ORIGINAL ARTICLE

# Melatonin Versus Pregabalin as Oral Premedication in Adult Patients Undergoing Lower-Extremity Amputation Under Spinal Anesthesia

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Abstract

*Objectives:* ***To assess how well pregabalin and melatonin work as premedication to reduce perioperative anxiety and post-surgical discomfort in individuals having lower limb amputations while given spinal anesthesia.***

*Methods:* ***Participants were split up into two sets of 25 patients, M and P, who were undergoing surgical lower limb amputation at Al-Zahraa University Hospital, either above or below the knee, under spinal anesthesia. About two hours before spinal anesthesia, one melatonin pill 6 mg (Group M) or 150 mg of pregabalin capsules (Group P) was given to them.***

*Results:* ***Compared to the pregabalin group, the melatonin group had more perioperative anxiousness. Pregabalin enhanced discomfort management and lessened the need for analgesics. The duration of motor block of spinal anesthesia was better for the pregabalin group. Higher levels of sedation were produced by melatonin.***

*Conclusion:* ***Pregabalin performed better in terms of pain score, but melatonin was more effective at reducing anxiety and promoting sedation.***

*Keywords:* postoperative pain; anxiety; VAS

## 1. Introduction

Preoperative anxiety and postoperative discomfort are two important factors that every anesthesiologist should take into account. An uncomfortable sense of tension or unease that results from a patient's concerns about getting sick, getting hospitalized, having surgery, getting anesthesia, or the unknown is known as preoperative anxiety. It has been connected to longer hospital stays, increased postoperative pain, and the demand for analgesics.[1]

One of the earliest and most prevalent surgical procedures that causes both physical and psychological impairment is extremity amputation. The associated mortality and morbidity rates are influenced by surgical procedures, anesthesia techniques, and amputation timing.[2] Significant disability results from lower limb amputations, and as much as 80 percent of individuals experience stump and phantom limb discomfort. One major effect in the early postoperative period that hinders amputees' rehabilitation is stump pain. Furthermore, one long-term effect of amputation that drastically reduces quality of life is chronic pain. The most popular medications for treating postoperative amputation pain are opioids. Opioids do that; however, they have significant side effects, such as drowsiness, nausea, and delirium.[3]

Some benefits of using regional anesthesia procedures during extremity surgeries, particularly in older patients, are early mobilization, a shorter stay in the hospital, an analgesic effect following surgery, a lower risk of thrombosis, a reduced need for transfusions, and cheaper expenses. Also, regional anesthesia procedures have a positive impact on the rates of perioperative and postoperative mortality and morbidity associated with extremity amputations.[4]

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Analgesia, sedation, and anxiety alleviation are some of the major objectives of premedication. Therefore, to enhance postoperative analgesia, early mobilization, and recovery, a multimodal strategy has been employed.[5] Adjuvant medications have been attempted and studied as protective analgesics for managing pain during the regional block, including acetaminophen, melatonin, gabapentin, or pregabalin.[6]

Pregabalin, an analogue of r-aminobutyric acid, exerts anticonvulsive, analgesic, and anti-anxiety effects via binding to the α2-δ portion of presynaptic voltage-gated calcium channels in the central nervous system (CNS). Preoperative oral pregabalin administration has been shown to decrease the duration of anesthesia and the need for postoperative analgesics. Its straightforward pharmacokinetics and pharmacological profile make it a popular preoperative medication for easing acute postoperative pain.[7]

The most significant neurohormone that the pineal gland produces is melatonin, also known as N-acetyl-methoxy tryptamine. Melatonin has been used as a natural pain reliever and novel analgesic medication for neuropathic and inflammatory pain, as well as during surgery. Melatonin influences COX-2 and nitric oxide activity to reduce inflammation and tissue damage.[8]

This study's goal was to inquire how pregabalin and melatonin, as premedication drugs, would lessen postoperative pain and perioperative anxiety in patients having lower limb amputations while under spinal anesthesia.

