Understanding the Prescribing Pattern of Escitalopram in Depression Patients

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Background and Objective of the Survey

Escitalopram, a selective serotonin reuptake inhibitor (SSRI), is a widely prescribed antidepressant for major depressive disorder (MDD) and generalized anxiety disorder (GAD) due to its proven efficacy and favorable side effect profile. Typically, the initial dose for adults is 10 mg once daily, which may be increased to a maximum of 20 mg based on the patient's response and tolerability. For elderly patients or those with hepatic impairment, a lower starting dose of 5 mg is recommended.

Escitalopram is chosen for its rapid onset of action and lower incidence of side effects compared to other antidepressants. Common side effects include nausea, insomnia, fatigue, and sexual dysfunction, which are generally mild and manageable. The medication is well-tolerated, making it suitable for patients who are sensitive to side effects or have comorbid conditions.

Treatment duration varies, often extending several months to prevent relapse of acute depressive episodes. For patients with recurrent depression, maintenance therapy may last a year or longer to sustain remission. Escitalopram is also sometimes combined with other medications, such as atypical antipsychotics or mood stabilizers, in treatment-resistant cases.

Regular follow-up is crucial to monitor efficacy, manage side effects, and ensure adherence. This comprehensive approach helps optimize therapeutic outcomes, improving the quality of life for patients with depression. Understanding prescribing patterns of escitalopram aids in refining treatment strategies to better meet patient needs.

The objective of the survey is:

To understand the prescribing pattern of escitalopram in depression patients

Methodology of the Survey

A survey was conducted to understand the prescribing pattern of escitalopram in depression patients. A total of 100 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- Pharmacological profile
- Clinical efficacy
- Long-term administration study
- Tolerability
- Abstracts

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Introduction

Escitalopram is a selective serotonin reuptake inhibitor (SSRI) that selectively binds to the human serotonin transporter (SERT). This activity inhibits serotonin (5-HT) reuptake and increases the amount of serotonin in synaptic clefts, which results in antidepressant action.

Racemic citalopram (RS-citalopram), an SSRI widely used in patients with major depressive disorder (MDD), possesses both an active S-enantiomer and clinically inactive R-enantiomer.[1] Escitalopram was produced by isolating the active S-enantiomer from RS-citalopram. In vitro and in vivo studies have shown that escitalopram inhibits the serotonin transporter protein more potently than citalopram.[2] For example, in vivo electrophysiological data indicated that escitalopram was four times more potent than citalopram in reducing the firing activity of presumed serotonergic neurons in the dorsal raphe nucleus of rat brain. In November 2011, escitalopram was approved in 100 countries in Europe, North America, and other regions. Escitalopram is indicated for generalized anxiety disorder, social anxiety disorder, obsessive-compulsive disorder, panic disorder, premenstrual dysphoric disorder, and MDD.

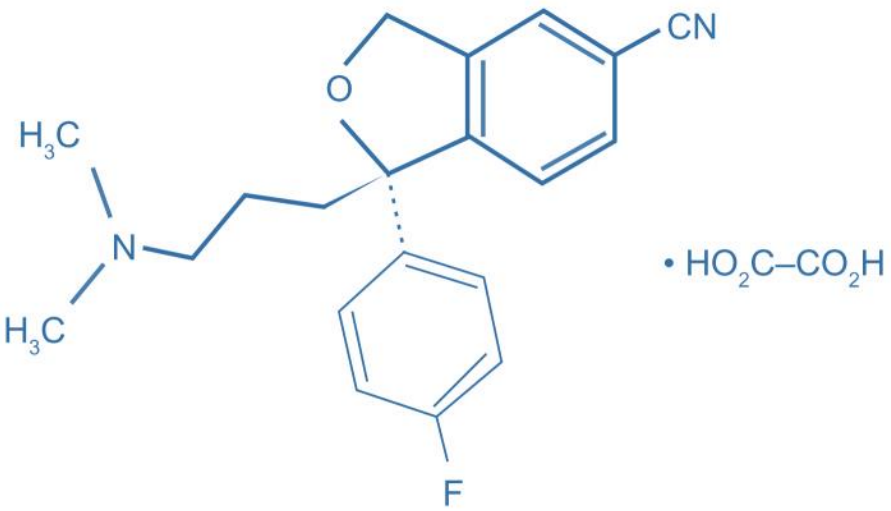

Figure 1. Chemical structure of escitalopram.

Pharmacological profile

Pharmacodynamic profile

Escitalopram has a highly selective, dose-dependent, inhibitory effect on SERT. Its antidepressant action arises from its inhibition of serotonin reuptake into presynaptic nerve ending, which enhances serotonin activity in the central nervous system.[7] Radioligand binding assays revealed that escitalopram showed particularly high selectivity for SERT compared to citalopram and several other SSRIs.[8] Escitalopram is "the most typical SSRI" of the SSRI agents, because it has virtually no binding affinity for other transporters.[7]

Escitalopram binds to two different sites of SERTs: the high-affinity binding site (primary site) of SERT, which controls serotonin reuptake in nerve endings; and the low-affinity binding site (allosteric site), which induces structural changes in SERT. The latter (allosteric action) is thought to stabilize and prolong binding of escitalopram to the primary site.[7,8]

Pharmacokinetic profile

The half-life of receptor occupancy for escitalopram was calculated to be approximately 130 hours, much longer than the half-life of the plasma concentration, which was approximately 30 hours.Figure 2 shows the binding occupancy of escitalopram on cerebral SERTs relative to its concentration changes in plasma. An allosteric action may be involved in this prolonged occupancy. Escitalopram is metabolized in the liver, mainly by cytochrome P-450 (CYP) 2C19 and also by CYP3A4 and CYP2D6. Escitalopram inhibits liver metabolic enzymes, but primarily only CYP2D6, with minimal inhibition of the other enzymes; the IC_{50} for CYP2D6 was higher than its effective blood concentration. In this regard, its interactions with other drugs would presumably be minimal.

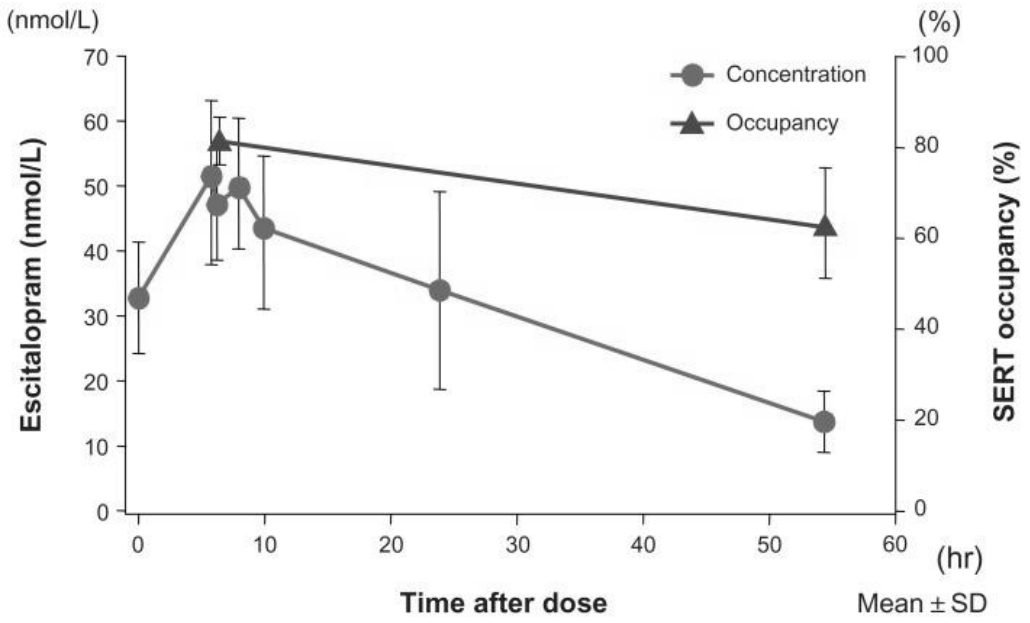

Figure 2. Escitalopram showed 5-HT transporter occupancy that outlived its plasma concentration.

Notes: Escitalopram (10 mg) was administered once daily for 10 consecutive days (the first 5 days are shown) to six healthy men. The 5-HT transporter occupancy rate was determined in the midbrain-hypothalamus region. The 5-HT transporter occupancy rate of escitalopram peaked at 80% and the occupancy half-life was 130 hours.

Clinical efficacy

Comparison with placebo

In a placebo-controlled study, patients with MDD received escitalopram at a dose of 10 mg/day, and a control group was given placebo. After 8 weeks of therapy, the total Montgomery–Asberg Depression Rating Scale (MADRS) score changed by −16.3 in the escitalopram group and −13.6 in the placebo group. Thus, escitalopram had significantly greater efficacy than placebo. The total MADRS score of the escitalopram group began to show significant improvement compared to that of the placebo group by the second week of therapy. This demonstrated its fast-acting property. In addition, the remission rate (the percentage of patients with a total MADRS score of 12 or less) was significantly higher in the escitalopram group than in the placebo group. Thus, the initial therapeutic dose (10 mg/day) was demonstrated to be effective. Likewise, in other studies,[,] escitalopram 10 or 20 mg/day was more effective than placebo in the treatment of MDD. Reduction in MADRS scores, the

primary endpoint, were greater with escitalopram than with placebo at the first or second week and were maintained throughout treatment. Furthermore, Clinical Global Impression-Improvement (CGI-I) and Clinical Global Impression-Severity (CGI-S) scores were reported, and support the MADRS score findings: escitalopram produced significant lower CGI-I scores from week 1 and CGI-S scores from week 3 than placebo, and this continued throughout treatment.

Comparison with SSRIs

Six randomized, double-blind, controlled studies[–] compared escitalopram and citalopram. Escitalopram was administered to patients with MDD for 4–8 weeks at 10–20 mg/day. All six studies[–] showed that the efficacy of escitalopram was equivalent to or greater than that of citalopram. Details of these studies follow.

In the study by Burke et al (n = 491; randomly assigned to placebo, escitalopram, 10 mg/day, 20 mg/day, or citalopram, 40 mg/day), escitalopram (10 mg/day) was at least as effective as citalopram at endpoint. In the study by Lepola et al, by week 8, significantly more patients had responded to treatment with escitalopram (n = 155) than with citalopram (n = 160). In the study by Lalit et al, response rates at the end of 2 weeks were 58% for escitalopram (10 mg/day) (n = 69) and 49% for citalopram (20 mg/day) (n = 74). Response rates at the end of 4 weeks were 90% for escitalopram (10–20 mg/day) and 86% for citalopram (20–40 mg/day). The remission rates at the end of 4 weeks were 74% for escitalopram and 65% for citalopram. Additionally, there were fewer dropouts and less requirement for dose escalation with escitalopram than with citalopram. In the study of Moore et al, MADRS scores decreased more in the escitalopram (n = 138) than in the citalopram (n = 142) arm. There were more treatment responders with escitalopram (76.1%) than with citalopram (61.3%), and adjusted remitter rates were 56.1% and 43.6%, respectively.

