

ARTICLE

Year : 2007 | Volume : 1 | Issue : 1 | Page : 6-

Sedation characteristics of melatonin and midazolam for premedication of adult patients undergoing cataract surgery under local anaesthesia

Rana Altaf Ahmad¹, Abdulhamid Samarkandi², Samir M Al-Mansouri³, Saleh A Al Obeidan³,

¹ Department of Anaesthesia, King Abdulaziz University Hospital, College of Medicine, King Saud University, Riyadh, Saudi Arabia

² Department of Anesthesia, College of Medicine, King Saud University Hospitals, Riyadh, Saudi Arabia

³ Department of Ophthalmology, King Abdulaziz University Hospital, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Correspondence Address:

Rana Altaf Ahmad

Consultant Anaesthetist, King Abdulaziz University Hospital, P.O. Box 245, Riyadh 11411
Saudi Arabia

Abstract

This prospective, double blind placebo controlled study is designed to compare the effects of sublingual melatonin versus midazolam for premedication of adult patients scheduled to undergo cataract surgery under local anaesthesia. Seventy five patients ASA1&2 ranged from 40-70 yr scheduled for cataract surgery procedure were studied. Patients were classified into 3 groups. Group 1 received midazolam, group 2 received melatonin and group 3 received placebo. Patients in group 1 received sublingual 0.5% midazolam solution 0.1mg/kg body weight. Group 2 received sublingual melatonin 0.05mg/kg body weight. The control group received sublingual placebo (saline). All drugs were given 100 min before the local block. Sedation, anxiety and orientation were quantified before and 10, 30, 60 min after premedication and 15, 30, 60 min after admission to the recovery room. One way ANOVA and non-parametric Kurskal-wallis test were for statistical analysis. Patients who received premedication with either midazolam or melatonin had significant decrease in anxiety levels compared with control group and midazolam group significant increase in level of sedation before operation was noticed compared with melatonin and control groups ($p < 0.05$). Midazolam produced highest scores of sedation at 30 and 60 min after administration and significant psychomotor impairment in the preoperative period compared with melatonin and placebo groups ($p < 0.05$). Postoperative patients who no significant difference between the groups for anxiety levels or trigger dot testing performance after received midazolam, melatonin premedication showed no increase in level of sedation at all intervals. There was operation compared with control ($p > 0.05$). Amnesia was not significant in both the groups. In conclusion, melatonin can be used effectively for premedication of adult patients without hangover effect compared to midazolam.

How to cite this article:

Ahmad RA, Samarkandi A, Al-Mansouri SM, Al Obeidan SA. Sedation characteristics of melatonin and midazolam for premedication of adult patients undergoing cataract surgery under local anaesthesia. Saudi J Anaesth 2007;1:6-6

How to cite this URL:

Ahmad RA, Samarkandi A, Al-Mansouri SM, Al Obeidan SA. Sedation characteristics of melatonin and

Full Text

Introduction

Midazolam belongs to a class of benzodiazepine derivative characterized by rapid onset of action [14] . Following oral administration, peak plasma concentration rises within 30 to 45 min. The onset of sedative effects has been reported within 15 min, with peak effects in 30 to 60 min. Elimination half-life after intravenous administration was reported to be 2.3 h. The bioavailability after the ingestion of 10, 20 and 40 mg midazolam in the form of a tablet ranged from 31 % to 73% due to extensive first pass hepatic extraction of midazolam [15] . In contrast, a single low melatonin dose produced no suppression of rapid eye movement sleep (REM). The pineal hormone melatonin (n-acetyl-5-methoxytryptamine) has several putative functions including regulation of circadian rhythms, regulation of the reproductive axis, and antioxidant activity [1],[2],[3] . Auto radiographic studies and receptor assays have demonstrated the presence of melatonin receptors in various regions of the central nervous system and in other tissues in humans [4] . Exogenous administration of melatonin has been found by several investigators to facilitate sleep onset and improve quality of sleep [5],[6] . Available data suggest that the sleep inducing properties of melatonin may differ from those of benzodiazepines. Benzodiazepine derivative reduces duration of (REM) sleep after single administration of high dose or long time administration of low dose [7],[8] . Benzodiazepine also reduce slow wave sleep thus negatively influencing sleep quality but in contrast single dose melatonin produce no suppression of REM sleep and there is no hangover effects like benzodiazepine [9],[10] . This prospective, randomized, double blind placebo controlled study was conducted to compare the effects of sublingual melatonin versus midazolam as premedication in local anaesthesia for cataract surgery in adult patients. The sedative, anxiolytic and amnesic effects of both drugs in addition to residual effects in the immediate postoperative period were evaluated.

