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Original Research Paper

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TO COMPARE SAFETY AND EFFICACY OF AGOMELATINE AND ESCITALOPRAM IN PATIENTS OF MAJOR DEPRESSIVE DISORDER

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ABSTRACT The objective of the study was to compare safety and efficacy of agomelatine and escitalopram in patients of major depressive disorder (MDD). This prospective, randomized, comparative and open labelled study was conducted in 140 patients of MDD with 70 patients in each group. Group A received agomelatine and group B received escitalopram. The efficacy was evaluated on the basis of percentage change in Hamilton Depression Rating Scale (HDRS) score. The safety was evaluated on the basis of by spontaneous adverse drug reaction reporting. In both groups A and B, there was a significant reduction in HDRS score from baseline. The mean HDRS score at baseline and follow up visits in both groups was found to be comparable. The safety profile of both drugs was found to be similar. In conclusion, the safety and efficacy of agomelatine and escitalopram in patients of MDD is similar.

KEYWORDS : Major depressive disorder, agomelatine, escitalopram.

INTRODUCTION

Major depressive disorder (MDD), or depression, is a syndrome characterized by a number of behavioural, cognitive and emotional features. It is associated with a sad or depressed mood[1]. Prevalence of MDD in India is 15.9%[2]. The link between depression and sleep disturbance is strong. About three quarters of depressed patients have insomnia symptoms[3]. The relative safety and better acceptability of selective serotonin reuptake inhibitors (SSRIs) has made them 1st line drugs in depression[4]. It has been postulated that antidepressants that benefit sleep quality and reset the disturbed circadian rhythms will have more therapeutic efficacy compared to the other antidepressants[5]. Agomelatine, a melatonin receptor MT1/MT2 agonist and 5-HT2c receptor antagonist, novel antidepressant has a comparable efficacy with SSRIs in depression and is known to have beneficial effects on subjective sleep in major depressive disorder patients also has lesser side effects; commonly seen side effects are headache, diarrhoea and constipation. The melatonergic modulation by agomelatine is suggested to be the main mechanism of its antidepressive action[6]. Escitalopram too has a significant beneficial effect in reducing sleep disturbance in patients suffering from MDD[7]. Commonly encountered side effects are gastrointestinal, others side effects are nervousness, restlessness, insomnia, anorexia, dyskinesia and headache[8]. Extensive search of the literature yielded no results for any study comparing safety and efficacy of agomelatine and escitalopram in patients with MDD in India. Hence, this study was planned to compare safety and efficacy of agomelatine and escitalopram in patients with MDD.

METHODS

Study design and procedure.

The study was conducted in patients visiting the department of Psychiatry, Christian Medical College and Hospital, Ludhiana. This was prospective, randomized and comparative study. The study was approved by institutional ethics committee and was not funded. 140 patients diagnosed with major depressive disorder (MDD), as per International Classification of Diseases 10 (ICD 10) criteria were assessed with Hamilton Depression Rating Scale (HDRS) and the patients having HDRS score >7 were recruited in the study. Written informed consent was obtained and patient information sheet was provided to all patients before enrolment. Patients of both sexes between 18 -70 years were included. Patients with history of hypersensitivity to study medication, pregnant and lactating female patients, patients with suicidal tendencies, patients with severe depression (HDRS score >18) were excluded from the study. The patients were randomized into two treatment groups using computer generated random numbers. Group A (n=70) received agomelatine 25-50 mg/day and group B (n=70) received escitalopram 10-20 mg/day). Efficacy was assessed using HDRS. Improvement in symptoms of depression was evaluated at 0, 3 and 6 weeks using HDRS. A HDRS score between 0-7 is normal; 8-13 signifies mild depression; 14-18 signifies moderate depression; 19-22 signifies severe depression and a score >23 signifies very severe depression. Response is defined as reduction of 50% or more of the HDRS score. A HDRS score ≤ 7 indicates patient is in remission[9]. The safety of the two drugs was recorded by frequencies of adverse drug reactions yielded by spontaneous adverse drug reaction reporting.

Statistical analysis

In the descriptive analysis, continuous variables are expressed as mean ± standard deviation and categorical variables are expressed as count. Univariate and multivariate analysis was performed as required. A p value less than 0.05 is regarded as statistically significant. All statistical analysis was performed using SPSS, version 21.

RESULTS

The patients were comparable in demographic profile. The patients had comparable HDRS score at baseline 15.2 (group A) and 15.4 (group B), table 1. Mean HDRS score of patients at baseline and subsequent visit in both the groups is shown in fig. 1.

Table 1. Demographic and clinical profile of patients in both groups at baseline

Characteristics	Group A	Group B
Total no. of patients	70	70
Age (years)	41.43	43.29
Sex (M:F)	36:34(51%:48%)	45:25(64%:35%)
HDRS Score	15.24 ± 0.21	15.43 ± 0.19

No significant difference between group A and B (p>0.05).

There was no significant difference in mean decrease in HDRS score at 3rd and 6th weeks, when both the groups were compared, depicted in figure 1. However there was significant ($p < 0.001$) difference in HDRS score of patients from baseline to 3rd and 6th week of treatment within each groups (Table 2 and 3).

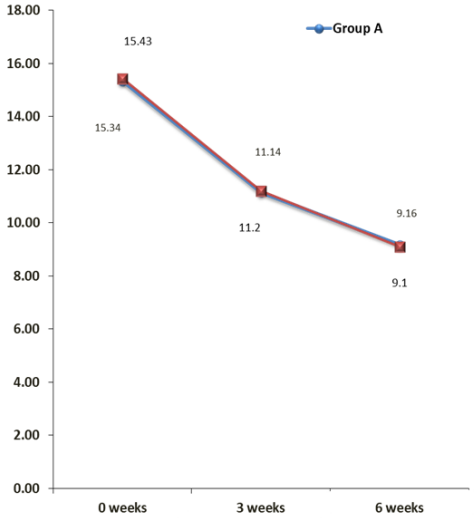

Figure 1: Comparison of mean HDRS score between the groups.

