A comparative study of Gabapentin and intravenous Lidocaine for post-operative pain control after total knee replacement

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ABSTRACT

Objective: To assess the side effects, efficiency, and outcomes of Gabapentin, Intravenous Lidocaine, and their combination for the reduction of postoperative pain after the total knee replacement.
Study Design: A Case-Control study was done.
Place and Duration: At Trauma and Orthopedic Department, Mukhtar A Sheikh Hospital Multan, from March 03, 2020 to August 03, 2020
Methodology: Sixty-six patients were included in the study who were placed in three study groups. Group A, B, and C were given recommended doses of intravenous lidocaine, Gabapentin orally, and their combination, respectively, a standard time before the start of operation. The administration of drugs was followed by giving anesthesia to the patients. The post-operative pain was measured through the visual analog score. According to which pain intensity was scored from 0 to 10 as per the information provided by the patients.
Results: Age, weight, gender, and duration of surgery were some factors that did not differ significantly in all groups. Pain relief was observed in all three groups within 24 hours with the mean VAS Rest Pan Score 50.0+-20.8, 40.7+-33.2 and 28.4+-19.3 in Group A, B, and C respectively which get reduced significantly to 17.5+-22.0, 16.4+-15.0 and 16.2+-18.0 in Group A, B, and C respectively till 48th hour. Nausea, vomiting, dizziness, headache and dry mouth was found as a complication of treatment in all treated groups. Nausea occurring is 22.7%, 9%, and 9%, Vomiting in 18.1%, 18.1%, and 4.5%, Dizziness in 18%, 27% and 31%, Headache in 18.1%, 13.6% and 18.1%, while Dry mouth in 18.1%, 27.2% and 27.2% in Group A, B and C respectively.
Conclusion: To reduce the postoperative pain by analgesic effect, intravenous lidocaine as well as Gabapentin, both are effective, safe, and significant but have some side effects too. Also, their combination reduces the pain, but the side effects are decreased by its use. For overcoming postoperative nausea and vomiting, Gabapentin is the most suitable drug.
Keywords: Anaesthesia, Gabapentin, intravenous lidocaine, postoperative pain, surgery, Total knee replacement

How to Cite This:
Hafeez J, Ahmad S, Mahmood A, Bandesha MY. A comparative study of Gabapentin and intravenous Lidocaine for post-operative pain control after total knee replacement. Isra Med J. 2021; 13(2): 87-91.

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Received for Publication: November 25, 2020
1st Revision of Manuscript: February 18, 2021
2nd Revision of Manuscript: May 16, 2021
Accepted for Publication: May 28, 2021

INTRODUCTION

End-stage Osteoarthritis, rheumatic arthritis, trauma, and other joint disorders can cause severe pain, restrict mobility and physical inactiveness. These joint destructive disorders are usually common in older and mid-aged adults. Inflammation of the synovial membrane and damage to knee cartilage are some of the consequences of these disorders. To have a pain-free life and increased mobility, total knee replacement, also known as total knee arthroplasty is recommended in these severe conditions[1,2]. The damaged cartilage and the bone are removed from that point where the femur and tibia meet on the knee parts in the surgery so that, you can move and bend your knee without any pain. Postoperative pain is usually associated with this procedure. 60% of the patients experience chronic pain whereas 30% face moderate pain. Moreover, thromboembolism risk and early ambulation are consequences of postoperative pain. So, the need for the management of postoperative pain after the knee replacement is obvious[3,4].

Several analgesics and anesthetic medications are used to overcome the pain. But, every medicine, along with its benefits, has some side effects[5]. Gabapentin (1-aminomethyl cyclohexane acetic acid) is an anticonvulsant drug that is usually used to treat migraine and other several neuropathic pain syndromes[6,7]. This non-epileptic drug has central and peripheral antalgic activity[6]. Some research has shown that Gabapentin shows its effect within 24 hours of the surgery. Fatigue, dizziness, uncoordinated movement, tiredness, blurred vision, uncontrolled or repetitive eye movements and, tremors can be some of the side effects of Gabapentin[7, 8].

Lidocaine is another anesthetic drug, also known as lignocaine, that is used to numb a specific area of the body to reduce pain[9,10]. The chemical formula of the drug is 2-(Diethyl amino)-N-(2, 6-dimethyl phenyl) acetamide. It can play a role as an anti-inflammatory and anti-hyper analgesic drug. Intravenous lidocaine has some benefits that the other local anesthetics lack including the perioperative infusion. It has been observed that postoperative pain is reduced after the introduction of lidocaine in the dorsum of the foot. Other benefits include a lesser opioid requirement. The common side effects are dizziness, vomiting, feeling hot or cold, confusion, ringing in your ears and, blurred vision. It has been suggested that the combination of both drugs can give the best results and reduce the pain after the surgery[11,12].

The time duration during which the Gabapentin's peak plasma level is obtained is 2-3 hours after its intake. Metabolism does not occur and it is removed from the body in some form, from the urine.