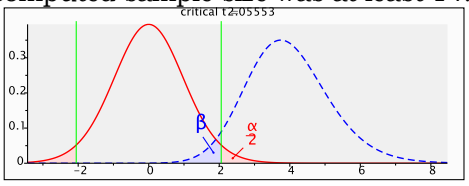
## 2. Patients and methods

Fifty patients of both sexes, who are 21 to 60 years, with American Society of Anesthesiologists (ASA) grades II and III physical statuses listed for surgical lower limb amputation above or below the knee pursuant to spinal anesthesia took part in this randomly allocated, double-blind comparative trial after receiving informed patient consent and local ethics committee approval (IRB N0-2023031870). From March 2023 to January 2025, this work was carried out at Al-Zahraa University Hospital at Al-Azhar University in Cairo.

Exclusion criteria: Any patient who is taking painkillers and opioid-containing supplements, has a history of allergic reactions to study drugs, has taken pregabalin or melatonin in the past, has taken antidepressants, antipsychotics, or any medication with tranquillizer or analgesic features, has acute or chronic neurological or psychiatric disorders, peripheral neuropathy, or is unable to communicate.

Sample size calculation:

The sample size was determined using the mean anxiety score between pregabalin and melatonin that was retrieved from earlier studies (Mishra et al.,[9] .With a 2-tailed test, α error = 0.05, power = 95%, and an effect size of 1.45, the G Power program iteration 3.1.9.7 was accustomed to compute the sample size. Each group's total computed sample size was at least 14.




Statistical analysis:

Version 26 of SPSS (Statistical Package for Social Sciences) was used to tabulate the records. The Shapiro-Wilk test was used to determine if quantitative data were regularly distributed. The findings were displayed as mean and standard deviation for regularly distributed records and median and range for records that were not. Numbers and percentages were used to represent qualitative data. Using the following recommended tests, the relevant statistical test was used based on the type of data. Continuous variables were correlated using the Spearman or Pearson correlation, the Mann-Whitney U test, the Student t test, and the Chi-Square test for categorical variables.

Methodology:

The individuals were split into two equal groups using a digitally produced random number approximately two hours prior to the initiation of spinal anesthesia. Each group received 20 ml of water, either one pregabalin capsule (150 mg; Lyrica, Pfizer Inc., Group P) or one melatonin tablet (Melatonin 6 mg tablet; Sigma Chemical, St. Louis, MO, Group M). All medications were produced in the same appearance as pills and placed in coded packets to preserve blindness. No further prior medication was given, and the study medications were delivered by the unit's nurse, who didn't take part in any subsequent research activities.

The primary outcome was the assessment of anxiety level (using Beck Anxiety Inventory) prior to administering the study medication, before giving spinal anesthesia in the operating theater, and following the conclusion of surgery.

The secondary outcomes were hemodynamic parameters, postoperative visual analog scale (VAS) for pain, painkiller usage, and degree of sedation utilizing Ramsay sedation score.

Electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximeter were connected and continuously checked after the patient was set up on the operating table. Ringer's lactate was used for preloading at a rate of 10–15

ml/ kg after the venous line was secured with an 18 G cannula. Using a 25-gauge spinal needle, a spinal block was carried out at the L3-L4 or L4-L5 interspace using 2.5–3 ml of hyperbaric bupivacaine 0.5% + fentanyl 25 µg, depending on the patient's age or a related medical condition, following skin infiltration with 3 ml of lidocaine 2% at the lumbar puncture site following aseptic technique.

Measured parameters: -

Before administering the study medication (Melatonin or Pregabalin) two hours prior to surgery, after moving to the operating room (OT), prior to spinal anesthesia, and right after surgery, the amount of anxiousness was measured using the Beck Anxiety Inventory (BAI). The BAI's total score can range from 0 to 63, with 21 questions and four possible values from 0 to 3. Based on scores, anxiety levels were divided into four categories: mild (8–15), moderate (16–25), severe (26–63), and minimal (0–7).

