Original Article

Comparing the Effects of Pre-Emptive Oxycodone, Diclofenac, and Gabapentin on Postoperative Pain After Tibia Fracture Surgery: A Randomized Clinical Trail

Abstract

Background: Postoperative pain (POP) is one of the most common and most important types of pain. **Objectives:** The aim of this study was to compare the effects of pre-emptive oxycodone, diclofenac, and gabapentin on postoperative pain (POP) among patients with tibia fracture surgery. **Materials and Methods:** This double-blind three-group randomised controlled trial was conducted in 2023. Participants were 111 candidates for tibia fracture surgery under general anaesthesia. They were randomly allocated to oxycodone, gabapentin, and diclofenac groups through block randomisation. Baseline arterial oxygen saturation, heart rate, and blood pressure were documented before surgery and POP and sedation status were measured during postoperative recovery and 2, 4, 6, 12, and 24 h after surgery. Postoperative opioid analgesic use was also documented. The data were analysed using the SPSS software (v. 20.0) at a significance level of less than 0.05. **Results:** Groups did not significantly differ from each other respecting participants' baseline age, gender, body mass index, arterial oxygen saturation, heart rate, blood pressure, and surgery duration ($P > 0.05$). Moreover, there were no significant differences among the groups respecting POP and sedation status at different measurement time points ($P > 0.05$), except for six hours after surgery at which the POP mean score in the gabapentin group was significantly less than the other two groups ($P = 0.001$). Among-group differences respecting postoperative use of opioid analgesics and medication side effects were also insignificant ($P > 0.05$). **Conclusion:** Pre-emptive oxycodone, diclofenac, and gabapentin significantly reduce POP among patients with tibia fracture surgery, though gabapentin may produce more significant analgesic effects. All these three medications can be used for pre-emptive analgesia. Of course, the best pre-emptive analgesic agent is determined based on the opinion of the treating physician.

Keywords: *Diclofenac, gabapentin, oxycodone, pain management, pre-emptive, tibia fracture*

Ramin Abrishami, Mehri Farhang Ranjbar, Amirreza Modir[1], Seyyed Kamal Hejazi

Research Center for Trauma in Police Operations, Directorate of Health, Rescue & Treatment, Police Headquarter, Tehran, Iran, [1]Student Research Committee, Arak University of Medical Sciences, Arak, Iran

Introduction

Postoperative pain (POP) is one of the most common and most important types of pain.[1] It may lead to different complications such as thromboembolism, myocardial ischaemia, and atelectasis. Combined analgesic regimens are usually used to manage POP and postoperative complications.[2] The effectiveness of these regimens depends on different factors such as patients' personality traits, psychological status, alcohol consumption, substance abuse, age, and surgery type. Currently, opioid analgesics are among the most effective analgesics for the management of POP. However, these analgesics have different side effects such as drowsiness, apnoea, nausea, vomiting, and ileus which limit their use.[3] In most cases, inadequate doses of these analgesics are administered to prevent their side effects. This practice is associated with ineffective pain management. Therefore, other strategies are essential to improve the effectiveness of POP management.

Pre-emptive analgesia is one of the strategies to improve the effectiveness of POP management. It refers to the administration of opioid or non-opioid analgesics before the onset of painful measures. This method helps use lower doses of opioid analgesics for effective POP management and hence, is associated with lower medication side effects.[4] Pre-emptive analgesia can reduce preoperative stress and postoperative mortality and improve prognosis, rehabilitation outcomes, and patient satisfaction.[4]

How to cite this article: Abrishami R, Ranjbar MF, Modir A, Hejazi SK. Comparing the effects of pre-emptive oxycodone, diclofenac, and gabapentin on postoperative pain after tibia fracture surgery: A randomized clinical trail. J West Afr Coll Surg 2024;14:301-6.

