

# Dealing with Depression in End Stage Renal Disease, Escitalopram vs Nortriptyline

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## ABSTRACT

**Background:** There is lack of consensus on the choice of anti-depressant for treatment of highly prevalent depression in patients with End Stage Renal Disease.

**Aim:** To compare the efficacy and safety selective serotonin reuptake inhibitor with a tricyclic antidepressant in ESRD patients

**Method:** A total of 30 End Stage Renal Disease patients were recruited in the study suffering from depression. They were further divided into two groups having 15 patient each. First group (group A) received Escitalopram (SSRI) and the second group (group B) received Nortriptyline (TCA). The Hamilton Rating Scale (HAM-D) for depression was used to assess the change in depression severity.

**Results:** Group A (n=14) showed a reduction in HAM-D scores from a mean of 23.6+6.9 to 10.4+3.2 (p=0.003), whereas, Group B (n=13) showed a reduction in HAM-D scores from a mean of 19.4+4.2 to 7.6+4.2 (p=0.002). The mean ASEC score of Group A was 5.67 and 7.86 for Group B.

**Conclusion:** The efficacy of both Escitalopram (SSRI) and nortriptyline (TCA) was comparable to each other with no drug standing out as having significant superiority over the other. However, both the drugs used in the trial established efficacy in depression treatment by showing statistically significant reduction HAM-D scores. The safety of both the drugs was also comparable and no drug stood out as significantly safer than the other.

**Keywords:** Escitalopra, nortriptyline, end stage renal disease

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## INTRODUCTION

Major Depressive Disorder (MDD) is referred to as persistence of five or more depressive symptoms for a period of 2 weeks or more in the Diagnostic and Statistical Manual of Mental Disorders V (DSM V)<sup>1</sup>. It has a very high prevalence among patient with Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD) and is associated with increased mortality<sup>2-5</sup>. Despite the high prevalence, depression in ESRD patient is under-diagnosed and undertreated, thereby, increasing its toll on the health of the patients. As compared to a prevalence of 2-10% in general population, about 20-27% of patients with chronic kidney disease suffer from depression of varying severities<sup>6-8</sup>. Depression causes significant social and occupational decline in patients with ESRD<sup>9-11</sup>. It has been shown that there is twofold increase in mortality and hospitalization requirement within a year in ESRD patients on chronic haemodialysis<sup>4</sup>.

There is very limited evidence available on treatment of depression in patients with ESRD. Treatment choices incorporate psychotherapy, pharmacologic treatment, electroconvulsive treatment (ECT), or a mix of a few of these modalities. As far as the pharmacotherapy is concerned, the NICE guidelines do not show a tilt in favor of any of the antidepressants' group for use in patients with ESRD<sup>12,13</sup>. However, there is a general recommendation for selection of SSRIs as the first line treatment as their efficacy has been found to be comparable to that of other antidepressant groups and much better side effects profile overall. Citalopram and Sertraline are particularly favored because of their lesser drug-drug interactions<sup>12,13</sup>, however, these suggestions are not specific to patients with Renal Impairment. The Maudsley prescribing guidelines takes a very similar stance on the subject with no antidepressant group given preference over the other for use in ESRD patients<sup>14</sup>. As a contrast to the maudsley prescribing guideline, the Psychotropic Drug Directory puts Sertaline in the High Risk category for use in patients with ESRD<sup>15</sup>. This categorization is based on a trial of 12 patients with end stage renal disease who were on maintenance hemodialysis and were taking 25 mg/day sertraline. All 12 showed signs of serotonin syndrome and 11 discontinued within 3 weeks<sup>15</sup>. Furthermore, Nagler et al suggest dosage reduction

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of sertraline is required in patients with severe RI (eGFR<30mL/min)<sup>16</sup>.

The above discussion clearly hints to the disparities that exists in the choice of antidepressants for use in depressed ESRD patients. The purpose of this study is to add to the data that is available on this subject and compare the efficacy and safety of a Tricyclic Antidepressant (TCA) with a selective Serotonin Reuptake Inhibitor (SSRI) antidepressant in patients suffering from ESRD.

