TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2016) 46: 789-794
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doi:10.3906/sag-1409-101

The effect of addition of ketamine to lidocaine on postoperative pain in rhinoplasties

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Received: 23.09.2014 • **Accepted/Published Online:** 09.08.2015 • **Final Version:** 19.04.2016

Background/aim: The objective of this study was to examine the effect of addition of subanesthetic doses of ketamine to an epinephrine-lidocaine solution on postoperative pain, analgesic use, and patient comfort during rhinoplasties.

Materials and methods: Ninety patients were randomly divided into three groups: Group L, lidocaine with epinephrine; Group K, lidocaine with epinephrine plus ketamine; and Group S (control group), physiological saline solution with epinephrine. The local anesthetic solution was injected as preincisionally with intranasal submucosal infiltration following induction of general anesthesia. We evaluated visual pain score, analgesic demand, Wilson sedation score, and antiemetic demand at 5, 15, and 30 min and 1, 2, 4, 6, 8, 16, and 24 h after the operation. The patient satisfaction score was checked 24 h after the operation.

Results: Visual pain score was significantly reduced in Group K in comparison with the other groups and this group did not need any rescue analgesics ($P < 0.05$). The postoperative patient satisfaction scores were highest in Group K compared with the other groups ($P < 0.05$).

Conclusion: Addition of ketamine solution to lidocaine for infiltration block during rhinoplasty was successful in decreasing pain during postoperative periods and reducing analgesic consumption during the first 24 h after the operation.

Key words: Ketamine, lidocaine, rhinoplasty, postoperative pain

1. Introduction

Rhinoplasty is a reconstructive surgery that is frequently performed to correct nasal deformities. Local anesthesia alone or local and general anesthesia together can be used in this procedure. Patients experience distinct pain for 3 days after the operation, which is especially severe during the first day (1). Good analgesia should be provided during the postoperative period in order to ensure patient compliance and comfort (2). Local anesthesia is frequently used because it also contributes to analgesia. The addition of vasoconstrictors and adjuvant agents to local anesthetics reduces side effects and facilitates analgesic effect and duration with reduced local anesthetic concentrations. Epinephrine increases the duration of local anesthesia and provides good exposure (3). Agents such as neostigmine, clonidine, or opioids may also be added to increase the duration of anesthesia. However, neostigmine and opioids are not suited for rhinoplasties because they may cause nausea and vomiting, and clonidine is unavailable in many countries (4,5). Therefore, ketamine and its enantiomers are frequently used in multimodal anesthesia approaches. Ketamine has been shown to be better among other adjuvant agents in terms of efficacy and safety, pharmacokinetics, and pharmacodynamics (6).

Ketamine allows preventative analgesia via 2 mechanisms: central desensitization due to antihyperalgesic effect and pain control as an N-methyl-D-aspartate antagonist. It has been shown that preincisional infiltration anesthesia with subanesthetic ketamine increases block time, thereby decreasing postoperative analgesic demand (7). The use of ketamine alone as a preventative analgesic remains questionable (8,9).

Lidocaine-epinephrine combinations are used frequently in addition to general anesthesia for intranasal infiltration during rhinoplasty, but, to date, there is no published study on the effect of added ketamine. The objective of our study was to determine the usefulness of subanesthetic ketamine as an adjuvant to the infiltration block in terms of postoperative pain scores, analgesic demand, and patient satisfaction.

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2. Materials and methods

2.1. Ethics consideration

This study was approved by the Malatya Clinical Studies Ethics Board (2012/130, Malatya, Turkey). The study was registered with the Clinical Trials Registry, NCT01827020 (https://clinicaltrials.gov/). Written and oral consent was obtained from all patients. Ninety ASA class I patients who were scheduled for rhinoplasty under general anesthesia were included. Exclusion criteria are the following: systemic diseases (hypertension, diabetes, coronary artery and valve disease), drug allergy, psychiatric disorders, chronic pain, and chronic alcohol intake.

2.2. Patients and controls

Patients were randomly divided into three groups by closed envelope method and were instructed to fast for at least 8 h prior to surgery. Upon arrival for surgery, routine monitoring (electrocardiogram, heart rate, pulse oximeter, noninvasive arterial blood pressure) was initiated following intravenous (I.V.) cannulation and 0.03 mg/kg I.V. midazolam premedication. Anesthesia induction was provided with fentanyl (1 to 2 μg/kg) and propofol (2 to 3 mg/kg). Patients were intubated after myorelaxation with rocuronium (0.6 mg/kg). Anesthesia maintenance was achieved with 2% to 3% of sevoflurane and 60% nitrous oxide in O_2.