*Table 1. Beck Anxiety Inventory (BAI):*

| | NOT AT ALL | MILDLY, BUT IT DIDN'T BOTHER ME MUCH | MODERATELY – IT WASN'T PLEASANT AT TIMES | SEVERELY – IT BOTHERED ME A LOT |
|---|---|---|---|---|
| NUMBNESS OR TINGLING | 0 | 1 | 2 | 3 |
| FEELING HOT | 0 | 1 | 2 | 3 |
| WOBBLINESS IN LEGS | 0 | 1 | 2 | 3 |
| UNABLE TO RELAX | 0 | 1 | 2 | 3 |
| FEAR OF WORST HAPPENING | 0 | 1 | 2 | 3 |
| DIZZY OR LIGHTHEADED | 0 | 1 | 2 | 3 |
| HEART POUNDING / RACING | 0 | 1 | 2 | 3 |
| UNSTEADY | 0 | 1 | 2 | 3 |
| TERRIFIED OR AFRAID | 0 | 1 | 2 | 3 |
| NERVOUS | 0 | 1 | 2 | 3 |
| FEELING OF CHOKING | 0 | 1 | 2 | 3 |
| HANDS TREMBLING | 0 | 1 | 2 | 3 |
| SHAKY / UNSTEADY | 0 | 1 | 2 | 3 |
| FEAR OF LOSING CONTROL | 0 | 1 | 2 | 3 |
| DIFFICULTY IN BREATHING | 0 | 1 | 2 | 3 |
| FEAR OF DYING | 0 | 1 | 2 | 3 |
| SCARED | 0 | 1 | 2 | 3 |
| INDIGESTION | 0 | 1 | 2 | 3 |
| FAINT / LIGHTHEADED | 0 | 1 | 2 | 3 |
| FACE FLUSHED | 0 | 1 | 2 | 3 |
| HOT / COLD SWEATS | 0 | 1 | 2 | 3 |

Prior to administration of Melatonin or Pregabalin, intraoperatively at five-minute intervals until twenty minutes, and subsequently every ten minutes until the conclusion of surgery, hemodynamic variables (MAP and HR) were collected as baseline. A fluid bolus and a 6 mg intravenous ephedrine bolus were employed to treat any hypotension (defined as MAP <20% of preoperative value). Atropine 0.01 mg/kg was administered intravenously to alleviate bradycardia (heart rate of 50 beats per minute).

A visual analogue pain scale (VAS) with an array of 0 to 10 (0 = none, 1–3) = mild, (4–7) = moderate, and (8–10) = severe) It is used to measure postoperative pain at the following intervals: immediately after surgery, on the fourth, sixth, twelfth, and twenty-four hours after surgery. Every eight hours, all patients were given oral paracetamol 1 g as part of their regular analgesic regimen. As soon as the patient arrived at the ward, the first dose of this medication was administered. I.M. Ketorolac 30 mg was used to provide rescue analgesia (when VAS was ≥4).

The total quantity of doses utilized in the 24 hours following surgery as well as the length of the initial ketorolac dosage request were recorded.

The degree of sedation at various points during the procedure was evaluated using the Ramsay Sedation Score (RSS), including before the study drug was administered (preoperative), during the procedure, just after the procedure, and on the fourth, sixth, twelfth, and twenty-four hours after the procedure.

