

# Preemptive melatonin versus pregabalin for perioperative anxiety and sedation in patients undergoing cataract surgeries: A double blind, prospective randomized clinical trial

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## Abstract

Cataract surgery is a day care surgery, mostly in aged patients and is usually done under topical anaesthesia. Using a premedicant with anxiolytic and sedative properties significantly improves comfort of patient and surgeon. We compared oral melatonin (6mg) and pregabalin (150 mg) on perioperative anxiety and sedation in patients undergoing cataract surgery. In this double blind, randomized clinical trial, 80 patients of 40-80 years, of both sex, ASA I and II, undergoing cataract surgery underwent simple random sampling to either receive oral melatonin 6mg [group I] or oral pregabalin 150mg [group II] one hour before the surgery. Anxiety and Sedation were assessed using Visual analogue scale [VAS] and Ramsay sedation score respectively just before administering study drug T1, one hour after administering T2 and immediately after cataract surgery T3. Oral melatonin (6mg) given one hour before cataract surgeries had better effect on the trend of perioperative anxiety than pregabalin. Oral Pregabalin(150mg) had a improved sedation score than melatonin which may not be desirable during the postoperative period in day care surgeries like cataract.

**Key Word:** Pregabalin, Melatonin, Cataract, Premedicant, Anxiety, Sedation.

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## INTRODUCTION

Cataract is a physiological change associated with ageing resulting in irreversible opacification of lens, the only remedy for which is replacement of the lens with an implantable artificial lens. Hence, cataract surgery mostly involves aged patients and is practiced as a day care

procedure in most centers. As cataract surgeries are mostly performed under topical anaesthesia, there is a need for a still and calm patient. This necessitates a premedicant which produces maximum anxiolysis with minimal sedation without affecting cognition, higher mental functions including memory. Many drugs like propofol, benzodiazepines, opioids, dexmedetomidine have been used as premedicants in cataract surgeries<sup>1</sup>. Benzodiazepines are probably the most commonly used premedicants to produce anxiolysis and sedation but are associated with greater arousability from sleep, restlessness and hangover effects<sup>2</sup> necessitating the search for suitable alternatives. Melatonin is a natural hypnotic, sedative, analgesic, anti-inflammatory, antioxidative and chronobiotic lately gaining popularity as a premedicant<sup>3</sup>. Pregabalin, a GABA analogue and an anticonvulsant was introduced for chronic pain conditions and is now being used for postoperative pain<sup>4</sup>. Melatonin

exerts its hypnotic effects through activation of MT1 and MT2 receptors<sup>5</sup> and a part of its central actions by facilitating GABAergic transmission through modulation of GABA receptor<sup>6</sup>. As both these drugs have actions centered on GABA and specific guidelines for premedications in cataract surgeries are yet to evolve, we aimed at looking at the anxiolytic and sedative actions of oral melatonin [6mg] and oral pregabalin [150mg] given one hour before cataract surgeries.

### MATERIAL AND METHODS

This is a double blind, prospective, randomized clinical trial set in a tertiary care teaching hospital where the patient, investigators, anaesthesiologist and the surgeon were blinded to the given drug. After approval from institutional ethical committee and written informed consent from patient, 80 patients were divided into two groups of 40 each by simple randomized sampling. Group I received oral melatonin [6mg] and Group II received oral pregabalin [150 mg] one hour before cataract surgery. Inclusion criteria were patients of ASA status I and II of both sex in age group of 40-80 years undergoing cataract surgery under peribulbar block. Exclusion criteria included patients of ASA status III and IV, patients with sleep disorders and psychiatric diseases on treatment, patients on anxiolytics, sedative-hypnotics, psychotic drugs and patients having hypersensitivity to melatonin and pregabalin. After discussion with our statistician, in order to obtain a power of 80% with an error equal to 0.05% a sample size of 34 patients in each group was deemed to be sufficient. Keeping in mind dropouts and shifting from normality in data distribution we decided to enroll 40 patients in each group. One day before the surgery, patients were explained about the study and the visual analogue scale [VAS] used for anxiety assessment. A 10cm linear VAS was used to assess anxiety levels with zero being no

anxiety and ten being extreme anxiety with inability to focus. The patient was asked to score his anxiety and this was noted. Sedation was assessed using Ramsay sedation score as follows:

