Clinical Research in Practice: The Journal of Team Hippocrates

Volume 4 | Issue 2 Article 6

2018

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Recommended Citation
ARTHURS BJ. SSRI maintenance therapy reduces rate of recurrence for elderly patients with first episode of major depression. Clin. Res. Prac. 2018 Sep 14;4(2):eP1667. doi: 10.22237/crp/1533816120

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 4 ISS 2 / eP1667 / SEPTEMBER 14, 2018
doi: 10.22237/crp/1533816120

SSRI maintenance therapy reduces rate of recurrence for elderly patients with first episode of major depression

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ABSTRACT A critical appraisal and clinical application of Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. *N Engl J Med.* 2006 Mar 16;354(11):1130-8. doi: 10.1056/NEJMoa052619. Based on the appraisal, long term SSRI maintenance therapy is recommended for elderly patients suffering from first episode of major depression.

Keywords: *depression, elderly, old age, geriatric, maintenance, treatment, SSRI, antidepressant, recurrence, relapse*

Clinical Context

An 82 year old woman with past medical history of hypertension and osteoporosis presents with a 6 week history of depressed mood, loss of interest in usual activities, insomnia, loss of energy, impaired concentration, and feelings of guilt. The symptoms occur daily. She states that she has had no significant life changes recently and feels guilty that she is "depressed despite having no reason to be depressed." She experienced appropriate grief when her husband died five years ago, but she has never had feelings like this for an extended period of time. She was diagnosed with Major Depressive episode according to DSM-V criteria and started on escitalopram. Elderly individuals are at increased risk of recurrent depression due to medical comorbidities, disability, and psychosocial factors (increased social isolation, loss of loved ones) that can come with older age.[1] Our patient had experienced the death of her husband and told us that she was more socially isolated from her family. The current standard of practice for patients with first episode of depression is continuation therapy for 4-9 months after complete remission of symptoms, with no subsequent maintenance therapy.[9] The patient not only agreed to treatment but also mentioned she never wanted to feel this way again. We wondered if long-term maintenance therapy would decrease the high risk of recurrence for our patient.

Clinical Question

Does SSRI maintenance therapy decrease recurrence in elderly patients with first episode of depression?

Research Article

Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. *N Engl J Med.* 2006 Mar 16;354(11):1130-8. doi: 10.1056/NEJMoa052619

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ISSN: 2379-4550
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Related Literature

A PubMed and Google Scholar search was conducted using the terms “geriatric”, "old age", "depression", and "maintenance treatment" sorted by best match. References were also reviewed in articles on depression treatment in the elderly on UpToDate and DynaMed. Systematic reviews on the topic were analyzed for additional relevant studies cited.[2,3] Publications that focused on tricyclic antidepressants were excluded due to the unfavorable side effect profile in the geriatric population. The search yielded 7 results that were relevant to the clinical question and studied recurrence of depression as the primary outcome. [2,8]

Two systematic reviews exist on the topic, a 2016 updated Cochrane review and a review by Kok et al. The Kok review analyzed eight randomized control trials (RCT's) and reports a reduction in rates of relapse and recurrence of depression in elderly patients who continued antidepressant use. The Cochrane review states that the quality of evidence on this topic is low and that no treatment recommendations can be recommended, and that further high quality studies are necessary. However, this appraisal will focus on primary research articles.

Five double-blinded, randomized, placebo controlled trials studying selective serotonin reuptake inhibitors (SSRI’s) were found in the search.[4,8] The Gorwood paper studied escitalopram use in 305 elderly patients. Maintenance treatment was only 6 months in duration. Additionally, there was no record of the patients that had first episode of depression.[5]

The Dombrovski paper studied paroxetine use in 116 elderly patients, with maintenance treatment lasting 2 years. 59% of those patients were experiencing their first episode of major depression. However, only 54 patients remained in the trial for the 2nd year and there was no subgroup analysis of patients with first episode of depression.[4]

