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Research Article

Preoperative gabapentin augments intraoperative hypotension and reduces postoperative opioid requirements with functional endoscopic sinus surgery

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KEYWORDS

Gabapentin;
Hypotensive anesthesia;
Analgesia;
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Opioids

Abstract *Background:* Functional Endoscopic sinus surgery (FESS) is a delicate and time consuming procedure; it is performed routinely under general anesthesia. Hypotensive techniques should be employed for best visualization of operative field. Gabapentin is a structural analog of gamma amino butyric acid. The aim of this study was to determine the analgesic efficacy of gabapentin and its role in deliberate hypotension during and after FESS.

Methods: Eighty patients ASA physical status I–II patients were scheduled to undergo elective FESS under general anesthesia. Patients were randomly assigned to one of two groups using a computer-generated table. Patients in the control group (40 patients) received oral placebo capsules and the study group (40 patients) patients received oral gabapentin (Conventin 400 mg; Evapharma Egypt) 1.2 g 1 h before surgery. Intraoperative, mean arterial blood pressure, infusion rates of the hypotensive agent (sodium nitroprusside) were recorded at 15 min interval. Assessments of pain, opioid usage, and side effects were performed at 1 h interval after arrival in the PACU.

Results: Gabapentin group patients required significantly lower (p value <0.05) infusion rates and total doses of hypotensive agent (sodium nitroprusside) than the placebo group patients at all measured intervals. Postoperative assessment of pain scores revealed that gabapentin group recorded significantly lower mean values of VAS than the control group (p value <0.05).

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Conclusion: Oral gabapentin, 1200 mg decreased dose requirements of intraoperative hypotensive agent (sodium nitroprusside) and postoperative morphine. In addition, patients receiving gabapentin had suffered less from opioid side effects (nausea, vomiting and urinary retention) than those receiving placebo.

1. Introduction

The multiplicity of mechanisms involved in pain requires a multimodal analgesia regimen, suggesting that a combination of opioid and non-opioid analgesic drugs may improve analgesic efficacy and reduce opioid requirements and side effects after surgery. A number of analgesic regimens can be used for pain relief in day-case surgery patients. These regimens include the use of opioids, local anesthetics, nonsteroidal antiinflammatory drugs (NSAIDs), and cyclooxygenase-2 inhibitors [1].

Gabapentin, a structural analog of gamma amino butyric acid, which was first developed as an antiepileptic drug. It was first reported to be effective for treatment of neuropathic pain [2] and diabetic neuropathy [3]. It has also been shown to reduce postoperative pain and opioid analgesic requirements in a variety of acute postoperative pain models [4–8].

As Functional Endoscopic sinus surgery (FESS) is a delicate and time consuming procedure, it is performed routinely under general anesthesia, so anesthesiologists have to plan the technique in such a way that will facilitate the operating team for achieving a bloodless field for better visualization of the intranasal structures and minimize intraoperative bleeding. Because very little bleeding can obstruct the view of the operating endoscope, hypotensive anesthesia should be employed [9].

Although postoperative pain is typically regarded as a type of nociceptive pain involving peripheral mechanoreceptor stimulation, it is clear that inflammatory, neurogenic, and visceral mechanisms also contribute to acute pain symptoms. It has been suggested that postoperative pain can be associated with a transient, reversible type of neuropathic pain [10]. An animal study demonstrated that gabapentin could reduce visceral nociception [11,15].

Early clinical studies of surgical patients suggested that preoperative administration of gabapentin decreased postoperative pain scores and opioid analgesic requirements after mastectomy [12,13], spinal surgery [7], and otolaryngologic surgery [6].

These results should be validated and other surgical pain models used before a reliable conclusion can be reached. The aim of this study was to determine the analgesic efficacy of gabapentin and its role in deliberate hypotension during and after FESS.

2. Methods

The study was conducted in Ain Shams University hospitals at the ENT surgical department. After approval of the institutional ethics committee and written informed consent; 80 patients ASA physical status I–II patients were studied. All were scheduled to undergo elective functional endoscopic sinus surgery under general anesthesia. Patients were chosen to participate in the study if they were at least 18 years old, willing to comply with the postoperative follow-up evaluations, within 50% of ideal body weight, had no clinically significant cardiovascular or central nervous system disease, and could operate a patient-controlled analgesia (PCA) device.

