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Comparison of the Effects of Infusion of Propofol -Remifentanil with Midazolam-Remifentanil in Reducing Bleeding in Patients undergoing Middle Ear Surgery

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Abstract

Objective: This study compares the effects of infusion of Propofol - Remifentanil with Midazolam - Remifentanil in reducing bleeding in patients undergoing middle ear surgery.

Methods: This study was conducted as a double blinded randomized clinical trial among 86 patients undergone elective surgery of the middle ear, they were divided in two 43 members group. All of the patients received Isoflurane and N_2O as maintenance of general anesthesia. When entering the middle ear, in order to reduce bleeding and achieve surgeon's satisfaction, either the combination of Midazolam - Remifentanil (M-R) or the combination of Propofol - Remifentanil (P-R) was adjuvant in each group. The (M-R) group received 0.5-1 µg/kg/min Midazolam with intravenous infusion and (P-R) group received 50-100 µg/kg/min Propofol with intravenous infusion; 1.0 µg/kg/min Remifentanil was administered in both groups. Vital signs of the patients were measured and recorded in 5 minutes intervals during the surgical procedure. The BIS scores was monitored and recorded in each group. Satisfaction of the surgeon from surgical setting and the amount of bleeding was recorded based on the score 0-10.

Results: There was no significant difference in systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate and BIS scores between the two groups during the procedure (P>0.05). Surgeon satisfaction showed no significant difference between the two groups (P>0.05). The differences between surgical procedure duration and period of PACU staying were statistically of no important significance between the two groups (P>0.05).

Conclusion: It seems that in the middle ear procedures the combination of Propofol - Remifentanil and Midazolam - Remifentanil have not statistically significant differences in hemodynamic control, surgeon's satisfaction, duration of surgical procedure and discharge from PACU. Therefore, adjuvant drug selection might consider either of these two regimens in order to achieve better surgical condition. Further studies are recommended to confirm these findings.

Keywords: Midazolam; Remifentanil; Propofol; Middle ear

Introduction

Each new technique and anesthetic drug has more beneficial effects and less toxic effects than the previous drug and method. Middle ear surgery is one of the microsurgeries that require the use of special methods of anesthesia provided with fewer amounts of bleeding, motion less patients during the procedure and lack of nausea and vomiting in post operation period. This means deep and adequate level of anesthesia, minimal intraoperative movement, and rapid recovery beside fewer postoperative complications. Maintenance of middle ear homeostasis is of great significance for the anesthesiologist because even minimal blood disrupts the surgeon's vision and prolongs the procedure. In recent years, it has been shown that intravenous administration of Propofol in middle ear surgery has led to better condition during operation [1]. Another study reported that the use of combination of low-dose Propofol with Remifentanil in comparison with Propofol alone results in better hemodynamic stability, less patients movement and more rapid recovery and is associated with anti-emetic effects [2]. Midazolam is a short-acting Benzodiazepine with minimal cardiovascular depressant effects, due to its anti-anxiety and amnestic properties this drug is one of the popular agents of balanced anesthesia. Midazolam has sedative hypnotic effects that these effects reverse quickly by Flumazenil antagonists [3]. Midazolam is commonly used for sedation before surgery and ambulatory short-term endoscopic surgeries [4,5]. Blood pressure control and hemodynamic stability to reduce and minimize the bleeding during microscopic surgery of the middle ear cavity is of great significance for anesthesiologists and surgeons, considering the importance of hemodynamic stability in patients and importance of reducing bleeding in operation setting which provide surgeon's and anesthesiologist's satisfaction. This study was conducted to compare the effects of infusion of Propofol - Remifentanil with Midazolam - Remifentanil in reducing bleeding in patients undergoing middle ear surgery in Iranian General Hospital, Ear, Nose, Throat operating room.