Received: 09-Aug-2023
Accepted: 25-Aug-2023
Published: 24-May-2024

Address for correspondence:
Dr. Amirreza Modir, Student Research Committee, Medicine Faculty, Arak University of Medical Sciences, Arak 3848176341, Iran.
E-mail: modir.ar@gmail.com

Access this article online

Website: www.jwacs-jcoac.com

DOI: 10.4103/jwas.jwas_143_23

Quick Response Code:

Oxycodone hydrochloride is a semi-synthetic opioid compound that stimulates the μ opioid receptors more than the δ and κ receptors.[5] It reduces the synthesis of inflammatory cytokines by reducing intracellular cyclic adenosine monophosphate. It has rapid-onset and long-term analgesic effects with low risks of hemodynamic instability, nausea, and vomiting.[6] It is a good treatment option for acute POP, cancer pain, and moderate to severe pains.[7] Some studies assessed the effects of oxycodone on cancer pain, osteoarthritis-related pain, neuropathic pain, and POP.[8] Hassani *et al*.[9] and Cheung *et al*.[10] also reported the significant positive effects of oxycodone on POP.

Diclofenac is a non-steroidal anti-inflammatory drug with good anti-inflammatory and analgesic effects[11,12] that blocks both cyclooxygenase 1 and 2.[13] It is used to manage pains associated with arthritic disorders, renal colic, surgeries, inflammatory disorders, and osteoarthritis[13-16] as well as pain after major surgeries.[17] Two studies found that diclofenac was effective in significantly reducing POP.[18,19]

Gabapentin, a structural analogue of gamma-aminobutyric acid, is an anticonvulsant agent that exerts its effects through voltage-gated calcium channels. It is also effective in reducing itching, chronic pains, migraine pain, and anxiety and does not cause amnesia.[20] Studies show that gabapentin has significant positive effects on neuropathic pain, post-herpetic pain,[21,22] and POP.[20-24]

Cheung *et al*.[10] reported oxycodone as a good oral substitute for injectable opioid analgesics. However, further studies are necessary to produce conclusive evidence respecting the effects of oxycodone. Hassani *et al*.[9] found that high doses of gabapentin significantly reduced postoperative nausea, vomiting, pain, and the need for pethidine administration, and recommended further studies into the effects of the lower doses of gabapentin. Moreover, Tomic *et al*.[18] showed that diclofenac, as an adjacent to orphenadrine, was effective in significantly reducing POP. Similarly, Yuri *et al*.[19] found that diclofenac significantly reduced POP without any significant side effect. However, that study highlighted the necessity of further studies in this area due to the small number of participants in the intervention group and sampling from individuals who lived mostly in rural areas. In addition to the limitations of previous studies into the effects of pre-emptive analgesia, there is limited comparative study into the effects of pre-emptive oxycodone, diclofenac, and gabapentin and hence, further studies are essential to produce more reliable results in this area. Therefore, the present study was conducted to compare the effects of pre-emptive oxycodone, diclofenac, and gabapentin on POP among patients with tibia fracture surgery.

Materials and Methods

Design

This double-blind three-group randomised controlled trial was conducted in 2023.

Participants and setting

Participants were 111 candidates for tibia fracture surgery purposefully selected from Valiasr Military Hospital, Tehran, Iran. Inclusion criteria were candidacy for tibia fracture surgery, age of 17–65 years, no sensitivity to oxycodone, gabapentin, or diclofenac, serum creatinine level less than 1.5 mg/dL, platelet count more than 150,000 per mm^3, no family history of thromboembolism, no history of substance abuse, and no history of coagulopathic, renal, hepatic, or cardiac disorders. Exclusion criteria were voluntary withdrawal from the study.

Participants were randomly allocated to an oxycodone group, a diclofenac group, and a gabapentin group using block randomisation with a block size of 6 [Chart 1]. The randomisation sequence was generated using the Sealed Envelope software. For allocation concealment, the first author anonymized and coded the medications of the study intervention and provided them to the second author of the study who implemented the intervention. Accordingly, the second author as well as study participants were blind to the intervention and the study was double-blind.

