndromes associated with the episode of depression. SNRIs also have an important role as second-line agents in patients who have not responded to SSRIs. The pharmacokinetics, pharmacodynamics, uses, side effects, and contraindications of desvenlafaxine, an SNRI, and sertraline, an SSRI are compared in this article.

Keywords: Depression; Desvenlafaxine; Sertraline; Efficacy; Safety; Selective serotonin and norepinephrine reuptake inhibitors; Selective serotonin reuptake inhibitors

1 Introduction

Depression plays a major role in the burden of diseases, and it is expected to be the main cause of disability in high-income nations by 2030[1]. A major depressive episode (DSM-IV) is defined as a depressed or dysphoric mood that is prominent and generally persistent (almost every day for at least 2 weeks) and contains at least 5 of the following 9 symptoms: Depressed mental state, decreased interest in a regular routine, substantial changes in weight and/or appetite, insomnia or hypersomnia, irritability or retardation, tiredness, feelings of guilt or unworthiness, slowed thinking or loss of concentration, or suicidal behaviour or suicidal ideation are all signs of depression[2]. The pathogenesis of major depressive illness is not completely understood. The current research evidence suggests that the affective symptoms are caused by a complicated relationship between neurotransmitter supply, receptor modulation, and sensitivity. Clinical and preclinical studies point to a disruption in serotonin (5-HT) function in the central nervous system as a key cause. Norepinephrine (NE), dopamine (DA), glutamate, and brain-derived neurotrophic factor (BDNF) are among the other neurotransmitters implicated. Sertraline (ZOLOFT) is a popular antidepressant prescription known as a selective serotonin reuptake inhibitor (SSRI) which has been on the market since 1991[3]. Sertraline medication may be required for several weeks before therapeutic results are evident. Desvenlafaxine (PRISTIQ), a selective serotonin and norepinephrine reuptake inhibitor (SNRI), was licensed by the FDA in 2008 to treat major depressive disorder[2]. Its effectiveness was demonstrated in four eight-week placebo-controlled studies involving outpatients with the major depressive disorder who met DSM-IV criteria. The purpose of this review is to compare the pharmacokinetics, pharmacodynamics, uses, side effects, and contraindications of sertraline with desvenlafaxine.

* Corresponding author: Sree Sudha T Y

2 Pharmacodynamics

Sertraline inhibits serotonin (5-HT) reuptake at the presynaptic neuronal membrane, resulting in a higher synaptic concentration of serotonin in the CNS. These alterations are thought to be responsible for sertraline's antidepressant activity and therapeutic benefits in obsessive-compulsive disorder and other anxiety disorders[3-4]. It has been demonstrated in clinical investigations to improve cognition in depressed patients[5]. Because it does not exert considerable anticholinergic, antihistamine, or adrenergic blocking activity, it has fewer sedative, anticholinergic, and cardiovascular effects than tricyclic antidepressants[6]. In vitro, has little affinity for GABA, dopaminergic, serotonergic and benzodiazepine receptors. It has just a minor inhibitory effect on norepinephrine and dopamine absorption in neurons and does not affect the monoamine oxidase enzyme[3]. In animal studies, sertraline treatment causes down-regulation of norepinephrine receptors in the brain[3]. For reasons that are not fully understood and are now under investigation, the commencement of the action and favourable benefits are usually noted after 4-6 weeks[7-8]. Desvenlafaxine (O-desmethylvenlafaxine) the primary active metabolite of venlafaxine inhibits serotonin transporters with ten times the affinity of norepinephrine transporters and the least affinity of dopamine transporters[9]. Norepinephrine is also involved in sleep, attention, memory, and mood management in everyday life. Desvenlafaxine has extra benefits and helps to concentrate as well as alleviate depression by suppressing norepinephrine. It does not appear to block calcium, chloride, potassium, or sodium ion channels, and it also does not appear to inhibit monoamine oxidase [9]. In vitro, desvenlafaxine has essentially minimal affinity for muscarinic, cholinergic, H1-histaminergic, and alpha1-adrenergic receptors and was also demonstrated to have no action against the cardiac potassium channel, hERG[9-10]. Desvenlafaxine seems to have a simple metabolism, a reduced probability of drug-drug interactions and does not need to be titrated extensively to obtain a therapeutic dose when compared to other antidepressants[2].

