

A COMPARISON OF ORAL MELATONIN VERSUS ORAL PLACEBO DRUG AS A PREMEDICATION IN THE PATIENTS UNDERGOING POSTERIOR LUMBAR SPINE SURGERIES IN A TERTIARY CARE CENTRE AT CHENNAI

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Received : 08/06/2023
Received in revised form : 05/07/2023
Accepted : 19/07/2023

Keywords:
Melatonin; Placebo; Posterior lumbar spine; Surgeries.

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DOI: 10.47009/jamp.2023.5.4.205

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 1020-1023



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Abstract

Background: Melatonin has been reported to cause preoperative anxiolysis and sedation without impairing orientation. The current study aimed to compare the effects of oral melatonin with placebo as premedication in patients undergoing posterior lumbar spine surgeries. **Materials and Methods:** A study was conducted on 80 patients aged 20-60 years of the American Society of Anesthesiologists Grade 1 and 2 posted for elective surgery, with a group of melatonin (Group M) and placebo (Group P) comprising 40 patients each. Patients were given either 10 mg (Tablet) oral melatonin or a placebo 60-90 min before induction. Preoperative anxiety was studied before and 60 min after giving medications using a visual analogue scale (VAS) anxiety score and sedation score. Haemodynamic monitoring, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), was recorded preoperative and during operation. **Result:** Most patients were reported in the age group of 30 to 40 years, with male predominance in both groups. The parameters such as ASA PS classification, sedation at 60 min, PIC recognised, and mean SpO₂ were comparable between both groups. In comparing VAS between the groups during postoperative 0 minutes, no statistically significant difference was found, whereas, in other time durations, a statistically significant difference was reported. The hemodynamic parameters like mean SBP, DBP and MAP were found to be better controlled in Group M. In both group patients, no complication was reported. **Conclusion:** Melatonin oral administration as a premedication before the surgery has reduced anxiety considerably, facilitating stable hemodynamic status.

INTRODUCTION

Pre-surgical anxiety is a challenging problem in preoperative care for patients. A common low level of anxiety is an expected response to unexpected and potentially life-threatening situations, especially in the first patient's surgical experience.^[1] However, a high and extended preoperative anxiety causes slow wound healing and requires large doses of anaesthesia and recovery drugs. Many patients in the preoperative phase experience anxiety, which is often regarded as a normal patient response.^[2]

Pre-surgical anxiety has many postoperative complications in a patient, and one of these problems is pain. Pain is a common complaint of postoperative patients that occurs mainly due to pre-surgery anxiety as a common feature.^[3] Pre-surgical anxiety has been found to lead to many problems such as nausea, vomiting, cardiovascular disorders such as

tachycardia and high blood pressure, and increases the risk of infection. Studies have also shown that a large proportion of surgical patients experience significant anxiety before surgery, and this is reported to affect 60-80% of surgical patients.^[4,5]

The extent to which each patient exhibits anxiety depends on several factors, such as the patient's preferences for surgery, age, gender, experience with surgery, educational status, type and level of surgery proposed, current health status, and socioeconomic status.^[6] Identifying risk factors helps to provide psychological support during pre-surgical visits to reduce stress. A certain group of patients, for example, women, younger patients, and patients with no previous history of surgical resection have a higher rate of anxiety before surgery.^[7] Melatonin is an omnipresent molecule and ubiquitous hormone. It is produced by the pineal gland at night. It has the function of promoting sleep and restorative clock

functions in humans.^[8] The study aimed to compare the effect of oral melatonin against an oral placebo as a treatment for patients undergoing lumbar spine surgery at a tertiary care facility in Chennai.

MATERIALS AND METHODS

This prospective, double-blinded, randomised control study was conducted at the Neurosurgery Operation Theatre at Government Stanley Medical College Chennai on 80 in-patients undergoing elective Posterior Lumbar spine surgeries. Study subjects were selected randomly by using the following inclusion and exclusion criteria.

Inclusion Criteria

Patients of either sex, aged between 20 to 60 years, with ASA PS I and II, and patients who have given consent and are undergoing lumbar spine surgeries, were included.

Exclusion Criteria

Patients aged more than 60 years with ASA PS III and IV, patients who refused consent for the study and with Haemodynamic instability, and patients with emergency surgery allergy to study drugs were excluded.

This study was carried out after obtaining approval from the Institutional Ethics Committee and written informed consent from the patients. All 80 patients were randomly divided into two equal groups. Group M received 10 mg of oral melatonin tablet 60- 90 minutes before surgery. Group P received a placebo drug instead of melatonin 60-90 minutes before surgery. Placebo drug: vitamin C as a control drug, similar in colour and texture to melatonin tablets. After shifting the patients to the operation theatre, an intravenous (IV) cannula was inserted, and maintenance fluid of Ringer solution was given.