*Table 2. Ramsay Sedation Score:*

| LEVEL OF ACTIVITY | POINTS |
|---|---|
| PATIENT ANXIOUS, AGITATED OR RESTLESS | 1 |
| PATIENT COOPERATIVE, ORIENTATED AND TRANQUIL | 2 |
| PATIENT RESPONDING ONLY TO VERBAL COMMANDS | 3 |
| PATIENT WITH BRISK RESPONSE TO LIGHT GLABELLA TAP OR LOUD AUDITORY STIMULUS | 4 |
| PATIENT WITH SLUGGISH RESPONSE TO LIGHT GLABELLA TAP OR LOUD AUDITORY STIMULUS | 5 |
| PATIENT WITH NO RESPONSE TO LIGHT GLABELLA TAP OR LOUD AUDITORY STIMULUS | 6 |

## 3. Results

Two groups of 25 patients each were formed from the 50 study participants, and they were assigned at random to either group. They all finished their studies.

The two groups' demographics (age, ASA, length of surgery, weight, and height) were similar. (Table 3).

*Table 3. Demographic data:*

| DEMOGRAPHIC DATA | MELATONIN GROUP (N=25) | PREGABALIN GROUP (N=25) | TEST VALUE | P-VALUE |
|---|---|---|---|---|
| SEX | | | | |
| FEMALE | 11 (44.0%) | 13 (52.0%) | 0.321 | 0.571 |
| MALE | 14 (56.0%) | 12 (48.0%) | | |
| AGE (YEARS) | | | | |
| MEAN±SD | 56.00±9.27 | 58.64±8.69 | -1.039 | 0.304 |
| RANGE | 42-70 | 44-70 | | |
| WT (KG) | | | | |
| MEAN±SD | 88.60±8.96 | 91.60±7.46 | -1.287 | 0.204 |
| RANGE | 70-100 | 80-100 | | |
| DURATION OF SURGERY (MIN) | | | | |
| MEAN±SD | 49.20±5.53 | 50.80±6.40 | -0.946 | 0.349 |
| RANGE | 40-60 | 40-60 | | |
| ASA | | | | |
| II | 16 (64.0%) | 20 (80.0%) | 1.587 | 0.208 |
| III | 9 (36.0%) | 5 (20.0%) | | |
| HIGHT (CM) | | | | |
| MEAN±SD | 161.51±7.23 | 162.80±6.93 | 0.106 | 0.721 |
| RANGE | 150-175 | 155-175 | | |

Based on heart rate "beat/min" and MAP (mmHg), no statistically significant difference

exists among the pregabalin and melatonin groups. with a p-value of p>0.05. (figure 1-2)

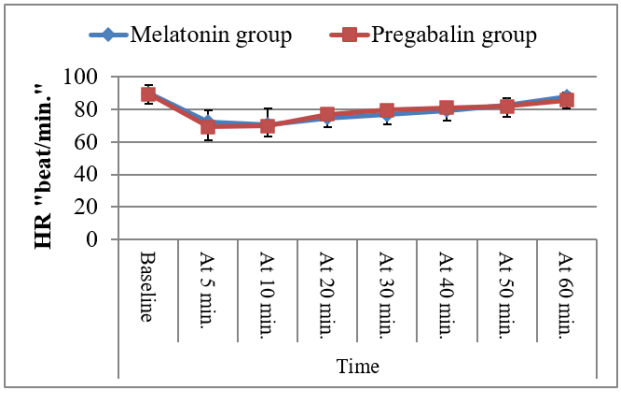



Figure 1. HR changes in both groups

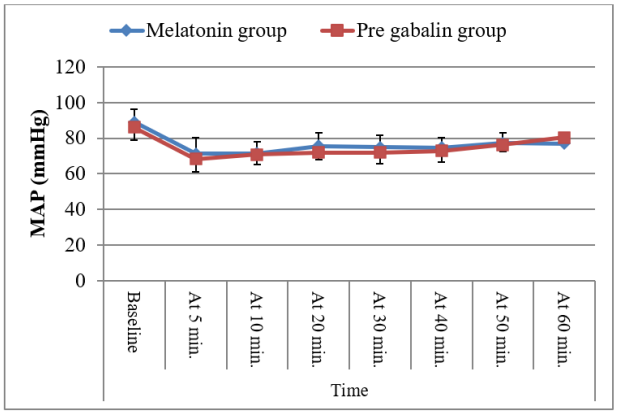



Figure 2. MAP changes in both groups

After moving to the operating room (OT), before spinal anesthesia, and immediately following surgery, the pregabalin group had a statistically significant higher median anxiety level than the melatonin group, with a p-value (p<0.001). (figure 3)