Patients and Methods

After obtaining institutional approval and informed consent from patients, we studied 75 ASA physical status I,II patients, Age (40 - 70 y) weigh 44-90 kg scheduled for cataract surgery . Patients who were taking centrally acting drugs consuming monoamine oxidase inhibitors, or allergic to study drugs were excluded. The day before study the principal investigator explained the study plan and showed the patients the different scales used in the assessment. Approximately 100 min before surgery patients were shifted to an isolated quiet room in the holding area. A pulse oximeter probe was placed on all patients and Spo₂, arterial blood pressure and heart rate were monitored continuously. Resuscitative equipment was immediately available at the bed side. Patients were allocated randomly to one of the three groups (n=25 each). First group received sublingual 0.5% midazolam 0.1 mg/kg. The second group received sublingual melatonin 0.05mg/kg body weight. The third group received sublingual placebo (saline). Study drugs and placebo were prepared to a volume of 3ml in a syringe from which needle was removed, marked only with coded label to maintain the double blind nature of study. The content of the syringe was given sublingually approximately 60 min before block of the eye by the anaesthesia technician who was not involved in data collection. At 180 sec the patient will be permitted to swallow the medication. A visual analogue scale (VAS) was used to evaluate sedation and anxiety levels. The scale was a 50 cm long and 10cm high card diagonally divided to a white and bright red triangle. The centimeter scale was on the rear side of the card [16] . The extremes are marked no sedation/anxiety at the white end and sedation/anxiety as bad as ever at the red end. The same interpreter-blinded to group assignment-evaluated VAS for anxiety; orientation score {0=none,

1=orientation in either time or place, 2=orientation in both}; Sedation score {1= awake, 2=drowsy, 3=asleep but arousable, 4=asleep but not arousable} before 10, 30, and 60 min after the administration of premedication and postoperatively at 15, 30, 60 min after admission to post anaesthesia care unit (PACU). Patients were asked to perform the trigger dot test (TDT) at these times. This test was used to quantitatively assess psychomotor activity. All patients positioned with 30 degree head elevation and used the same writing implement (ball point, medium point, black) for all tests. The TDT score represented the total number of dots (42) connected. TDT deviation represented the cumulative shortest distance in mm between the drawn lines and missed dots to account for inter-patient differences in test taking ability. TDT scores and TDT deviations were normalized to baseline scores and deviation for each patient. Changes in scores of different tests and TDT deviation and TDT time relative to baseline values were compared. Amnesia was assessed by showing patients two simple colored figures star and rectangle before premedication. Patients were queried 24 h later as to recall of the figures. In the holding area, an infusion of 5% D/W with \square NS was started. All the blocks were performed by the ophthalmologists. Peribulbar block was given to all patients using inferior and superior approach by 5ml of Xylocaine 2% and bupivacaine 0.5%. At each block toleration to the procedure was assessed. Standard monitoring were used i.e. pulse oximetry, non invasive blood pressure (NIBP), and Electrocardiography (ECG) (Datex-Ohmeda, Finland). The intraoperative sedation and tolerance to the procedure was done by the concerned anesthetist of the case. In the recovery room the same tests were repeated. Postoperative pain was treated with injection diclofenac sodium 1-2 mg/kg b.w. One way ANOVA was used to compare the mean values of quantitative variables across the three drug groups. A non-parametric Kurskal-wallis test was used to compare the scores of outcome variables across the three drug groups. A p- value 0.05) [Table 1]. There was no significant difference in VAS for anxiety measurement between the groups after giving premedication at 10, 30, 60 min as well as postoperatively at the same interval compared to baseline ($p>0.05$) [Figure 1].

