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Original Article

Comparative evaluation between two methods of induced hypotension with infusion of Remifentanil and Labetalol during sinus endoscopy

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ABSTRACT

Objective: This study aimed to compare two methods of controlled hypotension using labetalol and remifentanil in terms of capability to create controlled hypotension and to investigate the obtained complications, and satisfaction rate of surgeon and patient during functional endoscopic sinus surgery.

Methods: In this prospective clinical trial, 62 patients underwent endoscopic sinus surgery in Al-Zahra and Ayatollah Kashani Hospitals of Isfahan were divided into two groups: in the first group, 20 mg bolus dose of labetalol and then infusion of it, at a rate of 0.5–2.0 mg/min and in the second group, remifentanil with dose of 0.5–1 μg/kg started and then 0.25–0.5 μg/kg/min were prescribed. Hemodynamic parameters during anesthesia and recovery time, surgeon and patient satisfaction, and recovery time were measured and recorded.

Findings: Hemodynamics variable were comparable between two groups at different times of the study. The mean of bleeding and the frequency of side effects were higher in labetalol group (P = 0.033 and P < 0.0001, respectively). The median of surgeon satisfaction score in remifentanil group was statistically higher in labetalol group (P < 0.0001). Recovery time, fluid requirement, and pain score in labetalol group reported significantly more than remifentanil group. Richmond Agitation–Sedation Scale status at time points in the postanesthetic care unit showed differences between groups.

Conclusion: With infusion of labetalol and remifentanil after a bolus dose we can induce effective controlled hypotension under general anesthesia. Remifentanil is a short-acting narcotic drug; then, patient satisfaction was better and recovery time was shorter. From the economic aspect, labetalol prefers to remifentanil.

Keywords: Hypotension; Labetalol; Remifentanil; sinus endoscopy

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INTRODUCTION

Bleeding and its control shared by all surgeries. Its importance in major operation in which bleeding volume is large or surgeries that are performed in the limited field with microscope is more visible. Bleeding in sensitive areas such as sinus endoscopic are the main concerns of anesthesia and surgery team.[1] Endoscopy nowadays has found wide medical application, especially in the ear and nose and throat parts. However, bleeding in the area of the surgery led to the reduction in visibility of the surgeon,

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increase in duration of surgery, and reduction of surgery quality. Therefore, to cope with this problem, wide studies have been conducted in various parts of the world, and different methods have been suggested to overcome this problem that creation of controlled hypotension with using different drugs is one of these methods.[2] To create controlled hypotension (reduced systolic blood pressure to 80–90 mmHg or average arterial pressure to 50–60 mmHg) in the category of medications, a variety of drug such as inhaled anesthetics (halothane-isoflurane), vascular expanders (sodium nitroprusside and nitroglycerin), ganglion blockers (trimetaphan camsilate), beta and alpha-adrenergic blockers (phentolamine or labetalol), and the calcium channel blockers (nicardipine) are used. However, simultaneous use of them in some cases is not without risk and can cause a variety of cardiac arrhythmias such as ventricular fibrillation.[3]

Inhaler anesthetics, especially halothane used for this purpose, along with topical vasoconstrictor (epinephrine) injected by the surgeon increase the risk of cardiovascular complications including ventricular and supraventricular arrhythmia so that controlled hypotension has been reported as the fourth most common cause of death during anesthesia in England.[4,5] Therefore, to achieve optimal medication that has features such as ease of prescription, having a predictable effect, being faster the beginning and end of the effect, lack of toxic metabolites and at least impact on blood flow of vital organs is still not possible.[6] So far, various studies have been conducted, and various methods have been proposed while no single theory has been developed to create controlled hypotension.[5,7,8] Labetalol is a nonselective beta agonist that prevents vasoconstriction induced by alpha's receptor. Its overall effect is to reduce dose-dependent systemic resistance and blood pressure without reflex tachycardia to be caused cardiac output to be increased.[7] Remifentanil is among anesthesia drugs used mainly as prodrug to induce and maintain the anesthesia surgery and as an analgesic in anesthesia cares immediately after surgery. In addition, this drug is used in topical anesthesia under control conditions.[1]

As no paper has been used between labetalol and remifentanil in infusion form to create controlled hypotension in surgical operations and because with doses which needed for controlled hypotension, labetalol is cheaper than remifentanil then, the aim of this paper is to compare the two methods of controlled hypotension using labetalol and remifentanil in terms of capability to create controlled hypotension and to investigate the obtained complications, and satisfaction rate of surgeon and patient.