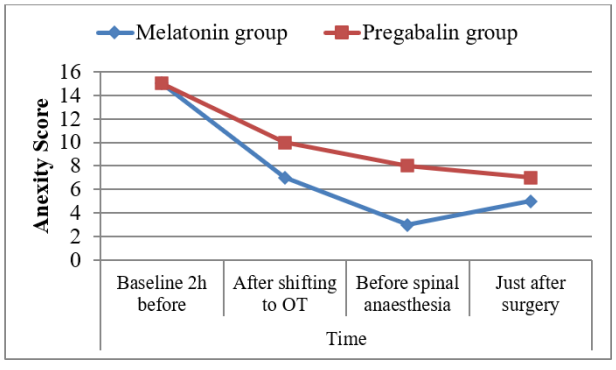



Figure 3. Anxiety score in both groups

With a p-value of less than 0.001, the pregabalin group's mean values for the length of motor block (min) and spinal anesthesia duration (min) were statistically significantly higher than those of the melatonin group. The groups do not differ statistically significantly based on onset of Motor Block (min) or onset of Sensory Block (min); nonetheless, the p-value exceeds 0.05. (table 4).

*Table 4. Onset and duration of both sensory and motor blocks in both groups*

| | Melatonin group (n=25) | Pregabalin group (n=25) | Test value | P-value |
|---|---|---|---|---|
| Onset of sensory block (min) | | | | |
| Mean±SD | 3.52±0.47 | 3.46±0.45 | 0.460 | 0.647 |
| Range | 3-4 | 3-4 | | |
| Duration of spinal anesthesia (min) | | | | |
| Mean±SD | 235.44±5.55 | 251.00±5.40 | -10.050 | <0.001** |
| Range | 225-245 | 240-260 | | |
| Onset of motor block (min) | | | | |
| Mean±SD | 7.40±0.50 | 7.44±0.51 | -0.281 | 0.780 |
| Range | 7-8 | 7-8 | | |
| Duration of motor block (min) | | | | |
| Mean±SD | 165.80±4.00 | 179.40±3.33 | - | <0.0 |
| Range | 160-170 | 175-185 | 13.066 | 01** |

After four, six, twelve, and twenty-four hours, the Melatonin group's median VAS score was statistically substantially greater than that of the Pregabalin category, with a p-value (p<0.001). (figure 4)

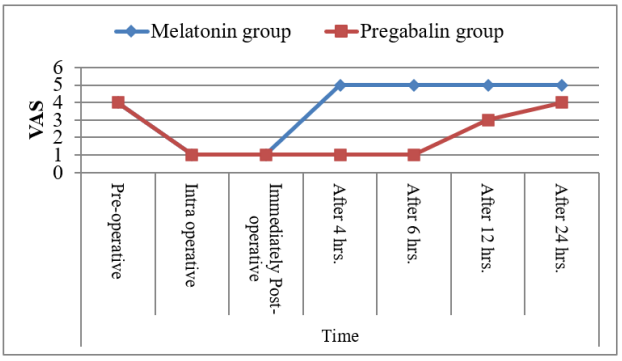



Figure 4. Changes in VAS scores in the two groups

Using a p-value (p<0.001), the melatonin category experienced a considerably quicker time to initial pain relief than the pregabalin category. (table 5)

*Table 5. Time to first rescue analgesia in both groups*

| TIME TO FIRST RESCUE ANALGESIA (MIN.) | MELATONIN GROUP (N=25) | PREGABALIN GROUP (N=25) | TESTVALUE | P-VALUE |
|---|---|---|---|---|
| MEAN±SD | 214.40±11.93 | 243.20±36.77 | 3.725 | <0.001** |
| RANGE | 200-240 | 200-320 | | |

The melatonin group had a considerably higher mean total analgesic demand (ketolarc 30 mg) than the pregabalin group (p<0.001). (figure 5).

