Alpha Psychiatry

LETTER TO THE EDITOR
Alpha Psychiatry 2022;23(1):40-41
DOI: 10.5152/alphapsychiatry.2021.21750

Reproducibility of the Efficacy of Escitalopram in Patients with Major Depression Who Had Previously Remitted with Escitalopram

Dear Editor,

Major depression (MD) is one of the most common and prevalent mental disorders and is characterized by low energy, low mood, low self-esteem, and cognitive impairments. It is one of the leading causes of disability worldwide and is associated with an approximate 15-18% lifetime prevalence rate.[1,2] Following each new episode, the condition of depression becomes worse, and the risk of subsequent relapse increases.[3] When relapse occurs after tapering off an antidepressant, clinicians generally restart the former antidepressant. However, the reproducibility of the former drug is unknown. Thus, we investigated the remission rate of escitalopram in MD patients who had remitted with escitalopram. Sixty-eight patients with drug-naïve, first-episode MD patients diagnosed with the *Diagnostic and Statistical Manual of Mental Disorders 5* (*DSM-5*)[4] and treated with escitalopram for at least 12 weeks were selected for the present study. Twenty-three patients (17/6: out-/in-patients) who had achieved remission for at least 8 weeks and had their escitalopram tapered off for at least 6 months or more and who then suffered a relapse with a major depressive episode were also included. The patients were retreated with escitalopram for the relapse episode. The dosage of escitalopram was 16.9 (4.6) mg/day. We evaluated the depressive state of MD patients with the 17-item Hamilton Rating Scale for Depression (HAMD),[5] at 0, 2, 4, and 8 weeks after restarting the treatment with escitalopram. The remission was defined as the score of HAMD was 7 points or less. This study protocol was approved by the Institutional Review Board at the University of Occupational and Environmental Health, Japan, and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent after being given a detailed description of the study.

The difference between the mean value of improvement in the HAMD in the previous treatment and the mean value of improvement in the current treatment was compared using a paired *t*-test. *P*-values were two-tailed and a $P < .05$ was considered a statistically significant difference. We used multivariable logistic regression to control for the potentially confounding roles of the number of recurrences and withdrawal period from a medical point of view. Patient backgrounds are as follows: 14 of 23 patients were female (61%) and the mean age was 44.22±12.21 (mean (SD) years). The mean number of recurrences was 2.8 (0.7). The average withdrawal period was 12.8 (7.8) months.

Ten of the 23 patients (43.4%) responded to escitalopram, and 6 of 23 (26.0%) patients achieved remission at week 8. The mean reduction in the HAMD score with the first escitalopram treatment was 17.3 (2.6) points. The mean reduction in the HAMD score with the current (second) escitalopram treatment was 10.3 (3.9) points. The reduction of the HAMD score was significantly higher with the first escitalopram treatment than with the second treatment ($P < .001$, paired *t*-test). We performed a logistic regression analysis with the presence of remission as the objective variable and the number of recurrences and withdrawal period as explanatory variables. The explanatory variables were selected based on previous medical observations. Multivariate analysis suggested that the number of relapses but not withdrawal period is a predictor of remission (odds ratio = 0.093, 95% CI; 0.012-0.723, $P = .023$). The cutoff value of the number of relapses was 2, as calculated by receiver operatorating characteristic curve (ROC) analysis. The sensitivity and specificity were 60.0% and 84.6%, respectively.

Reiji Yoshimura
Naomichi Okamoto
Ryohei Igata
Atsuko Ikenouchi

Department of Psychiatry, University of Occupational and Environmental Health, Kitakyushu, Fukuoka, Japan

Corresponding author:
Reiji Yoshimura
✉ yoshi621@med.uoeh-u.ac.jp

Received: October 28, 2021
Accepted: November 24, 2021

Cite this article as: Yoshimura R, Okamoto N, Igata R, Ikenouchi A. Reproducibility of the efficacy of escitalopram in patients with major depression who had previously remitted with escitalopram. *Alpha Psychiatry*. 2022;23(1):40-41.