METHODS

In this prospective clinical trial, 62 patients were participated. They underwent endoscopic sinus surgery under general anesthesia in AL-Zahra and Ayatollah Kashani Hospitals of Isfahan. Patients aged 15–65 years, the American Society of Anesthesiologist (ASA) I, II, who undergoing microsurgery with sinus endoscopic, nonuse of beta blockers, absence of heart diseases such as stable congestive heart failure and severe bradycardia (heart rate [HR] ≤60) and high blood pressure and lack of drug susceptibility were included in the study and Patients with these characteristics were excluded from the study: Changes method of surgery and anesthesia, surgery canceling, lack of follow up to the end of the study, drug susceptibility, patients who required blood transfusion. The sample size was estimated 34 patients, using the formula sample size to compare two means and by considering the confidence level of 95% ($Z_{1-a/2} = 1.96$), test power of 80% ($Z_{1-b} = 0.84$), the standard deviation of the mean arterial pressure (MAP) in patients underwent surgery that was considered 1.17, and the least significant difference between the two groups that was considered 0.8. This sample size was calculated based on a pilot study in the beginning of our project. Patients were assigned between two groups in which type and method of anesthesia were the same. Patients were divided into two groups: in the first group, at first, a bolus dose of labetalol (20 mg within 2 min in the supine position, this doses and speed of injection was selected according to labetalol intravenous usage policy for hypertension crisis), was injected; then, infusion of labetalol 0.5–2.0 mg/min with using syringe pump was prescribed until we received a suitable response or maximum dose of 300 mg. In the second group, remifentanil with dose of 0.5–1 μg/kg was started and then with a syringe pump of 0.25–0.5 μg/kg/min was injected until we received a suitable response (80–90 mmHg systolic blood pressure and 50–60 mmHg mean arterial blood pressure). The day before sinus endoscopic surgery, patients underwent preoperative anesthesia visit, and they went to operation room in nothing per oral (NPO) way. After obtaining informed consent, patients in two equal groups went randomly under capnography, electrocardiographic monitoring, blood pressure, saturation of arterial oxygenation (SaO_2), and heart rate. Patients went equally under the induction of anesthesia from sodium thiopental 5 mg/kg, atracurium 0.5 mg/kg, and fentanyl 2 μg/kg. The rest of surgery was conducted using isoflurane 1–1.5%, with 50% nitrous oxide in oxygen, and morphine 0.15 mg/kg. Mechanical ventilation was kept with a tidal volume of 10 ml/kg and respiratory