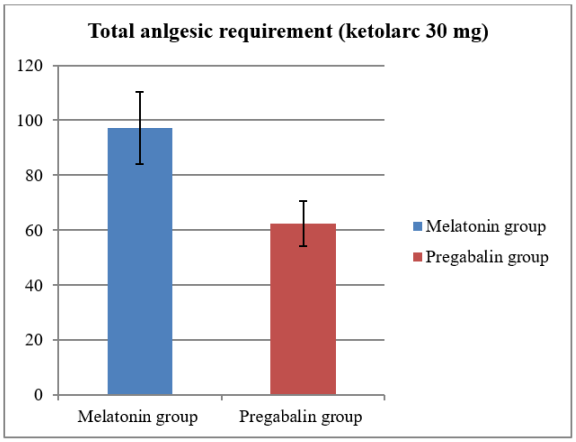



Figure 5. Total analgesic requirement in both groups.

The melatonin group had a statistically significant higher median RSS value than the pregabalin group during intraoperative, postoperative, and 4-hour periods, with a p-value ($p<0.001$) (figure 6).

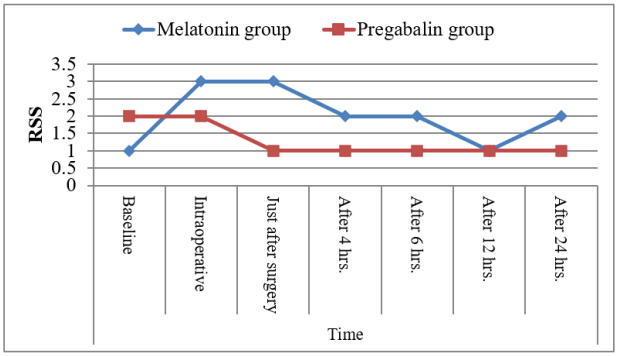



Figure 6. RSS value in both groups

## 4. Discussion

Fifty cases were recruited and split into two groups in order to assess how melatonin and pregabalin affected the sedation and anxiety of patients undergoing lower limb amputation under spinal anesthesia.

According to present research, the melatonin group experienced greater perioperative anxiolysis than the pregabalin group.

This appears to be comparable to those of Abbasivash et al.[10] who discovered that melatonin is linked to greater analgesia and decreases perioperative anxiety when compared to placebo.

Caumo et al.[11] administered melatonin preoperatively for anxiolysis in patients having abdominal hysterectomy; they observed similar outcomes.

According to a systematic evaluation by Madsen et al.[12] preoperative melatonin is more effective than a placebo or benzodiazepine at reducing perioperative anxiety.

The superiority of melatonin over pregabalin was also determined by Mohamed et al.[13] who evaluated the effects of oral melatonin against oral pregabalin in reducing the hemodynamic reactions to endotracheal intubation and influence on preoperative anxiety.

Conversely, Nasr et al.[14] found no difference in perioperative anxiety between pregabalin and melatonin. The use of different anxiety levels and patient age groups may be the cause of that discrepancy from current findings.

The level of discomfort following surgery was estimated using the Visual Analogue Scale (VAS), and the results showed substantial variations as soon as the patients were moved to the Post-Anesthesia Care Unit (PACU). Group P's VAS scores were noticeably lower than Group M's, suggesting that pregabalin provided better pain management and reduced the need for analgesics.

These findings are in line with those of Rajappa et al.[15] and Jokela et al.[16] who found that patients on pregabalin had a considerable decrease in VAS and a need for rescue analgesia.