Intervention

Study intervention was pre-emptive analgesia with a single dose of oxycodone 15 mg tablet (Faran Shimi Company, Iran)[7] for participants in the oxycodone group, a single dose of gabapentin 600 mg capsule (Jalinus Company, Iran) for participants in the gabapentin group,[21] and a single dose of diclofenac 100 mg tablet (Alborz Daru Company, Iran) for participants in the diclofenac group.[13] All participants were hospitalised one day before surgery, received nothing per mouth for at least 8 h before surgery, and received the allocated intervention one hour before surgery with at most 20 mL of water.[9] All participants received fluid therapy with Ringer's solution 10 mL/kg throughout surgery and their baseline arterial oxygen saturation, blood pressure, and heart rate were documented. General anaesthesia for all participants was induced with thiopental sodium 5 mg/kg, fentanyl 1.5 μg/kg, and atracurium 0.5 mg/kg, and was maintained using oxygen, nitrous oxide 50% inhalation, and isoflurane 1%–1.5%, as well as intravenous injections of fentanyl 50 μg and atracurium 10 mg every 30 min. All participants were intubated throughout general anaesthesia. After surgery, administration of inhalation and intravenous anaesthetic agents was terminated, the effects of muscle relaxants were reversed, the endotracheal tube was removed, and patients were transferred to the recovery room. POP in all groups was assessed using a visual analogue scale at six time points, namely during recovery and 2, 4, 6, 12, and 24 h after surgery. Patients' sedation status was also assessed at the same time points using the Ramsay Sedation Scale [Table 1]. Patients with a POP score of more than 4 received meperidine 25 mg/IM, which is a standard postoperative analgesic agent. The total dose of meperidine was documented for each patient.

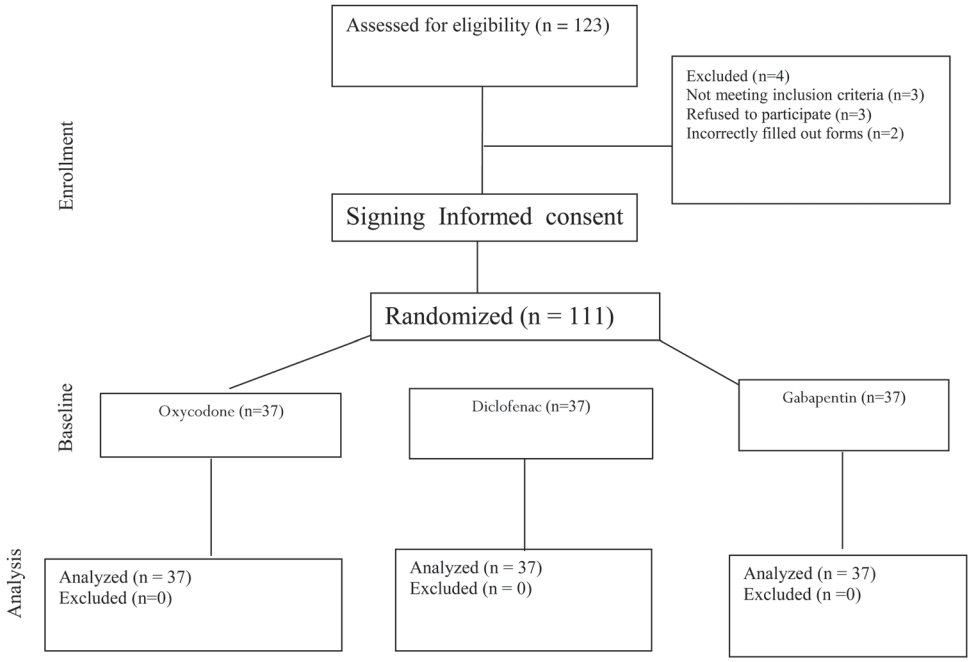

Chart 1: CONSORT diagram showing the flow of participants through each stage of a randomised trial

Table 1: The Ramsay Sedation Scale

1	Patient is anxious and agitated or restless or both
2	Patient is cooperative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

Intraoperative hypoxia (i.e., arterial oxygen saturation of less than 92%), hypotension (i.e., a blood pressure of less than 80% of baseline), and bradycardia (i.e., a heart rate of less than 40 bmp) were managed through oxygen therapy, Ringer's solution or sympathomimetic agents, and intravenous atropine 0.5 mg, respectively. Any other intraoperative or postoperative complication, such as shivering, nausea, vomiting, and altered consciousness, was also documented and managed using appropriate measures.