## METHOD

A total of 30 patients diagnosed as having End-Stage Renal Disease (ESRD) and clinical depression were recruited in the study and were randomly divided into two group of 15 patients each. The depression scoring of each patient in both groups was obtained by using Hamilton Depression Rating Scale (HAM-D). Group A was prescribed Escitalopram (SSRI) 10mg/day and group B was given Nortriptyline (TCA) 25mg/day which was crossed over to 50mg/days after 2 weeks. The HAM-D scoring of both groups was redone after 3 weeks of being on treatment to assess the efficacy of the antidepressant assigned to each group. The Antidepressant Side-Effect Checklist (ASEC) was filled by each patient on the 7th day after starting the assigned treatment. For each item on ASEC, the participants rated the severity of the specified symptom on a four-point scale (0 absent; 1 mild; 2 moderate; 3 severe) and specified whether a symptom (if present) was likely to be a side-effect of the antidepressant drug (yes or no). One participant from Group A and two participants from Group B dropped from the study due to severe side effects before the 7th day post-treatment. The results from rest of the participants were analyzed statistically using SPSS version 20.

## RESULTS

Group A (n=14) showed a reduction in HAM-D scores from a mean of 23.6±6.9 to 10.4±3.2 (p=0.003), whereas, Group B (n=13) showed a reduction in HAM-D scores from a mean of 19.4±4.2 to 7.6±4.2 (p=0.002). The mean ASEC score of Group A was 5.67 and 7.86 for Group B. Two participants from Group A had scored more than 8 on ASEC and three participants from Group B had done the same. However, one participant from Group A and two from Group B dropped out from the study because of severe side effects. No significant differences were found in the results based on age, sex, duration of illness and co-morbidities perhaps because of the relatively small sample size.

## DISCUSSION

The results of the study are in congruence with NICE guidelines and The Maudsley prescribing guidelines which do not point to superior efficacy or safety of any antidepressant group over the other regarding pharmacotherapy of the depression in patient having CKD or ESRD. Perhaps, one more reason for the results obtained from this study could be the fact that Nortriptyline was chosen from the tricyclic antidepressants group. Nortriptyline is one the safest among TCAs and has the lowest propensity for causing anticholinergic side effect. TCAs have already been linked to causing cardiac problems when prescribed in patients with chronic kidney problems<sup>17</sup>. TCAs not only cause direct side effects such as excessive sedation, drowsiness, orthostatic hypotension, arrhythmias etc but also the anticholinergic effects like dryness of mouth can cause the ESRD patient to drink excessive water. The resulting hypervolemic state can further exacerbate ESRD symptoms. The lesser anticholinergic effects of Nortriptyline could have minimized the occurrence of such side effects.

The SSRIs are generally considered quite safe and tolerable. One potential beneficial effect of SSRI in patients with ESRD is that they can decrease orthostatic hypotension, a common problem especially in Hemodialysis patients<sup>17</sup>. SSRI may exacerbate preexisting uremic symptoms. They may increase the risk for bleeding<sup>18</sup>. This adverse effect can be particularly problematic in patients with ESRD and underlying qualitative platelet defects related to uremia. SSRI have also been associated with increased nausea as a result of increased serotonergic activity in the gastrointestinal tract<sup>19,20</sup>. Thereby, it is clear that both SSRIs and TCAs have their pros and cons when considered for use in patients with kidney impairment. Needless to say, much further research is needed on this subject. A larger sample size, longer follow up, control groups and incorporation of co-morbidities with ESRD in the analysis can yield better results and render further insight into the use of TCAs and SSRIs in patients with kidney impairment.

## CONCLUSION

The efficacy of both Escitalopram (SSRI) and nortriptyline (TCA) was comparable to each other with no drug standing out as having significant superiority over the other. However, both the drugs used in the trial established efficacy in depression treatment by showing statistically significant reduction HAM-D scores. The safety of both the drugs was also

comparable and no drug stood out as significantly safer than the other.

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