There was no significant difference in orientation score between the two groups compared with the baseline in preoperative and postoperative period except in two cases of midazolam group where patients were in deep sleep after pre-medication and surgery has to be cancelled ($p>0.05$). Furthermore, patients in the midazolam group showed significant (p [17]).

For a long period of time oral benzodiazepine are used as premedication for their anxiolytic effects in performing local blocks for cataract surgery [18] . Ophthalmologists are suffering because of its sedative and hangover effects. It is documented in other studies that premedication with midazolam was associated with preoperative anxiolysis, sedation and impairment of psychomotor skills [19],[20],[21] that combination effects were not good for a patient who underwent local block for ophthalmic surgery and in whom the ophthalmologist needs full cooperation of the patient while performing surgery.

In this study the dose of melatonin 0.05mg/Kg used showed no sedative effect compared with midazolam [22] . When compared in the preoperative period only patients in the midazolam group experienced significant impairment of psychomotor skills and significant sedation compared to melatonin and control groups. There was significant reduction in the anxiety in the melatonin and midazolam group when compared with control preoperatively. However, there was no significant difference between all the groups regarding anxiety, sedation scores and TDT performance postoperatively. Amnesia was notable only in the midazolam group for one preoperative event. The amnesic properties of benzodiazepines are already well documented [23] . Our results showed that melatonin had no amnesic effects. The TDT deviation and score impairment relative to the baseline was noted in the midazolam group in the preoperative period and sedative effect was at grade 4 (asleep not arousable). Our results are in accordance with the other studies on psychomotor functions produced by midazolam premedication [19],[20] . On the other hand, with melatonin the dose used in our study, there was no impairment in TDT scoring relative to baseline at peak effect time of 30, 60 min [24] . The peak sedation effects of midazolam were noted at 30 and 60 min respectively after sublingual administration [25] . No patient was asleep in the melatonin group at all levels. The use of melatonin in anaesthesia was started by the author as a premedication drug and found to be good when compared with the sublingual midazolam and even now onward melatonin is being tried as intravenous induction agent in rats [17],[26] .

We concluded that sublingual melatonin is better than sublingual midazolam for premedication of adult patients undergoing cataract surgery under local anaesthesia. .Furthermore, unlike benzodiazepines, melatonin does not induce hangover effects.[Table 3]

