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ORIGINAL ARTICLE

Effect of Gabapentin on Opioid Requirement in patients undergoing total Abdominal Hysterectomy

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ABSTRACT

Background: Pain following surgery has an effect on anesthesia and surgical recovery. To improve the benefits and lessen the problems of opioids, combination regimens of non-opioid and opioid medications are used.

Objective: The aim of this study was to determine the effect of gabapentin on opioid requirement in patients undergoing total abdominal hysterectomy.

Materials and method: The current double blind controlled trial was carried out at the department of anesthesia, Umer Clinic, PKLI and POF hospital from January 2023 to June 2023 after taking permission from the ethical committee of the hospital. A total of 80 individuals of different age groups (ranged 41-61 years) with ASA I and II performing total abdominal hysterectomy were enrolled. These individuals were classified equally in two groups. There are 40 individuals in each of the two groups, Group S (study group, experimental group) & Group C (control group). Two hours before to surgery, 40 patients in Group S got oral gabapentin 1200 mg, while 40 participants in Group C received oral placebo capsules. Both groups received the same anesthetic method. All patients were put under general anesthesia. Following surgery, patients' pain levels were assessed using the VAS score 1–10. The information above was gathered by the assigned nurse who was blind to the treatment groups. SPSS version 12 was used to process the data. Applying the Student's t-test was applied to the assess pain score and supplemental nalbuphine requirements. A p-value of < 0.05 was considered significant.

Results: 80 individuals were enrolled in this study and were classified in to control and study groups. In both groups, the hemodynamic results remained stable. In both groups, no individuals needed intraoperative rescue analgesics. Following surgery, the gabapentin group's VAS score at zero, two, eight, sixteen, and twenty-four hours were noticeably lower than the control group's pain scores. The study group took significantly fewer nalbuphine overall in the first 24 hours following surgery than the control group. The P-value was statistically significant ($p< 0.001$).

Conclusion: The present study concluded that the use of gabapentin greatly lowers intraoperative and postoperative pain. It also minimizes the requirements of opioids in individuals undergoing TAH.

Keywords: Gabapentin**,** TAH, pain, opioids.

INTRODUCTION

In post-operative care, pain management is crucial because it lowers the possibility of psychological and neurotic affects after surgery. Thus, it is important to encourage patients to have surgery when it is required since, in many situations, fear of pain might prevent patients from choosing to have surgery, endangering their live and restricted their applications. To limit the negative effects, other painkillers have been used either alone or in conjunction with opioids to manage post-operative pain and decrease the demand for opioids. The antiepileptic and anticonvulsive medication gabapentin has been used to treat neuropathic pain.[1-2] It is an analogue of gamma-aminobutyric acid (GABA) that has multiple mechanisms of reducing pain.[3] Numerous studies have studied the effects of gabapentin on pain relief using various administration routes, dosages , surgeries alone or in combination with other painkillers, as a single dose or in multiple doses.[4-5-6] Pre-operatively or post-operatively and practically all of the studies in question found that it might lessen postoperative pain and the quantity of painkillers required.[7-8] In surgical patients, postoperative pain, a kind of acute pain, is one of the upsetting circumstances that nearly always tests anesthetists' abilities to manage these patients. Many medications have been attempted to treat it, and a combination of therapies has been employed. Paracetamol, NSAIDS, local anesthetics, and opioids are remain the main medications prescribed for postoperative pain management. Additionally, it has been evaluated with various pain relievers such as cyclooxygenase-2 inhibitors, venlafaxine, paracetamol and ketamine. Both gabapentin and paracetamol together and gabapentin by itself reduced the need for opioids during abdominal hysterectomy. .[9]Gabapentin suppresses high threshold calcium channel currents in cultured rat dorsal root ganglion neurons, according to a research by Sutton et al.[10] Additionally, it has been used to treat a variety of chronic pain problems and has been demonstrated to be successful in doing so with little adverse effects .[1] Pain management following a hysterectomy can aid in early ambulation, reduce complications such as ileus, impaired pulmonary function, and post-operative fatigue, improve patient satisfaction, and avoid delayed convalescence because hysterectomy is one of the most common gynecological surgeries and the second most common surgery performed after caesarean section in many countries.[11]The present study was carried out to determine the Effect of gabapentin on opioid requirement in patients undergoing total abdominal hysterectomy.

