

The Effects of Propofol-Remifentanil Vs Midazolam-Remifentanil on Hemodynamic Stability during Stapedectomy: A Randomized Clinical Trial

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Abstract

Background: One of the essential components during stapedectomy is a good cooperation between patient and surgeon. Remifentanil is commonly used short – acting opioid to assess the results during the procedure.

Purpose: The aim of this study is to investigate the effects of propofol- remifentanil and midazolam -remifentanil on hemodynamic parameters intra- Stapedectomy.

Methods: In this randomized, double-blinded trial, 36 patients with otosclerosis were evaluated in two equal groups, which received propofol- remifentanil and midazolam-remifentanil each. We recorded cardio-respiratory parameters, side effects and intra-operative cooperation of the patients.

Results: There was a statistically significant difference in blood pressure reduction between two groups. The severity of the bleeding and desirable cooperation of patients in midazolam- based regimen was better than propofol- based regimen (p- value= 0.01 and 0.02 respectively). The average operative time in patients who received propofol was about 15 minutes more than the other group (p- value=0.01).

Conclusion: The midazolam - remifentanil is more appropriate sedative, because it provides hemodynamic stability and a better cooperation of patient intra - stapedectomy.

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INTRODUCTION

Stapedectomy is a successful method in the treatment of otosclerosis. In this surgery, stapes bone is partially or completely removed and a suitable prosthesis is implanted in the middle ear (1). This procedure has been proven to have both efficacy and safety, but it is not devoid of complications. Most complications such as vertigo, facial palsy, perilymphatic fistula, tinnitus and sensory- neural hearing loss are mild and self-limited (2, 3). There are two different methods of anesthesia in stapedectomy. It was traditionally conducted under general anesthesia. The

application of local anesthesia and sedation can be a safe and feasible method. The administration of sedative drugs decreases the hospitalization time, complications and cost of treatment, but the lack of adequate sedation and lack of experienced surgeon may lead to problems during operation (4). Propofol is the most common drug to induce anesthesia. It has a high total body clearance and a short half-time, which makes it a suitable choice of sedation (5). Remifentanil, a short – acting opioid, is commonly used in stapedectomy and provides rapid recovery. A combination of

low dose propofol and remifentanyl has minor respiratory depression (6). Midazolam is a short-acting benzodiazepine. It causes drowsiness and relieves anxiety. To achieve a conscious sedation in some procedures, midazolam is administered with narcotic agents (e.g., fentanyl). According to existing evidence, propofol and midazolam have similar sedative effects (5, 7). A systematic review showed that midazolam-based regimens have longer sedative effect than propofol-based regimens in endoscopy (8). We undertook this study to compare the remifentanyl/propofol and remifentanyl/midazolam regimes as sedative agents during stapedectomy.

PATIENTS and METHODS

This prospective, randomized, double-blinded trial was conducted in 2016. This trial was approved by the medical ethics committee of Shahid Beheshti university of Medical sciences (Code of Medical Ethics: IR.SBMU.REC.1395.910).

Considering the type 1 error of 5%, power of 80%, two-sided test and conventional effect size ($d = 0.8$), 36 patients with otosclerosis were enrolled in the study. The eligible patients were aged 18 - 65 years with ASA (the American society of anesthesiologists) score I and II (9), who had hearing loss. We excluded all patients with drug sensitivity to propofol, midazolam, lidocaine or remifentanyl, ASA > II, drug abuse, previous history of surgery in the last three years, meniere's disease, bleeding disorders, psychological disorders, additional surgeries with stapedectomy and pregnant subjects. The investigators and patients were masked to the identity of a patient's group. After the patients consented to participate, they were randomly divided into two groups, group P ($n = 18$) received propofol/ remifentanyl (remifentanyl 0.05 $\mu\text{g}/\text{kg}$ per minute and propofol 0.25 $\mu\text{g}/\text{kg}$ loading dose and then intravenous infusion with 0.25 $\mu\text{g}/\text{kg}$ per minute) and group M ($n = 18$) received midazolam/remifentanyl (remifentanyl 0.05 $\mu\text{g}/\text{kg}$ per minute and repeated doses midazolam 1mg). We carried out local anesthetic with lidocaine 5 ml in epinephrine 1/100,000 at the site of operation. Follow up and information was

collected in a specific form, which was before and intra-operation variables. This information included demographic characteristics, vital signs (pre-operation and 15, 30, 45 and 60 minutes post-operation), chief complaints and surgical duration. The patient's pain, nausea and bleeding rate were measured by visual analog scale (VAS). The patient's intra-operative cooperation was evaluated by a surgeon on a scaled score 1-10 by VAS, Score 10 represents "perfect" and score 1 is the opposite. The severity of these variables was categorized at three levels (score 1-3: low, 4-6: moderate, and 7-10: severe). To describe the variables, we used mean and standard deviation for the continuous variables and frequency and percentage for the qualitative variables. To compare outcomes, the independent samples t-test was used for continuous data that was normally distributed in each group. The Mann -Whitney U test and Chi -square test were applied for Non- normally distribution and nominal data respectively. All tests were conducted at significant levels less than 0.05.