Exclusion criteria were age younger than 18 years or older than 50 years, history of chronic pain, regular medications with analgesics, analgesic use within 24 h of surgery, drug or alcohol abuse, psychiatric disorders, known allergy or contraindications to anesthetics or any drug used, asthma, renal insufficiency, hepatic disorder, history of a peptic ulcer or bleeding diathesis and pregnancy. The patients were randomly assigned to one of two groups using a computer-generated table. Patients in the control group (40 patients) received oral placebo capsules and the study group (40 patients) patients received oral gabapentin (Conventin 400 mg; Evapharma Egypt) 1.2 g 1 h before scheduled time for surgery. All given capsules were prepared by the pharmacy in order to maintain double-blind conditions, and an appropriate code number was assigned to each patient. Baseline mean arterial blood pressure, heart rate, and peripheral oxygen saturation values were obtained using standard monitors. After giving the oral medication 22 gauge intravenous line was inserted and 500 ml lactated Ringer's solution i.v. infusion was started in all patients, then midazolam, 0.05 mg/kg intravenously 45 min were given before surgery. An intra-arterial catheter was inserted under local anesthesia in the radial artery for direct measurement of arterial blood pressure. After 1 h of oral medication, anesthesia was induced with propofol (2 mg/kg) and atracurium (0.5 mg/kg) and fentanyl 2 μg/kg intravenously. Endotracheal intubation was done followed by mechanical ventilation in order to maintain the end expiratory CO_2 values between 34–36 mm Hg. Anesthesia was maintained with isoflurane 1.5% at a fresh gas flow rate of 2 l/min. Intraoperative mean arterial blood pressure was recorded at 5 min interval. After successful induction, sodium nitroprusside infusion started at a rate of 0.5 μg/kg/min, this rate was subjected to change (increased or decreased) in order to maintain a mean arterial blood pressure (45–50 mm Hg). Rate of infusion of sodium nitroprusside were recorded every 5 min, then at the end of the procedure. Morphine 2 mg IV was administered immediately before discontinuing isoflurane. At the end of surgery, residual neuromuscular blockade was antagonized with neostigmine 50 μg/kg and atropine 0.01 mg/kg IV.

After arrival in the post anesthesia care unit (PACU), patients were connected to a PCA device and postoperative analgesia was provided using 2 mg IV bolus injections of morphine at a lockout interval of 10 min and with a maximum 4 h limit of 40 mg. The incremental bolus dose of morphine was increased to 3 mg if analgesia was inadequate (pain score by visual analogue scale (VAS) was more than 4 cm after the first hour of PCA use.

Assessments of pain, opioid usage, and side effects were performed at 1 h interval after arrival in the PACU by a research assistant blinded to the group allocation till end of PCA usage. The PCA device was discontinued when the patient made no demands for the opioid analgesic in the preceding 8 h interval. If the patient experienced sustained nausea or vomiting lasting longer than 5 min, ondansetron (4 mg IV) was administered.

Data analysis was made by using SPSS 14.0 for Windows. Comparison between the two groups as regards numerical variables was made by using Student-t-test for comparing means and standard deviation. Significant results were defined when the p value was less than 0.05.

3. Results

There were no significant differences between groups with respect to ASA classification, age, weight, duration of surgery, preoperative mean blood pressure or duration of anesthesia (Table 1). No patient was excluded after inclusion to study. All patients were able to complete the entire study and their data were included in the final analysis.

Gabapentin group patients had significantly lower (p value <0.05) infusion rates of sodium nitroprusside than the placebo group patients at all measured intervals (Fig. 1).

Table 1 Patient's characteristics and operative data

Variable	Gabapentin (n = 40)	Placebo (n = 40)
ASA classification (I/II)	35/5	36/4
Age (yr)	30.6 ± 6.1	33.7 ± 4.2
Weight (kg)	71.6 ± 5.3	69.1 ± 5.9
Duration of anesthesia (min)	82.7 ± 11.5	79.9 ± 9.5
Duration of surgery (min)	70.9 ± 10.2	68.3 ± 11.4
Preoperative mean blood pressure (mm Hg)	70.5 ± 11.1	71.2 ± 10.8
Average intraoperative blood loss (ml)	200.1 ± 40.3	250.6 ± 30.9