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rate so that end-tidal carbon dioxide ($ETCO_2$) = 35–40 was kept. Fluid therapy of patients since NPO time was calculated with using the 4.2.1 formula and was given with 1/3, 2/3 serum at room temperature. Intraoperative fluid therapy was given to patients at a dose of 6 ml/kg of normal saline at temperature equivalent to operation room temperature, and each 1 ml of blood loss is compensated with 3 ml of normal saline during surgery. If bleeding volume reaches to maximum allowable blood loss and need for transfusion, the patient was excluded from the study. The total volume of fluids in each patient was calculated and recorded. In addition, the total volume of blood was collected, and it was included to questionnaire. In both groups, diastolic and systolic blood pressure, HR, and arterial oxyhemoglobin saturation (SPO_2) before the induction of anesthesia, immediately after drug prescription, after intubation, and then every 10 min until the end of the surgery measured and recorded. In addition, these parameters were measured and recorded in the postanesthetic care unit (PACU) every 15 min. The mean intraoperative blood loss volume in ml was calculated based on the blood volume within the suction. Surgeon satisfaction was measured based on the 5 Likert scale. Duration of surgery and duration of anesthesia time (from induction to patient's extubation) were calculated. Stay in recovery time from the extubation of patient to meet the exclusion criteria based on the modified aldrete scale was calculated. Modified aldrete scale and level of sedation of patients in the PACU were calculated based on the Richmond Agitation–Sedation Scale (RASS) score every 15 min after extubation. Intraoperative complications included lower systolic blood pressure (≤80–90 mmHg and mean lower than 50–60 mmHg, bradycardia HR ≤60 beats/min and tachycardia HR ≥100 beats/min, SaO_2 ≤90% as well as any arrhythmia, nausea and vomiting were recorded. In addition, in the PACU systolic blood pressure drop <80 mmHg, arrhythmia and ischemia symptoms and the rate of bleeding were evaluated and recorded. The additional drug in the form of 50 microgram bolus of fentanyl was used during the surgery based on HR higher than 100 beats/min or blood pressure increase more than 20% of the basal value acutely and suddenly. It was repeated if needed. This additional dose of drug was calculated, and it was compared in two groups. The additional dose of nitroglycerin at the rate of 50–100 μg was given as a bolus dose, in the case of lack of providing controlled hypotension. It was repeated if needed. This additional dose of nitroglycerin was calculated at total, and it was compared in two groups. Additional doses of ephedrine were given 5 mg as bolus dose based on the sudden drop in blood pressure (systolic blood pressure lower than 80 mmHg). It was repeated if needed. This additional dose of ephedrine was calculated and compared between the two groups. Data were analyzed using IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp). Statistical tests of *t*-test student, one-way analysis of variance (ANOVA), Chi-square, Mann–Whitney test, and ANOVA were used for statistical analysis by repeating the observations.

RESULTS

Figure 1 shows the profile of the study, nine patients of 77 reviewed patients did not enter to the study because five patients refused informed consent and four patients were not eligible. Sixty-eight eligible patients randomly assigned into two intervention groups. During the study, one patient in remifentanil group due to drug allergy, and five patients in labetalol group due to drug allergy (two patients) and intraoperative blood transfusion (three patients) were excluded from the study. Finally, 33 patients in Remifentanil group and 29 patients in labetalol group completed the study and analyzed. Table 1 shows baseline characteristics of studied patients calculated by independent sample *t*-test or Chi-square test. No significant differences were noted between groups for age, sex, weight, and ASA status ($P > 0.05$). Table 2 shows compare of the studied variables during surgery between groups calculated by independent sample *t*-test or repeated measurements of ANOVA. As shown, systolic blood pressure in all time points in both groups was similar and also no significant differences were noted in its trend. Diastolic blood

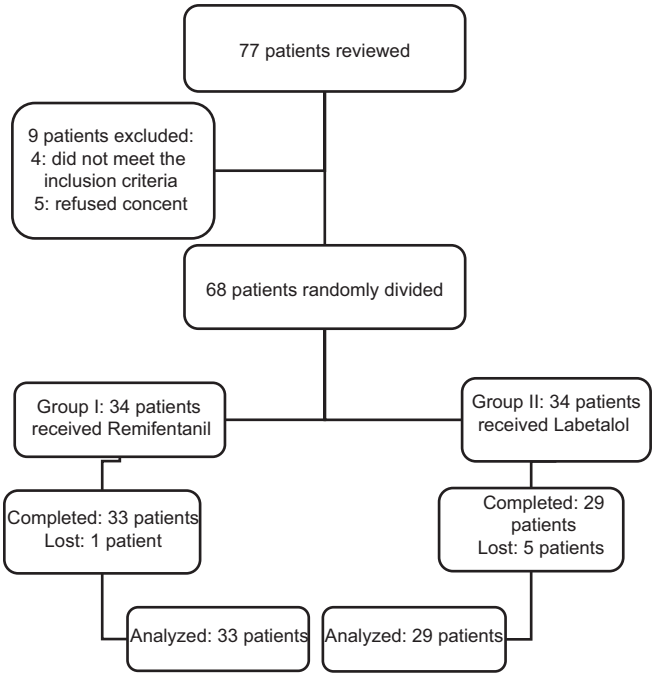

Figure 1: Study flowchart

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Table 1: Baseline characteristics between studied groups

