A Review on the prevalence of Depression and the effect of SSRIs on Depression.

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ABSTRACT

One of the main causes of disease in the globe is depression. Depressive disorder has a lifetime incidence, a young age of onset, a chronicity and role impairment, according to epidemiological studies. These Research have expanded our knowledge of how depressiondevelops over time, including remission, recovery, relapse and reoccurrence. Beginning with brief historical overview, its classification and a synthesis of the most recent data onprevalence and course, the review analysis the literature on major depression. With rareexpectations, girls are more likely than male to experience depressive disorder, with symptoms starting around mid-adolescence and lasting throughout adulthood. Accordingto epidemiological studies women (21.3%) have a much higher lifetime prevalence of Major Depressive Disorder (MDD) than men (12.7%). This ratio has been studied acrossnumerous nations and ethnicities.

Mood and Anxiety Disorders are commonly treated with Selective Serotonin Reuptake Inhibitors (SSRIs). There are description of the indication, pharmacological properties and dose administration because general medical settings treat more patients with SSRIs than mental ones. Despite having improved overall safety and tolerability than previous antidepressants, selective reuptake inhibitors have a high incidence and a variety of sideeffects than those seen in clinical trials.

Keywords: Depression, SSRIs, Fluoxetine, Anxiety

INTRODUCTION

A mental illness called depression results in enduring emotions of melancholy, emptiness, and lack of joy. It is distinct from the mood swings that people typically encounter on a dailybasis. Depression can be sparked by major life events such a bereavement or the loss of a job,according to Trusted Source. But depression is different from the unfavorable emotions someone would have after a trying life event. Depression frequently lasts despite a change in circumstances and results in sensations that are strong, persistent, and out of proportion to a person's situation. The symptoms of depression can include:

- a depressed mood
- reduced interest or pleasure in activities that a person previously enjoyed
- a loss of sexual desire
- changes in appetite
- unintentional weight loss or gain
- sleeping too much or too little
- agitation, restlessness, and pacing up and down
- slowed movement and speech
- fatigue or loss of energy
- feelings of worthlessness or guilt
- difficulty thinking, concentrating, or making decisions

- recurrent thoughts of death or suicide, or an attempt at suicide [1]

Among adults, depression is one of the mental diseases with the highest prevalence of diagnosis. Not only adults experience depression, but 2% of school aged children and 5% of teenagers do as well, and most of these causes go unreported. The most frequent cause of people to visit psychiatrist is depression, despite the fact that the general public believes that all psychiatric issues are depression. The myth about depression is what is typically observedin patient. Given the high price that depression exacts, its prevalence is a cause of concern.

Along with having a negative economic impact, it also has a negative social impact andcauses a great deal of individual and interpersonal misery.[2]

One of the most common and harmful types of psychopathologies is Major Depressive Disorder. In fact, depression continues to be the leading cause of disability worldwide (WHO,2017). According for nearly half of disability adjusted life years. Worldwide, Depression is a prevalent and significant cause of disease and mortality. Antidepressant arefrequently used to treat depression; however, some people may prefer alternative strategieslike exercise.[2]

CLASSIFICATION: Like many other illnesses, depressive illness can take manydistinct forms.

1. Major depression is characterized by a variety of symptoms that make it difficult for aperson to work, sleep, eat, and engage in once-pleasurable activities. These incapacitating bouts of despair can happen just once, twice, or multiple times throughout a lifetime.
2. Dysthymia, a less severe form of depression, is characterized by long-lasting, persistent symptoms that do not incapacitate you but prevent you from operating at"full steam" or from feeling happy. Major depressive episodes are occasionally experienced by people with dysthymia.
3. Bipolar disorder and manic-depressive disease are not nearly as common as other types of depression. Cycles of mania or exhilaration and despair are involved. The moodswings can be abrupt and dramatic at times, but most of the time they are gradual. Any or all of the other symptoms of a depressive illness may be present when one is in the depression cycle. Any or all of the symptoms described under "mania" may be present during the manic cycle. Mania frequently has an embarrassing and problematic impact on thinking, judgement, and social behavior.[3]

Major depressive disorder is defined by the Diagnostic and statistical manual of Mental disorder-fourth edition (DSM-IV-TR). (American Psychiatric Association {ADA},2000) asthe presence of a specific no. of symptoms that last for a specific amount of time. The symptoms are either those of a low mood or a loss of interest or pleasure. Additionally, the DSM-IV-TR(APA,2000) lists minimum five criteria must be met for a min of 2 weeks.[2]