Data analysis

Data were analysed using the SPSS software (v. 20.0). The one-way and the repeated measures analyses of variance were respectively used for among-group and within-group comparisons respecting POP, sedation status, heart rate, blood pressure, and arterial oxygen saturation. The Chi-square test was also used for among-group comparisons respecting intraoperative and postoperative complications and opioid intake.

Results

All 111 participants completed the study. Their age range and age mean were 19–44 and 27.37 ± 6.37 years, respectively. Moreover, the range and the mean of their body mass index were 19–34 and 22.96 ± 3.56, respectively. Most participants were male (66.7%). There were no significant differences among the three groups respecting participants' age, gender, body mass index, surgery duration, as well as baseline arterial oxygen saturation, heart rate, and blood pressure ($P > 0.05$) [Tables 2 and 3].

The difference among the groups respecting the mean score of POP was not statistically significant ($P > 0.05$), except for six hours after surgery at which the POP mean score in the gabapentin group was significantly less than the other two groups ($P = 0.001$). Among-group difference respecting the mean score of sedation was also insignificant at all measurement time points ($P > 0.05$) [Table 3]. Moreover, there were no significant differences among the groups in terms of opioid analgesic intake and postoperative complications ($P > 0.05$) [Table 4].

Discussion

This study aimed at comparing the effects of pre-emptive oxycodone, diclofenac, and gabapentin on POP among patients with tibia fracture surgery. Findings showed no significant differences among the groups respecting the mean score of POP, except for 6 h after surgery. At this time point, the mean score of POP in the gabapentin group was significantly less than the other two groups. Moreover, groups did not significantly differ from each other respecting sedation status, opioid analgesic use, and postoperative complications.

Our findings showed that pre-emptive oxycodone, diclofenac, and gabapentin significantly reduced POP and there was no significant difference among them respecting their

Table 2: Participants' characteristics

Group characteristics		Oxycodone	Diclofenac	Gabapentin
Age (years), Mean ± SD		27.37 ± 6.36	27.35 ± 6.44	27.40 ± 6.50
Body mass index, Mean ± SD		22.96 ± 3.56	22.97 ± 3.61	23.00 ± 3.56
Gender, *N* (%)	Female	13 (14.43)	12 (13.32)	12 (13.32)
	Male	24 (26.64)	25 (27.75)	25 (27.75)

Table 3: Group comparisons respecting the mean scores of postoperative pain and sedation

Outcomes	Time group	Recovery	2 h after	4 h after	6 h after	12 h after	24 h after	*P* value*
Sedation	Oxycodone	2.378 ± 0.491	2.108 ± 0.314	2.00 ± 00.00	2.00 ± 00.00	1.567 ± 0.502	1.513 ± 0.506	>0.05
	Diclofenac	2.405 ± 0.497	2.108 ± 0.314	2.00 ± 00.00	2.00 ± 00.00	1.567 ± 0.502	1.567 ± 0.502	
	Gabapentin	2.405 ± 0.497	2.108 ± 0.314	2.00 ± 00.00	2.00 ± 00.00	1.621 ± 0.491	1.648 ± 0.483	
	P value**	0.964	0.906	0.999	0.999	0.865	0.503	—
Pain	Oxycodone	0.567 ± 0.502	1.108 ± 0.393	1.891 ± 0.515	2.97 ± 0.371	4.05 ± 0.468	4.40 ± 0.497	<0.001
	Diclofenac	0.540 ± 0.505	1.08 ± 0.363	2.02 ± 0.371	3.135 ± 0.419	4.16 ± 0.373	4.43 ± 0.502	
	Gabapentin	0.513 ± 0.506	0.973 ± 0.287	1.73 ± 0.479	2.70 ± 0.570	4.08 ± 0.363	4.32 ± 0.474	
	P value*	0.899	0.220	0.08	0.001	0.491	0.617	—