Materials and Methods

This single blinded randomized clinical trial was conducted among patients undergoing middle ear surgery who were referred to an Iranian General Hospital. 86 individuals were selected by non-randomized simple method (Sequential), thus all patients who met the criteria entered the study until the completion of the sample size. The protocol was described for the patients to have their consent to entering the study. Exclusion criteria were as follows: Individuals who did not have consent to participate in the study, any underlying disease that limited daily activity, ASA Class > 2, emergency surgery, uncontrolled hyper-

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tension, cardiac functional class 3, and hypersensitivity to any of drugs used in each group. Then all patients were randomly divided into two groups; Propofol/Remifentanil (P-R) (I), Midazolam/Remifentanil (M-R) (II) by block randomization method as quadri blocks including 43 patients in each group. Middle ear surgery was performed by one ENT surgeon and anesthesia was done by one anesthesiologist. Neither the ENT surgeon nor the patients were informed about the adjuvant anesthetic administered while entering the middle ear, so the study was double-blinded. After placing the patient on the bed of the operating room, patients were preoxygenated for 5 minutes; blood pressure and heart rate were measured as the base rate through non-invasive methods. After injection of 1 μg/kg Fentanyl as premedication, the induction of anesthesia was performed similarly in both groups with the injection of 5 mg/kg Thiopental. Endotracheal intubation was facilitated with 0.6 mg/kg Atracurium. We used fentanyl in premedication in order to blunt the hemodynamic changes to laryngoscopy and tracheal intubation; because in bolus doses it has less adverse cardiovascular effects than Remifentanil such as bradycardia and hypotension. Maintenance of anesthesia was combination of 50% N_2O and isoflurane in both groups, when entering the middle ear the M-R group received 0.5-1 μg/kg/min Midazolam with intravenous infusion and the P-R group received 50-100 μg/kg/min Propofol with intravenous infusion; 0.1 μg/kg/min Remifentanil was administered with intravenous infusion in both groups. Depth of anesthesia was maintained 40-60 based on BIS in patients according to changes in inhaled gas; isoflurane, oxygen and nitrous oxide. After incision and opening the middle ear space the two protocols compared with each other and the data was recorded. Hemodynamic stability and lesser bleeding were detected in (M-R) group. Systolic and diastolic blood pressure, mean arterial blood pressure (MAP) and heart rate of each patient were measured and recorded in 5 minutes intervals during the surgical procedure with a non-invasive method using Saadat measuring device manufactured in Iran. Any episode of severe decline in blood pressure, decline in mean arterial blood pressure more than 30% compared to base MAP for 60 seconds, was treated with 5 mg intravenous ephedrine; and any episode of severe decline in heart rate, heart rate below 50 beats per minute for 60 seconds, was interfered with 0.5 mg intravenous atropine. Surgeon's Satisfaction Ratio about operation setting, including appropriate blood pressure control and amount of bleeding was recorded. The surgeon was asked about the condition with the expression of dissatisfaction, poor satisfaction, partial satisfaction and complete satisfaction. At the end of the surgery 0.05 mg/kg intravenous morphine was administered before transferring the patients to post anesthetic care unit (PACU) for post operation analgesia. After completion of skin sutures all drugs were discontinued; muscle relaxant was reversed when acceptable recovery of relaxation was obtained, and the patient was ventilated with 100% oxygen few minutes before transferring to PACU. The duration of recovery was recorded from the moment of drug discontinuation till leaving the PACU. All information about blood pressure, duration of surgery, duration of recovery and surgeon's satisfaction was recorded in data collection sheet. The data analyses were obtained by using SPSS software. The quantitative variables were compared between two groups by t-test and changes were assessed using repeated measurement ANOVA; qualitative variables were compared between two groups by chi-square test. Statistically $P<0.05$ was considered significant.

