Pregabalin in Monitored Anesthesia Care for Ear-nose-throat Surgery

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Abstract

Aim: The aim of this study was to determine intraoperative sedative and perioperative analgesic requirement and associated side effects of pregabalin (150 mg) for monitored anesthesia care during ear-nose-throat (ENT) surgeries. Materials and Methods: The study design was randomized and single-blinded; fifty patients undergoing elective ambulatory ENT surgeries under monitored anesthesia care were randomly allocated to receive either placebo (Group P) or pregabalin (Group PG) 150 mg, orally 1 h before surgery. All patients were then given intravenous (i.v.) midazolam 2 mg and fentanyl 1 μg/kg and local anesthesia at the site. Sedation was induced by administering an i.v. bolus of propofol 0.8 mg/kg and was maintained by continuous infusion of propofol. Level of sedation was assessed by Ramsay scale, and propofol infusion was titrated accordingly. Intraoperative pain was assessed by verbal rating scale (VRS) score. Patient having VRS >4 or complaint of pain was given fentanyl (0.5 μg/kg) i.v. bolus. Intraoperative sedative and analgesic requirement were recorded. Postoperative visual analog scale scores and requirement of analgesics were recorded for the first 24 h after surgery. Diclofenac 75 mg intramuscular (i.m.) was administered as rescue analgesic. Side effects (nausea/vomiting, sedation, dizziness, blurred vision) were also recorded. Results: Intraoperative propofol (212 ± 11 mg vs. 174 ± 9 mg; \( P = 0.013 \)) and fentanyl (120 ± 8 μg vs. 94 ± 6 μg; \( P = 0.02 \)) consumption was significantly lower in Group PG. Time to first analgesic request was longer (6.1 ± 0.4 h vs. 9.5 ± 1.2 h) with lesser requirement of analgesics (diclofenac) in the postoperative period. Incidence of side effects (sedation, nausea, vomiting) was found to be similar in both the groups. Conclusion: Premedication with pregabalin (150 mg) reduces intraoperative sedative and perioperative analgesic requirement in patients undergoing ENT surgeries under monitored anesthesia care with tolerable side effects.

Keywords: Analgesia, monitored anesthesia care, pregabalin

Introduction

Premedication with gabapentinoid drugs (gabapentin and pregabalin) has been found to decrease postoperative pain and reduce opioid consumption in patients undergoing major surgeries.\(^1\)\(^-\)\(^9\)

Limited data are available as far as their role in surgeries done under monitored anesthesia care is concerned.\(^10\) Adequate pain control with reduced opioid consumption with use of these drugs can benefit these patients by reducing postoperative nausea and vomiting (PONV), providing better patient satisfaction.

Previously, gabapentin has been studied in patients undergoing ear-nose-throat (ENT) ambulatory surgery under monitored anesthesia care. Gabapentin (1200 mg) was found to be effective in reducing analgesic requirement but was associated with dizziness in significant number of patients.\(^11\) Lower dose of gabapentin (600 mg) was found to reduce perioperative analgesic requirement without side effects.\(^12\)

The effects of pregabalin have not been studied for monitored anesthesia care in ambulatory ENT surgeries. A recent meta-analysis on role of pregabalin for acute pain management states that the analgesic effects and incidence of adverse effects of using pregabalin are not equal in different surgical categories. For major ENT surgeries, pregabalin premedication does not lead to reduced postoperative morphine consumption.\(^13\)

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hypothesized that premedication with pregabalin would reduce intraoperative sedative and perioperative analgesic requirement without side effects.

The aim of this study was to determine intraoperative sedative and perioperative analgesic requirement and associated side effects of pregabalin (150 mg) for monitored anesthesia care during ENT surgeries.

Materials and Methods

After obtaining the approval of the Institutional Ethics Committee and written informed consent of the patients, American Society of Anesthesiologists (ASA) physical status I–II patients undergoing elective ambulatory ENT surgeries (myringoplasty, septoplasty) under monitored anesthesia care were studied.

Exclusion criteria

Exclusion criteria were allergy or contraindications to local anesthetics or other drug used, asthma, renal insufficiency, a history of a peptic ulcer or bleeding diathesis, and pregnancy.