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MATERIALS AND METHOD

The current double blind controlled trial was carried out at the department of anesthesia, Umer Clinic, PKLI and POF hospital from January 2023 to June 2023 after taking permission from the ethical committee of the hospital. A total of 80 individuals of different age groups (ranged 41-61 years) with ASA I and II performing total abdominal hysterectomy were enrolled while individuals with a history of ischemic heart disease, hypertension, renal or hepatic insufficiency, coagulation problems, acid reflux illness, hypersensitivity to any medication, or those using calcium channel blockers or antidepressants were excluded. These individuals were classified equally in two groups. There are 40 individuals in each of the two groups, Group S (study group, experimental group) & Group C (control group). Two hours before to surgery, 40 patients in Group S got oral gabapentin 1200 mg, while 40 participants in Group C received oral placebo capsules. Following informed agreement, these individuals were randomized to one of two groups. Simple random allocation was used to create

a randomization list. Following that, a randomization list was used to assign a number to each patient. Prior to surgery, each individual was given the visual analogue scale and instructed on how to score their level of pain. The pharmacy used a randomization list to produce the trial medications into identical capsules. A qualified nurse who was not engaged in any other aspect of the trial packaged them in packages with sequential numbers and delivered them to the selected individuals in the same sequence. An individual who was blinded to the study documented the pain score assessment both intraoperative (by measuring a rise in blood pressure and heart rate related to pain) and postoperatively (by using the visual analogue scale, or VAS). The need for supplementary opioids (nalbuphine) both during and after surgery was also noted. Patients' weight and age were also recorded. Both groups received the same anaesthetic method. All patients were put under general anaesthesia. An hour before to the induction of anaesthesia, each participant was given a 7.5 mg pill of midazolam orally with a cup of water. During induction, individuals were given nalbuphine 0.15 mg/kg, atracurium besylate 0.5 mg/kg, and thiopentone 5 mg/kg. For three minutes, they were ventilated using a circular system with a flow of six litres of fifty percent oxygen in nitrous oxide (N2O) and 0.6% isoflurane. A 7.5 mm ID endotracheal tube was used to intubate the patients. 40% oxygen in nitrous oxide and 0.6% to 1.0% isoflurane were used to maintain anaesthesia, lowering flows to 3 litres per minute following 8 minutes. When one twitch appeared on the train of four (TOF), atracurium besylate (10 mg) was used to maintain muscle relaxation. For both deficit and maintenance, patients were given Ringer's lactate based on their body weight. To replace the lost blood, three times as much Ringer's lactate solution was used. Transfusions of blood were administered if the predicted hemoglobin level fell below 8 g/dl. Intraoperatively, isoflurane was raised by 0.2% if the baseline blood pressure or heart rate rose by more than 20%. Rescue analgesia was used if the alterations continued. Participants were given nalbuphine 0.05 mg/kg IV at intervals of two hours for postoperative analgesia based on VAS evaluation. The first post-operative dosage of nalbuphine was administered two hours after surgery. Rescue analgesia was administered in accordance with procedure if pain alleviation was insufficient. Following surgery, patients' pain levels were assessed using the VAS score 1–10. When arriving to the post-anesthesia care unit (PACU), as well as at 02, 08, 16, and 24 hours, the score is as follows: 1-3 indicates mild pain, 4-7 indicates moderate pain, and 8-10 indicates severe pain. A top-up intravenous dosage of 0.05 mg/kg of nalbuphine was given if the pain rating score was more than 3 (moderate pain), and this was recorded. The information above was gathered by the assigned nurse who was blind to the treatment groups. SPSS version 12 was used to process the data. Applying the Student's t-test was applied to the assess pain score and supplemental nalbuphine requirements. A p-value of < 0.05 was considered significant.