PREVALENCE OF DEPRESSION

In terms of Prevalence, misery, dysfunction, morbidity and economic cost, depression is an illness of substantial public health significance. Women experience depression more frequently than males. According to the global burden of disease report, unipolar depressive episodes had a point prevalence of 1.9% for men and 3.2% for females and a 1year of prevalence of 5.8% for males and 9.5% for females. If demographic and epidemiological trends continue, depression is predicted to account for 5.7% of all illness burden by 2020 andrank as the 2nd biggest cause of years lived with a disability adjusted for age.[4]

According to rural UP epidemiological study, neurotic depression was the most prevalent psychiatric morbidity, followed by manic depressive psychosis depression and anxiety state. Geriatric patient had higher rates of psychiatric morbidity (43.32%) than non-geriatric patient(4.66%). People with social economic and educational disadvantage had a higher rate of psychiatric illness. According to recent community-based studies, the prevalence ranges from21.7% to 45.90%.[4]

Studies from India have also shown that life events during the period preceding the onset ofdepression play a major role in depression.

The Indian council of medical research, a collaborative project at 4 center's (Bikaner,Goa, Patiala, Vellore) and the outcome.[3]

ICMR descriptive categories	Bikaner N=68%	Goa N=85%	Patiala N=102%	Vellore N=68%	All centers N=323%
Predominantly depressed type	5.9	11.8	11.7	11.8	11.8

Role and Importance of SSRI in the treatment of depression

Mood and anxiety disorder are commonly treated with selective serotonin reuptake inhibitors(SSRIs).[5] The first SSRI, fluoxetine was released in 1988 in US. The fluoxetine side effect profile was highly selective for serotonin receptors, making it significantly superior to any other Antidepressant that was currently in the market. Compared with the TCAs, SSRIs wereinitially considered almost free of side effects also could be prescribed for patient with multiple comorbidities.[6]

SSRIs are frequently administered and viewed as the first line of treatment for depression ora disorder characterized by a persistent low mood, anhedonia and feeling of worthlessness. [4,8] The monoamine hypothesis of depression first revealed the significance of serotonin (5- HT) in the etiology of major depressive disorder (MDD). Depression was an idea that, in itsmost basic form, chemical imbalances were the cause of major depressive disorder.

Noradrenaline (NA), serotonin and Dopamine (DA) amounts in limbic region.[8]

SSRIs continue to be the most effective medication for treating severe MDD, but their effectiveness is still unclear what causes mild to moderate depression. They have a long list of negative effects, among of which considering that lifestyle therapies including (exercise and mindfulness) may still have lingering after negative exposure effect, as alternative 1st linetreatments where possible ,the function of 5-HT2C and 5-HT1A receptors ,despite being investigated right now ,might eventually bring to light the variety of both negative and undesirable effect of SSRIs and encourage the creation of new antidepressant with fewer sideeffects that are not intended.[12]

Clinically important differences between SSRIs

Drug	Relationship b/w Dose and blood levels of drug	Half life	Dose range(mg/d)	Starting dose effective for most patient?	Dose adjustment inelderly	Drug interaction potential
citalopram	Linear over therapeutic dose range	33H	20-60	yes	40mg/d max	Relatively low
fluoxetine	Non-linear	4-6D	20-80	yes	Non recommendedfor healthy individual	high
fluvoxamine	Non-linear	15-26H	50-300	yes	Relatively low doses suggested	high
paroxetine	Non-linear	21H	20-60	yes	10mg/d to start;40mg/d maximum	Moderate to high
sertraline	Linear over therapeutic range	26H	50-200	Higher dose may be more effective.	Non recommended for healthy individual	Relatively low

Guidelines for choices of SSRIs

The choice of antidepressant should be matched to individual patients' needs as far as possible. This depends on the efficacy and tolerability of previous treatment with an SSRI; whether a particular side-effect such as sedation is required; and the risks of interactions and lethality in overdose. It is also good practice to limit the amount ofdrug available, especially if there is a serious risk of overdose.[11]