Result

In this study each group contained 43 subjects, with the study power of 20% considering $\alpha = 0.05$ and $\beta = 0.2$. Heart rate differences during the procedure in both studied groups are shown in figure 1 that was not statistically significant. Comparison the demographic characteristics are shown in table 1. Differences in systolic blood pressure during the procedure in both studied groups are demonstrated in figure 2 which was not statistically significant. Differences in diastolic blood pressure during the procedure in both studied groups are demonstrated in figure 3 which was not statistically significant. Differences in MAP during the procedure in both studied groups are demonstrated in figure 4 which was not statistically significant. Differences in BIS score during the procedure in both studied groups are demonstrated in figure 5 which was not statistically significant. Comparison of intra

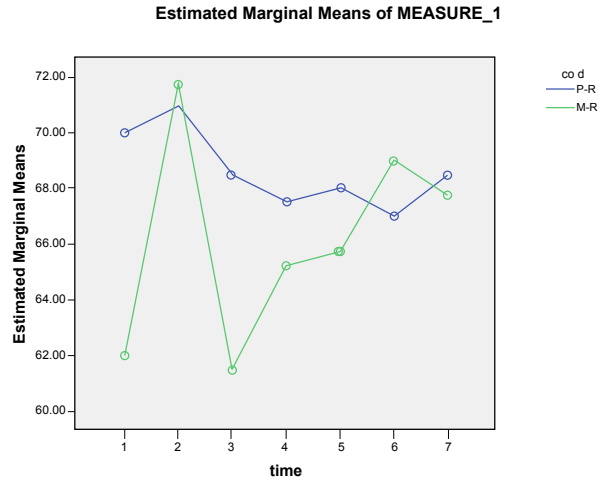

Figure 1: heart rate changes at different times during surgery in two groups (=0.716).

	P-R (n=43)	M-R (n=43)	P Value
0.112	35 ± 10	33 ± 13	Age
0.895	26:17	20:23	Sex; Male: Female
0.725	74 ± 16	69 ± 15	Weight ;Kg
0.818	167 ± 9	160 ± 9	Height ; cm

Table 1: Comparison of demographic data in two groups.

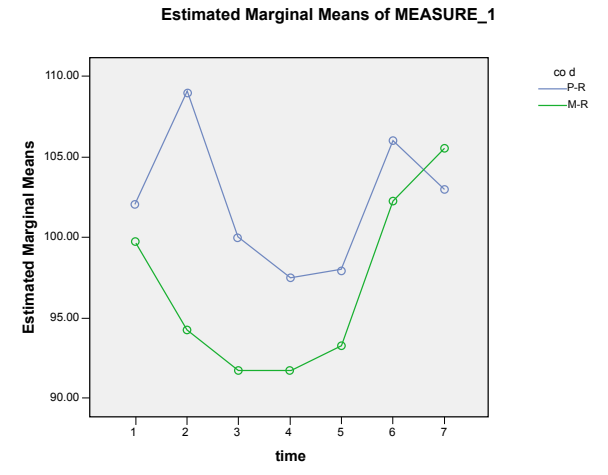

Figure 2: Systolic blood pressure changes at different times during surgery in two groups (=0.522)

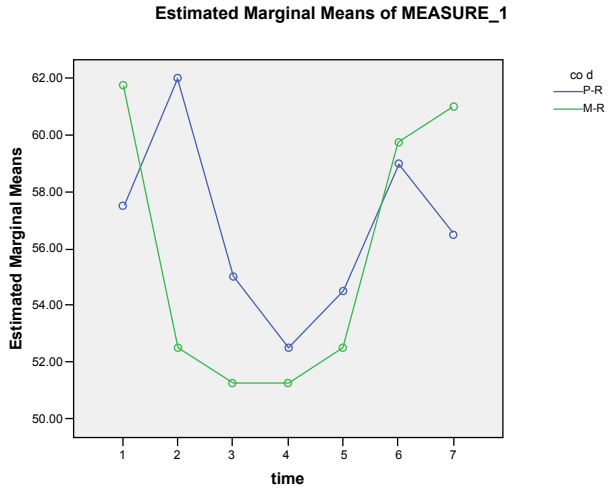

Figure 3: Diastolic blood pressure changes at different times during surgery in two groups (=0.696).

