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Revitalizing Postoperative Pain Management: Melatonin Vs Pregabalin – A Comparative Approach of Analgesic Innovation

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Abstract

Introduction: Inadequate postoperative analgesia has been a common problem in clinical practice, which can lead to the development of chronic pain. NSAIDs and opioids, while common, often fall short in managing postoperative and associated neuropathic pain and have side effects. Pregabalin and melatonin as pre-medicants, have analgesic, anxiolytic, and neuroprotective benefits. This study evaluated and compared the effectiveness of oral pregabalin and melatonin as pre-mendicant for postoperative analgesia.

Methods: The study included ASA grade I and II patients aged between 18 and 65 years of either sex, with a BMI of 18-30 kg/m^2. Patients were computer-randomized into three groups undergoing surgeries requiring more than 30 minutes of general anesthesia. Prescribed drugs were given 120 minutes before induction of general anesthesia. In the post-anesthesia care unit, patients were evaluated for postoperative analgesia according to the Visual Analogue Scale (VAS).

Results: Group P (pregabalin) patients had a mean VAS score of 3.3 SD 0.46, whereas Group M (melatonin) had

a score of 3.4 SD 0.46, and Group C (placebo) had a higher VAS score of 4.1 SD 0.66. Statistically, the distribution was significant with a p value <0.0001.

Conclusion: We conclude that premedication with oral pregabalin (150 mg) and oral melatonin (6 mg) before surgery could help with decreasing postoperative pain and thereby analgesic consumption. The comparison of the visual analog score was statistically significant.

Keywords: post-operative pain, melatonin, pregabalin, visual analogue pain score.

Introduction

Preanesthetic medicine is a crucial component of anesthetic care universally given prior to any type of anesthesia. The ideal pre-medicant should be safe to take orally, have sedative, anti-anxiety, analgesic, anti-emetic, and anti-sialagogue qualities, not impair cardiovascular stability or depress breathing, and successfully ease the patient's anxiety[1].

Around 75% of surgical patients suffer acute pain following their surgery, which is frequently of a medium-to-high intensity[2]. Fewer than half of surgical patients report adequate postoperative analgesia[3]. This percentage represents a significant problem as inadequate postoperative pain control may lead to adverse physiologic effects among patients in the immediate postoperative period; thereby increasing their risk of developing chronic pain associated with the procedure[4]. The goal of postoperative pain control is to reduce the negative consequences of acute post-surgical pain and help the patient transition smoothly back to normal function.

Traditionally, NSAID's & opioid analgesic therapy have served as the mainstay of treatment for acute postoperative pain. However, both these analgesics are unable to cover neuropathic component of pain. Also, the associated side effects like respiratory depression and opioid misuse have led to increasing demands for more investigative efforts into developing pain treatment strategies that emphasize using a multimodal approach.

Pregabalin, a gabapentinoid compound, is structurally related to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). It acts by decreasing the synthesis of neurotransmitter glutamate to act on the central nervous system, and possesses analgesic, anticonvulsant and anxiolytic activity and is effective in preventing neuropathic component of acute nociceptive pain of surgery. It is well absorbed and tolerated after oral administration, with peak plasma concentrations occurring within 1 hour. It undergoes negligible hepatic metabolism. It is non-narcotic, with clinically important reduction in pain[6].

Melatonin (*N*-acetyl-5-methoxytryptamine) is an endogenous sleep-regulating hormone secreted by pineal gland. The role of melatonin in anaesthesia and critical care has been elaborately discussed in the literature; it has been mentioned as a wonder drug with a wide spectrum of beneficial uses in anaesthesia and critical care including antioxidant and neuroprotective properties besides hypnosis, anxiolysis, and analgesia[7].

In this premise, this study was conducted to evaluate and compare the effectiveness of oral pregabalin and melatonin as pre-medicants for post operative analgesia.

Material and methods

The study was conducted in the Department of Anesthesiology and Intensive Care ASCOMS Jammu after getting approval from institutional ethics committee. The Study included 90 patients of ASA grades I and II, aged between 18 and 65 years of either sex, with a BMI of 18-30kg/m^2. Patients were computer-randomized into three groups undergoing surgeries

requiring more than 30 minutes of general anesthesia. Patients classified ASA III and IV, with psychiatric illness, and sleep disorders were excluded. Group P (Pregabalin) included 30 patients who received pregabalin 150 mg orally. Group M (Melatonin) included 30 patients receiving melatonin 6mg orally. Group C (Control) were the control patients who received a placebo drug. All the patients were given the prescribed drug 120 minutes before induction of general anesthesia with a sip of water.

General anesthesia was induced with fentanyl 1µg/kg, propofol 2mg/kg, and rocuronium 0.6mg/kg, further maintained with an oxygen & nitrous-oxide mixture with the inhalational isoflurane. At the end of the surgery, the residual neuromuscular paralysis was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). The patients shifted to the post-anesthesia care unit were evaluated for postoperative analgesia according to the Visual Analogue Scale (VAS). The VAS (Visual Analogue Scale) ranges from 0-10, with 0 defining no pain, and 10 defining maximum intolerable pain. Any side effects were also noted.

Statistical analysis was done by using IBM SPSS 21. Descriptive data was expressed in terms of percentages and proportions. Continuous data was expressed in terms of mean and standard deviation and was compared by using Analysis of variance (ANOVA) where a non-parametric data was compared by using chi square test. A value of p <0.05 was considered statistically significant, otherwise non-significant.