PATIENT RESPONSE	SCORE
Anxious and agitated or restless or both	1
Cooperative, oriented and tranquil	2
Responds to commands only	3
Brisk response to light glabellar tap or loud auditory stimulus	4
Sluggish response to light glabellar tap or loud auditory stimulus	5

The VAS anxiety score and Ramsay sedation score were assessed before giving study drugs T1, 60 minutes after giving the study drugs T2 before shifting to the OT and after cataract surgery T3. On the day of surgery, patient was shifted to the preoperative room one hour before surgery and a 20G I v line secured, followed by anxiety assessment and sedation assessment by the investigator. Subsequently, the study drug was administered by a nurse with sips of water. After one hour of administering drug, the anxiety and sedation scores were recorded and patient shifted to OT for the cataract surgery under peribulbar block administered by the surgeon. The duration of surgery was noted. After surgery, patient was shifted to recovery room and anxiety, sedation scores were recorded by the investigator. Any undesirable side effects like nausea, vomiting, dizziness and headache were noted. Vital parameters like heart rate, blood pressure and oxygen saturation were noted at baseline, an hour after drug administration, continuously during the surgery and after shifting patient to the recovery room. The data obtained was compared using t-test and repeated ANOVA on SPSS16 software. A p value  $\leq 0.05$  was taken as significant.

### RESULTS

Both groups were comparable with respect to demographic profile and duration of surgery. The VAS anxiety scores and Ramsay sedation scores before administering drugs T1, one hour after administering drugs T2 and after cataract surgery T3 are shown in table 2 and 3 respectively. Table 1 showing demographic variables and duration of surgery in both groups

VARIABLE	Group I	Group II
Number of patients	40	40
Gender[M:F]	18:22	15:25
Age in years[mean $\pm$ SD]	61.3 $\pm$ 7.92	62.7 $\pm$ 7.15
Duration of surgery in minutes[mean $\pm$ SD]	47.5 $\pm$ 5.61	48 $\pm$ 6.02

Table 2: showing Anxiety scores

Anxiety Score	Group I	Group II	P value
T1	4.03 $\pm$ 0.86	3.28 $\pm$ 0.99	0.001
T2	1.28 $\pm$ 0.45	2.23 $\pm$ 0.80	0.0001
T3	1.00 $\pm$ 0.00	1.00 $\pm$ 0.00	0.0001

Table 3: showing Sedation scores

Sedation Score	Group I	Group II	P value
T1	1.00±0.00	1.00±0.30	0.05
T2	1.85±0.36	1.47±0.60	0.001
T3	2.20±0.41	3.78±0.77	0.0001