Patients in Group L received 1 mg/kg lidocaine (Arythmal 2%, 5 mL amp, Osel®, İstanbul, Turkey) + 0.0125 mg/mL epinephrine; in Group K 1 mg/kg lidocaine + 0.5 mg/kg ketamine (racemic ketamine, Ketalar 500 mg vial, Pfizer®, İstanbul) + 0.0125 mg/mL epinephrine; and in group S 0.0125 mg/mL epinephrine completed with saline to a total of 12 mL. Intranasal submucosal infiltration volume was administered in all groups and surgery was started 5 min after local infiltration. The plastic surgeons and anesthetists were blinded to the contents of the injections for each patient. Myorelaxation was reversed with 0.05 mg/kg neostigmine and 0.02 mg/kg atropine following the return of spontaneous respiration at the end of each surgery.

An increase of >30% in systolic arterial pressure from baseline was treated with 100 μg/kg nitroglycerine and a decrease of >30% was treated with 10 mg of ephedrine. Bradycardia (heart rate of <50 beats/min) was treated with 0.5 mg of atropine sulfate.

2.3. Postoperative evaluation

After extubation, patients were evaluated 5, 15, and 30 min and 1, 2, 4, 6, 8, 16, and 24 h after the operation. Pain was evaluated using a visual pain score (VPS) of 0 to 100, where 0 indicated no pain and 100 indicated unbearable pain, and 8 mg of lornoxicam (Xefo® I.V., 2 mL vial, A.İ. İstanbul) was administered if the VPS was ≥40. When nausea or vomiting occurred, patients were treated with chlorpropamide (1 mL amp, Primperan®). Sedation was monitored via the Wilson sedation scale, where 1 = fully awake and oriented, 2 = drowsy, 3 = eyes closed but rousable to command, 4 = eyes closed but rousable to mild physical stimulation, and 5 = eyes closed and unrousable to mild physical stimulation. Patients were also checked for hallucination and dizziness. Patient satisfaction was evaluated 24 h after the operation using a patient satisfaction score where 1 = low satisfaction, 2 = medium, 3 = good, and 4 = excellent.

2.4. Statistical analysis

The postoperative VPS at 30 min was considered the primary endpoint and was used to estimate the sample size of 30 patients in each group with 80% power to detect a 10% difference in the VPS between Group S, Group L, and Group K. Data were recorded and calculated using SPSS 13.0 for Windows version. Results of continuous variables were expressed as mean, standard deviation, and median (min–max) and categorical variables were expressed as number and percent. Normality for continuous variables in groups was determined with the Shapiro–Wilk test. The Unpaired t-test, paired t-test, Wilcoxon test, and one-way analysis of variance (ANOVA) were used for statistical analysis. A value of $P < 0.05$ was considered significant.

3. Results

The patients were similar in terms of age, height, weight, sex, and operation times. Patient data are summarized in Table 1. There were no statistically significant differences among the groups in terms of mean arterial pressure, SpO_2, and heart rate. There were no cases of bradycardia or hypertension throughout the study

The VPS values in Group S were significantly higher than in the other groups at 15 min and 8 h after the operations ($P = 0.0001$ and $P = 0.000$, respectively). The VPS values in Group L were significantly higher than in the other groups at 30 min and 16 h after the operations (respectively $P = 0.001$ and $P = 0.000$; Table 2).

There was no difference in nausea and vomiting among the three groups (Table 3). Patients in Group K had no postoperative analgesic demands, but this was not statistically significant ($P = 0.093$; Table 4). The rate of demand for antiemetics as determined at the end of the 24-h postoperative period in each group was 10% (3 patients) in Group L, 10% (3 patients) in Group K, and 6.7% (2 patients) in Group S.

The Wilson sedation score at 5 and 15 min was 2 for all patients in Group L; in Group K, 7 patients (23.3%) had Wilson score = 1, 22 (73.3%) had Wilson score = 2, and 1 (3.3%) had Wilson score = 4. In Group S, 15 patients (50%) had Wilson score = 1 and 15 (50%) had Wilson score = 2. At 30 min, 25 patients (83.3%) in Group L had reached Wilson score 1 and 5 (16.7%) had Wilson score

Table 1. Demographic characteristics.

	Group L (n = 30)	Group K (n = 30)	Group S (n = 30)
Age (years)	26.6 ± 4.9	25.8 ± 4.8	26.1 ± 5.3
Height (cm)	168.4 ± 8.6	166.4 ± 9.2	167.4 ± 8.0
Weight (kg)	64.8 ± 9.1	61.1 ± 11.1	65.4 ± 10.5
Sex (F/M)	18/12	22/8	21/9
Duration of surgery (min)	89.0 ± 11.2	90.5 ± 9.7	90.8 ± 7.6

Data are expressed as mean ± SD and sex as number.

