Article

Agomelatine Efficacy in Treating First-Episode Senile Depression

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ABSTRACT

Objective: To investigate agomelatine effects on first-episode senile depression patients.

Methods: One hundred and sixteen elderly patients with first-episode senile depression were randomly and evenly divided into an observation group and a control group. The observation subjects were treated with agomelatine. The control subjects were treated with sertraline. The treatment effects, sleep improvement, and adverse reactions were compared.

Results: After one week of treatment observation group The Hamilton Depression Rating Scale (HAMD) and Pittsburgh Sleep Quality Index (PSQI) scores after one week of treatment decreased significantly. After two weeks of treatment control group scores also decreased significantly ($p < 0.01$). Observation group HAMD scores were significantly lower than control group scores after weeks 1, 2, 4, and 8 ($p < 0.05$). Observation group PSQI scores were significantly lower than control group at the end of weeks 4 and 8 ($p < 0.05$). Observation group adverse incidence rate during administration was significantly lower than the control group ($p < 0.05$).

Conclusion: Both agomelatine and sertraline are effective in treating first-episode depression elderly patients. Agomelatine has an earlier response, fewer adverse reactions and superior insomnia improvement.

Keywords: First-episode senile depression; Agomelatine; Sertraline

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1 INTRODUCTION

As populations age, the number of those with senile depression [SD] increases. SD has become an important disease which affects the quality of life and physical health of the elderly [1]. In clinical practice, the elderly have a lower recognition of the therapeutic value of psychotherapy. Somatization are more significant in depressed elderly patients. Choice of medications for first-episode senile depression patients is becoming crucial.

Recently, biological rhythm mechanism studies have found that biological rhythm disorders may be a pathological mechanisms of depression. Some antidepressants may adversely effect biological rhythms [2] and sleeping patterns. Agomelatine is a melatonin receptor agonist and 5-HT2C antagonist. Combinations of these receptors may determine appropriate and effective anti-depression treatments [3]. This paper reports comparisons of treatment effects, sleep improvements, and adverse reactions in first-episode senile depression patients treated with agomelatine and sertraline.

2 SUBJECT AND METHODS

2.1 Research subjects

Inclusion criteria: Included were first-episode patients who satisfied the diagnostic criteria for depressive disorders contained in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), which is gender-specific, aged 60-75, with HAMD [4] (17 items) score ≥ 20 points. Written informed consent was obtained from the patients. Exclusion criteria: patients with severe suicidal tendencies, complicated with other systematic severe diseases, whose baseline HAMD score decreased by ≥ 25 % compared to the screening controls, who had prior allergic reactions to research medications, administered along with other antidepressants within two weeks, or or failed to follow the treatment instructions.

The subjects in this study came from the Psychological Clinic of the Affiliated Hospital of Qingdao University. A total of 116 eligible patients were enrolled between February 2015 and February 2016. The group was evenly divided and randomly assigned to either an agomelatine group or an sertraline group. Two subjects in the agomelatine group were left the study in weeks 4 and 6. One sertraline group subject, withdrew due to headaches and two patients withdrew due to poor therapeutic results. A total of 56 agomelatine group subjects and 55 sertraline group subjects remained for the sample assessment.

There were 29 male and 27 female patients in the agomelatine group having a mean age of 65.8 ± 3.5; a baseline HAMD total score of 26.7 ± 5.2 points; and a baseline PSQI total score of 15.1 ± 2.9 points. The 25 male and 30 female patients in the sertraline group had a mean age of 67.6 ± 4.7; a baseline HAMD total score of 27.5 ± 4.9 points; and a baseline PSQI total score of 14.3 ± 2.7 points. These group differences were not statistically significant ($p > 0.05$) in terms of gender, age, HAMD total score, or PSQI total score. The two groups were comparable.

2.2 Treatment method

Agomelatine group subjects were administered agomelatine (25 mg/tablet, lot No.: H20143375), beginning with a a small dosage and which was increase to in the second week. The minimum treatment dosage was 12.5 mg and the maximum dosage was 50 mg. Sertraline group subjects were administered a 50 mg/tablet, (lot No.: H10980141), started from a small dosage and then added to treatment dosage within two weeks.

The minimum treatment dosage was 25 mg and the maximum dosage was 100 mg. During treatment, no other antipsychotic or anti-anxiety drugs were used and any electro-shock or systematic psychotherapies were discontinued during the course of the study.

2.3 Assessment method

Subjects depression and sleeping status of patients for both two groups were assessed using HAMD and PSQI at the end of weeks 1, 2, 4, and 8. Adverse reactions were assessed using TESS. These scales are commonly used clinical tools and they have a high reliability and validity index.

2.4 Statistical analysis

Statistical software SPSS13.0 performed data calculations. Measurement data were compared using the paired t test method. Counting data was analyzed using an χ^2 test. $p < 0.05$ was defined as statistically significant.

3 RESULTS

3.1 HAMD score comparison between two groups before and after treatment

HAMD scores for both groups decreased at each time point measured. Time points were after weeks 1, 2, 4, and 8 which were compared to the immediately prior period. The agomelatine group HAMD scores decreased after the first week. Sertraline group HAMD scores decreased after the second week ($p < 0.01$). Comparing the two , there was a significant difference in HAMD scores between the two groups at the end of weeks 1, 2, 4, and 8 ($p < 0.05$) (Table 1).