The study design was randomized and single-blinded; patients were randomly allocated using computer-generated randomization table. Group P (n = 25) received oral placebo (Vitamin B complex), and Group PG (n = 25) received oral pregabalin (150 mg), 1 h before surgery by a nurse in the preoperative room who was not involved in the study. After the patients had been taken to the operating room, crystalloid infusion was started through a 20-gauge intravenous (i.v.) cannula inserted in an appropriate antecubital vein, and the mean arterial blood pressure, heart rate, and peripheral oxygen saturation were recorded (IntelliVue MP20 Monitor). All patients were then given i.v. midazolam 2 mg and fentanyl 1 μg/kg. After local anesthesia (lidocaine 2% with epinephrine) performed by the surgeon, sedation was induced by administering an i.v. bolus of propofol 0.8 mg/kg and was maintained by continuous infusion of propofol adjusted to maintain sedation at a 2–3 level on the Ramsay scale. The propofol infusion was started with 2 mg/kg/h and titrated according to sedation levels, and total propofol consumption was determined. The patients were evaluated during surgery at 5, 15, 30, 45, and 60 min for sedation levels and pain, which were assessed using verbal rating scale (VRS). If the VRS score was >4 or on patient request, i.v. fentanyl 0.5–1 μg/kg was administered. The total fentanyl consumption by each patient was determined and noted.

Postoperatively, pain scores were recorded at 30 min and 1, 2, 4, 6, 8, 12, 16, 20, and 24 h using visual analog scale (VAS) score. VAS and VRS were explained to the patients during the preoperative visit. Additional analgesic needed by each group within 24 h and the time to first analgesic need were determined according to the VAS; when VAS values were >4, diclofenac 75 mg i.m. was administered and noted. The first analgesic need was regarded as the time when administration of an additional analgesic was done in the postoperative period, following surgery. Patients were questioned for the first 2 h in the postanesthesia care unit. They were later questioned on the ward every 2 h about the occurrence of any side effect, PONV, shivering headache, sedation, vision abnormalities (blurring of vision, double vision). On patient request or if nausea and vomiting occurred, ondansetron 4 mg i.v. was given.

A power analysis suggested sample size to be 25 patients per group to detect a 40% reduction in analgesic consumption, with a power of 0.8 (α =0.05) Student’s t-test and Chi-square test were used to analyze data. Significance was determined at P < 0.05.

Results

A total of fifty patients were enrolled, and all the patients were ASA grade I. There were no dropouts.

There were no significant differences in demographic profile; type and duration of surgery were similar in both the two groups [Table 1].

Requirement of propofol was found to be 212 ± 11 mg in Group P and 174 ± 9 mg in Group PG. The difference was found to be statistically significant (P = 0.0137) [Table 2].

Intraoperative fentanyl requirement was 120 ± 8 μg in Group P and 94 ± 6 μg in Group PG. The difference was found to be statistically significant (P = 0.02) [Table 2].

Patients who received pregabalin 150 mg (Group PG) had comparatively lower intraoperative VRS scores at all time points compared with Group P [Table 2].

| Variable                                      | Placebo (Group P) | Pregabalin (Group PG) |
|-----------------------------------------------|-------------------|-----------------------|
| Age (years)                                   | 26.6±0.75         | 30.76±10.7            |
| Sex (male:female)                             | 21:4              | 18:7                  |
| Weight (kg)                                   | 50.6±8.45         | 52.63±10.15           |
| Type of surgery (myringoplasty/septoplasty)   | 22:3              | 21:4                  |
| Duration of surgery (min)                     | 0.94±0.26         | 1.03±0.35             |

No significant difference between the groups

Table 2: Total propofol, fentanyl, diclofenac consumption and time to first analgesic request

| Variable                                      | Placebo (Group P) | Pregabalin (Group PG) | P   |
|-----------------------------------------------|-------------------|-----------------------|-----|
| Total propofol consumption (mg)               | 212.5±11.19       | 174±9.8               | 0.013 |
| Total fentanyl required (μg)                  | 120.8±8.34        | 94.5±6.9              | 0.02 |
| Total diclofenac consumption (mg)             | 161.3±12          | 71.2±10               | 0.001 |
| Time to first analgesic request (h)           | 6.1±0.4           | 9.5±1.2               | 0.017 |
intervals compared those who received placebo (Group P). The difference was not statistically significant [Figure 1].