In the study by Yevtushenko et al (n = 322; randomly assigned to escitalopram, 10 mg/day or citalopram, 10–20 mg/day), at study end, the mean change from baseline in MADRS total score was significantly greater in the escitalopram arm than in the 10 and 20 mg/day citalopram arms. Changes in the CGI-S and CGI-I scores and the rates of response and remission were significantly greater in the escitalopram group compared with those in the citalopram 10 and 20 mg/day groups. On the other hand, in the study by Ou et al (n = 240, randomly assigned to

escitalopram, 10–20 mg/day or citalopram, 20–40 mg/day), no significant differences were found between the two groups.

The meta-analysis of Montgomery et al, comparing escitalopram and citalopram, supported these controlled studies: escitalopram was significantly more effective than citalopram in overall treatment effect, with an estimated mean treatment difference of 1.7 points at week 8 on the MADRS and in responder rate (8.3 percentage points) and remitter rate (17.6 percentage points) analyses, corresponding to number-needed-to-treat (NNT) values of 11.9 for response and 5.7 for remission. The overall odds ratios were 1.44 for response and 1.86 for remission, in favor of escitalopram. However, Trkulja reported that MADRS reduction was greater with escitalopram, but 95% confidence intervals (CIs) around the mean difference were entirely or largely below two scale points (minimally important difference) and CI around the effect size (ES) was below 0.32 ("small") at all time points. Risk of response was higher with escitalopram at week 8 (relative risk, 1.14; 95% CI, 1.04 to 1.26) but NNT was 14 (95% CI, 7 to 111). All 95% CIs around the mean difference and ES of CGI-S reduction at week 8 were below 0.32 points and the limit of "small," respectively. The report concluded that the claims about clinically relevant superiority of escitalopram over citalopram in short- to medium-term treatment of MDD are not supported by evidence.

A long-term, double-blind, controlled study compared paroxetine to escitalopram given for 24 weeks to patients with severe depression. In that study, escitalopram at 20 mg/day showed better efficacy than paroxetine at 40 mg/day. The total MADRS score changed by −25.2 in patients given escitalopram and by −23.1 in those given paroxetine. Thus, the outcome was significantly better for the escitalopram group, with an intergroup difference of 2.12. Furthermore, the total Hamilton Depression Rating Scale (HAM-D17) score changed by −16.9 and −15.0 in the two groups, respectively; again, significantly better outcomes were shown for the escitalopram group than for the paroxetine group. In addition, the remission rate (percentage of patients with a total MADRS score of 12 or lower) was significantly higher (75.0%) in the escitalopram group than in the paroxetine group (66.8%). On the other hand, another study that compared variable doses of escitalopram (10–20 mg/day) and paroxetine (20–40 mg/day) revealed equivalent efficacy in the two groups.

In Japan, the superiority of escitalopram to placebo and its noninferiority to paroxetine (20–40 mg/day) were documented in a double-blind, parallel-group study⁻ that compared escitalopram (10 mg/day and 20 mg/day for 8 weeks) to placebo or paroxetine in patients with MDD. shows

the changes in the total MADRS scores. Based on the *P*-values, significant improvement was found in both escitalopram groups compared to the placebo group. Furthermore, based on the difference between the combined escitalopram groups and the paroxetine group, the upper limit of the 95% CI was below the noninferiority threshold limit (3.2); this demonstrated the noninferiority of escitalopram to paroxetine. In addition, previous studies have shown that the efficacy of escitalopram was equivalent to that of either fluoxetine or sertraline.

Table 1. Comparison of changes in total MADRS scores at 8 weeks (last observation carried forward) among patients with MDD treated with escitalopram, paroxetine, or placebo

	Escitalopram 10 mg (n = 120)	**Escitalopram 20 mg (n = 119)**	**Escitalopram combined groups (n = 239)**	**Paroxetine (n = 121)**	**Placebo (n = 124)**
Total score[a]					
At baseline	29.4 ± 5.8	29.8 ± 6.0	29.6 ± 5.9	29.8 ± 5.9	29.0 ± 5.6
At week 8	15.6 ± 11.0	16.2 ± 10.1	15.9 ± 10.5	15.6 ± 10.0	18.3 ± 10.1
Change					
At week 8[a]	−13.7 ± 10.0	−13.6 ± 8.8	−13.7 ± 9.4	−14.2 ± 9.9	−10.7 ± 9.5
Difference from the placebo group[b]	−3.0	−2.7	−2.8	−3.2	–
***P*-value[c]**	0.018	0.021	0.006	0.009	–
Difference from the	0.3 (−2.2, 2.8)	0.6 (−1.7, 3.0)	0.5 (−1.6, 2.6)	–	–

paroxetine group[d]					
***P*-value[e]**	0.796	0.612	0.652	–	–

Notes: Both escitalopram administration groups showed significant improvement compared to the placebo group. The upper limit of the 95% confidence interval for the difference between the combined escitalopram groups and the paroxetine group was below the noninferiority margin (3.2); this confirmed the noninferiority of escitalopram to paroxetine.

[a]Mean ± SD;

[b]least squares mean;

[c]versus the placebo group (ANCOVA);

[d]least squares mean (two-sided 95% confidence interval);

[e]versus the paroxetine group (ANCOVA). The threshold limit of noninferiority is 3.2.

Abbreviations: ANCOVA, analysis of covariance; MADRS, Montgomery–Asberg Depression Rating Scale; MDD, major depressive disorder.

Comparison with SNRIs

In a double-blind, controlled study of escitalopram (10–20 mg/day) versus duloxetine (60 mg/day) for 8 weeks, the changes in the total MADRS scores were −18.0 ± 9.4 and −15.9 ± 10.3, respectively. This result showed that escitalopram was significantly superior to duloxetine. In another long-term, double-blind, controlled study of escitalopram (20 mg/day) versus duloxetine (60 mg/day) for 24 weeks, the total MADRS score improved significantly to a greater extent in the escitalopram group than in the duloxetine group at 1 week. This trend persisted until the 16th week. Escitalopram has also shown equivalent or superior efficacy to that of sustained-release venlafaxine (venlafaxine SR).[,]

Long-term administration study

In addition to the two long-term, double-blind studies with paroxetine and duloxetine, two other long-term studies with escitalopram were carried out in Japan, which involved patients of different age groups. The first study involved patients 20–64 years of age (under 65), and the second study involved older patients of at least 65 years of age (65 and older). Both studies examined open-label, 52-week administrations of variable doses in outpatients. The remission rate (percentage of patients with a total MADRS score of 10 or lower) increased over the administration period; after 52 weeks, the remission rate was about 70% in both groups. Patients that reached remission by the eighth week were followed, and 20 of 23 of patients in the under-65 age group maintained remission until the end of study. In the 65-and-older age group, the five patients that reached remission by the eighth week also maintained remission.

Relapse and recurrence prevention study

An MDD relapse prevention study was carried out in another group of patients aged 65 and older. Escitalopram was administered at a dose of 10 or 20 mg/day for 12 weeks. Patients that reached remission (a total MADRS score of 12 or lower) were allocated to receive either escitalopram at 10 or 20 mg/day or placebo. The two groups were followed to determine the relapse rate. The cumulative non-relapse rate remained high in the escitalopram group but decreased over time in the placebo group (Figure 3). At the end of study, relapses were observed in only 9% of the escitalopram group and 33% of the placebo group; thus, the relapse rate was significantly lower in the escitalopram group.

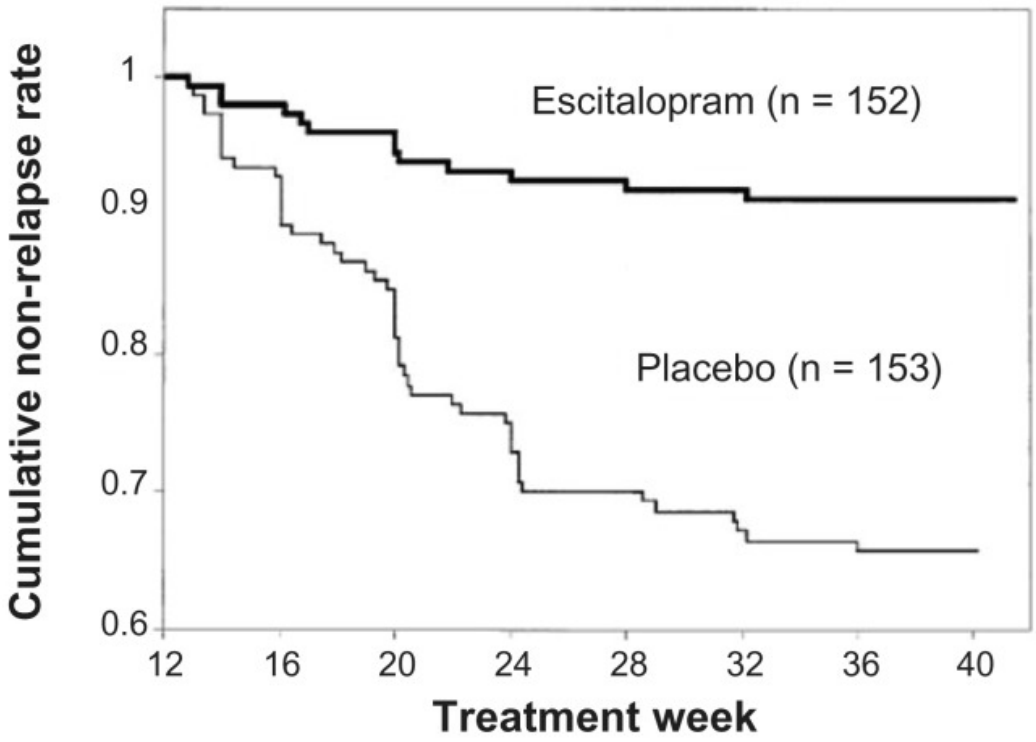

Figure 3. Changes in the cumulative non-relapse rate.

Notes: Escitalopram exhibits a low relapse rate, demonstrating a significant relapse-preventing effect compared to placebo.

An MDD recurrence prevention study examined recurrences after 16 weeks of continuous therapy with escitalopram. Patients given escitalopram at a fixed dose of 10 or 20 mg/day were compared to controls given placebo for 52 weeks of maintenance therapy. MDD recurrence was 27% in the escitalopram group – significantly lower than the 65% observed in the placebo group.

Tolerability

Patients with MDD generally exhibited favorable tolerance to escitalopram, regardless of whether they received short-term or long-term therapy. Adverse events were typically mild and temporary. The most frequent adverse events that occurred during escitalopram therapy included insomnia, nausea, excessive sweating, fatigue/somnolence, dysspermatism, and decreased libido.

Comparison with SSRIs or SNRIs

Escitalopram was compared to other SSRIs or SNRIs in a meta-analysis of patient data from 16 double-blind, controlled studies. When attention was focused on adverse events that occurred at a frequency of 5% or more, escitalopram showed significantly lower frequencies of diarrhea, dry mouth, and the presence of more than one adverse event compared to the other SSRIs. Escitalopram was also associated with significantly lower frequencies of nausea, insomnia, dry mouth, vertigo, excessive sweating, constipation, and vomiting than the SNRIs.