RESULTS

80 individuals were enrolled in this study based on the inclusion criteria. 2 individuals in the gabapentin group were excluded as surgery was delayed because of an adverse response to a blood product transfusion. Thus, information from 78 patients—40 out of 40 in the control group and 38 out of 40 in the preemptive (gabapentin) group—was included and examined. Thus, group S (study group) contributed 95% of the study's patients, while group C (control group) contributed 100% as presented in table1. The mean weight of the study participants was 78±4.11 kilogram. While their ages ranged from 41 to 61 years, with a mean of 47±1.22 years as shown in table 2. In two groups, the hemodynamic results remained stable. In both groups, no individuals needed intraoperative rescue analgesics. Following surgery, the gabapentin group's VAS score at zero, two, eight, sixteen, and twenty-four hours were noticeably lower than the control group's pain scores. The study and control groups' mean VAS scores at zero hour were 5.89±1.37 cms and 9.03±1.21 cms, respectively. These were 3.327±1.11 cms in the control group and 0.942±0.73 cms in the study group at 24 hours. After applying the Student's t test to the VAS scores the P-value less than 0.001 was considered significant as presented in table 3. The study group took significantly fewer nalbuphine overall in the first 24 hours following surgery than the control group. The control group used 23.30±9.275 mg of nalbuphine, whereas the study group used 12.20±4.707 mg. the P-value was statistically significant (p< 0.001) as shown in table 4.

Table 1. Group wise distribution of the study participants

Group	Frequency %
Control group	40(100%)
Study group	38(95%)
Total	80

Table 2. Demographic features of the study population

Features	Mean (± SD)
Age in years	47±1.22
Wight in kilogram	78±4.11

Table 3. Postoperative VAS Pain Scores (In centimeters)

Time in hours	Group	Frequency	Mean± SD	Value of P
Time zero	Study group	38	5.89±1.37	0.000
At zero hour	Control group	40	9.03±1.21	
Time 2	Study group	38	3.352±0.779	0.000
At 2 hours	Control group	40	5.971±1.200	
Time 8	Study group	38	2.617±1.338	0.000
At 8 hours	Control group	40	4.200±1.051	
Time 16	Study group	38	2.088±0.864	0.000
At 16 hours	Control group	40	4.028±1.173	
Time 24	Study group	38	0.942±0.73	0.000
At 24 hours	Control group	40	3.327±1.11	

Table 4. Postoperative nalbuphine consumption (in milligrams)

Group	No of individuals	Mean (± SD)	P value (student test)
Study group	38	12.20±4.707	0.000
Control group	40	23.30±9.275	

DISCUSSION

Pain following surgery has an effect on anesthesia and surgical recovery. Although they are often used to treat pain, opioids have side effects that restrict their usage. To enhance the benefits and lessen the problems of opioids, combination regimens of non-opioid and opioid medications are used.[11] One anticonvulsant medication that works via voltage-dependent calcium channels is gabapentin .[12] This medication reduces the reaction to neural inputs and releases amino acids in the spinal cord's dorsal horn, which lowers or stabilizes the activity of the injured neurons. [13] Therefore, gabapentin can be used to treat chronic pain caused by herpetic neuralgia, diabetic neuropathy, and other neuropathic

illnesses .[14]Recently published studies examined gabapentin's efficacy and usefulness in treating postoperative pain and inhibiting brain excitability.[15] The present study was carried out to explore the efficacy of of gabapentin on opioid requirement in patients undergoing total abdominal hysterectomy. In order to reduce the need for opioids in patients receiving total abdominal hysterectomy, the study's null hypothesis stated that gabapentin and a control group should have the same preemptive analgesic effect. The findings defied our null hypothesis and demonstrated that a single 1200 mg dosage of gabapentin administered two hours before to surgery considerably lowers the need for postoperative opioids during the first twenty-four hours. Individuals receiving gabapentin reported pain scores (VAS) that were comparatively lower than those of individuals receiving a control group.

