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Effect of clonidine premedication on postoperative sore throat and hoarseness after total intravenous anesthesia

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Abstract
To determine the effect of oral clonidine premedication on postoperative sore throat and hoarseness, we evaluated the incidence and severity of each of these complications in patients who underwent elective surgery in the supine position. The subjects were 82 patients, American Society of Anesthiologists (ASA) status I–III, aged 15–82 years. They were premedicated with either 150 μg oral clonidine and 20 mg raftidine (clonidine group; $n = 41$) or with 20 mg raftidine only (control group; $n = 41$) 2 h before anesthesia induction. General anesthesia was maintained with propofol, ketamine, fentanyl, and vecuronium, with or without epidural anesthesia. Postoperative sore throat and hoarseness were evaluated immediately after surgery and on the day after surgery. The incidences of sore throat and hoarseness tended to be higher in the clonidine group than in the control group; however, the difference did not reach statistical significance. There were no significant differences in the severity of these symptoms between the two groups. In conclusion, oral premedication with 150 μg clonidine did not prevent postoperative sore throat or hoarseness, and may have exacerbated these symptoms.

Key words Intubation · Complications · General anesthesia · Premedication · Clonidine

Sore throat and hoarseness are minor but frequent complications of general anesthesia with tracheal intubation, and occasionally require treatment with supplementary analgesics. Clonidine, an α-2 adrenergic agonist, provides sedation and anxiolysis, improved intraoperative hemodynamic stability, and reduction in the amount of anesthesia required [1–5]. It also reduces the need for postoperative rescue analgesics [6,7]. However, its analgesic effect on postoperative sore throat and hoarseness has not been evaluated. The purpose of the present study was to prospectively evaluate the effect of premedication with oral clonidine on the incidence and severity of sore throat and hoarseness after total intravenous anesthesia.

This prospective study was approved by the ethics committee of Iida Municipal Hospital, and informed consent was obtained from all patients. We initially enrolled 82 patients, American Society of Aresthesiologists (ASA) physical status I–III, aged 15–82 years, who were scheduled for elective surgery in the supine position. The patients were to undergo neck or oral surgery; patients with nasogastric tube placement or for whom delayed extubation was planned were excluded. The patients were randomly assigned to one of two groups: the clonidine group (41 patients who received 150 μg clonidine and 20 mg raftidine orally 120 min before induction) or the control group (41 patients who received 20 mg raftidine orally 120 min before induction). Randomization was achieved as follows. For each group, the treatment assignment was written on sheets of paper. The sheets of paper were folded, placed in an envelope, and shuffled. For each patient, one folded sheet was taken from the envelope by the anesthesiologist the day before surgery, and the patient was assigned to the treatment indicated on the sheet.

Blood pressure (BP) and heart rate (HR) were recorded for each patient before premedication as baseline values, before induction as preinduction values, and 3 min after intubation as postintubation values. Electrocardiography, noninvasive blood pressure monitoring, and pulse oximetry were performed in the operating room. After the application of 100% oxygen at 6 l·min^{-1} for several min, total intravenous anesthesia was induced with 1–2 mg·kg^{-1} propofol, 0.5–1 mg·kg^{-1} ketamine, 1–2 μg·kg^{-1} fentanyl, and 0.1 mg·kg^{-1} vecuronium. Two milliliters of 2% lidocaine was first administered intravenously to alleviate pain from the i.v. propofol administration. Laryngoscopy was performed 3 min after the vecuronium injection. The duration of laryngoscopy was measured, and the difficulty of