Discontinuation symptoms

Discontinuation symptoms typically occur at the end of treatment with antidepressant drugs. A detailed study compared discontinuation symptoms in patients with MDD during the post-therapy observation period after 27 weeks of therapy with escitalopram (20 mg/day) or paroxetine (40 mg/day). Discontinuation symptoms were evaluated in terms of the Discontinuation Emergent Signs and Symptoms (DESS) score. During the observation period, the drug doses were gradually decreased over 1–3 weeks, followed by 1 week of alternate-day dosing and, subsequently, 1–3 weeks of placebo. The escitalopram group exhibited smaller changes in the total DESS score and significantly less frequent discontinuation symptoms compared to the paroxetine group, both at the end of alternate-day dosing and after 1 week of placebo administration (Figure 4).

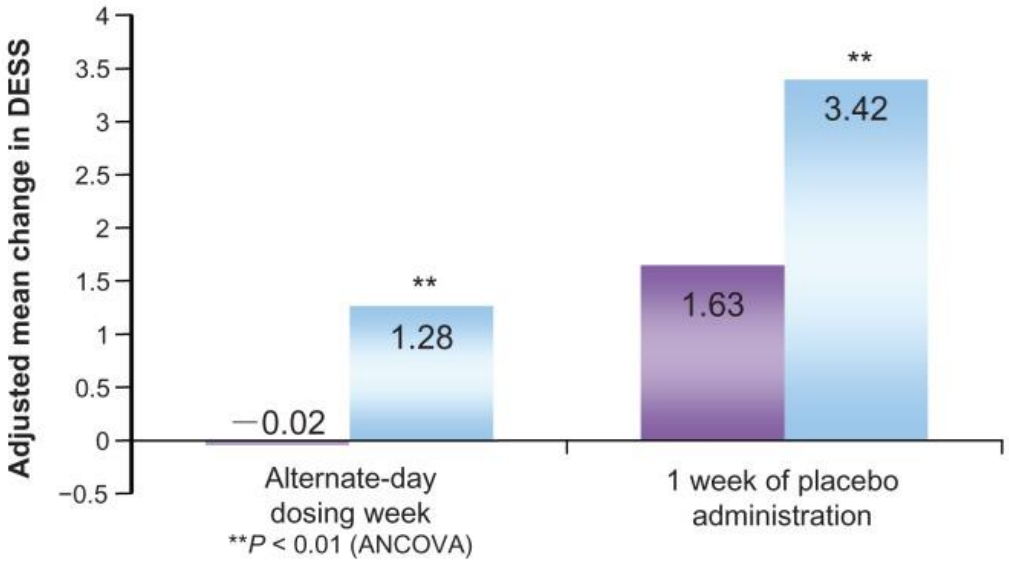

Figure 4. Discontinuation Emergent Signs and Symptoms (DESS 47) scores in the post-therapy observation period.

Notes: The change in the total modified DESS 47 score was calculated from the beginning of post-therapy observation to the end of one week with either alternate-day dosing or placebo. The mean scores are indicated in the bars. Scores were −0.02 for the escitalopram group and 1.28 for the paroxetine group. The corresponding values at 1 week of placebo administration were 1.63 for the escitalopram group and 3.42 for the paroxetine group. Significantly fewer post-therapy symptoms were observed in the escitalopram group than in the paroxetine group at all times.

Suicidality

Suicidality was studied in a detailed meta-analysis conducted on data from 34 placebo-controlled studies on SSRIs. The analysis included >40,000 patients, approximately 2600 of whom had been treated with escitalopram. They found one instance of suicide, which occurred 6 days after treatment cessation. Another analysis of placebo-controlled studies specifically included patients with MDD or anxiety disorders that used escitalopram. They reported no suicides during the first 2 weeks of treatment or during the entire period of escitalopram (,24 weeks), but one suicide occurred in the placebo group. Furthermore, there was no indication of increased risk of nonfatal self-harm or suicidal thoughts among patients that received escitalopram compared with those that received placebo. Rather, escitalopram reduced the MADRS item-10 (“suicidal thought”) or HAM-D item-3 (“suicidal thought”) scores to a significantly greater extent than placebo.” For an estimated >12 million patients with MDD and/or anxiety disorders treated with escitalopram, pharmacovigilance information revealed a suicide rate of 1.8 per 1 million patients; this rate was similar to that in patients treated with citalopram (2 per 1 million) and considerably lower than that in patients treated with tricyclic antidepressants (12 per 1 million) or monoamine oxidase inhibitors (MAOIs) (14 per 1 million).

Sexual dysfunction

A small, retrospective study (n = 47) indicated that two-thirds of patients with SSRI/SNRI-induced sexual dysfunction reported mild or marked improvements after switching to a regimen with escitalopram. However, several reports have suggested that escitalopram may be

associated with increased sexual dysfunction in both men and women compared to bupropion or sertraline.[9]

QT prolongation

In a clinical trial in Japan, the QT interval in heart rate was examined with Fridericia's correction formula (QTcF = QT/cubic root of relative risk). They found no difference in the QTcF values between patients that received escitalopram (10 mg/day) and those that received placebo. However, QTcF was significantly prolonged in patients treated with escitalopram (20 mg/day) compared to that of patients treated with placebo; nevertheless, no clinically problematic adverse events related to QT prolongation were observed. The trial report argued that caution was required in administering escitalopram to aged individuals, patients with liver dysfunction, patients with defective CYP2C19 activity, or patients that received other drugs that conferred a risk of QT prolongation.

Overdosage

In a retrospective analysis of 28 patients that underwent a supratherapeutic ingestion of escitalopram (5–300 mg), only one patient reported adverse events. That patient was admitted to a hospital for persistent lethargy, but the outcome was good. However, when escitalopram is taken at high doses or in poly-substance ingestions, CNS depression may occur. Patients (n = 13) that had taken escitalopram (mean dosage 126 mg) as a coingestant in poly-substance ingestions exhibited CNS depression (54%), cardiovascular effects (54%), and ECG changes (23%). In one case report, after an overdose of escitalopram (100–200 mg), a 38-year-old man exhibited severe, prolonged serotonin syndrome and elevated serum escitalopram concentration.

Patient acceptability

Another meta-analysis reported on the efficacy and patient acceptability of 12 new antidepressant drugs. In that meta-analysis, patient acceptability was defined as the persistence observed in taking a drug during an 8-week therapy. Among those 12 drugs, escitalopram was

associated with the highest rate of patient acceptability. The result of that meta-analysis was illustrated for family physicians using fluoxetine as the standard (Figure 5).

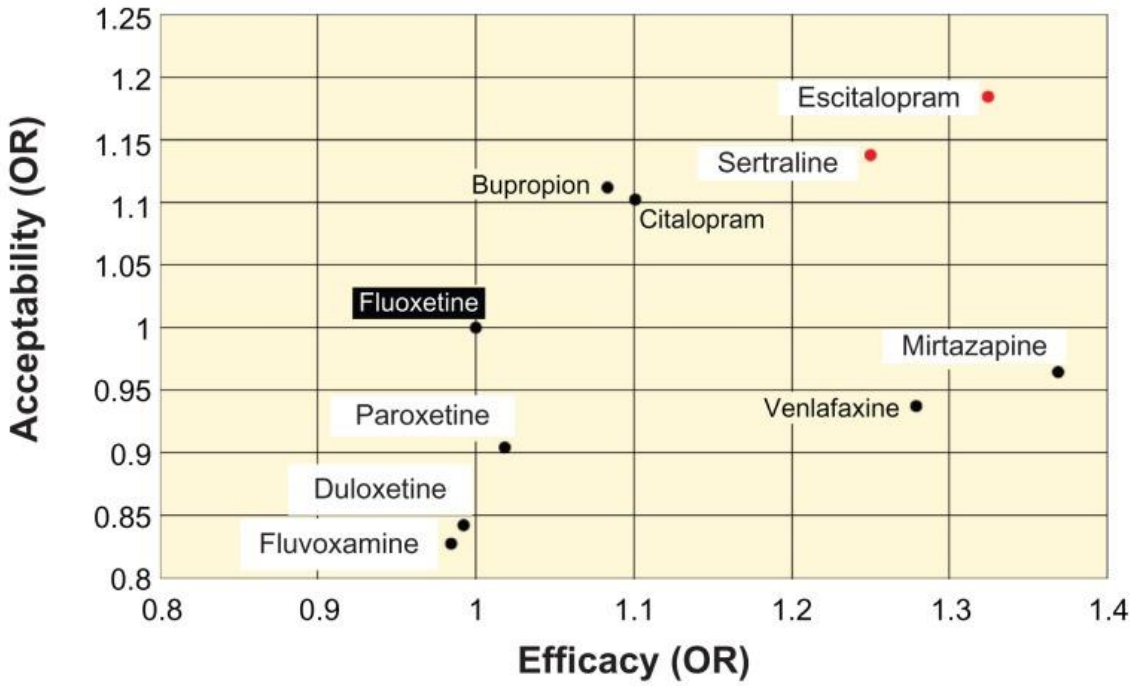

Figure 5. Efficacy and patient acceptability of new antidepressant drugs.

Notes: The odds ratios (OR) of acceptability and efficacy were based on a value of 1 for fluoxetine. Acceptability of escitalopram was highest among the new antidepressant drugs examined.

The rates of discontinuing therapy were analyzed among pooled data from double-blind, controlled studies of escitalopram versus paroxetine or duloxetine. The pooled data for paroxetine was derived from two studies, that treated patients for 24 and 27 weeks, respectively. The discontinuation rate at the end of the study period was significantly lower for patients on escitalopram (16.8%) than for those on paroxetine (27.9%). When the reason for discontinuing therapy was restricted to adverse events, the discontinuation rates remained significantly lower for escitalopram (6.6%) than for paroxetine (11.7%).

The pooled data for duloxetine were derived from two studies, that treated patients for 8 and 24 weeks, respectively. The discontinuation rate at the end of the study period was significantly lower for escitalopram (12.9%) than for duloxetine (24.6%). When the reason for discontinuing therapy was restricted to adverse events, the discontinuation rates remained significantly lower

for escitalopram (4.6%) than for duloxetine (12.7%). Thus, escitalopram was associated with high therapy continuity.

MDD has a relatively high likelihood of recurrence. Thus, high therapy continuity with escitalopram represents an advantage for patients with this disease. There may be several reasons for the high therapy continuity of escitalopram. First, it has high efficacy and good tolerability, as shown in the clinical studies discussed previously. Thus, dropouts from escitalopram therapy due to insufficient efficacy or adverse events appeared to be limited. Furthermore, the demonstrated efficacy of escitalopram at an initial dose of 10 mg could be detected in the early therapeutic phase by patients.' It was speculated that early signs of improvement most likely led to increased adherence, which, in turn, led to prevention of relapse and recurrence.

The fact that escitalopram demonstrated preventive effects on relapse and recurrence represented major benefit to patients that desire to be reintegrated into society. For instance, for a company employee that wants to return to work, escitalopram may facilitate the return-to-work program, and, thus, the patient would expect to return to work smoothly.