Table 1. Pre and Post-Treatment HAMD Scores Comparison ($\bar{x} \pm s$)

Group	Case	Before treatment	Week 1	Week 2	Week 4	Week 8
Agomelatine	56	26.7 ± 5.2	22.6 ± 6.8[ab]	16.2 ± 3.7[ab]	10.1 ± 3.6[ab]	6.2 ± 3.7[ab]
Sertraline	55	27.5 ± 4.9	25.8 ± 7.1	18.1 ± 4.2[a]	13.2 ± 4.4[a]	8.4 ± 4.1[a]

Note: [a]$p < 0.01$, compared with pre-treatment; [b]$p < 0.05$, for comparison of two groups at the same time point.

3.2 Pre and Post-Treatment PSQI Scores Comparison

The average PSQI total scores for both groups decreased at each time point after for weeks 1, 2, 4, and 8. The range of decrease range increased with treatment duration. Agomelatine group PSQI scores significantly decreased after the first week. The sertraline group PSQI scores significantly decreased after the end of week two ($p < 0.01$). A comparison shows significant PSQI scores differences between the two groups at the end of week 4 and 8 ($p < 0.05$). (Table 2)

Table 2. Pre and Post-Treatment PSQI scores comparisons the groups ($\bar{x} \pm s$)

Group	Before treatment	Week 1	Week 2	Week 4	Week 8
Agomelatine	15.1 ± 2.9	12.6 ± 3.8[a]	10.1 ± 3.2[a]	6.9 ± 3.1[ab]	4.7 ± 2.8[ab]
Sertraline	14.3 ± 2.7	13.2 ± 3.7	11.7 ± 3.4[a]	9.5 ± 4.4[a]	6.4 ± 4.1[a]

Note: [a]$p < 0.01$, compared with pre-treatment; [b]$p < 0.05$, for comparison of two groups at the same time point.

3.3 TESS score comparison during the treatment

Agomelatine group subjects were subject to gastrointestinal symptoms, such as nausea, diarrhea, and dyspepsia. Sertraline group subjects were subject to headache, dizziness, dry mouth, and loss of appetite. Agomelatine group TESS scores at the end of week 2, 4, and 8 were significantly lower than the sertraline group ($p < 0.05$) (Table 3).

Table 3. Post-treatment TESS scores compared ($\bar{x} \pm s$)

Time	Agomelation	Sertraline	t value
Week 1	8.93 ± 2.67	9.26 ± 3.07	0.84
Week 2	7.11 ± 2.05	9.17 ± 2.58	2.78[b]
Week 4	5.12 ± 2.07	8.32 ± 3.46	3.19[b]
Week 8	4.27 ± 1.55	6.67 ± 3.58	2.97[b]

Note: [b]$p < 0.05$, for comparison of two groups at the same time point.

4 DISCUSSION

Depression can cause severe suffering in the elderly and it is one of major causes of suicide [5]. Effective rapid treatment of senile depression and lessening elderly patient insomnia is critical. Agomelatine acts on the MT1, MT2, and 5-HT2C receptors and it exerts antidepressant effects by restoring the normal biological rhythms [6]. Specifically it increases the prefrontal NA and DA levels. Agomelatine's affinity for other receptors is negligible and it is safe for the elderly population. As a commonly-used 5-HT re-uptake inhibitor, sertraline is used to treat depression by inhibiting the 5-HT re-uptake by the presynaptic membranes to increase 5-HT contents in the synaptic cleft. Cipriani A [7], *et al.* showed that sertraline can be considered as a reference standard for antidepressant efficacy due to of its effectiveness and acceptability.

This study reports that agomelatine begins to become effective by the end of the first week. Sertraline begins to become effective by the end of the second week. Agomelatine acts more than the sertraline in treating senile depression. After 1, 2, 4, and 8 weeks of treatment, agomelatine patient HAMD scores were lower than sertraline group scores ($p < 0.05$).

This suggests that the overall therapeutic effect of agomelatine on depressed elderly patients is superior to sertraline. The rapid onset of agomelatine effects may associate with the improved sleep and the rapid recovery of daytime functionality [8]. This study confirms this conclusion. Agomelatine group insomnia was alleviated by the end of the first week. Agomelatine group PSQI scores were lower than that sertraline group ($p < 0.05$) after the fourth week and eighth weeks. This indicates that agomelatine is superior to sertraline in elderly schizophrenia patient sleep improvement. It has a rapid onset effect. Senile depression patients are sensitive sleep problems. Agomelatine, by relieving insomnia symptoms, will tend to increase senile depressive patient treatment compliance. This study also found that, after the second treatment week, agomelatine group TESS scores were lower than sertraline group TESS scores ($p < 0.05$). This suggests that agomelatine improved patient tolerance to the medication which may associated with the fact that the agomelatine itself does not increase 5-HT concentration in the blood [9]. It may avoid, or reduce, adverse reactions caused by SSRI drugs. The limititations of this study should be mentioned. Randomization method may have been too simple. Blind blindness is not used. Sample size was small. These limitations should be addressed in future studies.

In conclusion, agomelatine and sertraline are both effective at lessening improve depressive symptoms of first-episode depressive patients. Agomelatine has faster onset effects, is a better promoter of patient sleep improvement and has fewer adverse reactions. These effects recommend agomelatine to clinicians for its wider use in clinical practice.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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