3 Pharmacokinetics

The pharmacokinetic characteristics of sertraline and desvenlafaxine were compared in table 1

Table 1 The pharmacokinetic properties of sertraline and desvenlafaxine

Properties	Sertraline	Desvenlafaxine
Absorption	Bioavailability is expected to be greater than 44%. Cmax and AUC are slightly increased when given with meals. 3-11	Bioavailability - approximately 80% Unaffected by food 9,14,15
Volume of distribution	>20L/kg. 5	3.4L/kg 2
Protein binding	98%-99%. 3,12	30% 2,9
Metabolism	N-demethylation occurs in the liver, resulting in N-desmethylsertraline, which has significantly less pharmacological efficacy than sertraline11. N-hydroxylation, oxidative deamination, and glucuronidation are also involved3. Its degradation is mostly catalyzed by CYP3A4 and CYP2B6, with CYP2C19 and CYP2D6 accounting for minor activity 5,13.	It is primarily metabolized by conjugation, although it also undergoes some oxidative N-demethylation via CYP3A4. Its degradation is not mediated by CYP2D62.
Half-life	Approximately 26 hours3,5.	Approximately 11.1 hours 2
Route of elimination	Extensively metabolized, unaltered drugs are eliminated in the urine and feces 5.	In the urine, 45% of the dosage remains unaltered, 19% is eliminated as a glucuronide metabolite, and 5% is excreted as N,O-didesmethylvenlafaxine 2.

4 Indications

Adults with major depressive disorder can use desvenlafaxine to help them feel better. Sertraline is used to treat depression, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), panic disorder (PD),

premenstrual dysphoric disorder (PMDD), and social anxiety disorder (SAD) [3]. In some studies, sertraline outperformed desvenlafaxine in terms of clinical outcomes in patients with serious depression.[16]

5 Available formulations

Sertraline hydrochloride is available in 25 mg, 50 mg, and 100 mg tablet form. Also, it is available in a 20 mg/ml oral solution [3]. The available product ingredients are desvenlafaxine fumarate, desvenlafaxine fumarate monohydrate, desvenlafaxine hydrochloride, and desvenlafaxine succinate. Each tablet contains 76 mg or 152 mg of desvenlafaxine succinate, which is comparable to 50 mg or 100 mg of desvenlafaxine, respectively [2].

6 Dosing

6.1 Sertraline

In MDD, OCD, PD, PTSD, and SAD, titrate in 25-50 mg per day increments once weekly if the initial dose is insufficient. In mild cases of hepatic impairment, the suggested starting and maximum dosage is half of the prescribed dosage, and not recommended in moderate and severe cases. Reduce the dose gradually while stopping. Make sure it's diluted before using the oral solution. Table 2 shows the suggested sertraline doses for various disorders [3].

Table 2 Recommended sertraline doses for various disorders

DISORDERS	Start Dose	Maximum Dose
Major depressive disorder (MDD)	50 mg per day	200 mg per day
Obsessive-compulsive disorder (OCD)	6-12 years age - 25 mg per day ≥ 13 years age - 50 mg per day	200 mg per day
Panic disorder (PD), Post-traumatic stress disorder (PTSD), Social anxiety disorder (SAD)	25 mg per day	200 mg per day
Premenstrual dysphoric disorder (PMDD) - Continuous dosing	50 mg per day	150 mg per day
Premenstrual dysphoric disorder (PMDD) - Intermittent dosing	50 mg per day during the luteal phase only	100 mg per day during luteal phase only

6.2 Desvenlafaxine

The drug is to be taken orally 50 mg once a day, with or without food is the suggested dose. Dosages of 50-400 mg/day were found to be effective in clinical investigations, while there was no further benefit at doses larger than 50 mg/day, and side events and discontinuations were more common at higher doses. To avoid withdrawal effects, a stepwise dose reduction is advised while ending therapy [2].