Abstracts

Comparative Analysis of the Effects of Escitalopram, Pramipexole, and Transcranial Magnetic Stimulation on Depression in Patients With Parkinson Disease: An Open-Label Randomized Controlled Trial[2]

Abstract

Objective: This study aimed to compare the effects of different antidepressant therapies on depression in patients with Parkinson disease (PD) and to provide a reference for clinical treatment.

Methods: A total of 328 patients with idiopathic PD were selected consecutively. Subjects met Diagnostic and Statistical Manual of Mental Disease , Fourth Edition , criteria for a depressive disorder, or operationally defined subsyndromal depression, and scored greater than 17 on the 17-item Hamilton Depression Scale (HAMD-17). One hundred thirty-one patients with PD accompanied with depression were enrolled into the experimental group. The subjects were randomly divided into 4 groups, and 118 were eventually completed: routine treatment group

(n = 29), routine treatment + escitalopram group (n = 29), routine treatment + pramipexole group (n = 31), and routine treatment + transcranial magnetic stimulation (TMS) group (n = 29). After 4 weeks of treatments, the efficacy of each treatment was evaluated using HAMD score and reduction rate.

Results: After 4 weeks of treatment, the HAMD score was used for pair-to-pair comparison between the 4 groups. The therapeutic efficiency of escitalopram, pramipexole, and repetitive TMS was superior to routine anti-PD treatment, and the differences were statistically significant ($P < 0.05$). There was no statistical difference between escitalopram and pramipexole, but all of them were superior to rTMS. Further logistic regression analysis suggested that 50% reduction in HAMD score from baseline was associated with the treatment method. Among them, escitalopram had statistical significance ($P < 0.05$).

Conclusions: Escitalopram, pramipexole, and high-frequency TMS had better efficacy in patients with PD complicated with depression. At 4 weeks, escitalopram showed better antidepressant effects and improved patients' quality of life and did not worsen motor function.

Efficacy and safety of escitalopram in treatment of severe depression in Chinese population[3]

Abstract

Severe depression accounts for one-third of depressed patients. Increasing severity of depression usually hinders patients from achieving remission. This study evaluated the efficacy and safety of escitalopram in acute-phase treatment of severe major depressive disorder (MDD). A total of 225 participants with severe MDD (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria), with a current depressive episode and Montgomery-Asberg Depression Rating Scale (MADRS) score of ≥30 were enrolled. Participants received flexible dose escitalopram (10-20 mg/d) treatment for 8 weeks. Symptoms status was assessed by MADRS, Hamilton Depression Rating Scale (HAM-D-17), and Hamilton Anxiety Rating Scale (HAM-A). Quality of life was assessed by Short Form-12 (SF-12) and safety by adverse events, laboratory investigations, vital signs and physical findings. The remission (MADRS total score ≤ 10) rate in the intent-to-treat set (n = 207) was 72.9% at week 8. Significant improvement in symptoms compared to baseline, as evaluated by MADRS, HAMD-17 and HAMA scores at baseline, week 1, week 2, week 4, and week 8 ($p < 0.0001$ for all), was noted.

Mean (SD) reduction from baseline in MADRS total score was 26.6 (11.38). Improvements in SF-12 score were significant (p = 0.000) and positively related to symptom improvement and negatively related to treatment-emergent adverse events (TEAEs). TEAEs were reported in 28.38% of participants. Most common TEAEs (>4%) were somnolence (9.0%), nausea (7.7%), hyperhidrosis (4.5%), dry mouth and dizziness (4.1% each). No serious TEAEs were reported. Escitalopram was effective and well-tolerated for acute-phase treatment of severe depression in Chinese population.

Clinical features and efficacy of escitalopram treatment for geriatric depression[4]

Abstract

This study investigated the psychological characteristics and clinical features of 55 patients with geriatric depression, and evaluated the efficacy and safety of escitalopram in the treatment of geriatric depression, in a randomized controlled trial. Fifty-five patients with geriatric depression were randomly assigned to receive 8 weeks of escitalopram 10 mg, daily, orally (n = 29) or placebo (n = 26). At baseline, these patients had significantly higher neuroticism and psychoticism scores on the Eysenck Personality Questionnaire - Adult scale than Chinese population norms. General Severity Index scores and the mean values of the nine subscales of the Symptom Checklist-90 - Revised scale were also significantly higher in these patients than in Chinese population norms. The response rate to escitalopram after 8 weeks' treatment was 74.1% (20/27 patients). Adverse reactions included nausea, dry mouth and dizziness. In conclusion, depressed geriatric patients were found to have abnormal personality traits, and escitalopram was efficacious and had a good safety profile in the treatment of geriatric depression.

Escitalopram: an open-label study of bereavement-related depression and grief[5]

Abstract

Background: Approximately 8 million Americans suffer the loss of an immediate family member each year. Chronic depression may develop following bereavement-about 15% of the bereaved are depressed at 1 year. Several studies of psychotropic medications have

demonstrated improvement in depression ratings, but little data exists for selective serotonin reuptake inhibitor treatment in bereavement-related depression.

Methods: Thirty adults were treated with escitalopram for 12 weeks in open fashion for a major depressive episode following loss of a close family member (parent, sibling, child, or spouse/significant other). Main outcome measures were the Hamilton Depression Rating Scale, the Montgomery-Asberg Rating Scale, the Texas Revised Inventory of Grief, and the Inventory of Complicated Grief.

Results: Twenty-nine of thirty participants returned for at least one set of efficacy measures after starting medication. Nineteen subjects (66%) experienced a 50% or greater improvement on the Hamilton Depression Scale. Fifteen subjects (52%) achieved remission, defined as a final score of 7 or less on the Hamilton Depression Scale. Escitalopram significantly reduced depressive symptoms ($P<0.001$) over time. Subjects with uncomplicated grief and those with complicated grief improved similarly over time. Subjects with and without PTSD improved to a similar degree. Escitalopram was well tolerated.

Limitations: Open-label design, psychotherapy was not controlled, relatively short treatment period, variation in grief scales make comparisons to other studies difficult, all subjects with complicated grief also were clinically depressed, and gender discrepancy of sample.

Conclusions: Escitalopram improved depressive, anxiety, and grief symptoms in individuals experiencing a major depressive episode related to the loss of a loved one.

Escitalopram for comorbid depression and anxiety in elderly patients: A 12-week, open-label, flexible-dose, pilot trial[6]

Background: Comorbid depression and anxiety may result in greater symptom severity and poorer treatment response than either condition alone. Selective serotonin reuptake inhibitors have been found to be effective in treating both depression and anxiety; however, pharmacodynamic and pharmacokinetic changes associated with aging warrant special attention in medication trials in older patients.

Objective: The objective of this study was to assess the efficacy and tolerability of short-term (12-week) administration of escitalopram oxalate 10 to 20 mg/d for moderate to marked comorbid depression and anxiety in elderly patients.

Methods: This open-label, flexible-dose (10-20 mg/d), pilot trial was conducted at the Psychiatry Service, Veterans Affairs Medical Center, Cincinnati, Ohio. Outpatients aged > or =65 years were included if they met the criteria for comorbid major depressive disorder (MDD) and generalized anxiety disorder (GAD), as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, for > or =4 weeks and had a baseline Montgomery-Asberg Depression Rating Scale (MADRS) score of >22 and a Hamilton Rating Scale for Anxiety (HAM-A) score of > or =18. All patients received escitalopram 10 to 20 mg/d. The primary efficacy variables were the mean changes from baseline in total MADRS and HAM-A scores at 12 weeks (last observation carried forward). The secondary efficacy end point was the change from baseline in Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) 8 subscale scores. Adverse events were assessed at each visit (treatment weeks 1, 2, 3, 4, 6, 8, 10, and 12) with the use of open-ended questioning.

Results: Twenty patients were enrolled (mean [SD] age, 73.0 [4.8] years; 6 [30%] women; race: 17 [85%] white, 2 [10%] black, and 1 [5%] "other"). Seventeen (85%) of 20 patients completed the study; 3 (15%) withdrew: 1 (5%) due to lack of efficacy and 2 (10%) due to adverse events (dizziness and somnolence [1 (5%) patient each]). Statistically significant improvements from baseline to end point were found with escitalopram treatment (MADRS: t19 = 7.38, P < 0.001, effect size = 2.93; HAM-A: t19 = 4.19, P < 0.001, effect size = 1.83). Significant changes from baseline in scores on 4 (Social Functioning, Role Functioning-Emotional, Mental Health, and Energy/Fatigue) of the 8 subscales of the SF-36 were also found (all, P < 0.01).

Conclusion: In this small study in elderly patients with comorbid MDD and GAD, treatment with escitalopram 10 to 20 mg/d for 12 weeks was associated with significant improvements in symptoms of depression and anxiety.

Escitalopram and problem-solving therapy for prevention of poststroke depression: a randomized controlled trial[7]

Abstract

Context: Depression occurs in more than half of patients who have experienced a stroke. Poststroke depression has been shown in numerous studies to be associated with both impaired recovery in activities of daily living and increased mortality. Prevention of depression thus represents a potentially important goal.

Objective: To determine whether treatment with escitalopram or problem-solving therapy over the first year following acute stroke will decrease the number of depression cases that develop compared with placebo medication.

Design, setting, and participants: A multisite randomized controlled trial for prevention of depression among 176 nondepressed patients was conducted within 3 months following acute stroke from July 9, 2003, to October 1, 2007. The 12-month trial included 3 groups: a double-blind placebo-controlled comparison of escitalopram (n = 59) with placebo (n = 58), and a nonblinded problem-solving therapy group (n = 59).

Main outcome measures: The main outcome measure was the development of major or minor poststroke depression based on symptoms elicited by the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV) and the diagnostic criteria from DSM-IV for depression due to stroke with major depressive-like episode or minor depression (ie, research criteria).

Results: Patients who received placebo were significantly more likely to develop depression than individuals who received escitalopram (11 major and 2 minor cases of depression [22.4%] vs 3 major and 2 minor cases of depression [8.5%], adjusted hazard ratio [HR], 4.5; 95% confidence interval [CI], 2.4-8.2; P < .001) and also more likely than individuals who received problem-solving therapy (5 major and 2 minor cases of depression [11.9%], adjusted HR, 2.2; 95% CI, 1.4-3.5; P < .001). These results were adjusted for history of mood disorders and remained significant after considering possible confounders such as age, sex, treatment site, and severity of impairment in the model. Using an intention-to-treat conservative method of analyzing the data, which assumed that all 27 patients who did not start randomized treatment would have developed depression, and controlling for prior history of mood disorders, escitalopram was superior to placebo (23.1% vs 34.5%; adjusted HR, 2.2; 95% CI, 1.2-3.9; P

= .007), while problem-solving therapy was not significantly better than placebo (30.5% vs 34.5%; adjusted HR, 1.1; 95% CI, 0.8-1.5; P = .51). Adverse events, including all-cause hospitalizations, nausea, and adverse effects associated with escitalopram were not significantly different between the 3 groups.