* The results of the repeated measures analysis of variance
** The results of the one-way analysis of variance

Table 4: Group comparisons respecting opioid use and postoperative complications

Groups outcomes		Oxycodone, *N* (%)	Diclofenac, *N* (%)	Gabapentin, *N* (%)	*P* value
Opioid use	No	17 (56.75)	16 (43.24)	21 (56.78)	0.501
	25 mg	20 (54.05)	20 (54.05)	16 (43.24)	
	50 mg	0	1 (2.70)	0	
Complications	No	26 (70.27)	25 (67.56)	26 (70.27)	0.958
	Yes	11 (29.72)	12 (32.43)	11 (29.72)	

effects on POP. Accordingly, all these medications reduced the need for opioid analgesic administration. Similarly, a review study on 26 clinical trials published in 2003–2015 showed that oxycodone had significant positive effects on POP among patients with laparoscopic cholecystectomy and abdominal, pelvic, breast, or spinal surgeries, and considered oxycodone as a good substitute for injectable opioid medications.[10] Eizadi *et al*.[25] also showed that oral oxycodone was as effective as intravenous morphine sulphate in significantly reducing pain among patients with acute musculoskeletal injuries due to blunt limb trauma. In contradiction to our findings, Hassani *et al*.[9] found that pre-emptive gabapentin was more effective than oxycodone in significantly reducing POP, had less frequent postoperative nausea and vomiting, and was associated with lower need for postoperative pethidine administration among patients with abdominal hysterectomy. This contradiction may be due to the administration of the low doses of gabapentin in the present study.

Thenarasu *et al*.[13] also assessed the effects of pre-emptive diclofenac and paracetamol and found that oral diclofenac administration was associated with more effective and longer analgesia and concluded that diclofenac is better than paracetamol for pre-emptive analgesia. Diclofenac in the present study also had significant pre-emptive analgesic effects but its effects did not significantly differ from the effects of oxycodone and gabapentin. Yeganeh Mogadam *et al*.[22] also compared the effects of diclofenac and gabapentin on POP among patients with tonsillectomy and found that POP and meperidine administration in the diclofenac and gabapentin groups were significantly less than the control group. A reason for the contradiction between our findings and the findings of Yeganeh Mogadam *et al*.'s study is that we had no control group for comparison.

Simone *et al*.[26] compared the pre-emptive effects of dexamethasone and diclofenac after third molar surgery and reported that pain intensity in the dexamethasone group was significantly less than the diclofenac and the placebo groups but there was no significant among-group difference respecting patients' request for analgesia. They finally concluded that pre-emptive dexamethasone is effective in significantly reducing POP. The findings of this study respecting the effects of diclofenac on POP were similar to our findings but corticosteroid administration was more effective in significantly reducing POP in that study. Bafna *et al*. also compared the effects of pre-emptive oral gabapentin 600 mg and pregabalin 150 mg on acute POP and found that both of them significantly reduced the need for analgesia and significantly prolonged the period of

postoperative analgesia.[21] Our findings were in agreement with the findings of this study.

Javaherforooshzadeh *et al*.[20] compared the effects of melatonin and gabapentin on pain and surgery after spinal surgery and found that both melatonin and gabapentin were effective in significantly reducing pain and anxiety. Hosseini *et al*.[27] also assessed the effects of melatonin, clonidine, and gabapentin among patients with cholecystectomy and found that gabapentin was as effective as clonidine and melatonin in reducing preoperative anxiety, POP, and the need for opioid analgesics. Moreover, Khezri *et al*.[28] assessed the effects of melatonin and gabapentin on anxiety and pain after cataract surgery and reported that both melatonin and gabapentin significantly reduced anxiety and gabapentin significantly reduced pain and the need for sedation during retrobulbar eye block which is in line with our findings. However, we found no significant difference among the effects of oxycodone, diclofenac, and gabapentin. This contradiction is attributable to the difference between these two studies respecting the medications used in their interventions.