Preoperative parameters such as pulse rate, oxygen saturation, and blood pressure were recorded. At this time, the anxiety level of the patients before surgery was recorded using a Verbal analogue score (VAS from 0: no anxiety to 10: maximum anxiety).⁹ After this, all patients were given a fixed amount of anaesthesia with glycopyrrolate 10µg/kg, Fentanyl 2µg/kg, sodium thiopental (STP) 5mg/kg and atracurium 0.5mg/kg, Nitrous and oxygen levels and

sevoflurane (up to 2%). Haemodynamic monitoring, including SBP, DBP, MAP, HR, sPO2 and continuous ECG, was monitored continuously during the operation. Campbell Sedation scale was used to assess sedation after drug administration, and the patient was evaluated for any adverse effects 24hr postoperatively.

Statistical Analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). Percentage analysis was used for categorical variables, and the mean and SD were used for continuous variables to describe the data descriptive statistics frequency analysis. The unpaired sample t-test and the Mann-Whitney U test were used to find the significant difference between the bivariate samples in Independent groups. The Chi-Square test was used similarly to find the significance in categorical data; Fisher's Exact was used if the expected cell frequency was less than 5 in 2×2 tables. In all the statistical tools, the probability value of 0.05 is considered a significant level.

RESULTS

Most patients were reported in the age group of 30 to 40 years (50%), with male predominance (68.8%) in both groups. The parameters such as ASA PS classification, sedation at 60 min, PIC recognised, mean SpO2 and IV cannulation recalled were comparable between both groups [Table 1].

The comparison of VAS between the groups by Mann-Whitney U- test showed no statistically significant difference during postoperative (post-op) 0 minutes. In other time durations, a statistically significant difference between the groups was reported for the VAS score [Table 2].

The hemodynamic parameters, like mean SBP, were comparable between groups at 0 min time points and statistically significant ($p < 0.05$) at all other points. Mean DBP and heart rate were statistically significant ($p < 0.05$) at all points. MAP was comparable between groups at 0 and 10 min time points and statistically significant ($p < 0.05$) at all other points. In both group patients, no complication was reported in our study [Figure 1].

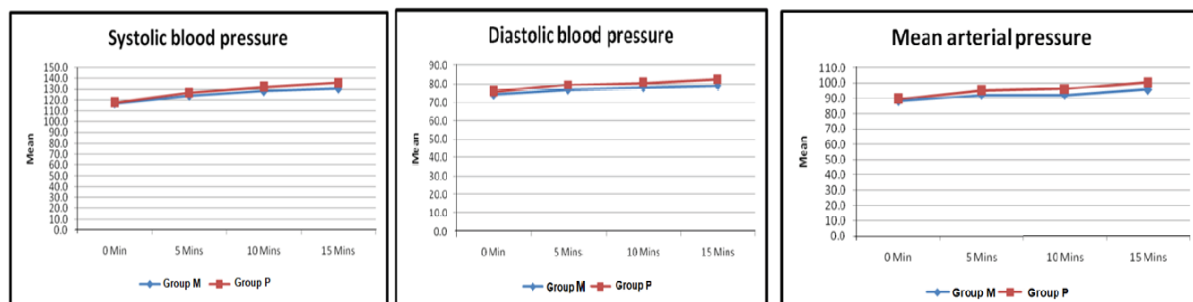


Figure 1: Observation of mean (A) SBP, (B) DBP and (C) MAP among patients of Group M and Group P

Table 1: Observation of demographic and other parameters of patients of both groups

Parameters	Observation N (%)		P-value
	Group A (N=40)	Group P (3=40)	
Gender			
Male	27 (67.5%)	28(70%)	0.809
Female	13 (32.5%)	12 (30%)	
Age group (years)			
Up to 18	6 (15%)	6 (15%)	0.541
31-40	20 (50%)	20 (50%)	
41-50	14 (35%)	12 (30%)	
> 50	0 (0%)	2 (5%)	
ASA PS classification			
I	18(45%)	24(60%)	0.342
II	22(55%)	16(40%)	
Sedation at 60 min			
I	24 (60%)	20 (50%)	0.369
II	16 (40%)	20 (50%)	
PIC recognised			
No	1 (2.5%)	2 (5%)	1.00
Yes	39 (97.5%)	38 (95%)	
IV Cannulation recalled			
No	1 (2.5%)	1 (2.5%)	1.00
Yes	39 (97.5%)	39 (97.5%)	

Table 2: Observation of VAS score, Mean HR and SpO2 among patients of both groups

