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24 Hours Pain-free after Combined Preoperative Gabapentin and Intrathecal Opioid: A Case Report

Marwa Ahmad Mahrous, Elhaisam Mohamed Taha, Ahmed M.A. Ismail*
Department of anesthesia and intensive care, Faculty of Medicine, Sohag University, Egypt
***Corresponding author:** Ahmed M.A. Ismail, **Mobile:** (+20) 01006774710, **E-Mail:** ahmed.aly25.aa@gmail.com

ABSTRACT
Background: Gabapentin is used as an anti-epileptic and in chronic pain but can be used also in acute postoperative pain by giving it preoperatively in a single or in two divided doses combined with intrathecal morphine.
Objectives: This study aimed to detect the role and value of gabapentin as analgesic in postoperative analgesia.
Presentation of the case: A case with orthopedic surgery that had no postoperative pain for 24 hours and needed no analgesia with good (near normal) mobility after taking preoperative gabapentin and intrathecal morphine with spinal anesthesia intraoperative. **Results:** It is a rare condition in which the patient is pain-free completely for 24 hours without any postoperative analgesia, most researchers stated that patients who received preoperative gabapentin need less postoperative analgesia or morphine but still there is pain.
Conclusion: Preoperative gabapentin has a great effect on postoperative pain, decreasing analgesic doses especially morphine with good and early postoperative mobility.
Keywords: Gabapentin, Intrathecal opioid, Postoperative analgesia, Pain.

INTRODUCTION

Gabapentin is used originally as an anti-epileptic and it is 1-(aminomethyl) cyclohexane acetic acid originating from a gamma-aminobutyric acid (GABA)-mimetic compound for management of spasticity with the good anticonvulsant property. At first, it was approved to be used in partial seizures, but then had a good effect in treating chronic pain syndromes as neuropathic pain [(1)]. Gabapentin is an oral preparation only and its absorption is from the small intestine, it occurs by diffusion and facilitated transport. An unidentified receptor which is related to a transport mechanism by a saturable l-amino acid binds to gabapentin in the gut after its oral intake to facilitate its transport. It is eliminated in the urine without change as it doesn't expose to metabolism in the human body. Elimination of gabapentin is by first-order kinetic so its elimination is affected by kidney impairment strongly correlated to creatinine clearance. Hemodialysis removes gabapentin. Gabapentin does not cause hepatic microsomal enzyme system induction or inhibition contrary to other anticonvulsants [(1)].

The aim of studying this case was to detect the role and value of gabapentin as analgesic in postoperative analgesia.

MECHANISM OF ACTION

Though gabapentin is a (GABA)-mimetic compound it is without GABAergic action and causes no interference with GABA uptake nor its metabolism. It causes a block of the nociception tonic phase, which is induced by formalin and carrageenan and causes inhibition of neuropathic pain, which is in the form of mechanical hyperalgesia and mechanical/thermal allodynia [(1)].

It is of most significance to treat postoperative pain effectively. Inadequately treated postoperative pain has a negative effect on the patient's recovery and the whole operative experience for the patient. Not only pain not well managed will cause patient immediate discomfort but also will increase patient morbidity and mortality and so affect patient life quality [(2)].

In addition to the above chronic pain which is the pain lasting for 2 months or more will result postoperatively and not related to a previous illness [(3)].

Most patients have good and rapid postoperative recovery and return to their normal wellbeing but others cannot and depend on opioid analgesia for longer periods with resulting postoperative chronic pain [(4)]. Though opioids have an extremely good pain-relieving effect on postoperative pain, it also has serious side effects such as bradycardia, hypotension, respiratory depression, decreasing level of consciousness, nausea and vomiting, pruritus, and constipation [(5)]. Postoperative opioid intake should be decreased as it leads to opioid-related complications, increased morbidity as well an increased period of hospital stay, so consequently increasing health care costs, all of that means another method of pain-relieving is needed [(6)]. Many institutions considered and used multimodal analgesia techniques in the standard treatment of postoperative pain [(7)].

Multimodal analgesia is combining multiple medications and therapies so there are different mechanisms of action acting both on the central and peripheral nervous system and offering individualized targeted patient therapy considering pharmacogenetics in the form of single gene allelic differences and responses to medications decreasing opioids intake and so decreasing their side effects [(8-9)]. Gabapentin is a drug with anti-hyperalgesic properties. These anti-hyperalgesic effects are caused by gabapentin effects at the dorsal root ganglia and spinal cord [(10)]. Gabapentin has few associated adverse side effects [(11)].

A review of four randomized control trials (RCTs) with 190 patients having an abdominal hysterectomy, reported a significant decrease in morphine doses in cases using gabapentin. But there was a good number of RCTs that demonstrated

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conflicting results as regards using gabapentin preoperatively [12].

In another study, gabapentin was administered to patients (n=40) undergoing mastectomy (20 received gabapentin and 20 received placebo) and revealed a decrease in morphine doses needed in the first 24 hours postoperative in patients took gabapentin [13].