Conclusions: In this study of nondepressed patients with recent stroke, the use of escitalopram or problem-solving therapy resulted in a significantly lower incidence of depression over 12 months of treatment compared with placebo, but problem-solving therapy did not achieve significant results over placebo using the intention-to-treat conservative method of analysis.

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6. Mohamed S, Osatuke K, Aslam M, Kasckow J. Escitalopram for comorbid depression and anxiety in elderly patients: A 12-week, open-label, flexible-dose, pilot trial. *Am J Geriatr Pharmacother*. 2006;4(3):201-209.
7. Robinson RG, Jorge RE, Moser DJ, et al. Escitalopram and problem-solving therapy for prevention of poststroke depression: a randomized controlled trial [published correction appears in JAMA. 2009 Mar 11;301(10):1024]. *JAMA*. 2008;299(20):2391-2400.

Survey Form

1. How often do you prescribe Escitalopram as a first-line treatment for depression?

a) Always

b) Often

c) Sometimes

d) Rarely

2. In what dosage do you typically start patients on Escitalopram?

a) 5 mg

b) 10 mg

c) 15 mg

d) 20 mg

3. What is the average duration of Escitalopram treatment in your patients?

a) Less than 6 months

b) 6-12 months

c) 1-2 years

d) More than 2 years

4. How do you determine the appropriate dose escalation for Escitalopram in your patients?

a) Based on symptom improvement

b) Based on side effects

c) Based on patient preference

d) Following standard guidelines

5. Which patient population do you find responds best to Escitalopram treatment?

a) Adolescents

b) Adults

c) Elderly

d) Pregnant women

6. How effective do you find Escitalopram in treating anxiety symptoms associated with depression?

a) Very effective

b) Effective

c) Moderately effective

d) Not effective

7. How do you handle discontinuation symptoms when stopping Escitalopram in patients?

a) Gradual tapering

b) Switching to another medication

c) Supportive therapy

d) Immediate cessation

8. Do you recommend any complementary therapies along with Escitalopram for better management of depression?

a) Cognitive-behavioral therapy (CBT)

b) Mindfulness-based stress reduction (MBSR)

c) Exercise programs

d) All of the above

9. How do you manage sexual dysfunction in patients taking Escitalopram?

a) Dose reduction

b) Switching medication

c) Adding another medication

d) Lifestyle modifications

10. What percentage of your patients on Escitalopram experience significant symptom improvement?

a) 0-25%

b) 26-50%

c) 51-75%

d) 76-100%

11. In your experience, how soon do patients typically begin to show improvement in depressive symptoms after starting Escitalopram?

a) Within 1 week

b) 1-2 weeks

c) 2-4 weeks

d) More than 4 weeks

12. Do you use any specific scales or tools to measure the effectiveness of Escitalopram in your patients?

a) Yes, PHQ-9

b) Yes, HAM-D

c) Yes, Beck Depression Inventory

d) No, I don't use specific scales

13. How often do you encounter treatment-resistant depression in patients taking Escitalopram?

a) Rarely

b) Occasionally

c) Frequently

d) Very frequently

14. What percentage of your patients on Escitalopram achieve full remission of depressive symptoms?

a) 0-25%

b) 26-50%

c) 51-75%

d) 76-100%

15. How satisfied are you with the overall effectiveness of Escitalopram in treating depression in your patients?

a) Very satisfied

b) Satisfied

c) Neutral

d) Dissatisfied

Survey Findings

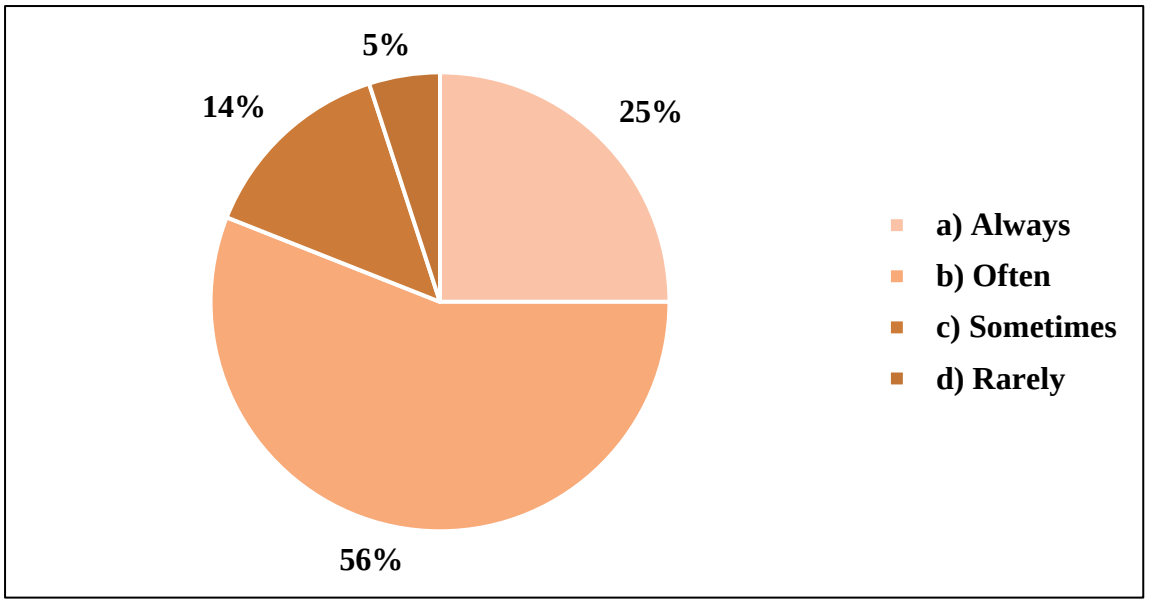
1. How often do you prescribe Escitalopram as a first-line treatment for depression?

a) Always

b) Often

c) Sometimes

d) Rarely



According to 56% of doctors, they often prescribe Escitalopram as a first-line treatment for depression.

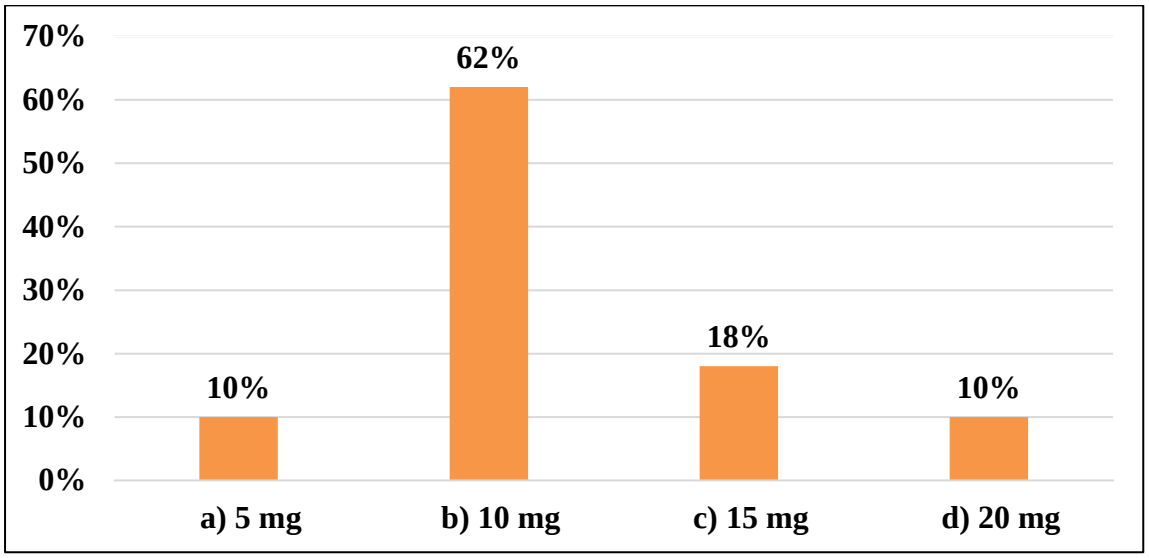
2. In what dosage do you typically start patients on Escitalopram?

a) 5 mg

b) 10 mg

c) 15 mg

d) 20 mg



As per 62% of doctors, they typically start patients on Escitalopram with 10 mg.

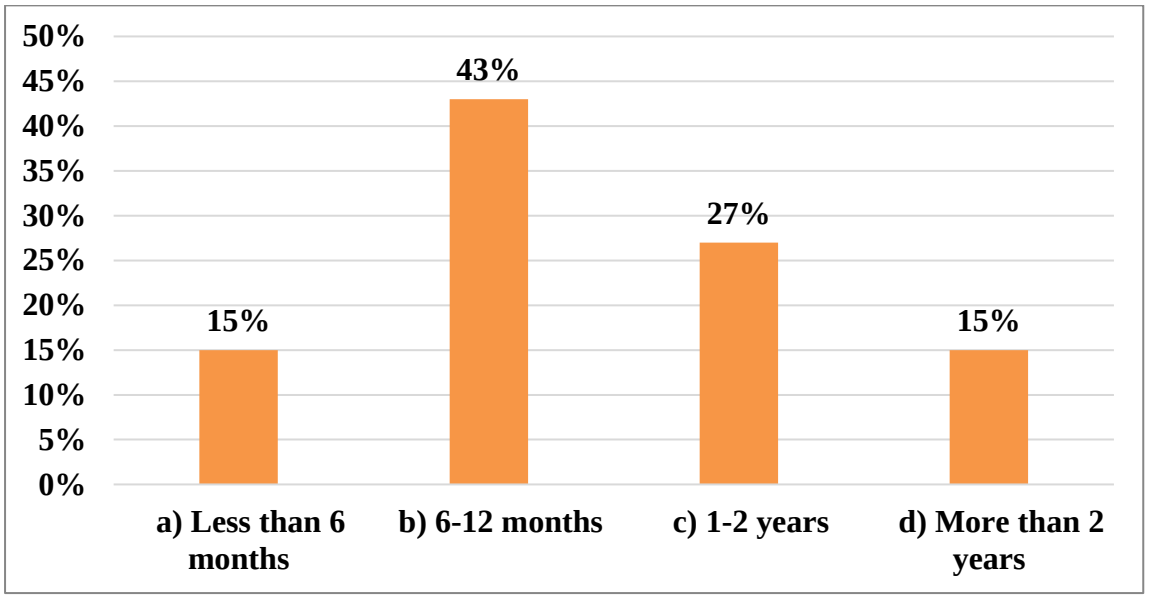
3. What is the average duration of Escitalopram treatment in your patients?

a) Less than 6 months

b) 6-12 months

c) 1-2 years

d) More than 2 years



As per 43% of doctors, 6-12 months is the average duration of Escitalopram treatment in their patients.