Table 2. Visual pain score (VPS 0 to 100) in each group.

	Group L (n = 30)	Group K (n = 30)	Group S (n = 30)	P-value
VPS, 5 min	20 (10–40)	10 (10–20)	30 (30–70)	0.057
VPS, 15 min	30 (20–70)	10 (10–20)	70 (30–80)*	0.000
VPS, 30 min	60 (30–70)#	10 (10–20)	20 (20–30)	0.001
VPS, 1 h	30 (20–70)	10 (10–20)	20 (20–30)	0.062
VPS, 2 h	20 (20–30)	15 (10–30)	20 (20–30)	0.990
VPS, 4 h	20 (20–30)	20 (10–20)	20 (20–30)	0.300
VPS, 6 h	20 (20–30)	20 (10–20)	20 (20–30)	0.109
VPS, 8 h	20 (20–70)	15 (10–30)	70 (20–80)*	0.001
VPS, 16 h	60 (30–70)#	20 (10–60)	20 (20–70)	0.000
VPS, 24 h	20 (20–30)	20 (10–20)	20 (20–30)	0.011

VPS presented as median value (min–max) in each group. #Group L compared with Group K and Group S. *Group S compared with Group L and Group K.

Table 3. Postoperative nausea and vomiting in each group.

	Nausea / Vomiting Group L (n = 30)	Nausea / Vomiting Group K (n = 30)	Nausea / Vomiting Group S (n = 30)
5 min	7 (23.3%) / 11 (36.7%)	8 (26.7%) / 1 (3.3%)	1 (36.7%) / 2 (6.7%)
15 min	- / -	- / -	11(36.7%) / 2 (6.7%)
30 min	(3.3%) / -	- /-	9 (3%0) / 6 (20%)
1 h	5 (16.7%)/ 5 (16.7%)	-/-	-/-
2, 4, 6, 8, 16, and 24 h	-/-	-/-	-/-

Data are presented as number (percentage).

Table 4. Need of analgesics in each group.

	Group L (n = 30)	Group K (n = 30)	Group S (n = 30)
None	-	30 (100%)*	-
One time	3 (10%)	-	26 (86.7%)
Two times	12 (40%)	-	22 (73.3%)

Need of analgesics presented as number (percentage).
*There was no requirement for analgesics in Group K.

2; 26 (86.7%) were at Wilson score 1 in Group K, 3 (10%) were at Wilson score 2, and 1 (3.3%) was at Wilson score 3. At 1 h postoperatively, all patients in all groups were fully awake (Wilson score = 1), and all remained so throughout the remainder of the 24-h observation period.

Three patients (10%) in Group K experienced hallucinations 30 min postoperatively. Hallucinations were not recorded at any other time during the observation period in this group, and no patient in Group L or Group S experienced hallucination at any time. Dizziness was not reported for any patient in any group.

The patient satisfaction score was significantly higher in Group K compared to either of the other groups (Table 5).

4. Discussion

Our results demonstrated that the addition of 0.5 mg/kg ketamine to lidocaine with an epinephrine solution in patients undergoing rhinoplasty under general anesthesia provides effective postoperative analgesia with decreased analgesic demand during the first 24 h after the operation. These results were accompanied by higher patient satisfaction scores.

Local anesthetic combinations with epinephrine are frequently used in many surgeries, including nasal surgeries, in order to provide good exposure, increase the duration of local anesthesia, and decrease the toxic side effects of local anesthetics (10). Demiraran et al. compared levobupivacaine and epinephrine-added lidocaine infiltration anesthesia in nasal surgeries, similar to our study, and determined that in addition to giving better exposure, postoperative analgesic consumption was significantly decreased (11). Addition of vasoconstrictors also offers the important advantage of decreasing the systemic toxic effects of the local anesthetic agent. Thevasagayam et al. found that using lidocaine infiltration anesthesia during rhinoplasty decreased systemic absorption of cocaine, thereby decreasing cardiac side effects while allowing safe increases of the cocaine dose (3). Significant decreases in VPS and analgesic use have also been reported during the first 24 h after septorhinoplasty operations in which naphazoline nitrate, a vasoconstrictor derivative, was used in combination with lidocaine (12). In the present study, there was no demand for analgesics in Group L until 30 min postoperatively, and the level of analgesic consumption in this group was lower than that observed in the control group.