Patients characteristics	Remifentanil group (*n*=33)	Labetalol group (*n*=29)	*P*
Age	36.36±12.35	34.34±10.91	0.5*
Sex			0.79†
Male	14 (42.4)	14 (48.3)	
Female	19 (57.6)	15 (51.7)	
Weight	70.44±13.23	68.35±10.38	0.54*
ASA status			0.35†
I	27 (81.8)	21 (72.4)	
II	6 (18.2)	8 (27.6)	

Data are presented as mean±SD, or *n* (%), where applicable. *P* value calculated using *Independent sample *t*-test or †Chi-square test. SD=Standard deviation, ASA=American Society of Anesthesiologist

pressure after induction in remifentanil group was significantly more than labetalol group, but in other time points and its trend were similar and no significant differences were noted. The MAP in time points in both groups was not significantly different. In addition, the trend of MAP was not significant. The mean of HR and SaO_2 in all time points in both groups was similar, and no significant differences were noted between groups. In addition, the trend of HR and SaO_2 were not significant between groups. The mean of $ETCO_2$ before induction and after intubation in Labetalol group was significantly more than in remifentanil group also, the trend of $ETCO_2$ between studied groups was statistically significant, however, after controlling the values before and after induction and intubation as covariates, the trend of $ETCO_2$ between studied groups was not statistically significant.

Results to compare studied variables every 10 min in 1st h at recovery room are calculated by independent sample *t*-test or repeated measurements of ANOVA and reported in Table 3. Systolic blood pressure in min 60 in labetalol group was significantly more than remifentanil group. Diastolic blood pressure at min 10 and min 20 in remifentanil group was significantly more than labetalol group. MAP, HR, and SaO_2 in all time points in both groups were similar, and no significant differences were noted between groups. Repeated measurements of ANOVA showed that the trend of systolic and diastolic blood pressure, MAP, HR, and SaO_2 at recovery room were not statistically significant between groups ($P > 0.05$). Table 4 shows findings of studied variables and side effects during surgery between groups calculated using independent sample *t*-test, Chi-square test, or Mann–Whitney test. Duration of anesthesia and surgery were similar in both groups ($P > 0.05$). The mean of the fluid requirement in patients in labetalol group was more than remifentanil group but was not statistically significant. The mean of bleeding in labetalol group was 295.2 cc which was significantly more than 225 cc in remifentanil group ($P = 0.033$). Morphine dose was similar in both groups, but fentanyl dose in labetalol group was significantly more than remifentanil group. The frequency of side effects in labetalol group was significantly more than remifentanil group ($P < 0.0001$). In labetalol group, 17 patients had bleeding but in remifentanil group, only one patient had bleeding as side effect ($P < 0.0001$). The frequency of hypotension and bradycardia between groups was similar. Surgeons in remifentanil group were more satisfied during surgery. The median of surgeon satisfaction score in remifentanil group was 5, and in labetalol group was 3 ($P < 0.0001$).

Table 5 shows findings of studied variables and side effects at recovery room between groups calculated using independent sample *t*-test, Chi-square test, or Mann–Whitney test. Recovery time in labetalol group was significantly more than remifentanil group ($P = 0.007$). The use of narcotic in labetalol group was significantly more than remifentanil group ($P = 0.07$), but dose of the narcotic was not statistically significant between groups. The fluid requirement in labetalol group was significantly more than remifentanil group ($P < 0.0001$). Side effects in labetalol group were significantly more occurred than remifentanil group ($P < 0.0001$). The frequency of nausea and hypotension in labetalol group was significantly more than remifentanil group ($P < 0.0001$). Vomiting was similar between groups. The mean of Aldrete score was similar between groups. Pain score in labetalol group reported significantly more than remifentanil group ($P < 0.0001$). The severity of nausea and vomiting in labetalol group reported significantly higher than remifentanil group ($P < 0.0001$).

RASS status at time points was assessed using Chi-square test and results showed in Figure 2. As shown that at recovery room at first, min 15, min 75, min 90, and min 120 frequency of RASS was similar and no significant differences were noted between groups ($P > 0.05$). At min 30, min 45, and min 60, majorities of the patients in remifentanil group were alert and calm, whereas in labetalol group, some of the patients were drowsy and the differences between groups for the frequency of RASS status were statistically significant ($P < 0.05$).