References

- 1 Weaver DR, Stehle JH, Stopa EG, Reppert SM. Melatonin receptors in human hypothalamus and pituitary: implications for circadian and reproductive responses to melatonin. *J Clin Endocrinol Metab* 1993; 76:295-301.
- 2 Tamarkin L, Baird CJ, Almeida OF. Melatonin: a coordinating signal for mammalian reproduction?. *Science* 1985; 227:714-20.
- 3 Reiter RJ, Tan DX, Poeggeler B, Menendez-Pelaez A, Chen LD, Saarela S. Melatonin as a free radical scavenger: implications for aging and age-related diseases. *Ann NY Acad Sci* 1994; 719:1-12.
- 4 Stankov B, Fraschini F, Reiter RJ: Melatonin binding sites in the central nervous system. *Brain Res Brain Rev* 1991; 16:245-56.
- 5 Cramer H, Rudolph J, Consbruch V, Kendel K: On the effects of melatonin on sleep and behaviour in man. *Adv Biochem Psychopharmacol* 1974; 11:187-91.
- 6 Wurtman RJ, Zhdanova IV: Improvement of sleep quality by melatonin. *Lancet* 1995; 346:1491-2.
- 7 Kales A, Kales JD, Scharf MB, Tan TL: Hypnotics and altered sleep-dream patterns: all night EEG studies of chloral hydrate, flurazepam and methaqualone. *Arch Gen Psychiatry* 1970; 23: 219-25.
- 8 Dement WC, Zarcone VP, Haddes E, Smythe H, Carskadon M: Sleep laboratory and clinical studies with flurazepam, The benzodiazepines. Edited by Garrattini S, Mussini E, Randall LO. New York, Raven Press, 1973, pp 599-611.
- 9 Frederickson PA, Krueger BR: Insomnia associated with specific polysomnographic findings, Principles and practice of sleep medicine. Edited by Kryger MH, Roth T, Dement WC. Philadelphia, WB Saunders, 1989, pp 484-5.
- 10 Zhdanova IV, Wurtman RJ, Lynch HJ, Ives JR, Dollins AB, Morabito C, Matheson JK, Schomer DL. Sleep-inducing effects of low doses of melatonin ingested in the evening. *Clin Pharmacol Ther* 1995; 57:552-8.
- 11 Petrie K, Conaglen JV, Thompson L, Chamberlain K. Effect of melatonin on jet lag after long haul flights. *BMJ* 1989; 298:705-9.
- 12 Arendt J. Melatonin. *Clin Endocrinol* 1988; 29: 205-29.
- 13 Dawson D, Encel N. Melatonin and sleep in humans. *J Pineal Res* 1993; 15:1-12.
- 14 Karl HW, Rosenberger JL, Larach MG, Ruffle JM: Transmucosal administration of midazolam for premedication of pediatric patients. Comparison of the nasal and sublingual route. *Anesthesiology* 1993; 78:885-91.
- 15 Kontinen VK, Maunuksela E-L, Sarvela J: Premedication with sublingual triazolam compared with oral diazepam. *Can J Anaesth* 1993; 40: 829-34.
- 16 Aitken RC: Measurement of feelings using visual analogue scale. *Proc R Soc Med* 1969; 62:939-43.
- 17 Naguib M, Samarkandi AH. Premedication melatonin, a double-blind placebo-controlled comparison with midazolam. *Brit J Anaesth* 1999; 82(6) :875-80.
- 18 Lang E, Schafer M, Brunisholz V. Midazolam as oral premedication for local anesthesia. *Anaesthesist* 1987; 36(5) :197-202.
- 19 Richardson MG, Christopher LW, Asadullah H. Midazolam premedication increases sedation but does not prolong discharge times after brief outpatient general anesthesia for laparoscopic tubal sterilization. *Anesth Analg* 1997; 85:301-5.
- 20 Ghoneim MM, Block RI, Sum PST, El-Zahaby HM, Hinrichs JV. The interactions of midazolam and flumazenil on human memory and cognition. *Anesthesiol* 1993; 79:1183-92.
- 21 Shafer A, White PF, Urquhart ML, Doze VA. Outpatient premedication: use of midazolam and opioid analgesic. *Anesthesiol* 1989; 71:495-501.
- 22 Naguib M, Samarkandi AH. The comparative dose-response effects of melatonin and midazolam for premedication of adult patients: a double blinded placebo-controlled study. *Anesth Analg* 2000; 91(2) :473-9.
- 23 Ghoneim MM, Mewaldt SP. Benzodiazepines and human memory. A review. *Anesthesiol* 1990; 72:926-38.
- 24 Lieberman HR, Waldhauser F, Garfield G, Lynch HJ, Wurtman RJ. Effects of melatonin on human mood and performance. *Brain Res* 1984; 323:201-7.
- 25 Lim TW, Thomas E, Choo SM. Premedication with midazolam is more effective by the sublingual than oral route. *Can J Anaesth* 1997; 44:723-6.
- 26 Naguib M, Hammond DL, Baker M, Cutkomp J, Queral L. Indication of general anesthesia by melatonin: Comparative dose-effect studies with thiopental and propofol. *Anesthesiol* 2001; 95:A1373.

Wednesday, April 20, 2016

[Site Map](#) | [Home](#) | [Contact Us](#) | [Feedback](#) | [Copyright and Disclaimer](#)