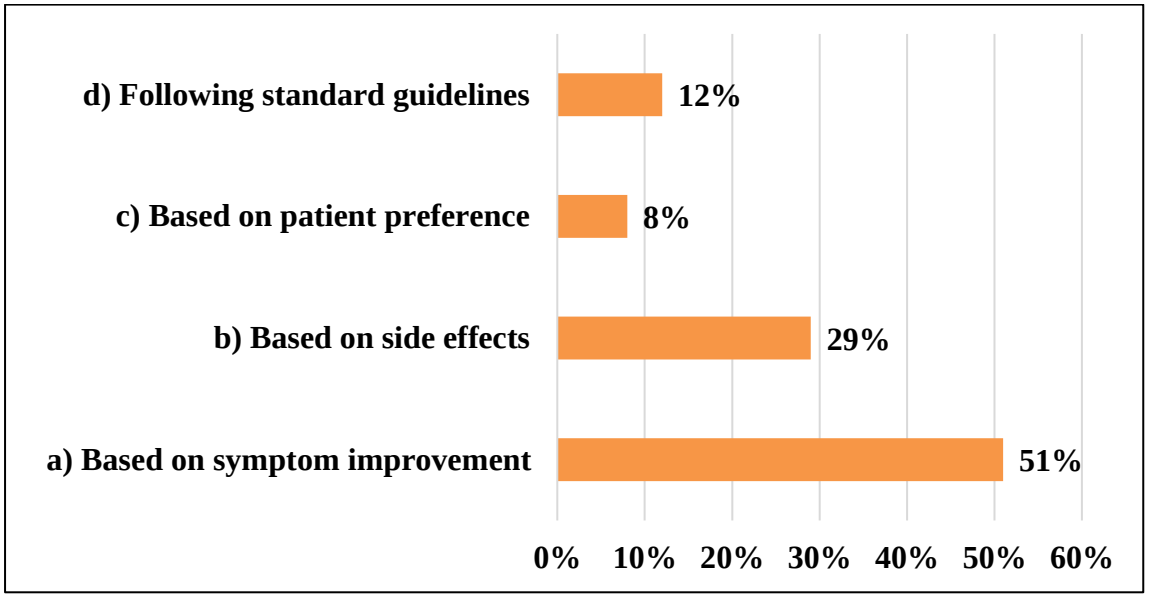
4. How do you determine the appropriate dose escalation for Escitalopram in your patients?

a) Based on symptom improvement

b) Based on side effects

c) Based on patient preference

d) Following standard guidelines



According to 51% of doctors, they determine the appropriate dose escalation for Escitalopram in their patients based on symptom improvement.

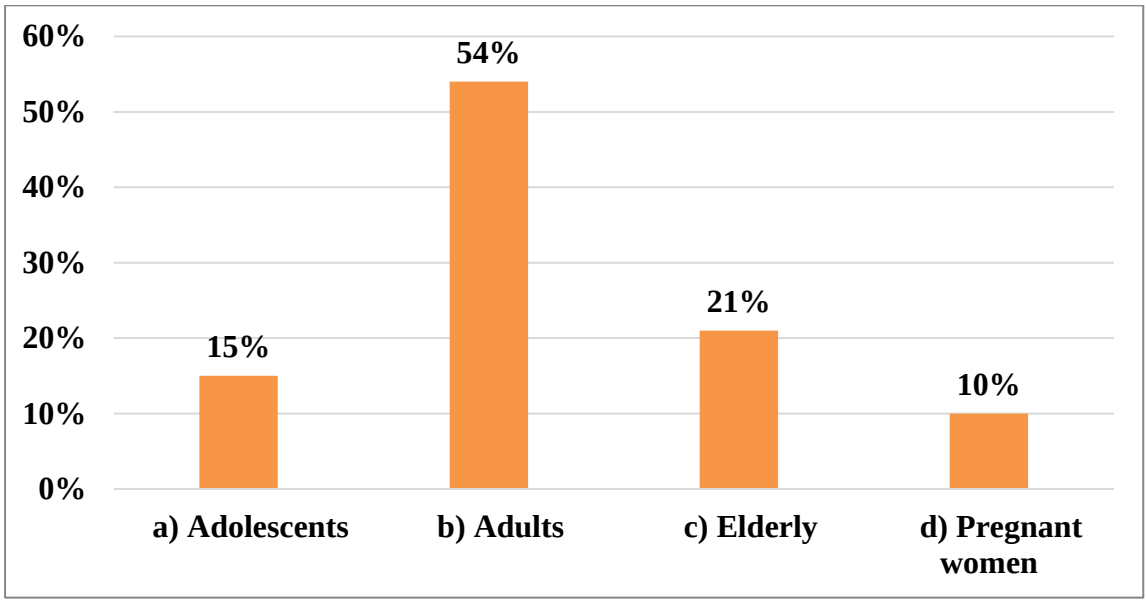
5. Which patient population do you find responds best to Escitalopram treatment?

a) Adolescents

b) Adults

c) Elderly

d) Pregnant women



According to 54% of doctors, adults responds best to Escitalopram treatment.

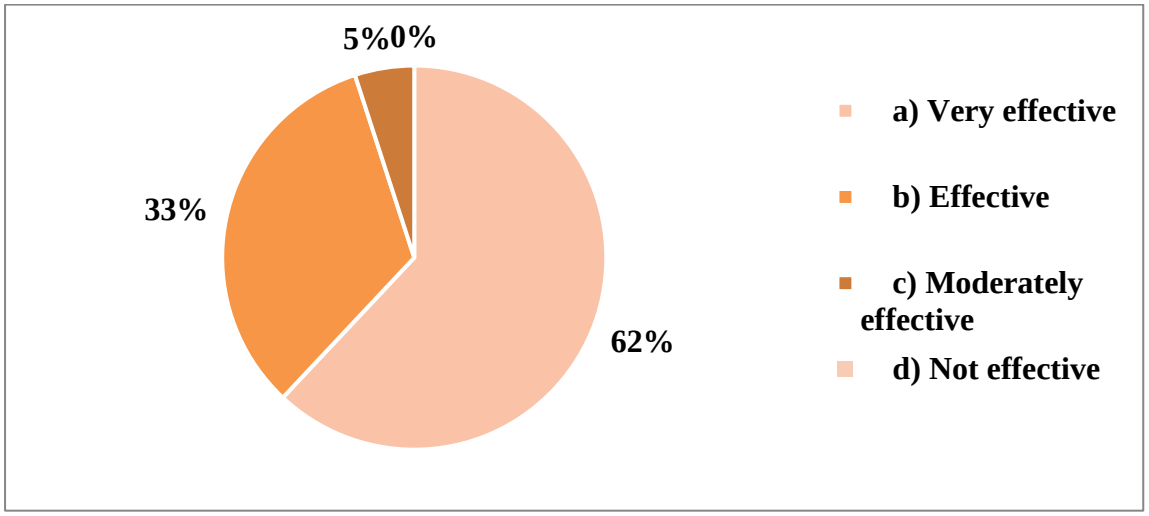
6. How effective do you find Escitalopram in treating anxiety symptoms associated with depression?

a) Very effective

b) Effective

c) Moderately effective

d) Not effective



As per 62% of doctors, they find Escitalopram very effective in treating anxiety symptoms associated with depression.

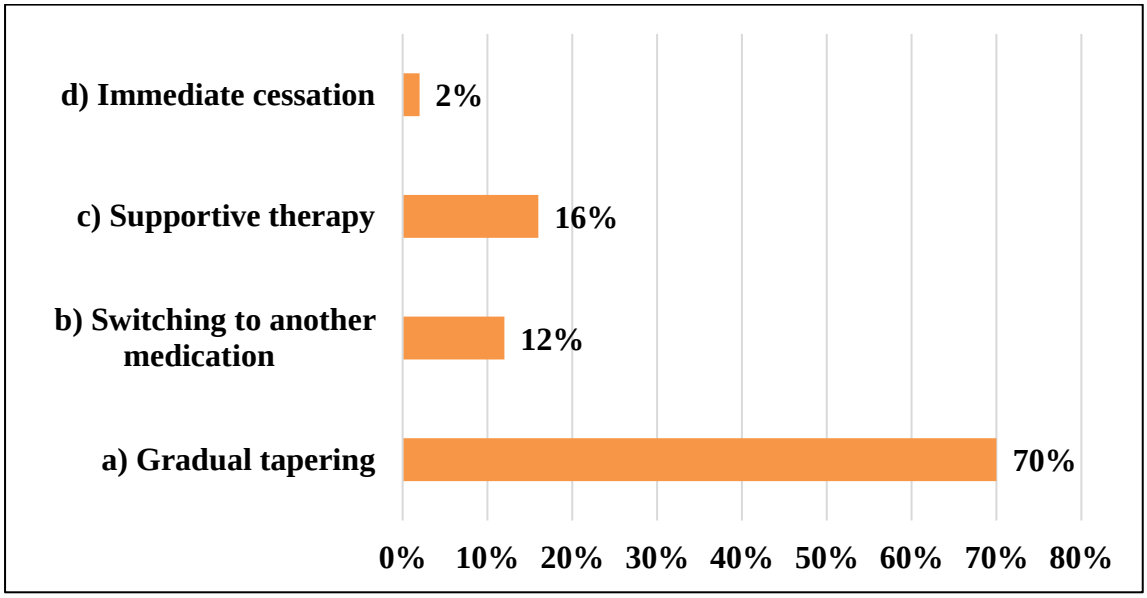
7. How do you handle discontinuation symptoms when stopping Escitalopram in patients?

a) Gradual tapering

b) Switching to another medication

c) Supportive therapy

d) Immediate cessation



According to 70% of doctors, they handle discontinuation symptoms when stopping Escitalopram in patients by gradual tapering.

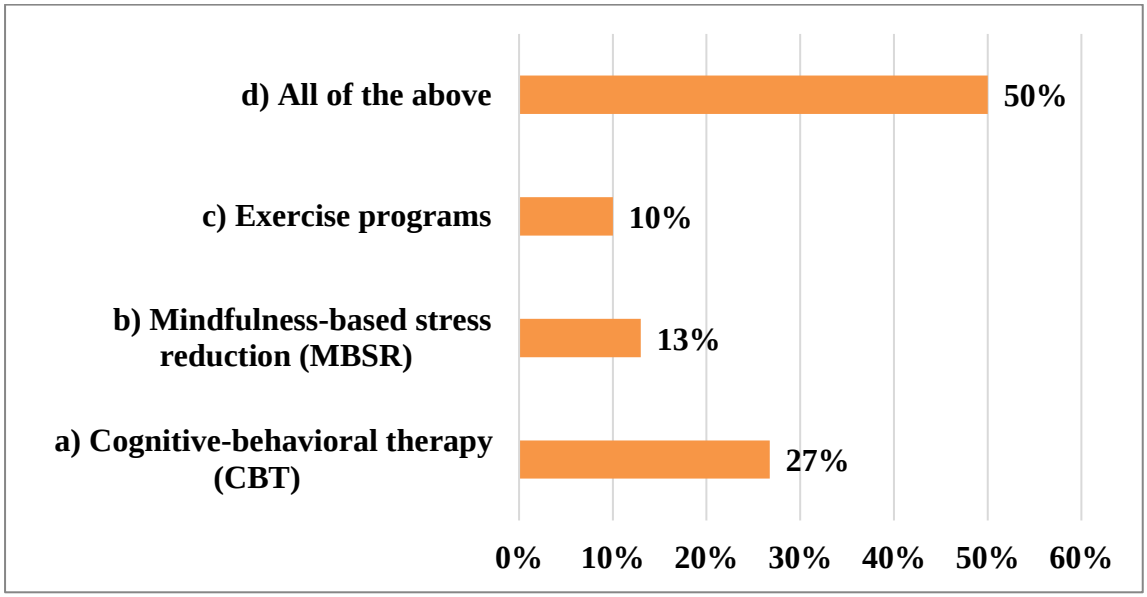
8. Do you recommend any complementary therapies along with Escitalopram for better management of depression?

a) Cognitive-behavioral therapy (CBT)

b) Mindfulness-based stress reduction (MBSR)

c) Exercise programs

d) All of the above



As per 50% of doctors, they recommend cognitive-behavioral therapy, mindfulness-based stress reduction, and exercise programs as complementary therapies along with Escitalopram for better management of depression.