DISCUSSION

Controlled hypotension is commonly used to decrease intraoperative blood loss and avoid transfusions and is essential for endoscopic sinus surgery under general anesthesia to provide better surgical field condition and decreased important complications

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Table 2: Comparison of studied variables during surgery at time points between groups

Variable	Group	Time points										*P**	*P***
		Before induction	After induction	After intubation	Min-10	Min-20	Min-30	Min-40	Min-50	Min-60	Min-70		
Systolic BP	R	131.8±25.1	120.6±30.1	130.4±33.9	105.3±18.5	93.3±15.6	88.3±16.3	84.5±9.1	83.3±9.4	81.1±9.3	82.9±10.3	0.24	0.65
	L	126.9±17.7	106.9±22.3	116±23.4	101.1±15.3	90.8±12.7	87.8±9.9	84.2±11.8	86.2±10.2	74.7±9.9	85.2±7.3		
	P†	0.61	0.053	0.07	0.26	0.41	0.67	0.85	0.41	0.27	0.34		
Diastolic BP	R	83.4±14.9	75.7±19.3	83.2±23.3	64.2±16.6	58.3±17.1	53.6±15.4	49.3±7.8	49.6±8.3	47±7.8	49±9.8	0.08	0.59
	L	78.3±9.5	62.8±14.3	71.5±16.9	60.5±13.7	51.8±10.8	51.9±9.8	49±11.8	48.2±10.2	47.7±9.6	50.6±11.9		
	P†	0.15	0.004	0.03	0.24	0.88	0.91	0.72	0.79	0.77	0.61		
MAP	R	92.5±23.1	84.6±22.9	93.9±25.8	71.7±15.7	64.4±14.1	62.4±14.2	59±7.2	59.2±7.9	57.2±6.3	61±9.6	0.41	0.84
	L	91.2±17	75.8±15.8	85±20.9	73.8±13.9	63.7±10.4	62±9.1	58.7±9.7	58.2±8.9	57.6±9	62.1±9.3		
	P†	0.77	0.07	0.19	0.78	0.3	0.53	0.68	0.58	0.96	0.53		
HR	R	83.8±12.8	85.7±16.2	86.2±16.4	74.8±14.3	70.5±13.7	69.5±11.4	68.9±11.9	67.5±11.9	68.7±11.4	70.7±13.7	0.11	0.059
	L	85±13	91.2±21.6	88.8±15.1	76.8±13.3	76.7±13.3	76.1±13.6	71.1±17.5	73.1±13.8	75.3±10.7	77.8±12.1		
	P†	0.81	0.31	0.63	0.98	0.35	0.07	0.84	0.44	0.07	0.05		
SPO_2 (%)	R	97.9±2.1	98.4±1.7	98.6±2	99.2±0.9	99.3±1	99.4±0.8	99.3±0.9	99.3±0.9	99.7±2.2	99.4±0.9	0.22	0.28
	L	94.1±17.5	98.3±2.2	99±1.4	98.7±2.9	98.7±2.9	98.2±5.4	98±6.5	99.7±6.9	98±6.7	98.8±3		
	P†	0.23	0.64	0.58	0.31	0.24	0.22	0.3	0.19	0.22	0.36		
$ETCO_2$	R	30.7±2.3	30.8±2.3	31±2.5	31.4±2.3	31.6±2.3	31.6±2.6	32.3±2.4	32.4±2.4	32.6±2.2	34.4±1.1	0.016	0.92
	L	33.8±3.2	33.2±3	33.8±2.5	33.3±2.7	33.4±2.7	33.6±2.8	33.6±2.4	33.9±2.9	34.1±2.8	34.9±3.1		
	P†	0.002	0.18	0.035	0.16	0.08	0.07	0.056	0.05	0.1	0.15		