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laryngoscopy was graded as follows: grade 1, no difficulty; grade 2, only posterior extremity of the glottis visible; grade 3, only the epiglottis visible; grade 4, no recognizable structures visible [8]. Intubation was facilitated with a tracheal tube with a standard cuff (Trachelon; Terumo, Tokyo, Japan) and an internal diameter of 7–8 mm for women and 8–9 mm for men. The cuff was inflated until no air leak could be heard with peak airway pressure at 20 cmH2O. Anesthesia was maintained by total intravenous anesthesia with propofol, fentanyl, ketamine, and vecuronium, with or without epidural block. The occurrence of cough reflex or body movement during anesthesia was defined as bucking, and a supplemental anesthetic agent or neuromuscular blocker was administered. The anesthesiologist in charge asked the patients about sore throat and hoarseness before they left the operating room and on the morning after surgery. No additional analgesics were administered before the first evaluation. At the time of the first evaluation, the degree of sedation was assessed according to a modified Ramsey Sedation Score (modified RSS: 1, patient anxious or agitated or both; 2, patient cooperative, oriented, and tranquil; 3, patient responds to commands only; 4, patient responds to a glabellar tap; 5, patient does not respond) [9]. Patients with a modified RSS of 1, 4, or 5 were regarded as inappropriate candidates for this study and were excluded. Symptoms of sore throat were graded for severity as follows: 0, absent; 1, minimal; 2, moderate; 3, severe. Symptoms of hoarseness were graded for severity as follows: 0, absent; 1, slight; 2, severe; 3, preventing speech.

Values for results are expressed as means ± SD or as percentages. The unpaired *t*-test and χ^2 test were used to analyze differences in patient characteristics, BP, and HR, and differences in the incidences of sore throat and hoarseness. The Mann-Whitney *U*-test was used to compare grades of difficulty of laryngoscopy and the severity of symptoms between groups. $P < 0.05$ was considered significant. Statistical analysis was performed with StatView version 5.0 (SAS Institute, Cary, NC, USA).

Of the 82 patients initially enrolled, 67 patients comprised the final study group. Five patients were excluded because of inappropriate sedation, and 10 patients were excluded because of multiple attempts at laryngoscopy. Patient characteristics are shown in Table 1. Sex, age, height, weight, duration of laryngoscopy, duration of intubation, difficulty of laryngoscopy, factors contributing to difficult intubation, and incidence of intraoperative bucking did not differ significantly between the two groups.

Mean preinduction BP and postintubation BP were significantly lower in the clonidine group than in the control group (Table 2). Postintubation HR was also significantly lower in the clonidine group (Table 2). The

Table 1. Patient characteristics

	Clonidine group ($n = 33$)	Control group ($n = 34$)
Sex (F/M)	24/9	21/13
Age (years)	49.2 ± 18.7	54.5 ± 15.9
Height (cm)	158.8 ± 9.0	159.6 ± 8.1
Weight (kg)	58.2 ± 12.5	60.5 ± 10.5
Duration of laryngoscopy (s)	14.2 ± 9.1	14.6 ± 10.1
Duration of intubation (min)	131.3 ± 64.8	152.9 ± 63.4
Difficulty of laryngoscopy (grade I/II/III/IV)	(23/9/1/0)	(27/6/1/0)
Factors contributing to difficult intubation		
None	30	31
Stiff cervical spine	0	1
Short neck	1	1
Micrognathia	1	0
Limited jaw mobility	1	1
Intraoperative bucking (%)	54.5 (18/33)	52.9 (18/34)

Table 2. Changes in mean blood pressure and heart rate

	Group	Baseline	Preinduction	Postintubation
Mean blood pressure (mmHg)	Clonidine ($n = 33$)	88.3 ± 9.9	82.4 ± 12.8**	89.8 ± 17.3*
	Control ($n = 34$)	90.0 ± 12.6	93.2 ± 13.1	99.4 ± 17.1
Heart rate (beats/min)	Clonidine ($n = 33$)	67.5 ± 8.7	69.3 ± 14.1	79.6 ± 17.9*
	Control ($n = 34$)	65.3 ± 9.0	73.2 ± 12.9	90.0 ± 15.5

Values are means ± SD
* $P < 0.05$; ** $P < 0.01$, compared to control group

Table 3. Incidences of postoperative sore throat and hoarseness

	Clonidine group ($n = 33$)	Control group ($n = 34$)	P value
Day of surgery			
Sore throat (%)	42.4 (14/33)	26.5 (9/34)	0.169
Hoarseness (%)	66.7 (22/33)	47.1 (16/34)	0.105
Day after surgery			
Sore throat (%)	27.3 (9/33)	14.7 (5/34)	0.206
Hoarseness (%)	12.1 (4/33)	23.5 (8/34)	0.223