In comparing SSRIs, limitations regarding the available evidence must be recognized. In general, there are fewer comparative data for citalopram and fluvoxamine than the other SSRIs, possibly because fluvoxamine has made less market impact than the others and because citalopram is a more recent entry intothe market in most countries.[11]

SITUATION	GUIDELINES
1. General	Fluvoxamine not first line owing to poor tolerability.
2. Previous good response or tolerability to a particular SSRI.	Choose the same SSRI unless other consideration.
3. Previous poor response or tolerability to a particular SSRI.	Choose different SSRI.
4. Rapid Anti-Depressant response particularly desirable.	Consider any SSRI other than fluoxetine. Consider Citalopram or Sertraline.
5. Concomitant medication or combination with TCA.	Consider Fluoxetine, avoid paroxetine.
6. Poor compliance with medication or likely tomiss doses or interrupt treatment.	Avoid paroxetine, consider fluoxetine; slowly taper SSRI.
7. Previous troublesome SSRI discontinuation reaction.	Consider any SSRI other than citalopram.
8. High Risk of self-poisoning limit amount of SSRI available.	Consider any SSRI other than paroxetine. Consider any SSRI other than fluoxetine.
9. Previous troublesome sedation on an SSRI.	
10. Previous agitation on an SSRI.	Consider any SSRI other than paroxetine, in particular fluvoxamine; an alternative class ofAnti-Depressant.
11. Alternative class of Anti-Depressant may be more appropriate.	Consider fluoxetine.
12. Previous troublesome several side-effectson an SSRI may be more appropriate.	Consider sertraline.
13. Pregnancy.	Avoid fluoxetine.
14. Breast-feeding.	
15. Likelihood of need to initiate or switch todrug with adverse interaction with SSRIs.	

Pharmacology of SSRIs

Selective serotonin reuptake inhibitors vary in their potency and selectivity in inhibiting serotonin reuptake, and they may have significant effects on other transporters and receptors,indicating that they are not as selective as their manufacturers claim. For example, it has beenproposed that fluoxetine's effects on 5-HT2C receptors may explain its proclivity to cause agitation; paroxetine's affinity for muscarinic receptors explains its increased proclivity to produce discontinuation effects; sertraline's affinity for the dopamine transporter results in greater efficacy in severe depression; and sertraline's and fluvoxamine's affinity for sigma1 opioid receptors explains their effect. However, at our current state of knowledge pharmacodynamic differences between the SSRIs are of minor practical importance in determining choice.[11]

The variations in pharmacokinetics amongst SSRIs are more significant. Compared to its competitors, which vary from roughly 0.5 to 1.5 days, fluoxetine has a significantly longer elimination half-life (1-3 days, paroxetine, its active metabolite, norfluoxetine, 7-15 days). This means that if medications that interact with fluoxetine are taken, a significantly longer washout period is needed and that it takes longer to achieve steady state (and perhaps effective) plasma concentrations. The ability of SSRIs to inhibit hepatic cytochrome P450 (CYP) isoenzymes, which are in charge of many medicines' metabolism, is a significant areawhere they vary from other antidepressants.[11]

Consequences of SSRIs discontinuation and Potential mitigation strategies [10]

CONSEQUNCES	STRATEGIES
Worsening of Depressive Disorder	1.Cross-Titration with SSRI or SNRI. 2.Resume same SSRI. 3.Alernative treatment.
Discontinuation symptoms	1. Brief trial of fluoxetine. 2. Cross-Titration with SSRI or SNRI. 3. Resume same SSRI. 4.Gradual taper and discontinue.
No change in symptoms	1.Watchful monitoring. 2. Gradual taper and discontinue.
Improved symptoms	1.Alernative treatment. 2.Watchful monitoring.
Worsening of Depressive associatedsymptoms	1. Cross-Titration with SSRI or SNRI. 2. Resume same SSRI. 3.Alternative treatment

CONCLUSION

Depression is becoming more common in the world, which is concerning given the related costs to society, the economy, the individual, and interpersonal relationships. The global costof depression significantly transcends the expense of appropriately diagnosing it and effectively treating people who experience it. The WHO has listed depression as the single most years-burdensome disease in the globe because to its high rates of lifetime prevalence, early age of onset, high chronicity, and function impairment.[2]