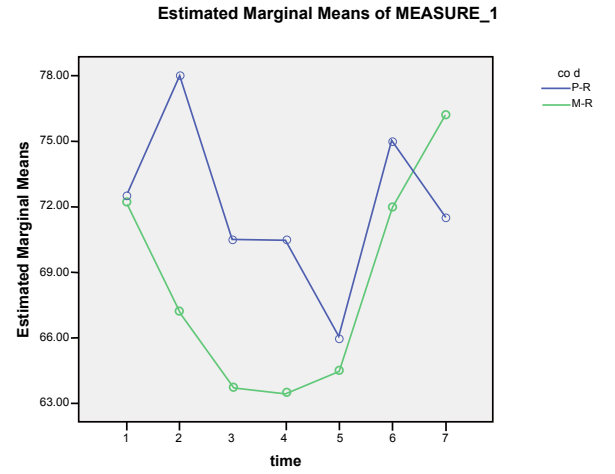

Figure 4: MAP changes at different times during surgery in two groups (=0.122).

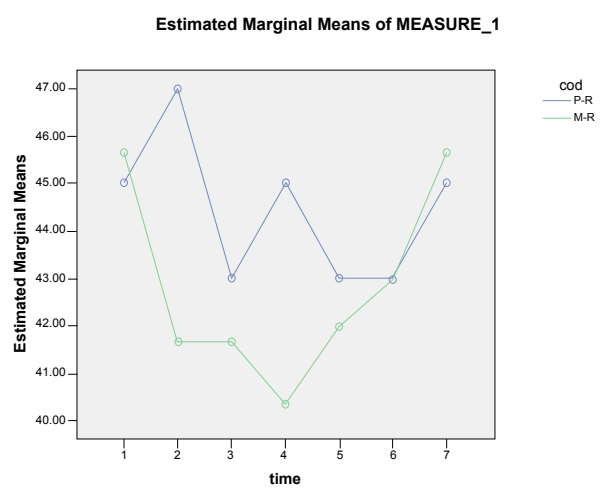

Figure 5: BIS changes at different times during surgery in two groups (=0.734).

	P-R (n=43)	M-R (n=43)	P Value
0.796	98.3 ± 5.4	96 ± 4.9	Anesthesia time (min)
0.261	43 ± 14.5	34.2 ± 4.9	Middle ear surgery time (min)
0.228	9.5 ± 0.8	7.7 ± 0.5	Eye opening time (min)
0.163	10 ± 0.8	8.5 ± 0.6	Extubation time (min)
0.720	43 ± 14.5	40 ± 18.7	Recovery time (min)

Table 2: Comparison of intraoperative and recovery data in two groups.

	P-R (n=43)	M-R (n=43)	Total (86)	P Value
No satisfaction	0 (0%)	0 (0%)	0 (0%)	0.586
Poor satisfaction	4 (4.7%)	1 (2.3%)	3 (7%)	
Partial satisfaction	36 (41.9%)	17 (39.5%)	19 (44.2%)	
Complete satisfaction	46 (53.4%)	25 (58.2%)	21 (48.8%)	

Table 3: Comparison of surgeon's satisfaction in two groups.

operative and recovery data in the two study groups is shown in table 2 and none of them was statistically significant. Comparison the surgeon's satisfaction between the P-R and M-R groups is shown in table 3 which was not statistically significant.

Discussion

Middle ear surgery is one of the microsurgeries that require the use of special methods of anesthesia provided with fewer amounts of bleeding, motion less patients during the procedure and lack of nausea and vomiting in post operation period. This means deep and adequate level of anesthesia, minimal intraoperative movement, and rapid recovery beside fewer post operation complications. Blood pressure control and hemodynamic stability to reduce and minimize the bleeding during microscopic surgery of the middle ear cavity is of great significance for anesthesiologists and surgeons, considering the importance of hemodynamic stability in patients and importance of reducing bleeding in operation setting which provide surgeon's satisfaction.