Data are presented as mean±SD. *P* value calculated using †Independent sample *t*-test, *Repeated measurements of ANOVA, and **Repeated measurements of ANOVA after controlling baseline values (induction and intubation values). SD=Standard deviation, R=Remifentanil, L=Labetalol, BP=Blood pressure, MAP=Mean arterial pressure, HR=Heart rate, SPO_2=Arterial oxyhemoglobin saturation, $ETCO_2$=End-tidal carbon dioxide, ANOVA=Analysis of variance

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Table 3: Comparison of studied variables in recovery room at time points between studied groups

Variable	Group	Time points						*P**
		Min-10	Min-20	Min-30	Min-40	Min-50	Min-60	
Systolic BP (mmHg)	R	108.8±24.9	108.2±30.6	104.9±31.2	103.8±30.4	102.8±32.4	100.9±32.3	0.63
	L	102.1±20	98.8±19.1	97±23.2	93.1±25.2	98±22.3	120.3±14.6	
	P†	0.19	0.15	0.49	0.29	0.87	0.007	
Diastolic BP (mmHg)	R	70.6±15	69.3±18.7	69.1±20	68.8±23.3	68.1±22.7	68.8±22.8	0.16
	L	60.7±15.8	60.8±14.2	59.4±17.6	57.2±18.8	61.6±18	74.4±8.4	
	P†	0.012	0.036	0.16	0.11	0.45	0.23	
MAP	R	81.3±19.6	85.1±26.6	82.7±25.8	80.9±23.4	79.8±24.6	77.4±24.2	0.33
	L	75.6±18.4	73.4±14.7	72.8±19.1	70.4±21.3	73.5±17.9	88.3±10.7	
	P†	0.13	0.036	0.17	0.15	0.56	0.04	
HR	R	82.6±14.1	85±18.1	82.6±17.8	79.9±14.9	81.8±14.9	79.9±11.4	0.25
	L	78.8±13.5	78.3±12.7	76.8±10.8	73.8±11.4	77.4±10.3	81.9±11.4	
	P†	0.17	0.16	0.17	0.17	0.2	0.52	
SPO_2 (%)	R	98.5±2	98±2.1	97.6±2.1	97.4±2.8	97.1±3.6	97.2±3.9	0.12
	L	98.7±1.2	98.6±1.5	98.7±1.5	98.5±2.1	98.5±2	98.3±1.8	
	P†	0.92	0.32	0.09	0.12	0.07	0.14	

Data are presented as mean±SD. *P* value calculated using †Independent sample *t*-test and *Repeated measurements of ANOVA. SD=Standard deviation, R=Remifentanil, L=Labetalol, BP=Blood pressure, MAP=Mean arterial pressure, HR=Heart rate, SPO_2=Arterial oxyhemoglobin saturation, $ETCO_2$=End-tidal carbon dioxide, ANOVA=Analysis of variance

Table 4: Comparison of studied variables during surgery between studied groups

	Remifentanil group	Labetalol group	*P*
Duration of anesthesia	117.2±50.7	125.7±44.8	0.49*
Duration of surgery	95.6±50.9	108.6±42.7	0.49*
Transfusion	1 (3)	0	0.55†
Fluid requirements	953.1±312.1	1086.2±346.1	0.12*
Bleeding	225±95.9	295.2±151.7	0.033*
Morphine dose	9.7±2.3	9.9±2.2	0.7*
Fentanyl dose	183.9±96.9	280.7±144.7	0.003*
Nitroglycerin dose	166.6±115.5	184.6±108.4	0.79*
Side effects	3 (11.5)	23 (88.5)	<0.0001†
Bleeding	1 (3)	17 (58.6)	<0.0001†
Hypotension	1 (3)	5 (17.2)	0.08†
Bradycardia	1 (3)	1 (3.4)	0.72†
Surgeon satisfaction score	5 (4-5)	3 (2-4)	<0.0001**

Data are presented as mean±SD, median (IQR), or *n* (%), where applicable. *P* value calculated using *Independent sample *t*-test, †Chi-square test, and **Mann-Whitney U-test. SD=Standard deviation, IQR=Interquartile range