According to the literature, both methods have some better results as well as side effects. In the current study, we studied the effect of oral Gabapentin and intravenous lidocaine in patients with a total knee replacement. The current study was conducted with an objective to assess the side effects, efficiency, and outcomes of Gabapentin, Intravenous Lidocaine, and their combination for the reduction of postoperative pain after the total knee replacement.

METHODOLOGY

This case-control study was performed at Tertiary Care Hospital Trauma and Orthopedic Department of Mukhtar A Sheikh Hospital Multan, from March 03, 2020 to August 03, 2020. Patients that were suffering from any kind of arthritis or knee joint disorder were selected for the study. Ethical statement of the patient was the priority and written consent was also taken from every patient as a record. The whole procedure was explained to all patients and the choice of with-drawl at any time was provided as well. The inclusion criteria for the study included patients of age more than 18 years, both gender, patients undergoing surgery with general anesthesia, and mainly the patients that were suffering from any kind of arthritis or knee joint disorder. Whereas the exclusion criteria included patients with neoplastic etiology, infection, traumatic fracture, metal sensitivity, obstructive sleep apnea, revision surgery, mental diseases, and use of the local anesthetic technique or a nerve block. Three groups were made and named A, B, and C. Patients were divided equally so that each group consists of 22 patients.

The patients of the A group were given placebo capsules 1 hour before the surgery. Then, just before giving anesthesia, IV bolus injection of 1.0 mg/kg lidocaine (Xylocaine 2%; AstraZeneca, 600 Capability Green, Luton, LU1 3LU, UK) was introduced to the patients. The solution was diluted by normal saline to a 10 ml volume. Then, it was infused continuously, until the skin was closed. A syringe was pumped at the rate of 2 mg/kg/h during surgery. In group B, 1 hour before the surgery, patients were given 600 mg gabapentin capsules (Neurontin; Pfizer, Cairo, Egypt). They were allowed to ingest the capsule. Then, before giving anesthesia the patients were given 10 ml of the saline bolus. After that saline infusion was done intraoperatively (the same volume as lidocaine infusion in group A). The same syringe pump was used for the procedure until the closure of the skin. Whereas in group c, patients were allowed to ingest 600 mg gabapentin capsules. Similar to groups A and B, it was done 1 hour before surgery. Then, just before having anesthesia, they received an IV bolus of 1.0 mg/kg lidocaine. After that, the same syringe pump was used in this procedure for intraoperative lidocaine infusion. Before the closure of the skin, the process was done at the rate of 2 mg/kg/h. there was no specific dose for the administration of IV drugs. The amount to be given was calculated according to the weight of the patient. All the persons involved in the research including the surgeons, patients as well as anesthetist were unaware of group allocation. The Preoperative condition of the patients including their assessment was done 12 hours before the surgery. The patients were explained how to express the intensity of pain ranging from 0-10 by using the visual analog score (VAS; 0 = no pain and 10 = worst pain- imaginable)[13] at 12, 24, 36, and 48 hours following the operation. All three groups were contrasted with patients in a placebo group who were not given any pain-reducing treatment.

Data Analysis: For the data analysis procedure, SPSS software (Statistical Package for the Social Science; SPSS Inc, Chicago, IL, USA) was used with version 22. In statistical analysis, data were explained as mean ± standard deviation (±SD), or frequencies (number of cases) and percentages when appropriate. All of the three groups were evaluated and the results were compared by one-way analysis of variance (ANOVA) test. Mann-Whitney U test was used to evaluate the independent samples. If the frequency was less than 5, the Exact test was used. P-values less than 0.05 were considered significant[14,15].

RESULTS

The study was completed by sixty-six patients that were undergoing total knee replacement surgery by using general anesthesia. Among them, 22 patients were present in each group (n=22 in groups A, B, and C). No significant difference was found in the mean values of age, weight, gender, duration of surgery, Intraoperative fentanyl, and extubation time among participants from all groups (Table-I).

Table-I: Baseline characteristics of patients (N=66)

Variables	(A) Group (n=22)	(B) Group (n=22)	(C) Group (n=22)
Age (years)	46.9 ± 7.7	45.4 ± 6.7	47.8 ± 8.2
Male/female (n)	6/16	5/17	7/15
ASA class 1 / 2 (n)	8/14	6/16	8/14
Weight (kg)	89 ± 8.7	90.2 ± 8.2	88.7 ± 8.6
Duration of surgery (min)	130 ± 28	134 ± 29	132 ± 28
Intraoperative fentanyl	227 ± 39.8	220 ± 34.2	180 ± 30.4
Extubation time (min)	10.4 ± 1.4	9.8 ± 1.7	10.6 ± 1.2

Variation in VAS was observed during different observed hours postoperatively. Patients from Group A reported the highest intensity of the pain (50.0+-20.8) after 24 hrs of operation while group B and C complained of maximum pain, 44.5+-21.2 and 36+-26.2 respectively, at the 36th hour of reporting following the infections. However, a comparative decrease in pain intensity was observed in all groups at the 48th hour after the surgery. Similarly, at every reporting hour, no significant difference was found between the measured pain intensity of the participants of all 3 groups (Table-II).