7 Drug interactions

Both desvenlafaxine and sertraline interact with other drugs in the same way. They may interact with antiplatelet medications like aspirin and clopidogrel, as well as NSAIDs like naproxen and anticoagulants like dabigatran. MAO inhibitors including isocarboxazid, linezolid, metaxalone, methylene blue, moclobemide, phenelzine, procarbazine, rasagiline, safinamide, selegiline, and tranylcypromine should be avoided since they might induce a dangerous and perhaps fatal drug interaction. It is recommended to avoid most MAO inhibitors for at least two weeks before to and following treatment with this drug. The risk of serotonin syndrome is increased by additional drugs that raise serotonin, including ecstasy, St. John's wort, certain antidepressants (including other SNRIs like duloxetine, SSRIs like fluoxetine), and tryptophan. Alcohol, marijuana, antihistamines, sleep or anxiety medications including alprazolam, diazepam, zolpidem, muscle relaxants, and opioid pain medicines like codeine and hydrocodone can all cause drowsiness. This medicine may interfere with some lab tests, such as amphetamine urine testing, resulting in erroneous test findings. As a result, taking both desvenlafaxine and sertraline at the same time is not recommended. Also, Venlafaxine and desvenlafaxine are quite similar. When taking desvenlafaxine, avoid taking any drugs that contain venlafaxine. [2,3,17,18]

8 Adverse drug reactions

Common side effects are Nausea, dizziness, drowsiness, dry mouth, loss of appetite, increased sweating, gastrointestinal symptoms, or trouble sleeping may occur. Prolonged usage can cause easy bruising, decreased interest in sex, changes in sexual ability, muscle cramps, tremors, and unusual weight loss. Fast heartbeat, fainting, black stools, vomit that looks like coffee grounds, eye discomfort, enlarged pupils, and impaired vision are all major side effects. Tachycardia, hallucinations, lack of coordination, severe dizziness, severe nausea, vomiting, diarrhoea, twitching muscles, inexplicable fever, and unusual restlessness are all symptoms of serotonin syndrome. It is uncommon for this drug to cause a severe allergic response. Males may occasionally experience a painful or protracted erection that lasts 4 hours or more. Desvenlafaxine also raises norepinephrine levels, which aids concentration and reduces depression. Higher norepinephrine levels might generate sensations of euphoria. They can, however, produce panic attacks, elevated blood pressure, and hyperactive behaviour. Because of these side effects, desvenlafaxine may not be appropriate for patients with certain heart conditions, a history of panic attacks, or hyperactivity disorders.[2,3,17,18]

9 Contraindications/ precautions

- Abnormal Bleeding - Concomitant use of aspirin, NSAIDs, other antiplatelet drugs, and anticoagulants may increase this risk.
- Concomitant use of monoamine oxidase inhibitors (MAOIs) or use within 14 days of stopping MAOIs
- Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions
- Activation of Mania/ Hypomania - patients with bipolar/ manic-depressive Disorder
- Angle Closure/ narrow Glaucoma
- Seizure disorder
- Patients with suicidal thoughts
- Discontinuation syndrome - Taper the dose when possible and monitor
- Hyponatremia
- Hypersensitivity to sertraline or excipients
- Avoid alcoholic beverages [2-3]

Table 3 Drug specific Contraindications

Desvenlafaxine	Sertraline
Venlafaxine should not be used concomitantly with desvenlafaxine Hypertension Cardiovascular/ Cerebrovascular Disease Cholesterol and Triglyceride Elevation Interstitial Lung Disease and Eosinophilic Pneumonia	QT prolongation and ventricular arrhythmias when taken with pimozide The liquid forms alcohol. Concomitant use of disulfiram can cause a serious reaction disulfiram-alcohol response.

10 Special population

10.1 Renal impairment

Renal impairment does not appear to alter sertraline exposure. So, dose change is not required. But, renal Impairment reduces the clearance of desvenlafaxine. The suggested dose of desvenlafaxine for moderate renal impairment is 50 mg per day and for severe and end-stage renal disease (ESRD), 50 mg every other day. But, the dose should not be increased in individuals with moderate or severe renal impairment or ESRD [2-3].

10.2 Hepatic impairment

Due to increased exposure in this patient population, the recommended dose of sertraline in individuals with mild hepatic impairment is half the usual dosage. Sertraline is not recommended for moderate or severe hepatic impairment

since it is extensively metabolized, and the effects on moderate and severe hepatic impairment have not been studied. In the case of hepatic impairment, dose-escalation above 100 mg/day is not recommended for desvenlafaxine [2-3].

10.3 Pregnancy and lactation

Medication should be taken only when necessary, during pregnancy and lactation. It has the potential to harm an unborn child. Also, the risk of chronic pulmonary hypertension and withdrawal in the infant may be increased in babies delivered to mothers who took this medication during the last three months of their pregnancy. The medication, which passes into breast milk, may harm a breastfeeding baby [2-3].