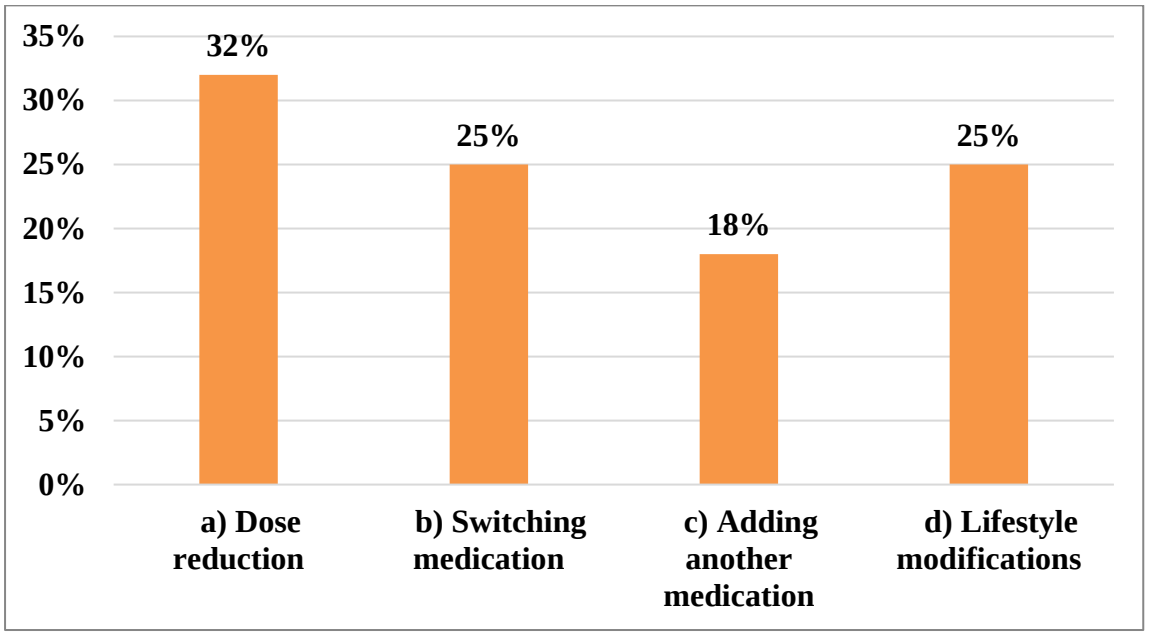
9. How do you manage sexual dysfunction in patients taking Escitalopram?

a) Dose reduction

b) Switching medication

c) Adding another medication

d) Lifestyle modifications



As per 32% of doctors, they manage sexual dysfunction in patients taking Escitalopram by dose reduction.

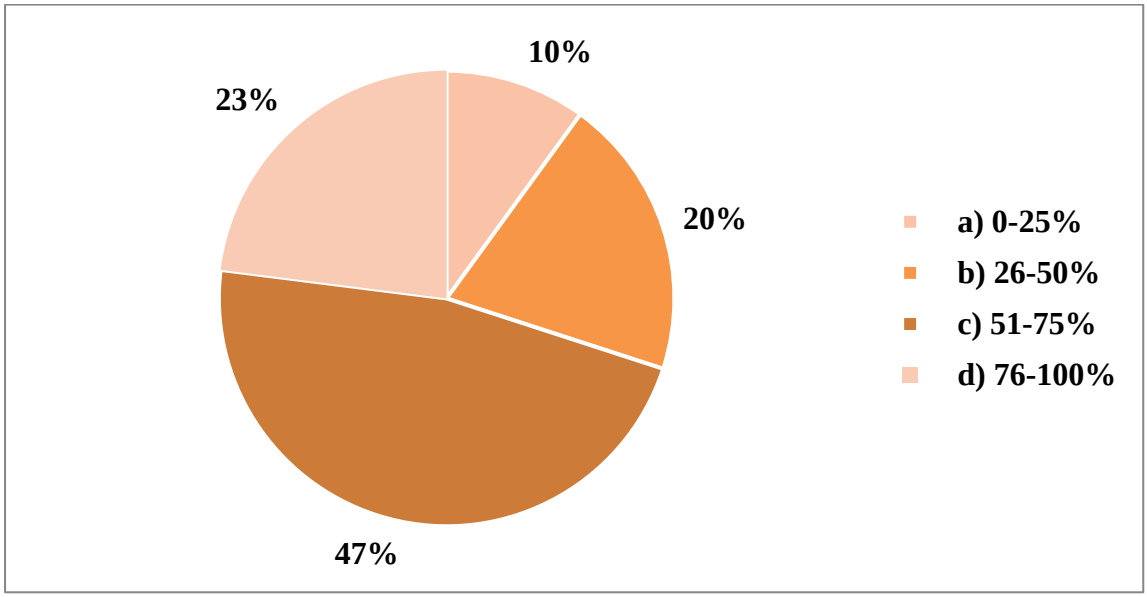
10. What percentage of your patients on Escitalopram experience significant symptom improvement?

a) 0-25%

b) 26-50%

c) 51-75%

d) 76-100%



As per 47% of doctors, 51-75% of patients on Escitalopram experience significant symptom improvement.

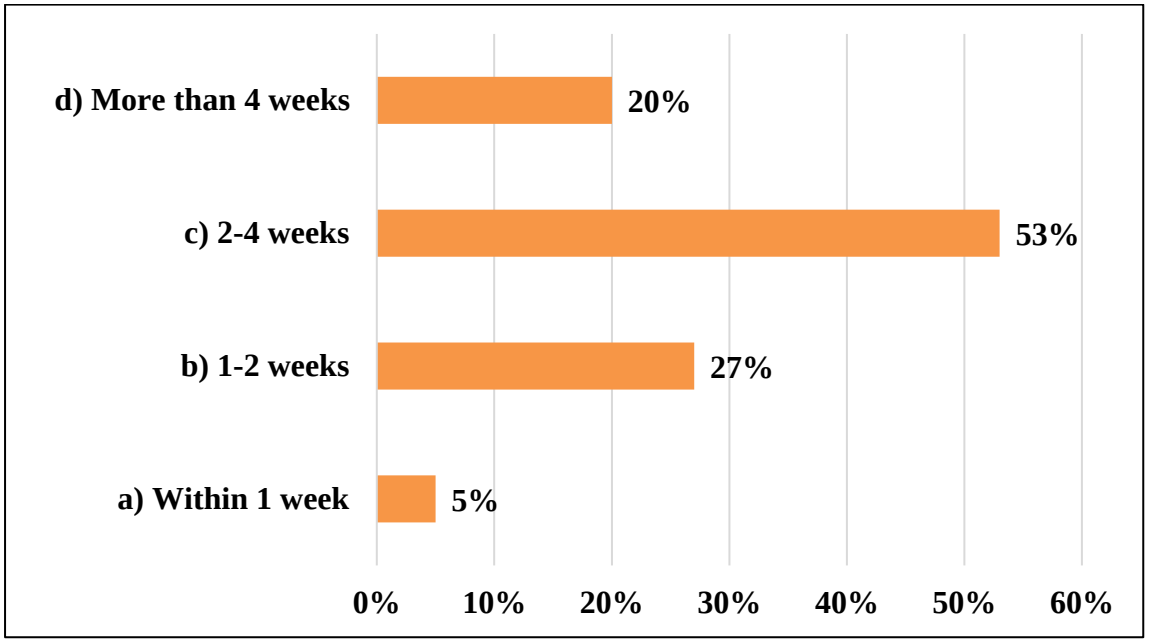
11. In your experience, how soon do patients typically begin to show improvement in depressive symptoms after starting Escitalopram?

a) Within 1 week

b) 1-2 weeks

c) 2-4 weeks

d) More than 4 weeks



According to 53% of doctors, patients typically begin to show improvement in depressive symptoms 2-4 weeks after starting Escitalopram.

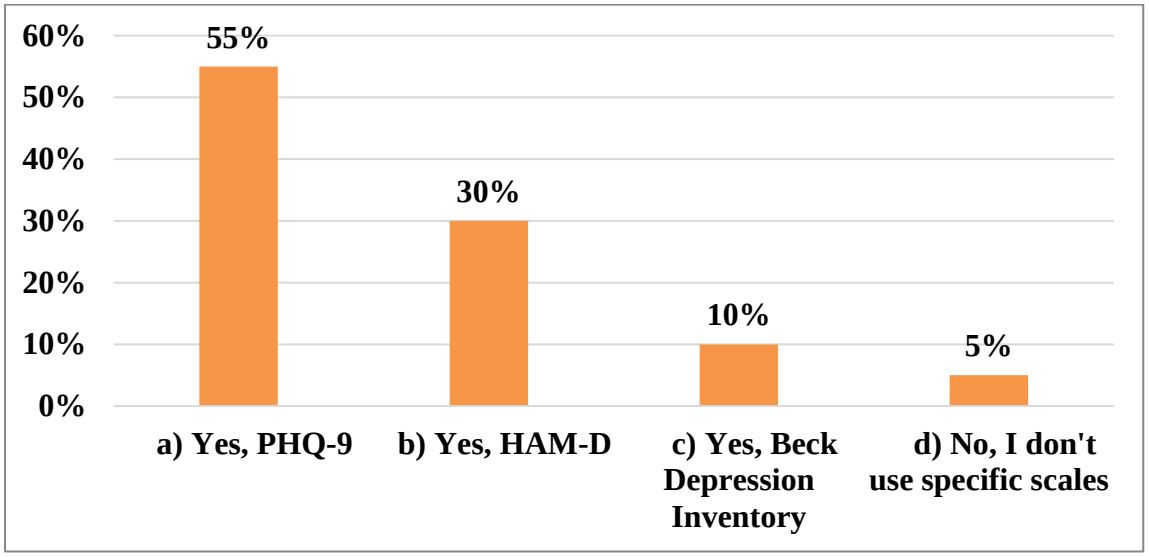
12. Do you use any specific scales or tools to measure the effectiveness of Escitalopram in your patients?

a) Yes, PHQ-9

b) Yes, HAM-D

c) Yes, Beck Depression Inventory

d) No, I don't use specific scales



As per 55% of doctors, they use PHQ-9 to measure the effectiveness of Escitalopram in their patients.

