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EFFECTIVENESS OF RAMELTEON AND AGOMELATINE AS PREMEDICATION BEFORE ANAESTHESIA INDUCTION

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How to cite: A comparison of the effectiveness of Ramelteon and Agomelatine as premedication before anaesthesia induction.

ABSTRACT

Background Ramelteon is the first melatonin receptor agonist class medicine used in hypnotic therapy, and it was just licensed by the FDA to treat insomnia. Melatonin MT2 and MT1 receptors are thought to help maintain heart rhythm and regulate the sleep-wake cycle.

Aim: The current study sought to compare the effectiveness of Ramelteon and Agomelatine as premedication prior to anaesthesia induction.

Methods: The research evaluated 120 ASA class I participants of both genders who had elective surgery under general anaesthesia . These 120 participants were separated into two groups: Group I received Agomelatine, whereas Group II received Ramelteon as a premedication prior to anaesthesia induction.

Results: There were 24 subjects in Group I and 20 subjects in Group II who took ramelteon between the ages of 31 and 40. Group I and II had 16 and 20 participants, respectively, ranging in age from 41 to 50 years. Groups I and II each had two and four participants aged 51 to 60 years old. No change in orientation score was noticed on intergroup comparisons reflecting non-statistical differences.

Conclusions: The current study suggests that orientation is unaffected by either Ramelteon or agomelatine administered 60 minutes before surgery as a pre-anaesthesia drug.

Keywords: Agomelatine, anaesthesia induction, assessment of orientation, ramelteon, pre-anesthetic medication

INTRODUCTION

Servier Laboratories, a European pharmaceutical business, produced a structural counterpart of melatonin called agomelatine. Agomelatine was originally approved for clinical usage in the European Union in 2009, and it is now being approved by the US FDA. Agomelatine is a synthetic naphthalene analogue of melatonin that acts as an agonist of the melatonergic MT1 and MT2 receptors. It has a longer half-life, with an average terminal half-life of 140 minutes. It has a higher affinity for the receptors than melatonin.1,2

Agomelatine's antidepressant effectiveness is mostly dependent on its serotonin 5-HT2 receptor antagonist action, as well as its melatonergic characteristics. In addition to its depressive activity, agomelatone has been shown in animal models to have anxiolytic efficacy.3

Antagonism of 5-HT2c receptors induced by agomelatine, particularly in the frontal cortex, may be associated with sedative and anxiolytic properties, and in addition to blocking 5-HT2c receptors, agomelatine can increase extracellular noradrenaline levels, which increases the anxiolytic response.4

The FDA has authorized Ramelteon, the first melatonin receptor agonist medication in the hypnotic therapy class, for the treatment of insomnia. Melatonin receptors MT1 and MT2 are thought to have a role in regulating the sleep-wake cycle. Ramelteon's high affinity and specificity for melatonin receptors, MT1 and MT2, is thought to be responsible for its anxiolytic and sedative actions.[5] Ramelteon has been shown to be quite effective in treating patients with sleep onset problems since it was licensed for insomnia treatment in 2005. It is available as an 8mg tablet, with an average onset of action of roughly 1 hour and an elimination half-life of 2.6-5 hours.6

Ramelteon has a fast and efficient first-pass metabolism and linear pharmacokinetics. Cmax, or peak serum concentration, and the area under the concentration-time curve (AUC) show significant inter-subject variability, indicating a strong first-pass effect with a coefficient of variation of about 100%. Various metabolites have been detected in human urine and serum. There is limited information on the comparative effectiveness of Agomelatine and Ramelteon as pre-anaesthetic medications prior to anaesthesia induction in terms of orientation.[7] As a result, the current study intended to compare the effectiveness of Ramelteon and Agomelatine as premedications prior to anaesthesia induction.

MATERIALS & METHODS

The current prospective randomized controlled clinical trial aims to compare the effectiveness of Ramelteon and Agomelatine as premedication before anaesthesia induction. The subjects for the research were from the Institute's Department of General Surgery. All individuals provided verbal and written informed permission before participating in the study.

The study comprised 120 patients of both genders aged 18 to 60 who were undergoing elective surgical procedures at the institution under general anaesthesia . The study's inclusion criteria were individuals who granted informed consent for participation, people with a body weight of 40-70 kgs, and subjects aged 18-60 years.