SSRIs are the most effective class of antidepressant and even they are safer in overdose than the older tricyclic antidepressant. SSRIs are widely used to treat major depressive disorder and other mood or anxiety disorder because of their effectiveness and have lesser or no side effect. However, most SSRI side effects are dose related and can be attributed to serotonergiceffects, for example -nausea are the common side effect of SSRI therapy, most likely result from stimulation of 5-HT3 receptor and can usually be reducing the dose of SSRI. Accordingto practice point prevalence SSRI prescribing varied from 2.5% to 11.9% in some studies.[11]

REFERENCES

1) Goldman.L.,2022. What is depression and what can I do about it? Medical NewsKToday.
2) Richards.D.,2011. Prevalence and clinical cause of depression. Clinicallypsychological review, (31):1117-11125.
3) Iyer.K, khan.Z.A.,2012. Depression a review in school of bioscience and Technology,Vellore of technology, Vellore, Tamil Naadu. Research journal of Recent Science, 1(4):79-87.
4) Grover.S, Dutt.A, Avasthi.A.,2010. An overview of Indian research in depression.Journal of psychiatry, (52):187-188.
5) Balk.A, Weilburg.JB, Lee.J.,2022. An overview of SSRI and SNRI therapies fordepression. Europe PMC, 13(6):25-33.
6) Ferguson.J.M.,2001. SSRI antidepressant medication; adverse effect and tolerability.Journal of clinical psychiatry, 3(1):22.
7) Taylor.S, Stein.M.B.,2006. The future of SSRIs in psychiatric treatment. Medicalhypothesis, (66):14-21.
8) Joshi.A.,2018. Selective serotonin reuptake inhibitors. Psychiatria Danubina,(30):606-609.
9) Marken.P. A, Munro.J.S.,2000. Selecting a selective serotonin reuptake inhibitor: clinically important distinguishing features. Journal of clinical psychiatry, 2(6):205.
10) Jha.M. K, Rush.A. J, Trived.M.H.,2018. When discontinuing SSRIs antidepressants is a challenge: management tips. American journal of psychiatry, 175(2):1176-1184.
11) Anderson.I.M, Edwards.J, G.,2001. Guidelines for choice of SSRIs in depressiveillness. Advances in psychiatric treatment, 7(3):170-180.
12) Sullivan.F. P, Neale.M.C, Kendler.K.S.,2000. Genetic epidemiology of major depression: review and meta-analysis. American journal of psychiatry, 157(10):1552-1562.
13) Stahl.S.M.,2004. Selectivity of SSRIs: individualising patient care through rationaltreatment choices. International journal

of psychiatry in clinical practice, 8(1):3-10.
14) Mace.S, Taylor.D.,2000. Selective serotonin reuptake inhibitors: a review of efficacyand tolerability in depression. Export opinion on pharmacotherapy, 1(5):917-933.
15) Sussman.N.,2003. SNRIs Vs SSRIs: Mechanism of action in treating depression andpainful physical symptoms. Prime care companion J Clin Psychiatry, 5(7):19-26.
16) Nelson.J.C.,1994. Are the SSRIs really better tolerated than the TCAs for thetreatment of major depression. Psychiatric Annals, 24(12):628-631.
17) Johnson.C.F, Dougall.N.J, Williams.B, MacGillivray.S.A, Buchanan.A.,2014. Patientfactor associated with SSRI dose for depression treatment in general practice: a primary care cross sectional study. BMC family practice, 15(1):1-11.
18) Masand.P. S, Gupta.S.,1999. Selective serotonin-reuptake inhibitors: an update. Harvard review of psychiatry, 7(2):69-84.
19) Boden.J.M, fergusson.D.M., 2011. Alcohol and Depression. Addiction, 106(5):906-914.
20) Kehinde.O. A, Anyika.E. N, Abah.I.,2017. Drug utilization pattern of antidepressantsin federal neuropsychiatric hospital lagos, Nigeria. Journal of Hospital Administration,6(5):12.
21) Avanthi.E, Somashekar.H. E, Kumar.P, Sushma.H. K, Sudarshan.C. Y, Raja.B., 2014.Prescribing pattern of antidepressant in psychiatric unit of a tertiary care Hospital. Int J Basic Clin Pharmocol, 3(4):667-670.
22) Tripathi.A, Avasthi.A, Desousa.A, Bhagabati.D, shah.N, Abraham.R.,2016. Prescription pattern of antidepressant in five tertiary care psychiatric centres of India.The Indian journal of medical research, 143(4):507.