Fava et al[6] reported that patients who, after an initial response to fluoxetine, relapsed upon switching to placebo have a relatively high probability of responding to the reinitiation of fluoxetine treatment. This supports the reinitiation of the same antidepressant as a first-line treatment strategy in patients who relapsed after stopping a previously effective antidepressant. According to the recent systematic review, a failure to respond only seems to occur in a minority of patients restarting antidepressants (16.5%, range 3.8-42.9%), it is of clinical relevance given the high number of patients taking antidepressants, the occurrence of the phenomenon in all common classes of antidepressants.[7] The results of the present study are largely in accordance with that finding. The reason why the reduction of HAMD in the first treatment was greater than that in the present treatment remains unknown. The desensitization of the serotonin receptor might be involved in the reduced efficacy of escitalopram.[8] We also recommended that MD patients with 2 or fewer relapse episodes should reinitiate escitalopram, and those with 3 or more relapse episodes should change other antidepressants, that is, different classes of antidepressants such as serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, augmentation, or combination strategy. We must perform randomized controlled trials to ascertain whether changing to a dual-acting antidepressant, or strategy of augmentation, or combination, is superior to reinitiating escitalopram in patients with 3 or more relapses. The present study had several limitations: with 23 patients the sample was severely underpowered and statistical inferences were thus highly uncertain and most likely biased. Heterogeneity including symptom severity, clinical characteristics, and psychosocial factors exited. Moreover, the generalizability and representativeness of the study findings were limited. Finally, we could not check the compliance and measured blood levels of escitalopram. We should reconfirm these preliminary findings considering these points.

Ethics Committee Approval: *This study was approved by the Institutional Review Board at the University of Occupational and Environmental Health, Japan.*

Informed Consent: *Written informed consent was obtained from all participants who participated in this study.*

Peer Review: *Externally peer-reviewed.*

Author Contributions: *Concept - R.Y.; Design - R.Y., N.O., R.I., A.I.; Supervision - R.I., A.I.; Resource - R.Y.; Materials - R.Y., N.O., R.I., A.I.; Data Collection and/or Processing - R.Y., N.O., R.I., A.I.; Analysis and/or Interpretation - R.Y., N.O.; Literature Search - R.Y.; Writing - R.Y.; Critical Reviews - N.O., R.I., A.I.*

Conflict of Interest: *The authors have no conflict of interest to declare.*

Financial Disclosure: *The authors declared that this study has received no financial support.*

References

1. Malhi GS, Mann JJ. Depression. *Lancet*. 2018;392(10161):2299-2312. [CrossRef]
2. Kendler KS, Thornton LM, Gardner CO. Stressful life events and previous episodes in the etiology of major depression in women: an evaluation of the "kindling" hypothesis. *Am J Psychiatry*. 2000;157(8):1243-1251. [CrossRef]
3. Park LT, Zarate CA Jr. Depression in the primary care setting. *N Engl J Med*. 2019;380(6):559-568. [CrossRef]
4. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders: DSM-V*. 5th ed. Washington, DC: American Psychiatric Association; 2013.
5. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62. [CrossRef]
6. Fava M, Schmidt ME, Zhang S, Gonzales J, Raute NJ, Judge R. Treatment approaches to major depressive disorder relapse. Part 2: reinitiation of antidepressant treatment. *Psychother Psychosom*. 2002;71(4):195-199. [CrossRef]
7. Bosman RC, Waumans RC, Jacobs GE, et al. Failure to respond after reinstatement of antidepressant medication: a systematic review. *Psychother Psychosom*. 2018;87(5):268-275. [CrossRef]
8. Commons KG, Linnros SE. Delayed antidepressant efficacy and the desensitization hypothesis. *ACS Chem Neurosci*. 2019;10(7):3048-3052. [CrossRef]