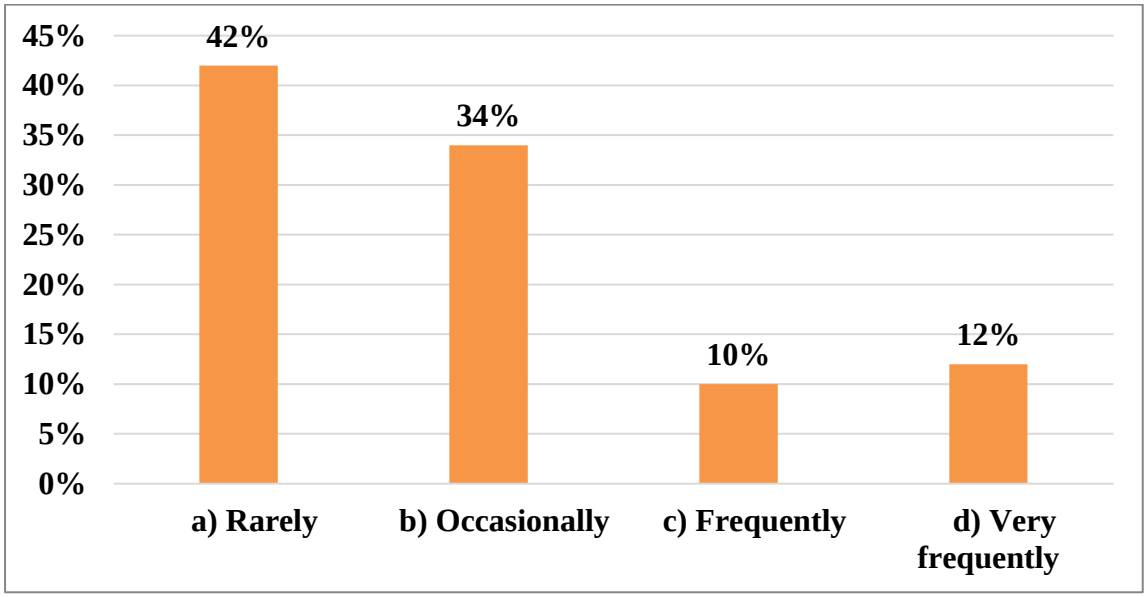
13. How often do you encounter treatment-resistant depression in patients taking Escitalopram?

a) Rarely

b) Occasionally

c) Frequently

d) Very frequently



As per 42% of doctors, they rarely encounter treatment-resistant depression in patients taking Escitalopram.

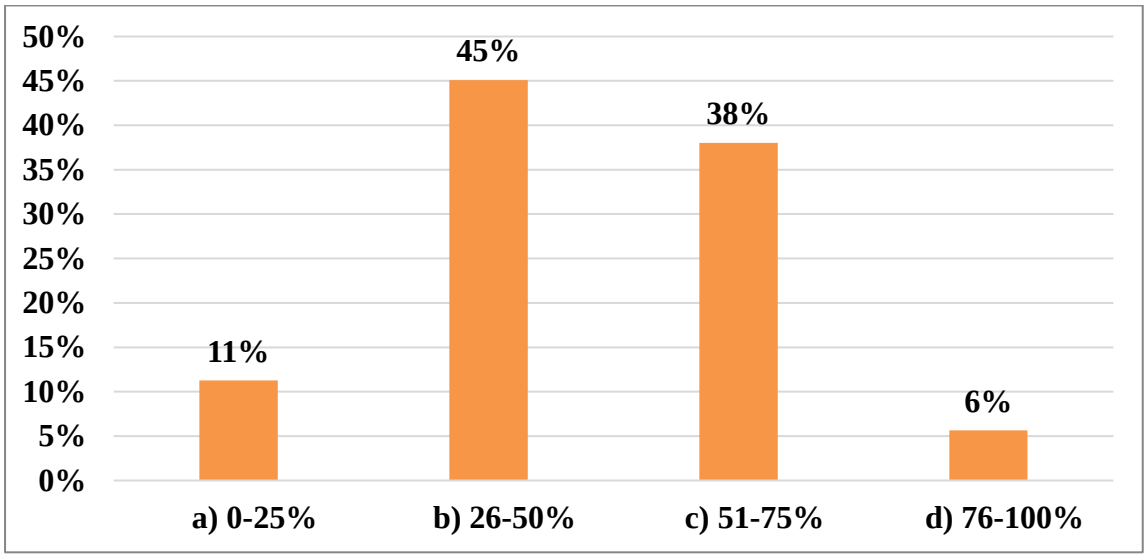
14. What percentage of your patients on Escitalopram achieve full remission of depressive symptoms?

a) 0-25%

b) 26-50%

c) 51-75%

d) 76-100%



According to 45% of doctors, 26-50% of patients on Escitalopram achieve full remission of depressive symptoms.

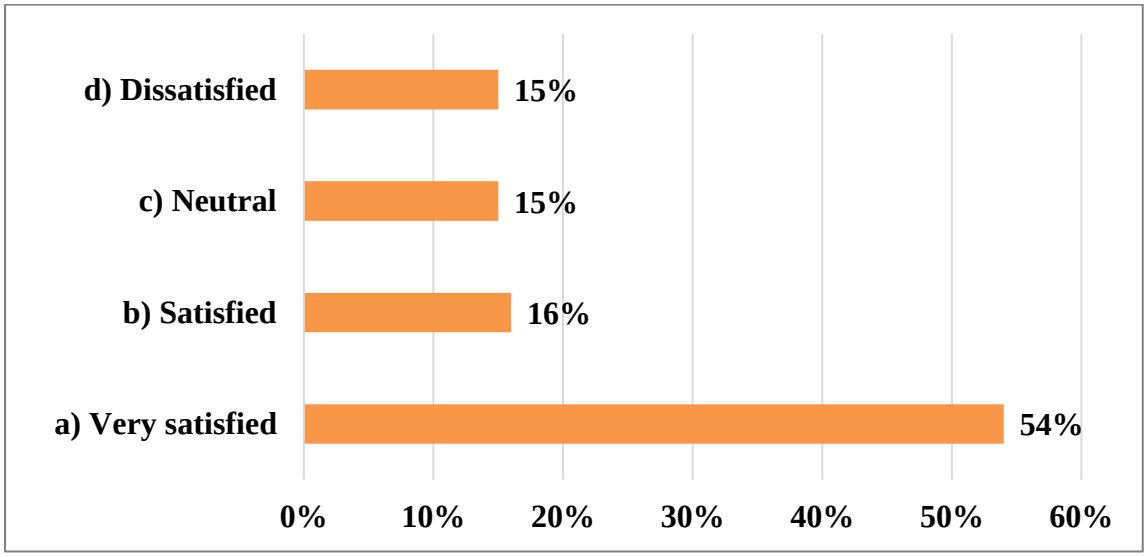
15. How satisfied are you with the overall effectiveness of Escitalopram in treating depression in your patients?

a) Very satisfied

b) Satisfied

c) Neutral

d) Dissatisfied



According to 54% of doctors, they are very satisfied with the overall effectiveness of Escitalopram in treating depression in their patients.

Summary

- According to 56% of doctors, they often prescribe Escitalopram as a first-line treatment for depression.
- As per 62% of doctors, they typically start patients on Escitalopram with 10 mg.
- As per 43% of doctors, 6-12 months is the average duration of Escitalopram treatment in their patients.
- According to 51% of doctors, they determine the appropriate dose escalation for Escitalopram in their patients based on symptom improvement.
- According to 54% of doctors, adults responds best to Escitalopram treatment.
- As per 62% of doctors, they find Escitalopram very effective in treating anxiety symptoms associated with depression.
- According to 70% of doctors, they handle discontinuation symptoms when stopping Escitalopram in patients by gradual tapering.
- As per 50% of doctors, they recommend cognitive-behavioral therapy, mindfulness-based stress reduction, and exercise programs as complementary therapies along with Escitalopram for better management of depression.
- As per 32% of doctors, they manage sexual dysfunction in patients taking Escitalopram by dose reduction.
- As per 47% of doctors, 51-75% of patients on Escitalopram experience significant symptom improvement.
- According to 53% of doctors, patients typically begin to show improvement in depressive symptoms 2-4 weeks after starting Escitalopram.
- As per 55% of doctors, they use PHQ-9 to measure the effectiveness of Escitalopram in their patients.
- As per 42% of doctors, they rarely encounter treatment-resistant depression in patients taking Escitalopram.
- According to 45% of doctors, 26-50% of patients on Escitalopram achieve full remission of depressive symptoms.
- According to 54% of doctors, they are very satisfied with the overall effectiveness of Escitalopram in treating depression in their patients.

Consultant Opinion

Market Opportunities:

- Increase awareness and education about the efficacy and management of Escitalopram, especially its use in treating anxiety symptoms associated with depression. Highlighting its benefits and providing clear guidelines can encourage more consistent use among healthcare professionals.
- Develop tools to help doctors monitor patient progress and manage side effects more effectively. Digital tools that integrate with electronic health records (EHR) can provide reminders for dose adjustments and track symptom improvement.

Value for Healthcare Professionals:

- Provide comprehensive clinical data and case studies that support the use of Escitalopram. Offering webinars and workshops on best practices for prescribing and managing Escitalopram can enhance doctors' confidence and competence in using this medication.
- Supply materials and training on integrating complementary therapies such as CBT, mindfulness, and exercise programs, to provide a holistic approach to treating depression.

Adverse Effect Management:

- Develop and disseminate clear guidelines for managing common side effects such as sexual dysfunction. This can include dose reduction strategies and other pharmacological or non-pharmacological interventions.
- Provide patients with information on what side effects to expect and how to manage them. This can help reduce anxiety and improve adherence to treatment.

Withdrawal Management:

- Ensure that doctors have access to detailed protocols for the gradual tapering of Escitalopram to manage discontinuation symptoms effectively. These protocols should be easy to follow and adaptable to individual patient needs.

- Facilitate support groups or counseling sessions for patients discontinuing Escitalopram to provide emotional support and guidance through the process.

Market Positioning:

- Emphasize the unique benefits of Escitalopram, such as its effectiveness in treating both depression and anxiety symptoms, its safety profile, and the rapid onset of symptom improvement. Use patient testimonials and success stories to reinforce its positive impact.
- Conduct and publish comparative studies that demonstrate the advantages of Escitalopram over other SSRIs, particularly in terms of efficacy, safety, and patient satisfaction.

Personalized Treatment Decisions:

- Encourage doctors to consider patient-specific factors such as age, overall health, and lifestyle when prescribing Escitalopram. Personalized care plans can lead to better adherence and outcomes.
- Advocate for regular use of assessment tools like PHQ-9 to monitor treatment effectiveness and make timely adjustments. This helps in personalizing the treatment plan based on patient progress.

Improving Patient Outcomes:

- Promote the integration of complementary therapies into treatment plans. By addressing multiple aspects of mental health, patients are more likely to experience significant improvements in their overall well-being.
- Provide continuous education for healthcare professionals on the latest research and developments in depression treatment, ensuring they are up-to-date with best practices and innovative approaches.

NOTES

NOTES

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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Weston Medical Education Foundation of India

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