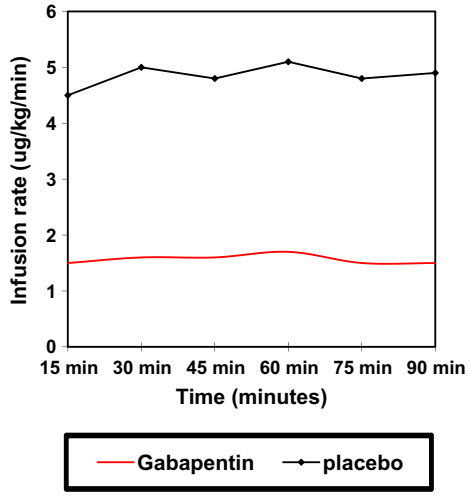

Figure 1 Intraoperative infusion rates of sodium nitroprusside in the two study groups.

Table 2 Cumulative morphine consumption at 8 h, and time to first morphine request in the post anesthesia care unit.

	Control (*Mean* ± *SD*)	Gabapentin (*Mean* ± *SD*)
First morphine request (min)	20 ± 8	40 ± 5
Morphine consumption (mg)	14 ± 2	8 ± 1

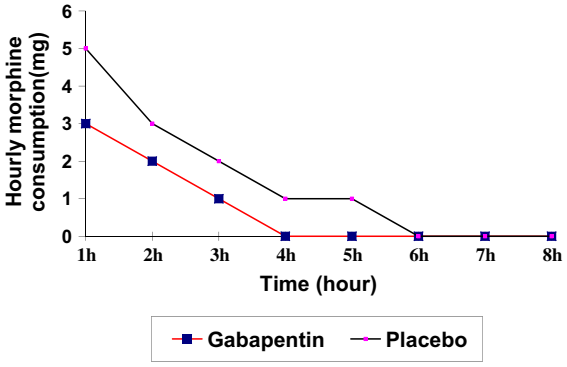

Figure 2 Postoperative morphine consumption.

Table 3 Incidence of nausea and vomiting in the two study groups.

	Control (n = 40)	Gabapentin (n = 40)
Nausea	10 (25%)	3 (7.5%)
Vomiting	5 (12.5%)	1 (2.5%)
Use of antiemetic drugs	10 (25%)	2 (5%)
Urinary retention	1	0

The time until the first request for analgesia (morphine) in the PACU was longer in the gabapentin than in the control group (40 ± 5 min) compared to the placebo group (20 ± 8 min) (Table 2). Compared with the control group, PCA morphine requirement was significantly lower in the gabapentin group at 1, 2, 3, 4, 5 and 6 h after surgery (Fig. 2). Postoperative assessment of morphine usage revealed that gabapentin group recorded a significantly lower values of morphine consumption than the control group (p value <0.05) (Table 2).

The most common side effects during the postoperative period were nausea and vomiting. The incidence of nausea was significantly less frequent in the gabapentin group compared with the placebo group (10) compared to the placebo group (3). Not surprisingly, antiemetic usage was also significantly reduced in the gabapentin (versus placebo) group. One patient of the placebo group suffered from urinary retention for 8 h postoperatively, not surprisingly, this patient received the highest amount of morphine of the whole study patients (Table 3).

4. Discussion

Perioperative administration of gabapentin, as part of a multimodal analgesic regimen with PCA morphine, led to improved

pain control and reduced opioid-related side effects by reducing the doses of opioids required. Moreover, intraoperative usage of intravenous hypotensive agent was significantly reduced.

In animal models of nociception, gabapentin reduced mechanical or thermal hyperalgesia [16] and incisional injury [11]. Pretreatment with gabapentin also blocked the development of hyperalgesia, suggesting a preventive effect of gabapentin, and had a selective effect on the nociceptive process involving central sensitization [14]. Studies have demonstrated that mechanical hyperalgesia surrounding the wound in postoperative patients and experimentally heat induced secondary hyperalgesia share a common mechanism and that central neuronal sensitization contributes to postoperative pain [10].

Thus, drugs such as gabapentin, which have been effective in reducing hyperalgesia in different models of pain, may play an important role in acute postoperative pain in humans [17].

Studies suggest that gabapentin may be useful in the perioperative setting, as an adjuvant to parenteral opioid analgesics in the postoperative period [4–8].

Our study shows a different usage through improving intraoperative hypotension required for sinus surgery.

In summary, oral gabapentin 1200 mg decreased the dose requirement of morphine and postoperative pain and improves intraoperative hypotension required for sinus surgery.

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