Surgical wounds, surgical drains, and tissue tension during surgery are the causes of surgical pain.[16] Effective pain management is necessary since the initial postoperative day is when the pain is at its worst. For this, a variety of analgesic medications have been employed, and a combination of opioid and non-opioid medications has demonstrated a high level of postoperative pain management. Overuse of opioids can cause adverse consequences including respiratory depression, however gabapentin used prophylactically has been demonstrated to reduce the overall dosage of opioids needed in surgical patients, hence reducing the risk of adverse effects. Gozal et al.[17] found that individuals having thyroidectomies had significantly lower opioid needs after local wound infiltration of 0.5% bupivacaine before skin closure which support the findings of our study. Following thyroid and parathyroid surgery, Basto et al. reported that perioperative ketoprofen and paracetamol administration was linked to lower pain levels and a decrease in the need for morphine. [18] Preemptive analgesia with paracetamol has been attempted in one research with varying degrees of efficacy.[19] Bilateral superficial blocks considerably decreased postoperative pain intensity following thyroid surgery, according to another research. [20] Aunac et al. showed that bilateral superficial and deep cervical blocks given prior to thyroid surgery significantly decreased the need for anaesthetics and analgesics during the procedure and decreased pain scores.[21]Although the recommended dosage for treating neuropathic pain is 300–1200 mg three times a day,[22] the gabapentin dosage in our research (1200 mg) was within the range of a single daily dose. Gabapentin was given orally two hours prior to surgery in this trial because research on lab animals has shown that preemptive gabapentin therapy is more effective and long-lasting than post-treatment. In a rat model of postoperative pain, preemptive therapy with a single dosage of gabapentin prevented the onset of hyperalgesia for two days, while gabapentin administered an hour after the intervention only alleviated symptoms for three hours.[23] Positive outcomes have been shown in previous clinical trials using gabapentin to treat postoperative pain. When given orally one hour before to surgery, gabapentin 1200 mg reduced postoperative morphine consumption and pain scores in the early postoperative phase for individuals having spinal surgery, which in turn reduced opioid-related adverse effects such nausea and vomiting.[24] Gabapentin 3000 mg given before to and during the first 24 hours following a complete abdominal hysterectomy resulted in a 32% decrease in morphine use in another research, with no discernible impact on pain ratings during mobilization or at rest.[25] According to research by Rorarius et al., individuals having vaginal hysterectomy required 40% less postoperative pain management during the first 20 postoperative hours when a single dosage of 1200 milligrams gabapentin was administered 2 to 2.5 hours prior to the induction of anesthesia.[26] This study is consistent with ours, which demonstrates a 47% decrease in postoperative narcotic dosage. In our study, gabapentin- receiving participants undergoing TAH had considerably decreased postoperative nalbuphine intake and pain ratings (VAS). The majority of the aforementioned trials showed a substantial impact on postoperative analgesic needs, despite variations in surgical techniques and gabapentin dosages. Furthermore, there is a significant risk of vomit and nausea following gynecological surgery, and this risk is raised if opiates are used excessively in the first few hours following the procedure. Thus, gabapentin lowers the occurrence of these adverse effects by reducing the need for opioids during the postoperative phase. To achieve a maximal plasma concentration at the moment of surgical stimulation, it is reasonable to provide gabapentin orally around two hours prior to surgery. Since gabapentin is a highly lipophilic medication that is quickly absorbed from the stomach and penetrates the blood-brain barrier, its concentration in the brain tissue, where it acts, is almost as high as in the blood.[27] Two hours after surgery, Dierking et al. observed a substantial negative association between gabapentin plasma levels, suggesting a dosage response effect. According to earlier research, gabapentin is an anxiolytic medication.[28] Given the potential link between beforehand anxiety and surgical pain, gabapentin may lessen the need for opioids by producing preoperative anxiolytics and improving postoperative pain relief.[29] Furthermore, research has demonstrated that opioid and gabapentin work in concert in both human and animal investigations.[30] Gabapentin partly reverses existing morphine tolerance in rats and inhibits its growth.[31]

It has been proposed that central sensitization is crucial for both postoperative pain and chronic pain conditions. It is unknown how much each pain mechanism contributes in relation to postoperative pain.[32]Several anti-hyperalgesic techniques and medications have been studied to lessen central neuronal hyper excitability, which might potentially increase postoperative pain. In preclinical and clinical trials, gabapentin has shown strong anti-hyperalgesic properties in addition to being used to treat neuropathic pain disorders.[33] The participants in our study received gabapentin well, and during the preoperative phase, no notable adverse effects were noted when taking oral gabapentin. Our findings are comparable to those of previous published research.

CONCLUSION

The present study concluded that the use of gabapentin greatly lowers intraoperative and postoperative pain. It also minimizes the requirements of opioids in individuals undergoing TAH.

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