Limitations

This study faced no serious limitation and all steps of the study were taken according to the predetermined time schedule.

Conclusion

This study shows that pre-emptive oxycodone, diclofenac, and gabapentin can significantly reduce POP and post-operative opioid consumption, though gabapentin may be more effective than oxycodone and diclofenac. These medications are associated with no significant side effect and are well-tolerated by patients due to their administration through the oral route. Of course, the final decision for the best pre-emptive analgesic is based on the opinion of the treating physician.

Acknowledgements

This study was part of a research project ethically approved by the Ethics Committee of the Directorate of Health, Rescue, and Treatment of Iran Police Headquarter (code: IR.SBMU.TEB.POLICE.REC.1402.019). Moreover, the study was registered in the Iranian Registry of Clinical Trials (registration number: IRCT20230716058804N1). Hereby, we would like to thank the Clinical Research Council of Valiasr military hospital, Tehran, Iran, as well as the Directorate of Health, Rescue, and Treatment of Iran Police Headquarters, Tehran, Iran, for their intangible and tangible supports.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors report no declaration of interest.

References

1. Zoltie N, Cust MP. Analgesia in the acute abdomen. Ann R Coll Surg Engl 1986;68:209-10.
2. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. Yale J Biol Med 2010;83:11-25.
3. Abdallah FW, Hussain N, Weaver T, Brull R. Analgesic efficacy of cannabinoids for acute pain management after surgery: A systematic review and meta-analysis. Reg Anesth Pain Med 2020;45:509-19.
4. Wang N, Wang Y, Pang L, Wang J. Effect of preemptive analgesia with intravenous oxycodone in the patients undergoing laparoscopic resection of ovarian tumor. Pak J Med Sci 2015;31:300-3.
5. Wu J, Gui Q, Wang J, Ye J, Xia Z, Wang S, *et al*. Oxycodone preemptive analgesia after endoscopic plasma total adenotonsillectomy in children: A randomized controlled trial. Medicine (Baltim) 2020;99:e19004-04-e.
6. Sun C, Yang Q, Wang C, Zhao J, Dai M. Efficacy of different preemptive analgesia on postoperative analgesia, oxidative stress, and inflammatory response after gynecological laparoscopic surgery. Evid Based Complement Alternat Med 2021;2021:4233716.
7. Gaskell H, Derry S, Moore RA, McQuay HJ. Single dose oral oxycodone and oxycodone plus paracetamol (acetaminophen) for acute postoperative pain in adults. Cochrane Database Syst Rev 2009;2019:CD0027-63-CD.
8. Park J-H, Lee C, Shin Y, An J-H, Ban J-S, Lee J-H. Comparison of oxycodone and fentanyl for postoperative patient-controlled analgesia after laparoscopic gynecological surgery. Korean J Anesthesiol 2015;68:153-8.
9. Hassani V, Zaman B, Alimian M, Safaeian R, Mehdizadehkashi A, Karami S, *et al*. Comparison effect of pre-emptive gabapentin and oxycodone on pain after abdominal hysterectomy: A double blind randomized clinical trial. Acta Medica Iranica 2018;56:244-8.
10. Cheung CW, Ching Wong SS, Qiu Q, Wang X. Oral oxycodone for acute postoperative pain: A review of clinical trials. Pain Physician 2017;20:SE33-52.
11. Bajaj P, Ballary CC, Dongre NA, Baliga VP, Desai AA. Comparison of the effects of parecoxib and diclofenac in preemptive analgesia: A prospective, randomized, assessor-blind, single-dose, parallel-group study in patients undergoing elective general surgery. Curr Ther Res Clin Exp 2004;65:383-97.
12. Wattchow DA, De Fontgalland D, Bampton PA, Leach PL, McLaughlin K, Costa M. Clinical trial: The impact of cyclooxygenase inhibitors on gastrointestinal recovery after major surgery—A randomized double blind controlled trial of celecoxib or diclofenac vs. placebo. Aliment Pharmacol Ther 2009;30:987-98.
13. Thenarasu V, Gurunathan D, Selvarasu K. Comparison of efficacy of diclofenac and paracetamol as preemptive analgesic agent. Biomed Pharmacol J 2018;11:1699-706.
14. Chung C. The use of injectable nonsteroidal anti-inflammatory drugs in local accident & emergency practice. Hong Kong J Emerg Med 2002;9:65-71.
15. Dutta NK, Mazumdar K, Dastidar SG, Park J-H. Activity of diclofenac used alone and in combination with streptomycin against Mycobacterium tuberculosis in mice. Int J Antimicrob Agents 2007;30:336-40.
16. Coxib, traditional NTC, Bhala N, Emberson J, Merhi A, Abramson S, *et al*. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: Meta-analyses of individual participant data from randomised trials. Lancet 2013;382:769-79.