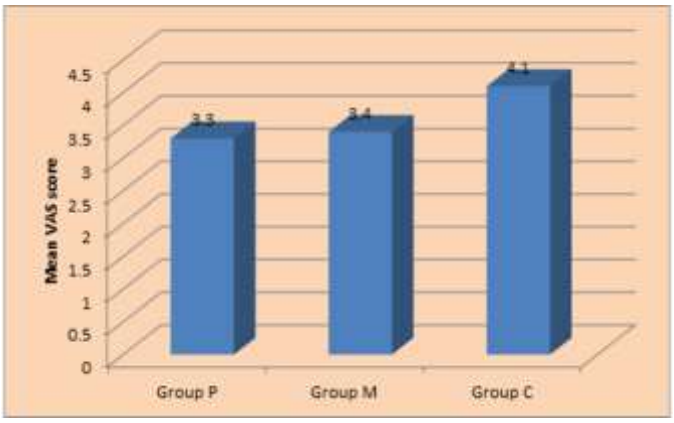
Results

The age ranged from 18-65 years, and the mean age of patients in Group P (pregabalin), Group M (melatonin), and Group C (placebo) was 42.43, 46.06, and 40.53 years respectively. Statistically, the difference between the mean age was not significant (p=0.25). The majority of patients in Group P (pregabalin), Group M (melatonin), and Group C (placebo) had ASA physical status class I (56.67%, 60%, and 56.67% respectively). Statistically, the distribution was comparable in all three groups (p>0.05). Comparison of the postoperative analgesia (Table 1 and graph 1) was done in the post anesthetic case unit using the VAS (visual assessment score). This score ranges from 1- 10. Group P (pregabalin) patients had a mean VAS score of 3.3 SD 0.46, whereas Group M (melatonin) had a score of 3.4 SD 0.46, and Group C (placebo) had a higher VAS score of 4.1 SD 0.66. Statically the distribution was significant with a p value <0.0001.

Table 1: Comparison of postoperative analgesia

Variable	Group P (n=30)	Group M (n=30)	Group C (n=30)
Mean VAS score ± SD (Range)	3.3 ± 0.46 (3 – 4)	3.4 ± 0.49 (3 – 4)	4.1 ± 0.66 (3 – 5)
Statistical inference (ANOVA)	F=18.92; p<0.0001; Highly significant		

Graph 1: Comparison of postoperative analgesia



Discussion

Pain is an expected outcome of surgery. Many people experience suboptimally managed postoperative pain.

Furthermore, current observational data support the existence of an "analgesic gap" in delivering adequate postoperative pain relief, despite evidence that aggressive postoperative pain control improves outcomes[8]. Postoperative pain is thought to affect both medical resource use and patients' ability to resume the normal activities of their lives after discharge from the hospital to home[9].

Various pharmacological methods are being used to manage postoperative pain, mostly NSAID's and opioids but each of them present with their own drawbacks. Pregabalin and Melatonin are known to have analgesic effects. They pose minimal side effects and unlike opioids, don't need monitoring postoperatively

The present study was conducted on 90 patients undergoing surgeries requiring general anaesthesia. Thirty patients each were randomly assigned to pregabalin 150 mg group, melatonin 6 mg group and placebo drug group. The two study groups were evaluated for efficacy as premedication for post-operative analgesic effects. All the three groups were identical in terms of age, sex, ASA status, Mallampati grade and type of surgical procedures

In the present study, mean VAS score was comparable in pregabalin and melatonin groups, though it was significantly more in placebo group ($p<0.0001$) (Table 1),

Jokela R *et al.* (2008) evaluated the quality of analgesia in women undergoing laparoscopic surgery and reported VAS scores for pain to be lower in the pregabalin (150 mg) group than that in the control group. Several mechanisms may contribute to the beneficial effects, which includes the modulation of visceral pain and central sensitization (Ben Menachem E, 2004; Stawicki SP, 2007).

Similar observations were found in the study conducted by Farshad Hassanzadeh Kiabi *et al.,* (2021) in which they investigated the effect of preoperative oral melatonin on pain intensity after cesarean section during spinal anesthesia and showed that the use of 10 mg of melatonin before cesarean section with spinal anesthesia is not only safe, but also reduces the severity of patients' pain, increases the duration of postoperative analgesia, reduces the need for analgesics after surgery and resumption of physical activity.

Identical to our study Katayoun Haryalchi *et al.,* (2024) compared the pretreatment effects of melatonin and pregabalin on postoperative pain intensity in total abdominal hysterectomy (TAH) and results found that both melatonin and pregabalin reduce the pain intensity throughout the first day after the TAH under GA, but preventive melatonin is more effective than pregabalin to reduce pain in the patients. In contrast our study reveals nearly similar analgesic potencies of Pregabalin and melatonin.

Conclusion

We conclude that premedication with oral pregabalin (150 mg) and oral melatonin (6 mg) before surgery could help with decreasing postoperative pain and thereby analgesic consumption. The comparison of the visual analog score was statistically significant. This offers a promising approach for optimizing analgesic management, potentially improving and enhancing overall clinical outcomes. Its integration into standard practice could lead to significant advancements in anesthesia care.

Limitations

The study's limitations, including the relatively small sample size of 90 patients (30 in each group) and the exclusion of patients with certain comorbidities (ASA III

and IV), must be considered when interpreting these results. Further research with larger, more diverse patient populations is warranted to validate these findings.

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