No significant difference between group A and B (p>0.05).

Table 2- HDRS score (Mean ± SD. error) in group A at baseline, 3 weeks and 6 weeks

Group A		
Follow Up	**HDRS Score**	**P Value**
0 Weeks	15.24 ± 0.21	
3 Weeks	11.21 ± 0.23#	< 0.001
6 Weeks	9.16 ± 0.16#	< 0.001

As compared with 0 weeks

Table 3- HDRS score (mean ± std. error) in group B at baseline, 3 weeks and 6 weeks

Group B		
Follow Up	**HDRS Score**	**P Value**
0 Weeks	15.43 ± 0.19	
3 Weeks	11.2 ± 0.2#	< 0.001
6 Weeks	9.1 ± 0.17#	< 0.001

As compared with 0 week

The mean percentage reduction in HDRS score from 0 to 6 weeks in both the groups is shown in figure 2. The mean percentage reduction was comparable in both the groups and no statistical significant difference (p>0.5) was observed.

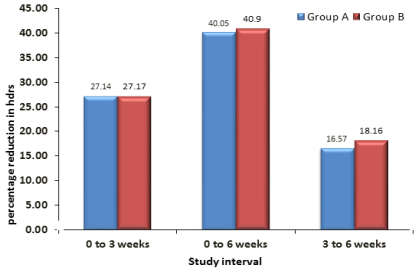

Figure 2. Comparison of percentage reduction of HDRS score between the groups.

No significant difference between the groups (p>0.05).

The difference in the number of remitters/responders was not found to be statistically significant (p>0.05), depicted in figure 3. No significant difference in the number of participants who encountered adverse drug reactions (ADRs) between both the groups was observed. Most of the adverse effects observed in both the groups were mild. Gastrointestinal (GI) side effects including nausea, dyspepsia and acid regurgitation were the most commonly encountered ADRs in both groups. No serious adverse events reported in both the groups.

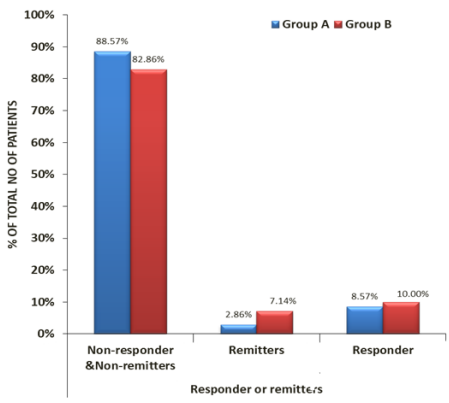

Figure 3- Comparison of the number of responders and remitter in both groups.

No significant difference between group A and B (p>0.05).

DISCUSSION

Depression is a common psychiatric illness encountered in clinical practice and is a leading cause of disability, workplace absenteeism, decreased productivity and high suicide rates[10].SSRIs are presently the most widely used drugs for the treatment of depression. However, about 40% of all depressed patients fail to show a response to first-line antidepressant drug treatment, and of those that do respond; only a proportion will achieve full recovery- thus the need for newer antidepressants[11]. Agomelatine is an antidepressant drug with a novel mechanism of action. It is the first antidepressants that targets the circadian system, sleep quality and mediates its therapeutic effect through the melatonergic system[12]. Extensive literature search yielded only very few results of studies done to compare the safety and efficacy of agomelatine and escitalopram in patients with MDD, with differing outcomes. Hence we conducted this study to compare the safety and efficacy of agomelatine and escitalopram in patients of MDD. A total of hundred and forty patients (n=140) were enrolled based on the inclusion criteria. We found a greater number of male participants compared to females, however this difference was not found to be statistically significant. This was not in agreement with previous studies like the study conducted by Marcus M et al (2012) in which the burden of depression was found to be significantly higher in women compared to men[13]. Ravi Babu Komaram et al (2015) conducted a study to compare the safety and efficacy of agomelatine and escitalopram in patients of MDD. They came to the conclusion that agomelatine 25–50 mg /day is as effective and safe as escitalopram 10–20 mg/day[14]. In agreement with this study we also found the same results. In our study we found there to be no significant difference in the number of participants who encountered adverse drug reactions (ADRs) between both the groups. These findings are in accordance with the above mentioned studies conducted by Ravi Babu Komaram et al (2015) and Urade et al (2015), which also found the safety profile of agomelatine and escitalopram to be comparable[14,15]. The number of responders and remitters in groups A and group B were found to be comparable. These findings of our study were found to be in agreement with a previous study conducted by Ravi Babu Komaram et al (2015), in which there was found to be no significant difference in the number of responders and remitters between both groups[14]. In the context of efficacy and safety, in our study we found the efficacy and safety of agomelatine and escitalopram to be comparable which was in agreement with a previous study done by Ravi Babu Komaram et al (2015)[14]. However, a study conducted by Urade et al (2015) found the efficacy of escitalopram to be greater than agomelatine [15]. This difference may be attributed to the longer period of the study. Hence, we propose that multi-centric trials with a larger sample size and longer duration of study must be conducted.

CONCLUSION

In conclusion, in our study we found that the safety and efficacy of

agomelatine and escitalopram in patients of MDD is similar.

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