10.4 Elderly

Maybe more sensitive to the drug's negative effects, including dizziness when standing, bleeding, or lack of coordination. Additionally, elderly adults are more prone to hyponatremia due to a salt imbalance, especially if they use diuretics. Desvenlafaxine in adults over the age of 65 had an increased risk of orthostatic hypotension. So, when calculating the dose for them, the possibility of impaired renal clearance of desvenlafaxine should be considered [2-3].

10.5 Children

May be more susceptible to the drug's side effects, such as loss of appetite and weight loss. The safety and effectiveness of sertraline in pediatric patients other than those with OCD have not been established [2-3].

11 Conclusion

There is no solid proof that one set of medications is always better than the other for all people. A randomized comparative clinical trial is recommended to demonstrate these drugs' superior efficacy and tolerability. Both sertraline and desvenlafaxine can help with a variety of mood disorders, but they take a while to work. When used under the guidance of a doctor, these medications can significantly improve a person's quality of life.

Compliance with ethical standards

Disclosure of conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

[1] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006, 3: e442.

[2] FDA Drug Approval Package for Desvenlafaxine. Last Accessed on April 30, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021992s030lbl.pdf

[3] FDA Approved Drug Products. Zoloft (sertraline hydrochloride). Last Accessed on April 30, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/019839S74S86S87_20990S35S44S45lbl.pdf

[4] Pittenger C, Bloch MH, William k. Glutamate abnormalities in obsessive compulsive disorder: neurobiology, pathophysiology, and treatment. PharmacolTher. 2011, 132(3): 314-32.

[5] Murdoch D, McTavish D. Sertraline. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in depression and obsessive-compulsive disorder. Drugs. 1992, 44(4):604-24.

[6] Shelton RC. The role of sertraline in the management of depression. Clin Ther. 1994, 16(5):768-82.

[7] Erb SJ, Schappi JM, Rasenick MM. Antidepressants Accumulate in Lipid Rafts Independent of Monoamine Transporters to Modulate Redistribution of the G Protein, Galphas. J Biol Chem. 2016, 291(38):19725-19733.

[8] Sertraline. Last Accessed on April 30, 2022. https://www.psychologytoday.com/ca/blog/the-superhuman-mind/201702/number-one-reason-ssris-take-four-six-weeks-work

[9] Liebowitz MR, Tourian KA. Efficacy, safety, and tolerability of Desvenlafaxine 50 mg/d for the treatment of major depressive disorder:a systematic review of clinical trials. Prim Care Companion J Clin Psychiatry. 2010, 12(3).

[10] Jasiak NM, Bostwick JR: Risk of QT/QTc prolongation among newer non-SSRI antidepressants. Ann Pharmacother. 2014 Dec, 48(12):1620-8.

[11] DeVane CL, Liston HL, Markowitz JS. Clinical pharmacokinetics of sertraline. Clin Pharmacokinet. 2002, 41(15):1247-66.

[12] Kristensen JH, Ilett KF, Dusci LJ, et al. Distribution and excretion of sertraline and N-desmethylsertraline in human milk. Br J Clin Pharmacol. 1998, 45(5):453-7.

[13] Sertraline. Last Accessed on April 30, 2022. https://www.pdr.net/drug-summary/Zoloft-sertraline-hydrochloride-474.3608

[14] Pae CU. Desvenlafaxine in the treatment of major depressive disorder. Expert Opin Pharmacother. 2011, 12(18):2923-8.

[15] Reddy S, Kane C, Pitrosky B, et L. Clinical utility of desvenlafaxine 50 mg/d for treating MDD: a review of two randomized placebo-controlled trials for the practicing physician. Curr Med Res Opin. 2010, 26(1):139-50.

[16] Ch S, Sudha S, Reddy CG, et al. A Comparative Study on Safety and Efficacy of Desvenlafaxine Versus Sertraline in Depression. Cureus. 2022, 14(2):e22717.

[17] Sertraline drug interaction. Last Accessed on April 30, 2022. https://www.webmd.com/drugs/2/drug-1/sertraline-oral/details#:~:text=Some%20products%20that%20may%20interact,such%20as%20warfarin%2Fdabigatran).

[18] Desvenlafaxine drug interaction. Last Accessed on April 30, 2022. https://www.webmd.com/drugs/2/drug-163933/desvenlafaxine-oral/details#:~:text=Some%20products%20that%20may%20interact,when%20used%20with%20this%20medication.