17. Daglar B, Kocoglu H, Adnan Celkan M, Goksu S, Kazaz H, Kayiran C. Comparison of the effects of lornoxicam versus diclofenac in pain management after cardiac surgery: A single-blind, randomized, active-controlled study. Curr Ther Res Clin Exp 2005;66:107-16.
18. Tomic J, Wallner J, Mischak I, Sendlhofer G, Zemann W, Schanbacher M, *et al*. Intravenous ibuprofen versus diclofenac plus orphenadrine in orthognathic surgery: A prospective, randomized, double-blind, controlled clinical study. Clin Oral Investig 2022;26:4117-25.
19. Yuri P, Ali Z, Rasyid N, Birowo P. Effects of pipemidic acid, phenazopyridine HCL and sodium diclofenac on pain perception following endoscopic urological surgery: Double-blinded randomized-controlled trial. Acta Med Indones 2016;48:184-92.
20. Javaherforooshzadeh F, Amirpour I, Janatmakan F, Soltanzadeh M. Comparison of Effects of melatonin and gabapentin on post operative anxiety and pain in lumbar spine surgery: A randomized clinical trial. Anesth Pain Med 2018;8:e687-63-e.
21. Bafna U, Rajarajeshwaran K, Khandelwal M, Verma AP. A comparison of effect of preemptive use of oral gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. J Anaesthesiol Clin Pharmacol 2014;30:373-7.
22. Yeganeh Mogadam A, Fazel MR, Parviz S. Comparison of analgesic effect between gabapentin and diclofenac on post-operative pain in patients undergoing tonsillectomy. Arch Trauma Res 2012;1:108-11.
23. Parikh HG, Dash SK, Upasani CB. Study of the effect of oral gabapentin used as preemptive analgesia to attenuate post-operative pain in patients undergoing abdominal surgery under general anesthesia. Saudi J Anaesth 2010;4:137-41.
24. Mahoori A, Noroozinia H, Hasani E, Hosainzadeh S. The effect of pre-operative administration of gabapentin on post-operative pain relief after herniorrhaphy. Saudi J Anaesth 2014;8:220-3.
25. Eizadi P, Jalili M, Dehpour A. Oral oxycodone compared with intravenous morphine sulfate for pain management of isolated limb trauma: A randomized clinical trial. Emerg (Tehran) 2018;6:e59-e59-e.
26. Simone JL, Jorge WA, Horliana AC, Canaval TG, Tortamano IP. Comparative analysis of preemptive analgesic effect of dexamethasone and diclofenac following third molar surgery. Braz Oral Res 2013;27:266-71.
27. Hosseini VS, Yekta R, 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. Arch Anesthesiol Critic Care 2015;1:120-25.
28. Khezri M-B, Oladi M-R, Atlasbaf A. Effect of melatonin and gabapentin on anxiety and pain associated with retrobulbar eye block for cataract surgery: A randomized double-blind study. Indian J Pharmacol 2013;45:581-6.