The Wilson paper studied sertraline use in 113 elderly patients, with maintenance treatment lasting 2 years. 73% of those patients were experiencing their first episode of major depression. This study was not chosen because there is no subgroup analysis of first episode patients and also due to the fact that the continuation phase of treatment was very short. There was only 1 month between remission of symptoms and randomization into the treatment and control groups. This is not a standard continuation phase in treatment of depression and may have led to higher rates of recurrence.[8]

The Klysner paper studied citalopram use in 121 elderly patients, 85% of which were experiencing their first episode of major depression. Maintenance treatment was only 11 months in duration. This study was not selected due to the shorter maintenance duration and the lack of subgroup analysis. Also, 41 patients withdrew from the study for reasons not related to recurrence of depression.[6]

The Reynolds paper studied paroxetine use in 116 elderly patients, with maintenance treatment lasting 2 years. This study includes a subgroup analysis of 69 patients with first episode of major depression, therefore this publication was chosen for critical appraisal.[7]

Critical Appraisal

This article describes a randomized, double-blinded, placebo controlled study with CEBM evidence level of 1b. The primary outcome studied was recurrence of depression over the two year maintenance treatment period.

The investigators recruited 116 patients over the age of 70 who had a DSM-IV diagnosis of major depression and responded to treatment with paroxetine and weekly psychotherapy. Participants also had to have a Hamilton Rating Scale of Depression (HRSD) score of at least 15 and a Mini Mental Status Exam (MMSE) score of at least 17. This ensures the study population has moderate to severe depression and does not have severe dementia, which could affect outcomes. Exclusion criteria include psychotic or bipolar depression. This prevents more complicated types of depression from affecting results.

The majority of study participants were Caucasian women with an average age of 77 experiencing their first episode of major depression. This is similar to our patient, her age of 82 falls within the standard deviation of the study population. The median duration of the current episode of depression was between 26 and 57 weeks, but our patient's episode was only 6 weeks in duration. Episodes of longer duration might be more difficult to treat, and could potentially have higher rates of recurrence. Despite this difference, the study population is sufficiently similar to our patient.

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The participants are the patients who responded to initial paroxetine therapy and then remained in remission for a 16 week treatment period. There were 38 patients who required augmented pharmacotherapy with bupropion, nortriptyline, or lithium during the initial phase. For the maintenance phase, these patients were randomized using stratification; 19 were in the treatment group and 19 were in the placebo group. These nonstandard treatments among participants are not ideal because those requiring augmentation might be more prone to relapse. It is for this reason that the article was not included in the Cochrane review. It is unknown how many augmented patients were experiencing their first episode of depression.

Additionally, seven of the 116 participants only had a partial recovery, which may make them more prone to relapse. It is unknown how many of the 7 were randomized into each group. If more ended up in the placebo group, this could potentially affect the rates of recurrence. ClinicalTrials.gov reports 225 subjects, which does not match the published results. Twenty of the 63 patients in the active paroxetine groups did not complete the trial (32%), whereas only nine of 53 patients in the placebo groups did not complete the study (17%). By using a Cox Hazzard Ratio, they took this into account, but it should be noted that active treatment was harder to sustain.

The patients were randomized by a project statistician into 4 groups: paroxetine with psychotherapy, paroxetine with clinical management (counsel on symptoms, adverse effects), placebo with psychotherapy, and placebo with clinical management. Randomization was stratified by augmentation and first episode of depression. There were no statistically significant differences between the groups aside from duration of current episode of depression (longer duration in paroxetine group). However, statistical analysis reports no significant difference relating to the duration of episode and time to recurrence. It is notable that the investigators put 63 patients in the treatment group and 53 patients in the control group, which they claim is to "maximize the number of observations in the active-treatment groups to test for pairwise differences in recurrence rates."

Those in the placebo group were slowly tapered off paroxetine (and augmented pharmacotherapies) over a 6 week period, which was appropriate tapering. The primary outcome was time to recurrence of depression, which was determined by DSM-IV criteria and HRSD of at least 15. Study subjects were assessed monthly. A single geriatric psychiatrist confirmed each recurrence to standardize the process. The authors state that adherence to treatment was tracked by pill counts. The article shows that two members of the paroxetine group were dropped due to noncompliance, but there are no details as to what this means. It is unknown how adherent the rest of the participants were, which could obviously affect outcomes. Psychotherapy was standardized with a manual for care and the sessions were audiotaped to verify each subject received comparable treatment.