Postoperative pain scores (VAS) were lower in Group PG as compared to Group P at all intervals, and statistically, significant difference was observed at 4, 6, and 12 h [Figure 2].

Time to first requirement of analgesic was 6.1 ± 0.4 h in Group P and 9.5 ± 1.2 h in Group PG. In Group PG, 24% of the patients did not require additional analgesics in the first 24 h. Total consumption of diclofenac was lower in Group PG than in Group P, 161 ± 12 mg versus 71 ± 10 mg ($P < 0.001$) [Table 2].

The most common side effects observed were sedation (4% in Group P vs. 8% in PG) and nausea and vomiting (8% in Group P vs. 12% in PG), and the difference was not statistically significant ($P = 0.66$). No other side effects were observed in any of the groups.

**DISCUSSION**

There are rather sparse data regarding the use of gabapentinoid drugs as a part of the pain management after ambulatory surgery. Our study was designed with an aim to determine intraoperative sedative and perioperative analgesic requirement and associated side effects of pregabalin (150 mg) for monitored anesthesia care during ENT surgeries.

A dose of 150 mg pregabalin was selected based on the results of previous studies. Preoperative pregabalin (75–150 mg) has been found to be effective in reducing postoperative pain and analgesic consumption, following septoplasty under general anesthesia.\[14,15\] Lower dose of pregabalin (50–75 mg) has been found to decrease pain score but does not reduce opioid consumption, following laparoscopic cholecystectomy.\[16\] Furthermore, higher doses of pregabalin (300 mg) can produce side effects such as sedation, dizziness, and blurred vision which are unwarranted in ambulatory surgeries.\[17\]

The results of our study show reduced intraoperative requirement of propofol in patients who received pregabalin as compared to placebo ($P < 0.013$). Intraoperative fentanyl consumption was also significantly lower in Group PG as compared to Group P ($P < 0.02$).

Patients who received pregabalin 150 mg (Group PG) had lower intraoperative VRS scores, compared those who received placebo (Group P). The difference was not statistically significant. This could be explained by the fact that all the patients were kept pain free using additional doses of fentanyl.

Similar results were observed in a study by Kazak et al. in patients undergoing nasal septal or nasal sinus surgery under monitored anesthesia care combined with preoperative analgesia with a low dose of 600 mg oral gabapentin. They observed reduced consumptions of remifentanil ($P = 0.033$) and propofol ($P = 0.001$) in gabapentin group compared to placebo.\[11\]

Postoperative analgesic consumption was significantly reduced with pregabalin. Twenty-four percent of patients did not require additional analgesics for 24 h. Time to first rescue analgesic was 9.5 h compared to placebo 6.1 h.

The results of our study are supported by previous studies done using gabapentin as premedication; there was significant reduction in postoperative diclofenac consumption with a longer time to first analgesic request.\[10,11\]

Contrary to above findings, a recent meta-analysis shows no difference in total morphine equivalent consumption at 24 h between pregabalin and the control group for major ENT surgeries done under general anesthesia although there is reduction in both 2- and 24-h postsurgical pain in Group PG. Sedation was found to be statistically significant with pregabalin in cardiothoracic, orthopedic, spine, and miscellaneous procedures.\[13\]

A meta-analysis of nine studies on postoperative pain following nasal surgery shows that gabapentinoid drugs are effective but blurred vision was found to be a handicap.\[18\]

We observed side effects including sedation, nausea and vomiting, but the incidence was found to be similar in both the groups. Sedation in Group P may be due to higher dose of opioid analgesics required. PONV is more common after ENT procedures than other surgeries.
Time taken by patients to ambulate was not recorded, and comparing effects of pregabalin with placebo rather than gabapentin itself was a major limitation of our study. Not many studies are available comparing these two drugs regarding their efficacy.

We conclude that premedication with pregabalin (150 mg) reduces intraoperative sedative and perioperative analgesic requirement in patients undergoing ENT surgeries under monitored anesthesia care with tolerable side effects. Future studies are required to compare the effects of gabapentin and pregabalin in ambulatory ENT surgeries.

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Conflicts of interest

There are no conflicts of interest.

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