But in another study, there was no significant difference in cumulative morphine consumption at the first 24 hours postoperative in an RCT with patients undergoing thoracotomy (n=120; 57 patients received gabapentin and 63 patients received placebo) [14].

PRESENTATION OF THE CASE

A twenty-six-year-old young man presenting with an infected first stage revision of total hip joint replacement due to rheumatoid affection. He was coming for a repeat of first stage revision in Sohag university hospital. Full laboratory investigations were done (HB 11.5 mg/dl; WBC5.8 × 1000 cm^3, ESR 1st hour 21 mm 2nd hour 34 mm and CRP: 56). The patient uses both gabapentin and pregabalin (300 and 150 mg respectively) daily for chronic pain caused by rheumatoid arthritis affecting the other hip joint and pain caused by joint infection for 2 months preoperative.

Pr-eoperative fasting for 10 hours. The patient received preoperatively 600 mg gabapentin in two divided doses. The first dose was 12 hours before surgery and the second dose was 8 hours before surgery.

Intra-operatively, he received spinal anesthesia with intrathecal 500 µ morphine and received 2 L of intravenous fluids with an antibiotic. The surgery took 3 hours uneventfully. Post-operatively the patient had severe hypotension for 3 hours treated by ephedrine, dexamethasone, fluid, colloid, and blood transfusion. There was no pain for the next 24 hours with no need for any analgesics with good and early mobility inside and beside as the patient was having a temporary hip joint that sh ouldn't bear any weight. After 24 hours postoperatively the patient started to need analgesics, which were combined nalobuphine (2 mg every 8 hours) and NSAID for the next 24 hours.

Ethical approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Sohag University. Written informed consent was taken from all participants. The study was conducted according to the Declaration of Helsinki.

DISCUSSION

Gabapentin in the perioperative period may decrease postoperative pain, both incidence and intensity up to 6 months after otolaryngology, orthopedic, mastectomy, and abdominal/pelvic operations [15-18].

Gabapentin in the perioperative period is considered by professional guidelines as a part of multimodal analgesia [20], though the effectiveness of gabapentin as a part of multimodal analgesia has been mixed, and the routine postoperative care differs among surgeries and institutions worldwide [20-24].

Professional societies advise using gabapentin for optimum acute postoperative pain treatment after good evidence of decreased opioid doses with gabapentin multimodal analgesia [19].

A study by **Deniz *et al.*** [24] showed decreased pain scores in the early postoperative period (at 45 min, 60 min, and 2 h) as compared to controls after preoperative oral intake of 900 mg gabapentin. Moreover, the need for rescue analgesia is decreased with preoperative gabapentin intake and without significant side effects. But preoperative gabapentin did not decrease the overall tramadol dose.

Gabapentin was taken 1-2 hours preoperatively in a single dose in most studies that assessed its action in postoperative analgesia [25-27]. It is known that gabapentin reaches its peak plasma level in 2-3 hours after intake and it undergoes no metabolism and is excreted unchanged in urine after 5-9 hours elimination half-life. It has no drug interactions as it has no hepatic metabolism and a low level of protein binding [28].

A study by **Deniz *et al.*** [24] used gabapentin 2 hours preoperatively to reach its optimum blood level at the time of tissue incision.

Another study by **Zeng *et al.*** [29] showed that acute postoperative pain score significantly decreased both at rest and on movement up to 24 hours but with no effect at 48 hours. It also decreased the incidence of postoperative vomiting and the need to rescue antiemetics but it increased the sedation score at 2 hours postoperatively. Besides, it decreased the intraoperative propofol and remifentanil doses but it didn't cause a decrease in postoperative opioid doses [29].

In a study by **Gill *et al.*** [30]**,** they stated that gabapentin preoperatively didn't decrease opioid requirement and the postoperative discomfort following sinonasal surgery is mild, and opioid intake is minimal.

A metanalysis by **Han *et al.*** [31], showed that the administration of gabapentin could decrease the cumulative opioid dose at 24 hours postoperatively as compared to placebo. This meta-analysis of RCTs shows that preemptive gabapentin intake could significantly decrease VAS scores postoperatively, and decreases the incidence of some adverse effects in spinal surgery.

In our case gabapentin was administered in two divided doses each one was 300 mg at 12 and 8 hours preoperatively then he received intrathecal (spinal) anesthesia with bupivacaine (heavy 3.5 ml) and morphine 500 µ then underwent uneventful surgery with intraoperative antibiotic and fluids (2 liters of crystalloids), the surgery took 4 hours. In the immediate postoperative period, the patient suffered severe hypotension that continued for 2 hours treated with colloid. The patient has no pain (0 VAS score) and he didn’t ask for analgesic until 24 hours postoperative and showed good and early (near normal) mobility.

CONCLUSION

Gabapentin had effective analgesia for postoperative pain when used preoperatively. Multimodal analgesia was the best way to treat postoperative pain, decreasing drug side effects and at the same time increasing analgesia efficiency. Using gabapentin as a part of multimodal analgesia increased its efficiency. The combination of intrathecal opioids and preoperative oral gabapentin gave excellent postoperative pain relief.

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