Among the subgroup of 69 patients with first episode of depression, the results showed a recurrence rate of 27% in the paroxetine group and 56% in the placebo group over the 2 year span with p=0.03. This results in a number needed to treat (NNT) of 3.45.

Clinical Application

Our patient was going to receive pharmacotherapy, but we made no arrangements for psychotherapy. The results of the trial indicated very similar outcomes with or without psychotherapy, as long as the patient received maintenance pharmacotherapy.

Based on the current evidence available, SSRI maintenance therapy for at least two years is recommended for our patient. While the evidence presented in the Reynolds study is not without flaws, it is well designed and sufficiently able to answer the clinical question. Depression in the elderly is an under recognized and undertreated problem in our society.[4] Old age adults have a high risk of recurrence and higher suicide rates than the general population. It is a major cause of decreased quality of life in the elderly.[4] Our 82 year old woman expressed a desire to get back to enjoying life the way that she did previously, and decreasing her chance of becoming depressed again would aid in achieving her goal.

The strength of the evidence needs to be balanced with the risks of SSRI treatment. Because SSRI's are very well tolerated, there is a low risk in keeping the patient on long-term maintenance therapy. It is also an affordable medication. For these reasons, this appraisal recommends that elderly patients who experience a first episode of major depression and respond to SSRI therapy should remain on maintenance therapy in order to decrease the rate of recurrence.

ISSN: 2379-4550

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Take home points:

1. Depression in the elderly is treatable, yet recurrence can complicate treatment.
2. In critically appraising primary research to answer a clinical question for a specific patient, the strength of evidence needs to be balanced with risk of treatment and the patient's own goals of care.
3. Physicians can practice preventative medicine and improve quality of life in old age by recommending SSRI maintenance therapy to those with first episode of major depression.

References

1. Luijendijk HJ, et al. Incidence and recurrence of late-life depression. *Arch Gen Psychiatry*. 2008;65(12): 1394-1401. doi: 10.1001/archpsyc.65.12.1394
2. Kok RM, Heeren TJ, and Nolen WA. Continuing treatment of depression in the elderly: a systematic review and meta-analysis of double-blinded randomized controlled trials with antidepressants. *Am J Geriatr Psychiatry*. 2011;19(3): 249-255. doi: 10.1097/jgp.0b013e3181ec8085
3. Wilkinson P, Izmeth Z. Continuation and maintenance treatments for depression in older people. *Cochrane Database Syst Rev*. 2016;9:Cd006727. doi: 10.1002/14651858.cd006727.pub2
4. Dombrovski AY, et al. Maintenance treatment for old-age depression preserves health-related quality of life: a randomized, controlled trial of paroxetine and interpersonal psychotherapy. *J Am Geriatr Soc*. 2007;55(9):1325-1332. doi: 10.1111/j.1532-5415.2007.01292.x
5. Gorwood, P., et al., Escitalopram prevents relapse in older patients with major depressive disorder. *Am J Geriatr Psychiatry*. 2007;15(7):581-593. doi: 10.1097/01.jgp.0000240823.94522.4c
6. Klysner, R., et al., Efficacy of citalopram in the prevention of recurrent depression in elderly patients: placebo-controlled study of maintenance therapy. *Br J Psychiatry*. 2002;181:29-35. doi: 10.1192/bjp.181.1.29
7. Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. *N Engl J Med.* 2006 Mar 16;354(11):1130-8. doi: 10.1056/NEJMoa052619
8. Wilson C, et al. Older community residents with depression: long-term treatment with sertraline. Randomised, double-blind, placebo-controlled study. *Br J Psychiatry*. 2003;182:492-497. doi: 10.1192/bjp.182.6.492
9. Armstrong C. APA Releases Guideline on Treatment of Patients with Major Depressive Disorder. *Am Fam Physician*. 2011 May 15;83(10):1219-1227

ISSN: 2379-4550