Maintenance of middle ear homeostasis is of great significance for the anesthesiologist because even minimal blood disrupts the surgeon's vision under an operating microscope and prolongs the procedure. The procedures related to ear are very sensitive to stimulations particularly during the surgery, so creating a setting with minimal movements is inevitable which requires relatively deep anesthesia. Various sedative and hypnotic drugs have been used in numerous studies for middle ear surgery to facilitate the operation till now [1,2,6-9]. In recent years, it has been shown that intravenous administration of Propofol in middle ear surgery has led to better condition during operation [1]. Another study reported that the use of combination of low-dose Propofol with Remifentanil in comparison with Propofol alone results in better hemodynamic stability, less patients movement and more rapid recovery and is associated with anti-emetic effects [2]. Midazolam is a short-acting Benzodiazepine with minimal cardiovascular depressant effects, due to its anti-anxiety and amnestic properties this drug is one of the popular agents of balanced anesthesia. Midazolam is commonly used for sedation before surgery and ambulatory short-term endoscopic surgeries [4,5].

Previous studies had compared the administration of Propofol and Midazolam in middle ear procedures. In his study Benedik J et al. [8] reported that Propofol is more appropriate than Midazolam to make sedation in patients undergoing middle ear surgery, but in our study we recorded higher depth of anesthesia with Midazolam than Propofol, which was not statistically significant.

In previous studies it has been shown that Propofol - Remifentanil is an appropriate method in ear surgery procedure because of its rapid recovery, creating intraoperative well condition and reducing post operation nausea and vomiting [1,2]. Our study reveals that in Propofol - Remifentanil group the duration of anesthesia, middle ear surgery and PACU staying was shorter than Midazolam - Remifentanil group. Also eye opening time and patient's extubation were faster in Propofol - Remifentanil group than Midazolam - Remifentanil group but statistically showed no significance.

By determining Propofol titer the depth of anesthesia can be easily accessed and after discontinuation of the drug patient is rapidly awakened [10]. Propofol alone leads to longer duration of recovery from anesthesia in high concentrations [10]. It seems that Remifentanil combined with Propofol provides faster eye opening after discontinuation of anesthesia and faster extubation. According to previous studies another advantage of Remifentanil-Propofol is lessen blood pressure and subsequent decrease bleeding in the setting of surgery which reduces the time of the procedure [11,12]. According to this study Mean Heart Rate in Propofol - Remifentanil group is lower than Mean Heart rate in Midazolam - Remifentanil group, but there was no statistically significant difference between the groups. Also changes in systolic and diastolic blood pressure, MAP and BIS did not show statistically significant differences between the two study groups. In other studies it is reported that less changes in heart rate and MAP are observed with Remifentanil-Propofol during operation [2].

In Midazolam - Remifentanil group intraoperative heart rate was associated with greater fluctuations, these fluctuations were not clinically important. It seems that arterial pressure, cardiac output and peripheral vascular resistance are mildly decreased with Midazolam. Also increase in heart rate following Midazolam administration is because of mild changes in systolic blood pressure. Other studies also reported that Midazolam results in a mild decrease in systolic and diastolic blood pressure and mild increase in heart rate, neither of which are significant or clinically important [13-15].

In our study surgeon's satisfaction was more in Midazolam - Remifentanil group, due to higher depth of anesthesia and lesser amount of bleeding as a result of lower ranges of MAP but no significant differences between two groups were reported.

Conclusion

Considering the findings of this study it seems that in the middle ear procedures the combination of Propofol - Remifentanil and Midazolam - Remifentanil have not statistically significant differences in hemodynamic control, surgeon's satisfaction, decreasing bleeding in the surgical setting, duration of surgical procedure, time of eye opening and discharge from PACU. Therefore, adjuvant drug selection might consider either of these two regimens in order to achieve better surgical condition. Further studies are recommended to confirm these findings.

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