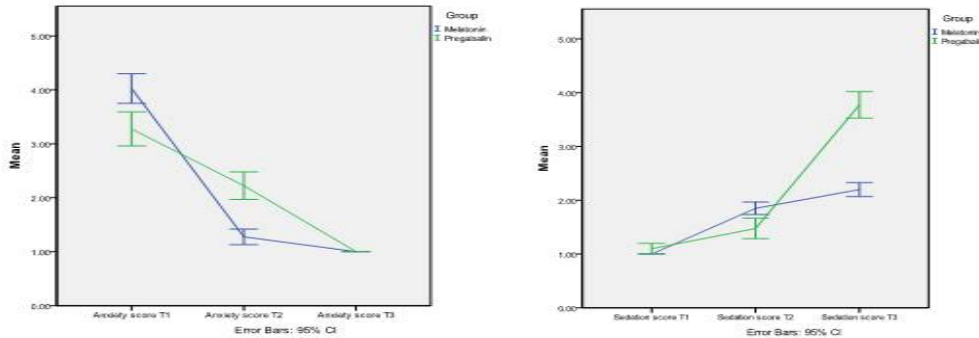


Figure 1: showing anxiety scores. Figure 2: showing sedation scores

## DISCUSSION

Melatonin is a naturally occurring pineal hormone which regulates circadian rhythm<sup>7</sup>. The exact mechanism of action is not known, but evidence points out a synergistic action between melatonergic and GABAergic systems<sup>6,8</sup>. Oral melatonin at doses of 0.2mg/kg produced loss of consciousness in humans<sup>3,6</sup> and produced EEG activity similar to intravenous and inhalational anaesthetics. Turkistani *et al* found that oral melatonin 3mg and 5mg as premedication reduced induction dose of propofol without prolonging recovery<sup>9</sup>. Nasr DA *et al* compared oral melatonin (6mg) versus oral pregabalin (150mg) and showed both reduced perioperative anxiety and postoperative pain in laparoscopic gynaecological surgeries and compared to melatonin, pregabalin produced less sedation<sup>10</sup>. After going through above studies we decided to use 6mg of oral melatonin 1 hour before surgery. Pregabalin a gabapentinoid and anticonvulsant<sup>11</sup> is effective in neuropathic pain, incisional, inflammatory, formalin induced injury, anxiety and sleep modulation. It binds to alpha-2-delta subunit of voltage gated calcium channels on the presynaptic membrane, reduces calcium influx and release of neurotransmitters like glutamate, noradrenaline, serotonin, dopamine, substance P. It is rapidly absorbed orally with blood concentration being attained in one hour and is 98% excreted unchanged in urine. FDA recommends an initial dose of 150mg of pregabalin and hence we decided to use 150mg in our study<sup>12</sup>. The State-Trait Anxiety Inventory (STAI) is the gold standard for anxiety evaluation. However, STAI has 20 multiple choice questions which limits its use in patients with cataract. Studies show that Visual analogue scale [VAS] correlates well with STAI and is a valid measure of

preoperative anxiety<sup>13,14</sup>. As it is easy to use in patients undergoing cataract surgeries, we used it in our study. In our study, both groups were comparable in their anxiety scores before administering study drugs. However, melatonin showed a greater effect on anxiety at T2 and T3 compared to pregabalin, as shown in figure 1. From figure 1, it is clear that the trend of anxiety scoring is better with melatonin leading to greater patient cooperation intraoperatively as compared to pregabalin. The baseline sedation scoring was not significant in both groups [p=0.05] but trend of sedation scoring was steeper with pregabalin as seen in figure 2 leading to sedated patients arousable to verbal commands which was not significant clinically. Too much of sedation [RSS>5] can be a hindrance in daycare surgeries like cataract Nasr DA *et al*<sup>10</sup> compared oral melatonin (6mg) with oral pregabalin (150mg) given one hour before Laparoscopic gynaecological surgeries and found that both reduced perioperative anxiety and postoperative pain with melatonin causing higher sedation than pregabalin contradictory to our study. Khezri M *et al*<sup>7</sup> compared oral melatonin (6mg) versus oral gabapentin(600mg) for anxiety and pain associated with retrobulbar block during cataract surgery and concluded that both had similar effects on anxiety, whereas gabapentin decreased pain and improved sedation scores during retrobulbar block. In our institute, peribulbar block was used and pregabalin improved sedation score compared to melatonin (p<0.001). Side effects of melatonin and pregabalin include headache, dizziness, drowsiness<sup>3,15,16</sup>. One patient who received pregabalin complained of dizziness in our study. The limitations of our study include small sample size and lack of plasma drug measurement which would have given us a better

perspective on drug actions. Further studies with bigger sample size and analysis of plasma drug levels are needed to formulate guidelines on premedication for cataract surgeries.

## CONCLUSION

Oral melatonin (6mg) given one hour before cataract surgeries had better effect on the trend of perioperative anxiety than pregabalin. Oral Pregabalin(150mg) had a improved sedation score than melatonin which may not be desirable during the postoperative period in day care surgeries like cataract.

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