Table-II: Mean vas rest pan score of participants belonging to 3 study groups (N=66)

Time after surgery(hr)	Placebo Group	GA (n=22)	GB (n=22)	GC (n=22)	P-Value
12	54+- 28.5	37.6+-26.5	32.2+-25.5	23.4+-19.8	0.75
24	48+-18.2	50.0+-20.8	40.7+-33.2	28.4+-19.3	0.056
36	44.3+-21.3	35.5+-11.8	44.5+-21.2	36+-26.2	0.89
48	37+-20.3	17.5+-22.0	16.4+-15.0	16.2+-18.0	1.0

Maximum patients (22.7%) from Group A reported nausea while 18.1% reported headache, vomiting, dry mouth, and dizziness as side effects of lidocaine. Similar, side effects were reported among group B and C participants but with a variable frequency of occurrence. Results have predicted the least side effects among group C while the equal frequency of complications was found among patients from group A and B (Table-III).

Table-III: Post-operative side effects (N=66)

Postoperative side effects	(A) Group (n=22)	(B) Group (n=22)	(C) Group (n=22)
Nausea	5 (22.7%)	2 (9%)	2 (9%)
Vomiting	4 (18.1%)	4 (18.1%)	1 (4.5%)
Dizziness	4 (18%)	6 (27%)	7 (31%)
Headache	4 (18.1%)	3 (13.6%)	4 (18.1%)
Dry mouth	4 (18.1%)	6 (27.2%)	6 (27.2%)

DISCUSSION

Pre-operative anxiety is usually a serious issue, but postoperative pain is more a center of attention here[11]. Both of them are somehow connected as anxiety leads to decreased pain thresholds as a result of which severe pain is suffered by the patients that have undergone knee surgery[3]. Also, pain and anxiety have a significant effect on wound healing time as well as the immune system[5]. So, to overcome the pain, analgesics are sued[16]. In this study, we used oral Gabapentin, intravenous lidocaine, and their combination to find out the most efficient analgesics in subsiding pain among the patients who had gone through knee replacement.

Our study indicated that all three treated analgesics were efficient in pain reduction following the operation. There was no significant difference found between pain reduction activity of the three treatment strategies used. Similar results were found in a study conducted by Kaba et al[17] who studied the post-operative pain reduction effect of intravenous lidocaine on patients who went through laparoscopic colectomy. He found that lidocaine was significant in reducing postoperative pain, along with the reduction in the need for opioid use. In another study, a methodology similar to our study was performed on thyroid-operated patients. The study contrasted with our results as patients who were administered combination of two analgesics recorded a significant decrease in pain intensity than the other two groups[18]. The use of gabapentin and lidocaine is aimed at reducing the utilization of opioids. Harvin et al[19], in their study, combined the two analgesics in a multimodal analgesic strategy and found the model effective in reducing opioid intake.

In contrast to our study, previously lidocaine has been proved inefficient in pain reduction in many studies. Martin et al. found that no difference was found between the placebo group who were infused with normal saline and lidocaine treated group in terms of pain on patients undergoing hip arthroplasty[20]. Similarly, De Oliveria et al[21] concluded lidocaine as ineffective. On the other hand, the pain reduction effect of Gabapentin has been validated in existing literature[22]. Sen et al[23] contrasted gabapentin treated group with the placebo group and found significant differences in pain reduction.

The result of the present study shows that group C having a combination of Gabapentin and lidocaine shows fewer postoperative complications and side effects than the other two groups. Postoperative sedation was found in all three groups in the study. The frequency of sedation along with headache, nausea, and mouth dry was different in the cases but the results are found to be consistent with previous studies[24,25]. Literature states that sedation level is higher in the gabapentin group just because of higher or repeated dosages. So, some research has shown that if the ideal amount of Gabapentin is used, i.e., 600-800mg is consumed, then all the postoperative effects can be overcome[25].

Limitations: Firstly, plasma lidocaine concentration was not measured. Also, the amount of lidocaine given to the patients in a short time was lesser as compared to other studies. Moreover, the study has a sample size that has not only limited the evaluation of the exact effect of analgesics but the difference of our results to previous studies can also be contributed to the same limitation. Similarly, better determination of the individual analgesic couldn't be done. The study recommends conducting further studies to evaluate the effect of analgesics on a larger sample population and by utilization of recommended doses.

CONCLUSION

To reduce the postoperative pain by analgesic effect, intravenous lidocaine as well as Gabapentin, both are effective, safe, and significant but have some side effects too including nausea, vomiting, headache, dizziness, and dry mouth. Also, their combination reduces the pain, but the main point is that their use also decreases the side effects. Whereas, for overcoming postoperative nausea and vomiting, among all three methods, oral Gabapentin is the most suitable drug.

AUTHOR'S CONTRIBUTION

Hafeez J: Conceived idea, Designed research methodology, Data analysis, Manuscript writing,
Ahmad S: Manuscript writing, Data collection, Data analysis, Literature review
Mahmood A: Manuscript writing, Data analysis, Data collection, Literature review
Ali L: Data collection and analysis, Literature review
Bandesha MY: Designed research methodology, Data analysis, Manuscript writing, Final critical review of manuscript

Disclaimer: None.
Conflict of Interest: None.
Source of Funding: None.

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