Additionally, Mansour et al.[17] examined the impact of pregabalin and melatonin on sedation and anxiolysis in patients having hip replacement surgery while under spinal anesthesia. For postoperative analgesia, they discovered that pregabalin is superior.

In variance with the current work, Hoseini et al.[18] revealed that melatonin, gabapentin, and clonidine were all equally effective at lowering postoperative pain and narcotic intake when contrasted to a placebo.

Additionally, melatonin and pregabalin did not differ in their ability to control postoperative pain, according to Nasr et al.[14]. This discrepancy from present findings could be the result of the use of various anesthetic methods.

The results of the present study demonstrated that there was no difference in either group's start of sensory or motor block. The pregabalin group fared better in terms of both the extent of spinal anesthesia and the length of motor block.

According to current results, Mishra et al.[9] examined the impact of pregabalin and melatonin on the duration, blockade features, perioperative anxiety, pain, and sedation of spinal anesthesia in patients having total hip replacement while receiving spinal anesthesia. They concluded that the pregabalin group experienced the longest durations of sensory and motor blocking, whereas the placebo group experienced the shortest.

This was also agreed with Park et al.[19] and Omara et al.[20].

However, Nethra et al.[21] noticed, in comparison to a placebo, preoperative melatonin prolongs the sensory and motor blockade of spinal anesthesia.

Based on the current findings, melatonin provides higher sedation during intraoperative procedures, immediately following surgery, and four hours later than pregabalin.

This was in line with Nethra et al.[21], who concluded that preoperative melatonin confers high RSS up to two hours after surgery.

Also, Nasr et al.[14] found that melatonin creates a higher level of sedation.

On the other hand, Mansour et al.[17] came to the conclusion that all groups' sedation scores were the same.

Limitations: Current investigation was limited to one center, and our sample size was small. The results we got could have been impacted by the single center study and limited sample size. Finally, the present study's postoperative observation follow-up period was somewhat brief.

*4. Conclusion*

Melatonin was better at lowering anxiety and encouraging sedation, whereas pregabalin was better on the pain scale and had less analgesic consumption. The pregabalin group experienced longer spinal anesthesia and a longer motor block.

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Authorship

All authors have a substantial contribution to the article

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## Conflicts of interest

There are no conflicts of interest.