	Group A (N=40)	Group P (3=40)	P-value
VAS score (mean+ SD)			
0 min	7.43 ±0.96	8.03 ±0.83	0.007
15 min	6.05 ±0.88	7.03 ±0.73	0.0005
30 min	5.35± 1.00	6.98± 0.70	0.0005
60 min	5.18± 1.17	7.15 ±1.10	0.0005
Post-Op 0 Min	0.00 ±0.0	0.00±0.00	1.00
Post-Op 15 Min	5.18± 0.55	5.75± 0.63	0.0005
Post-Op 30 Min	5.85± 0.58	6.50 ±0.64	0.0005
Post-Op 60 Min	5.88 ±0.72	6.63 ±0.77	0.0005
Heart Rate (beats per min) (mean+ SD)			
0 min	82.9 ±6.0	86.5± 4.6	0.004
5 min	87.3 ±5.5	91.4± 4.0	0.0005
10 min	88.8 ±5.4	93.5± 4.2	0.0005
15 min	90.2 ±5.4	95.5 ±4.6	0.0005
SpO2 (%) (mean+ SD)			
0 min	100.0 ±0.2	100.0 ±0.2	1.00
5 min	99.9 ±0.4	99.9 ±0.4	1.00
10 min	100.0± 0.0	100.0 ±0.0	NA
15 min	100.0 ±0.0	100.0± 0.0	NA

DISCUSSION

The comparison of Anxiety reduction effects between the two groups was the study's primary goal based on VAS anxiety scores. The secondary goals were comparing their efficacy in reducing postoperative pain, their hemodynamic statuses after induction and intubation, and their effect level in the Orientation, Sedation, and postoperative memory levels. In our study, the demographic profile in both groups regarding age, gender, and ASA status showed no statistically significant difference. Hence, both groups are comparable in the above said three parameters. The duration of surgery was around 2 to 2.5 hours in both groups. These findings in the present study follow earlier reported studies.^[10]

In Group M, there was a statistically significant difference in the reduction of preoperative anxiety levels of the patients compared to the baseline values. Whereas in Group P, there was no statistically significant difference in the reduction of preoperative

anxiety levels of the patients compared to the baseline values. Hence, we infer that Group M significantly reduced anxiety levels compared to Group P in the preoperative period. Khare et al., in their study, also reported similar findings where a significant difference was reported between melatonin and placebo groups.^[10]

In group M, there was a slight increase in the SBP at induction and intubation after 5, 10 and 15 min compared to baseline values. In group P, there was a higher increase in the systolic blood pressure at induction and intubation at 5, 10 and 15 min compared to baseline values. There was initially no statistical difference in the systolic blood pressure increase at baseline and 5 min between the two groups. Still, there was a highly significant statistical difference in the increase of systolic pressure between the two groups at 10 min and 15 min. Hence group P showed a statistical increase in systolic blood pressure after intubation compared to group M. There was a statistically significant difference in the

increase of DBP at intubation at 0 minutes between the two groups and a statistically significant difference in the increase of diastolic blood pressure at 5 min, 10 min and 15 min between the two groups. Hence group P showed a statistical increase in diastolic blood pressure after intubation compared to group M. Gupta et al. had similar findings in their investigations.^[9]

In group P, there was a higher increase in the MAP after induction and intubation at 5, 10 min and 15 min compared to baseline values. There was no significant difference between the two groups at 0 minutes, but a highly significant statistical difference in the increase of MAP at five and 15min. Hence group P showed a significant rise in the Mean arterial pressure after intubation compared to group M. These findings in the present study follow the earlier reported study.^[8,9] In group P, there was a higher increase in the heart rate after induction and intubation at 5, 10 and 15 min compared to baseline values. There was a highly significant difference in the heart rate increase between the two groups at all times. Hence there was a statistically significant increase in the heart rate after intubation in group P compared to group M. Ionescu et al. also reported similar findings in their investigations.^[11,12]

In both Group M and Group P, there was no drop in oxygen saturation at any time during the study. Hence there was no statistical difference in the oxygen saturation between the two groups. From the above observations, premedication with oral melatonin tablets where found to have greater anxiety reduction and better haemodynamic stabilities compared to the placebo premedication in the patients undergoing posterior lumbar spine surgeries.^[10-12]

In group M, very minimal sedation was observed at 60 minutes compared to group P. No statistical difference between the two groups was noted at 60 minutes in the sedation levels. Both Group M and Group P patients had no major complications. Corrigan et al. also reported an insignificant effect between the melatonin group and placebo for the sedation effect.^[13]

CONCLUSION

Melatonin oral administration as a premedication sixty minutes before the surgery has reduced the level of anxiety considerably, facilitating stable

hemodynamic status after induction and intubation with Minimal Sedation and also without any impact on the Memory Status of the patients undergoing Posterior Lumbar Spine Surgeries.

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