Combined preincisional local anesthetics can be used during general anesthesia or sedation. Infiltration block provides good intraoperative and postoperative analgesia when the anesthetic method is selected properly. In adolescents, a lidocaine and bupivacaine combination was administered preincisionally, and despite its use with the accompanying midazolam and fentanyl sedation, general anesthesia was required for most of the patients (9 out of 14) (13). In addition, when Jha et al. compared 0.5 mg/kg ketamine and 2 mg/kg bupivacaine preincisionally with epinephrine in palate repair of children following general anesthesia, they found, similar to our study, that postoperative pain scores (CHEOPS) and analgesic demand were significantly lower in the ketamine group (14).

Providing preemptive analgesia in parallel to the development of multimodal analgesia has gained importance. If pain transmission is stopped prior to incision, morbidity decreases along with the intensity and duration of postoperative pain (15). Ketamine is not used in pain treatment, but it enables effective postoperative analgesia via N-methyl-D-aspartate antagonism and by changing central sensitization. The antihyperalgesic effect of peripheral local ketamine has been shown in preclinical studies (16). Subanesthetic or low-dose ketamine (1 mg/kg) decreases postoperative analgesic consumption at a significant level without any side effects due to its analgesic effectiveness along with a proven harmony with local anesthetics and opioids (17). Doses of 0.5 and 1 mg ketamine were examined in a study of peritonsillar ketamine infiltration carried out by Honarmand et al., and because those authors did not find a difference between

Table 5. Patient satisfaction scores in each group.

Score	Group L (n = 30)	Group K (n = 30)	Group S (n = 30)
1	2 (6.7%)	-	5 (16.7%)
2	17 (56.7%)	5 (16.7%)	19 (63%)
3	11 (36.7%)	21 (70%)*	6 (20%)
4	-	4 (13.3%)	-

Data are presented as number of patients (percent) with satisfaction of patient score (1 = low, 2 = medium, 3 = good, and 4 = excellent).
*Satisfaction of patients is seen to be highest in Group K.

the doses in terms of preventing postoperative pain over 24 h, we used the 0.5 mg dose in our study (18). Savafi et al. used preincisional subcutaneous infiltration or I.V. ketamine to provide preemptive analgesia for patients undergoing cholecystectomy (19). Similar to our study, they determined that analgesia was attained during the first 24 h after the operation without any significant side effects. In fact, the local anesthetic effect of ketamine may last for as long as 1 week, but in the present study, we did not determine the absolute duration of the analgesic effect because our postoperative observation period ended at 24 h (20).

The subcutaneous, oral, rectal, topical, intranasal, sublingual, I.V., I.M., epidural, and caudal analgesic effect of ketamine were determined in a review by Tawfic (21). Yeaman et al. effectively used subanesthetic ketamine with an intranasal atomizer device (22). Analgesia was obtained in 56% of patients with 0.7 and 1 mg/kg ketamine administration due to decreased absorption of ketamine (30%–50%). Analgesia was obtained in all patients of our study with submucosal administration of the medications. Surendar et al. topically administered ketamine in a higher dose (5 mg/kg) to the nasal cavity with an intranasal syringe in pediatric dental patients. They achieved better postoperative analgesia with ketamine compared to midazolam and dexmedetomidine (23).

The efficacy of a ketamine and ropivacaine combination used in caudal blocks has also been examined. In a study of 2 mg/kg ropivacaine and 0.5 mg/kg ketamine administered in combination during the preoperative period in children undergoing inguinal hernia repair, it was determined that in addition to providing hemodynamic stability, the combination was associated with significantly increased analgesic duration and decreased analgesic use (24). Although those authors used ketamine in neuraxial blocks, in contrast to the submucosal block examined in the present study, our patients in the ketamine group also had significant reductions in VPS values and decreased analgesic consumption, in addition to hemodynamic stability, without any negative side effects.

The limitations of our study were as follows. First, local anesthetic with epinephrine was used in all three groups in our study, and hemoglobin and hematocrit were not monitored as a primary objective of our study of analgesia. Next, because the process of acquiring permission for the use of drugs for indications outside of the prospective scope is long, we did not include a group where only ketamine infiltration was used. The use of ketamine as infiltration anesthesia in rhinoplasty should be supported by further studies, and the effects on bleeding and pain control should also be further examined.

In conclusion, an infiltration block in addition to general anesthesia in rhinoplasties can be used successfully without any intraoperative or postoperative side effects. When ketamine is used as the adjuvant agent, it provides effective analgesia during the first 24 h after the operation, and it decreases analgesic use and increases patient comfort.

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