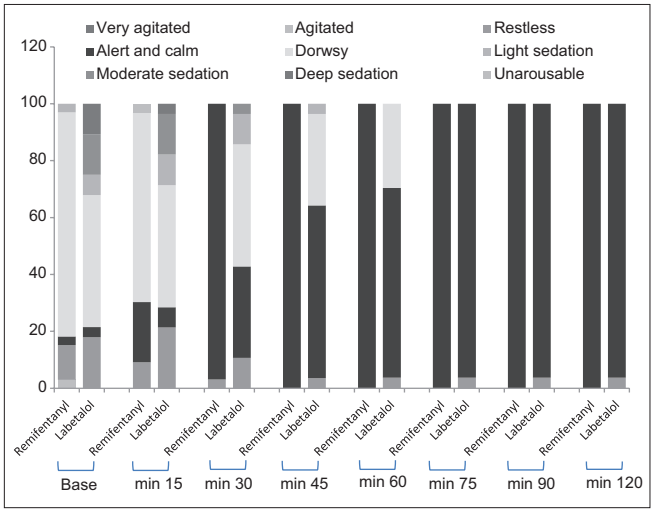

Figure 2: Comparison of the Richmond Agitation-Sedation Scale at time points between study groups. The frequency of sedation status at base and min 30, 45, and 60 were significantly different between groups

such as severe bleeding.[9,10] Remifentanil and labetalol the two anesthetic drugs that are used in anesthesia during endoscopic sinus surgery to controlled hypotension and providing the better field of operation, but no comparative study has been performed on the use of remifentanil or labetalol for controlled hypotension during endoscopic sinus surgery. The present study was designed to assess the efficacies of labetalol and remifentanil in terms of postoperative analgesia and other complications during and after controlled hypotension for in endoscopic sinus surgery. Controlled hypotension is defined as a reduction of the systolic blood pressure to 80–90 mmHg or reduction of MAP to 50–65 mmHg.[11] Both labetalol and remifentanil were effective to induce CH with similar hemodynamics during surgery and recovery, but findings in the present study revealed that bleeding and side effects during surgery in remifentanil group were lower than labetalol group. In addition, surgeons in remifentanil group were significantly more satisfied than surgeons in labetalol group. Other findings revealed that in remifentanil group at recovery time, use of narcotic, fluid requirement, side effects, and pain score was significantly lower than labetalol group. In our

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Table 5: Comparison of studied variables at recovery room between studied groups

	Remifentanil group	Labetalol group	*P*
Recovery time	75.2±29.3	93.4±20.0	0.007*
Narcotic usage	9 (27.3)	14 (48.3)	0.07†
Dose of narcotic	36.4±30.1	30.7±12.4	0.52*
Dose of ondansetron	5.0±1.8	11.0±12.1	0.48*
Fluid requirements	363.3±124.5	489.3±225.4	0.013*
Side effects	3 (9.1)	19 (65.5)	<0.0001†
Nausea	3 (9.1)	18 (62.1)	<0.0001†
Vomiting	0	1 (3.4)	0.47†
Hypotension	0	11 (37.9)	<0.0001†
ALdrete score	9.7±1.0	10.0±0	0.086*
Pain score (VAS)	2 (1.5-2)	2 (2-4)	<0.0001**
Nausea and vomiting (VAS)			<0.0001†
None	30 (96.8)	9 (31)	
Mild	1 (3.2)	18 (62.1)	
Moderate	0	2 (3.3)	

Data are presented as mean±SD, median (IQR), or *n* (%), where applicable. *P* value calculated using *Independent sample *t*-test, †Chi-square test, and **Mann-Whitney U-test. SD=Standard deviation, IQR=Interquartile range, VAS=Visual analog scale

study, patients who received Labetalol had more recovery time with more side effects than patients who received remifentanil. This can be explaining by higher number of patients in labetalol group who received additional doses of narcotic. This study showed that use of labetalol for induced hypotension is comparable with remifentanil and also from the economic aspect labetalol is better.