Subjects with ASA physical grade status I, as well as those undergoing elective surgical operations at the Institute under general anaesthesia . The exclusion criteria for the study were subjects who were unwilling to participate in the study, having preoperative hypotension, subjects with psychiatric illness or head injury, known allergy to melatonin, Ramelteon, or Agomelatine, respiratory problems, bronchial asthma, or COPD, impaired renal parameters or renal diseases, rheumatic/ischemic heart diseases, conduction defects, heart block, or sinus bradycardia, lactating and pregnant females, ASA physical status

Following the final inclusion of the research individuals, 120 were randomly divided into two groups. Each group had 60 patients, with Group I receiving Agomelatine as a premedication before anaesthesia induction and Group II receiving Ramelteon as a premedication before anaesthesia induction. Group I individuals were given Agomelatine in the form of a 10 mg pill orally, whereas Group II patients received Ramelteon in the form of an 8mg tablet.

During the preoperative period, all individuals had a full pre-anesthetic examination. All individuals provided a complete history, including drugs used before to surgery, a history of drug allergy, anaesthesia exposure, and a detailed history of previous and present medical disease. This was followed by a complete systemic and general physical examination. Routine and pertinent specific examinations were also conducted, as well as an evaluation of the ASA's physical state. Each participant's weight was reported in kilos.

The collected data were statistically analyzed using SPSS (Statistical Package for the Social Sciences) software version 21.0 (IBM Corp., Armonk, NY, USA) for descriptive measures, independent t-test, Mann Whitney U test, and chi-square test. The data were presented in the form of mean and standard deviation, as well as frequency and percentage. A p-value < 0.05 was considered statistically significant.

RESULTS

The current prospective randomized controlled clinical trial was designed to compare the effectiveness of Ramelteon and Agomelatine as premedication prior to anaesthesia induction.

The current study evaluated 120 participants who were randomly divided into two groups of 60 subjects each. Group I subjects were given Agomelatine as a premedication before anaesthesia induction, whereas Group II subjects were given Ramelteon as a premedication. Group I individuals were given Agomelatine in the form of a 10 mg pill orally, whereas Group II patients received Ramelteon in the form of an 8mg tablet. The study subjects' mean ages in Groups I and II were 37.24±9.72 and 36.61±9.2 years, respectively, with no statistically significant difference ($p>0.05$). The bulk of the research individuals were in the age range of 31-40 years, with 40% (n=24) and 33.3% (n=20) in Groups I and II, respectively followed by 30% (n=18) subjects in Group I from 18-30 years and Table 1 shows that 33.3% (n=20) of the subjects in Group II were 41-50 years old, 26.6% (n=16) were 41-50 years old in Group I, and 26.6% (n=16) were 18-30 years old in Group II, with the exception of 3.33% (n=2) and 6.66% (n=4) patients who were 51-60 years old.

The gender distribution in the two groups of research subjects was found to be 50% (n=30) men in the Agomelatine group and 33.3% (n=20) males in the Ramelteon group. Males made up 50% (n=30) of the Agomelatine group, whereas females made up 66.6% (n=40) of the Ramelteon group. Table 2 shows that there was no statistically significant difference in gender distribution between the Agomelatine and Ramelteon groups ($p>0.05$).

The research individuals in the Agomelatine and Ramelteon groups had a mean weight of 55.7±8.33 and 55.5±8.05 kg, respectively, which was not statistically significant ($p=0.722$). According to Table 3, there were 30% (n=18) and 33.3% (n=20) subjects in the Agomelatine and Ramelteon groups from the 40-50 kg age range, 40% (n=24) subjects in the Agomelatine and Ramelteon groups from the 51-60 kg weight group, and 29.6% (n=18) and 26.6% (n=16) subjects from the Agomelatine and Ramelteon groups in the 60-70 kg weight range, respectively.

Orientation ratings at different evaluation intervals of the day before surgery were shown to differ between the two groups of research individuals, Before premedication, at 0 minutes, 15 minutes, 30 minutes, 45 minutes, and 60 minutes were 2.00±0.00 in both groups and were unchanged at all evaluation periods, indicating no significance (see Table 4).

DISCUSSION

The current study evaluated 120 participants who were randomly divided into two groups of 60 subjects each. Group I subjects were given Agomelatine as a premedication before anaesthesia induction, whereas Group II subjects were given Ramelteon as a premedication. Group I individuals were given Agomelatine in the form of a 10 mg pill orally, whereas Group II patients received Ramelteon in the form of an 8mg tablet. The study individuals in Groups I and II had mean ages of 37.24±9.72 and 36.61±9.2, respectively.