Ratios are shown in parentheses

Table 4. Severity of postoperative sore throat and hoarseness

	Clonidine group ($n = 33$)	Control group ($n = 34$)
Day of surgery		
Sore throat	0 (0–3)	0 (0–1)
Hoarseness	1 (0–3)	0 (0–3)
Day after surgery		
Sore throat	0 (0–2)	0 (0–1)
Hoarseness	0 (0–1)	0 (0–2)

Each value represents the median; ranges are in parentheses
Sore throat was graded as 0, absent; 1, minimal; 2, moderate; 3, severe.
Hoarseness was graded as 0, absent; 1, slight; 2, severe; 3, preventing speech

incidences of sore throat and hoarseness on the day of surgery did not differ between the two groups (Table 3). On the day after surgery, the incidences decreased, without differences between the two groups (Table 3). The severities of hoarseness and sore throat did not differ significantly between the two groups (Table 4).

Sore throat and hoarseness are common postoperative complaints, and the incidence is reported to be 14.4%–50% for sore throat [10–16] and 10%–50.1% for hoarseness [10–12,15–17]. In the present study, the incidences of sore throat and hoarseness on the day of surgery were 42.4% and 66.7% in the clonidine group and 26.5% and 47.1% in the control group, respectively. Although the differences did not reach statistical significance, the incidences in the clonidine group were greater than those in the control group. In fact, the incidence of hoarseness in the clonidine group was greater than that reported previously.

One possible explanation for clonidine as a cause of postoperative throat complications may be its inhibition of salivary secretion. Clonidine has become popular as a premedication for patients undergoing general anesthesia because of its benefits [1–5]. However, it is also well known that clonidine significantly reduces salivary secretion by inhibiting parasympathetic reflexes [18–20]. Numazawa et al. [19] studied the effect of clonidine on salivary secretion when used as a premedication. Salivary volume before induction was significantly reduced, not only by a dose of $3\,\mu g \cdot kg^{-1}$ clonidine but also by a dose of $1\,\mu g \cdot kg^{-1}$. It is not unusual for routine intubation to cause laryngeal hematoma, tracheal mucosa impairment, or edema [21]. We used a water-soluble lubricant on the tracheal tube; however, reduction of salivary secretion before induction could have induced traumatic intubation and caused postoperative sore throat and hoarseness.

It is well known that the intracuff pressure increases when nitrous oxide is used in general anesthesia, increasing the risk of postoperative sore throat and hoarseness. Therefore, total intravenous anesthesia may have the advantage of decreasing the incidences of postoperative sore throat and hoarseness. However, careful titration of drugs is needed to maintain an adequate depth of anesthesia. Bispectral index monitoring or target-controlled infusion helps to provide adequate sedation in patients undergoing total intravenous anesthesia. However, these methods may not be available in every situation. Although clonidine has been reported to decrease the dose requirement for propofol anesthesia [5], it did not decrease the incidence of inadequate relaxation or bucking in the present study. Inadequate relaxation or bucking may also increase contact between the tracheal tube and the tracheal mucosa or vocal cords, increasing the incidence of postoperative throat problems.

This study was limited by small sample size. According to previous studies, clonidine premedication reduced the postoperative analgesic requirement by approximately 30% [6,7]. We recently reported that the frequency of sore throat was approximately 30% after total intravenous anesthesia [22]. More than 200 patients per group would be required to detect a decrease from 30% to 21% with a type I error probability of 0.05. Further studies with larger sample sizes are therefore needed.

In conclusion, we found that 150 μg oral clonidine premedication did not decrease the incidence or severity of postoperative sore throat or hoarseness. In fact, sore throat and hoarseness tended to be frequent with clonidine premedication. These complications may be trivial compared to the benefits of clonidine premedica-

tion; however, clinicians should recognize this potential effect.

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