Several anesthetic drugs have been studied with respect to the intraoperative conditions for the ENT-surgeons. Remifentanil as an ultra-short-acting l-opioid receptor agonist appears to provoke mild to moderate hypotension and bradycardia. Moreover, the effectiveness of remifentanil in compare to different opioids is assessed in several previous studies and although they had similar effects on achieving a bloodless surgical area, remifentanil had better short-act. A randomized, double-blind clinical trial to compare surgical field bleeding during endoscopic sinus surgery with clonidine-based or remifentanil-based hypotensive anesthesia was done by Cardesín *et al*.[12] Bleeding and the duration of surgery and anesthesia in this study was similar between clonidine and remifentanil, but authors concluded that the use of clonidine-based controlled hypotensive anesthesia achieves lower surgical field bleeding during endoscopic sinus surgery compare to remifentanil. In a study by Özcan *et al*., the effects and possible side effects of remifentanil and dexmedetomidine for controlled hypotension in during functional endoscopic sinus surgery are evaluated. In this study, operation time, duration of anesthesia and controlled hypotension time, SpO_2, and arterial blood pressure were similar in both remifentanil and dexmedetomidine groups, but recovery time in dexmedetomidine group was significantly longer than remifentanil group. Özcan *et al*. concluded that dexmedetomidine and remifentanil provided safe, controlled hypotensive anesthesia in patients undergoing functional endoscopic sinus surgery with a significantly lower recovery time in remifentanil infusion.[13] Other study by Yun *et al*. compared the effects of nitroprusside and remifentanil on hemodynamics for endoscopic sinus surgery. The conclusion of Utting JE study is that nitroprusside and remifentanil were effective to induce controlled hypotension in patients undergoing endoscopic sinus surgery with general anesthesia.[6] Lee *et al*. study reported that remifentanil and dexmedetomidine both enabled hypotensive anesthesia and good intraoperative fields for endoscopic sinus surgery although in postoperative period remifentanil shows faster recovery.[14] In a study by Wu, the clinic efficacy of compound-induced hypotension during functional endoscopic sinus surgery is evaluated. In this study, sodium nitroprusside alone and in combination with diltiazem or labetalol were used to induce hypotension during surgery. Results of this study show that induced hypotension with sodium nitroprusside compound of diltiazem or labetalol is an ideal way in the clinical use and produce satisfied synergistic effect.[15] Esmolol which is a β-adrenoreceptor antagonists like labetalol in a placebo-controlled trial is used to induced hypotension during endoscopic sinus surgery. Esmolol was better than saline to control HR, blood pressure, and improved surgical fields.[16] As shown, the studies have reported the efficacy of anesthetic agents inducing controlled hypotension and an ability to ensure a satisfactory operative field but there no comparative report about remifentanil and labetalol, so, to the best of our knowledge, the present study is the first study to assess the efficacy of remifentanil and labetalol induced hypotension during endoscopic sinus surgery. Our findings show the similar positive effects on hemodynamics during surgery and recovery, but remifentanil had better condition during surgery and recovery.[17] All these findings show that, however, remifentanil had similar effects on hemodynamics compare to different anesthetic agents but reported that remifentanil as an opioid with the shortest onset and offset due to its metabolism by a specific tissue and plasma esterase and have better surgical field condition.

Limitation of our study was about the limitation for increases of labetalol doses above the determined

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doses, if we did not achieve suitable responses because of long action of labetalol on cardiovascular and delay hypotension. We use nitroglycerin multiple doses if we need for desirable hypotension, to overcome this limitation.

Remifentanil and labetalol were effective to induce controlled hypotension in patients undergoing endoscopic sinus surgery with similar effects on hemodynamics. However, during surgery and at recovery time remifentanil was more efficient in compare to labetalol to improve bleeding, surgeons' satisfaction, lower side effects, use of narcotic, fluid requirement, pain score, and provide better surgical field condition. We recommended the use of labetalol infusion after bolus doses, for induced hypotension. Its properties are comparable with remifentanil and from the economic aspect, it prefers to remifentanil.

AUTHORS' CONTRIBUTION

P.S. contributed in the conception and design of the work, interpretation of data, revising of the draft and Final approval of the version to be published and agreed for all aspects of the work, A.R. and G.K. contributed to design of the work, acquisition, Drafting the work and Final approval of the version to be published.

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Conflicts of interest

There are no conflicts of interest.

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