The majority of the study subjects were between the ages of 31 and 40, with 40% (n=24) and 33.3% (n=20) in Groups I and II, respectively, followed by 30% (n=18) in Group I from 18 to 30 years and 33.3% (n=20) in Group II from 41 to 50 years of age, 26.6% (n=16) from 41 to 50 years in Group I and 26.6% (n=16) from 18 to 30 years in Group II, and at most 3.33% (n=2) and 6.66% (n=4) subjects between 51 and 60 years old. These findings were similar to those of Brown GM et al8 in 2009 and Sateia MJ et al9 in 2008, who investigated people with demographics similar to those in the current research.

The gender distribution of the two groups of research volunteers was found to be 50% (n=30) men in the Agomelatine group and 33.3% (n=20) males in the Ramelteon group. Males made up 50% (n=30) of the Agomelatine group, whereas females made up 66.6% (n=40) of the Ramelteon group. There was no statistically significant difference in gender distribution between the Agomelatine and Ramelteon groups ($p>0.05$). These distributions were congruent with the findings of Yu CL et al10 in 2023 and Komazaki M et al11 in 2002, who evaluated participants with comparable gender distributions who were undergoing elective operations under Ramelteon, as in the current investigation.

The study found that the mean weight of patients in the Agomelatine and Ramelteon groups was 55.7±8.33 kg and 55.5±8.05 kg, respectively, which was statistically non-significant ($p=0.722$). There were 30% (n=18) and 33.3% (n=20) subjects in the Agomelatine and Ramelteon groups, respectively, from the 40-50 kg age range, 40% (n=24) in the Agomelatine and Ramelteon groups, respectively, from the 51-60 kg weight group, and 29.6% (n=18) and 26.6% (n=16) in the Agomelatine and Ramelteon groups, respectively, from the 60-70 kg weight range. These findings were consistent with the findings of Buoli M et al in 2014 and Wilhelmsen M et al13 in 2011, who obtained results comparable to the current study in their separate investigations.

Orientation scores in both study groups were 2.00±0.00 at various intervals before surgery, including 0 minutes, 15 minutes, 30 minutes, 45 minutes, and 60 minutes, indicating no significant difference. These findings were consistent with those of Cardinali DP et al14 in 2011 and Dai X et al15 in 2007, who reported orientation scores comparable to the current study and found no significant difference in orientation scores with either pre-anaesthetic drug.

CONCLUSIONS

Given its limitations, the current study shows that orientation is unaffected by either Ramelteon or agomelatine administered 60 minutes before surgery as a pre-anaesthesia drug. Future studies in multi-institutional settings with patients from various geographical backgrounds and greater sample numbers are needed to assess the effectiveness of the study medications.

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S. No	Age (years)	Agomelatine group		Ramelteon group	
		n=60	%	n=60	%
1.	Mean age (years)	37.24±9.72		36.61±9.2	
2.	Age range				
a)	18-30	18	30	16	26.6
b)	31-40	24	40	20	33.3
c)	41-50	16	26.6	20	33.3
d)	51-60	2	3.33	4	6.66

Table 1: Age distribution in the study subjects

S. No	Gender	Agomelatine group		Ramelteon group	
		n=60	%	n=60	%
1.	Males	30	50	20	33.3
2.	Females	30	50	40	66.6
3.	Total	60	100	60	100

Table 2: Gender distribution in two groups of study subjects

S. No	Weight (kgs)	Agomelatine group		Ramelteon group	
		n=60	%	n=60	%
1.	Mean weight (kg)	55.7±8.33		55.5±8.05	
2.	40-50	18	30	20	33.3
3.	51-60	24	40	24	40
4.	61-70	18	29.6	16	26.6
5.	Total	60	100	60	100

Table 3: Distribution of study subjects based on body weight

S. No	Orientation scores	Agomelatine group	Ramelteon group	p-value
1.	Day before surgery	2.00±0.00	2.00±0.00	-
2.	Before premedication	2.00±0.00	2.00±0.00	-
3.	0 min	2.00±0.00	2.00±0.00	-
4.	15 min	2.00±0.00	2.00±0.00	-
5.	30 min	2.00±0.00	2.00±0.00	-
6.	45 min	2.00±0.00	2.00±0.00	-
7.	60 min	2.00±0.00	2.00±0.00	-

Table 4: Orientation scores in the two groups of study subjects