## References

1. Eapen I, Veerasamy RS, Hamsenandinie C, Anand S. Comparative study between oral melatonin and oral pregabalin on preoperative anxiety, preoperative sedation and postoperative analgesia in surgeries done under regional anesthesia: A randomized controlled study. Annals of Tropical Medicine and Public Health 23(15) DOI: 10.36295/ASRO.2020.231515
2. Fitzgibbons P, Medvedev G. Functional and clinical outcomes of upper ex-tremity amputation. J Am Acad Orthop Surg. 2015;23(12):751-60
3. Ayling OGS, Montbriand J, Jiang J, Ladak S, Love L, Eisenberg N, et al. Continuous Regional Anesthesia Provides Effective Pain Management and Reduces Opioid Requirement Following Major Lower Limb Amputation. European Journal of Vascular and Endovascular Surgery Volume 48 Issue 5 p. 559e564 November/2014
4. Dohlman LE, Kwikiriza A, Ehie O. Benefits and Barriers to Increasing Regional Anesthesia in Resource-Limited Settings. Local and Regional Anesthesia 2020:13 147–158
5. Pokharel K, Tripathi M, Gupta PK, Bhattarai B, Khatiwada S, Subedi A. Premedication with oral alprazolam and melatonin combination: A comparison with either alone- A randomized controlled factorial trial. Biomed Research International 2014:1-7.
6. Elrashidy A, Khattab AM, Elseify ZA, Oriby ME. Perioperative Anxiolytic and Analgesic Effects of Pregabalin in Vitreo-Retinal Surgery: A Randomized, Double-blind Study. Anesth Pain Med. 2021 August; 11(4): e117414.
7. Park M, Lee H, Jeon Y. Preoperative pregabalin prolongs the duration of spinal anesthesia and reduces early postoperative pain: A double blind, randomized clinical CONSORT study. Medicine (Baltimore), 2016;95(36). e4828.
8. Srinivasan V, Zakaria R, Jeet Singh H, Acuna-Castroviejo D. Melatonin and its agonists in pain modulation and its clinical application. Arch. Ital. Biol. 2012; 150: 274-89.
9. Mishra A, Srivastava VK, Prakash R, Mishra NK, Agarwal J, Kabi S. Perioperative anxiolysis and analgesic effect after premedication with melatonin and pregabalin in total hip arthroplasty under spinal anesthesia: A prospective comparative trial. Adv Biomed Res 2023; 12:185.
10. Abbasivash R, Salimi S, Ahsan B, Moallemi N, Sane S. The effect of melatonin on anxiety and pain of tourniquet in intravenous regional anesthesia. Adv Biomed Res 2019; 8:67.
11. Caumo W, Torres F, Moreira NL, Auzani JA, Monteiro CA, Londero G. The clinical impact of preoperative melatonin on postoperative outcomes in patients undergoing abdominal hysterectomy. Anesth Analg2007; 105:1263-71.
12. Madsen BK, Zetner D, Møller AM, Rosenberg J. Melatonin for preoperative and postoperative anxiety in adults. Cochrane Database Syst Rev 2020;12: 861.
13. Mohamed AK, Attia JA, Ahmed AA. Melatonin versus pregabalin for attenuation of stress response to endotracheal intubation. MJMR, Vol. 30, No. 2, 2019, pages (210-215).
14. Nasr DA, Abdellatif AA. Efficacy of preoperative melatonin versus pregabalin on perioperative anxiety and postoperative pain in gynecological surgeries. Egypt J Anaesth January 2014, Pages 89-93. DOI:org/10.1016/j.egja.2013.10.001
15. Rajappa GC, Vig S, Bevanaguddaiah Y, Anadaswamy TC. Efficacy of pregabalin as premedication for post-operative analgesia in vaginal hysterectomy. Anesth Pain Med 2016;6: e34591.
16. Jokela R, Ahonen J, Tallgren M, Haanpää M, Korttila K. Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynaecological laparoscopic surgery. Br J Anaesth 2008; 100:834-40.
17. Mansour MS, Soltan AA, Sedky AM. Efficacy of preoperative melatonin versus pregabalin on intraoperative anxiolysis and sedation during hip arthroplasty under regional anesthesia. Research and Opinion in Anesthesia & Intensive Care 10(4): p 341-347, October-December 2023. | DOI: 10.4103/roaic.roaic_13_23
18. Hoseini VS, Yekta RA, Marashi S, Marashi SM. The efficacy of melatonin, clonidine, and gabapentin in reducing Preoperative Anxiety and postoperative pain in patients undergoing laparoscopic cholecystectomy: A randomized clinical trial. Archives of anesthesiology and critical care. Autumn 2015; 1(4)120-125.
19. Park M, Lee H, Jeon Y. Preoperative pregabalin prolongs duration of spinal anesthesia and reduces early postoperative pain A double-blind, randomized clinical CONSORT study. Medicine (Baltimore) 2016;95: e4828.
20. Omara AF, Ahmed SA, Abusabaa MM. The effect of the use of pre-emptive oral pregabalin on the postoperative spinal analgesia in patients presented for orthopedic surgeries: Randomized controlled trial. J Pain Res 2019; 12:2807-14.
21. Nethra SS, Madhu KP, Sagar Srinivas K, Sudheesh K, Shubha S. Efficacy of preoperative oral melatonin on post operative pain in patients undergoing infraumbilical surgeries under subarachnoid block: A double-blind randomized control study. Indian J Clin Anaesth 2019;6(3):420-4.