RESULTS

We assessed 36 patients in this trial including 52.8% ($n=19$) female and 47.3% ($n=17$) male. The mean age of patients was $33(\pm 8.5)$ and $50(\pm 9.6)$ years in group P and group M respectively ($P = 0.83$). Table 1 shows the findings of comparison between two study groups regarding patients' characteristics, duration of surgery, severity of the bleeding, nausea and pain. The mean duration of surgery was 50 ± 14 minutes in group M and 65 ± 21 minutes in group P ($P = 0.015$). None of patients in group M had pain during operation. Blood pressure, pulse rate and respiratory rate were monitored before and during surgery. No significant differences were found in pulse rate and respiratory rate between the groups (Table 2); only four patients in group P were affected with apnea. Intra - operative systolic blood pressure was significantly lower in the group P than in group M, and the difference level was almost 10 mmHg (Table 2). In group P tinnitus was improved in 72.2% ($n=13$) and 22.2% ($n=4$) patients, respectively completely and partially, while one patient had worse outcome. Complete

cure was achieved in 83.3%(n=15) of group M (P =0.54). There was a significant difference in nausea severity between the groups. Moderate nausea was observed further in group M (P =0.017), but severe

nausea was not identified in both groups. The patients' cooperation rate was higher in group M than group P (75%, vs 40%, P=0.02).

Table 1: Demographic and clinical findings

variables	Group P(n=18)	Group M(n=18)	P-value*
Age(year)	33.4(±8.5)	50.3(±9.6)	0.83
Duration of surgery(minute)	65(± 21)	50(±14)	0.015
Severity of bleeding	5.7(±2.6)	3.7(±1.7)	0.011
Pain	0.17±0.12	0	0.17
Nausea(Mild: Moderate)	15:3	8:10	0.017
Gender(Male: Female)	8:10	7:11	0.72
* p- value categorical variables were calculated with the Chi-Square test, and Mann-Whitney U test was used for continuous variables. Significant level <0.05 Group P: Propofol/Remifentanil; Group M: Midazolam/ Remifentanil			

Table 2: Comparison of cardiorespiratory parameters in both groups

Variable	Group *	Pre-operation	Intra- operation(minute)			
			15	30	45	60
Blood pressure(systolic)	P	97.2±13.5	92.7±11.2	87.2±9.7	85.8±8.6	77.8±9.5
	M	103.1 ±13.58	102.9±11.7	97.3±16.8	100.9±10.7	93.0
P- value		0.236	0.013	0.044	.000	0.036
Pulse rate	P	77.4±8.9	85.0±10.8	77.9±13/3	82.2±7.8	71.2±29.7
	M	85.3±18.2	86.2±9.7	85.6±11.9	78.6±5.7	70.1±25.3
P- value		0.140	0.737	0.107	0.189	0.140
Respiratory	P	12.2±1.7	11.7±1.1	11.8±1.5	11.8±1.9	12.2±1.6
	M	12.2±0.4	12±0.6	12.2±0.4	12.2±0.4	12.0
P- value		0.978	0.570	0.346	0.531	0.845
*: Group P: Propofol/Remifentanil, Group M: Midazolam/ Remifentanil Significant level (p-value)<0.05						

DISCUSSION

Propofol and midazolam with remifentanil are suitable for sedation during stapedectomy. In the manipulation of the stapes, a good collaboration between patient and surgeon should be established, which can be immediately ascertained by recovery of hearing function during surgery. In Our study, cardiorespiratory parameters were stable throughout the sedation period, but four patients in group P experienced apnea. The pulse rate and respiratory rate of the patients were similar in both groups. In propofol group, low systolic blood pressure remained during intra- operative times, which was related to the severity of the bleeding and inadequate dose of propofol. Consistent with the negative inotropic effect

of propofol, blood pressure dropped following infusion of propofol (10, 11, 12). The severity of the bleeding was significantly higher in propofol group. In order to prevent dose- dependent respiratory depression and risk of apnea, we had to use propofol less than sedative-dose (10-50 µg/kg/min) (13). On the other hand, the role of interaction between propofol and remifentanil is important, remifentanil decreases propofol clearance and reduces the required dose of propofol infusion (14). Propofol vs midazolam showed less intra-operative patient cooperation, which can be due to the inadequate amounts of propofol. Remifentanil, as an opioid analgesic, reduces the side effects of stapedectomy

(15); consequently, we couldn't detect the severe nausea in patients. Of course mild / moderate nausea was found only in midazolam group, not in propofol group this finding was similar to khurana P, study (11). Similar to some previous studies, despite the midazolam group, there was pain on receiving propofol (11, 12, 15). The duration of surgery was longer in propofol group, which is interpretable due to the usage of low dose propofol infusion and individual variation in response. Some studies showed that propofol-based regimen has faster recovery time (16, 17), but in our study, recovery time and postoperative complications weren't measured. Therefore, it is recommended to investigate the long term outcomes in another study.

CONCLUSION

Propofol and midazolam with remifentanyl were evaluated in terms of hemodynamic stability during stapedectomy. Both regimes are effective, but hypotension and intra-operative blood loss were more observed in propofol with remifentanyl than midazolam with remifentanyl. Cardiorespiratory stability and desirable cooperation of patients throughout the surgery were noted in patients who received midazolam. We believe that the midazolam –based regimen is more appropriate for sedation in middle ear surgery.

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CONFLICT of INTEREST

The authors declared no conflicts of interest with this article.

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