

ORIGINAL RESEARCH

ANESTHESIOLOGY

Comparison of two different doses of intravenous remifentanil on cardiovascular response to endotracheal intubation: a randomized controlled trial

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Abstract

Background & Objectives: Endotracheal intubation is one of the most potent stimuli as an integral part of general anesthesia with several risks such as a sudden increase in blood pressure and pulse rate. One of the drugs that can be used to prevent hemodynamic spikes in endotracheal intubation is remifentanil. It has rapid onset and peak effect with short duration of action. Various authors have used different doses of this drug. We compared the effect of two different doses of remifentanil on hemodynamic response to endotracheal intubation.

Methodology: It was a randomized clinical trial on 35 patients, aged 19-65 y, physical status ASA I-II, body mass index (BMI) 18.5-29.99 kg/m², who underwent elective surgery under general anesthesia. Subjects were randomly assigned into 2 groups, Group R1, who received remifentanil 0.5 µg/kg intravenously (IV), followed by an infusion @ 0.1 µg/kg/min; and Group R2, who received remifentanil 1 µg/kg followed by 0.1 µg/kg/min intravenously. Systolic, diastolic and mean arterial pressure, and pulse rates were noted on arrival in the operating room T₀, then measurements were performed 2 min after induction (T₁), 1 min after intubation (T₂), and continued at 3 and 5 min after intubation (T₃ and T₄). The data was analyzed with SPSS v21.0 for Windows. T-test or Mann-Whitney U test was performed to analyze the data.

Results: Based on this study, the hemodynamic parameters were significantly lower in systolic blood pressure (113.35 ± 4.66 vs. 107.83 ± 6.37, P = 0.008), diastolic blood pressure (68.88 ± 4.22 vs. 61.83 ± 4.22, P = 0.004), mean arterial pressure (83.76 ± 4.22 vs. 77.28 ± 5.84, P = 0.001) and pulse rate (83.71 ± 8.20 vs. 76.11 ± 9.70, P = 0.013) after 1 min of endotracheal intubation in the remifentanil 1 µg/kg group compared to the 0.5 µg/kg remifentanil group.

Conclusion: Administration of remifentanil 1 µg/kg followed by maintenance of 0.1 g/kg/min can cause a statistically significant decrease in blood pressure and heart rate compared to remifentanil 0.5 µg/kg followed by maintenance of 0.1 µg/kg/min, when administered for endotracheal intubation.

Abbreviation: BMI: body mass index; IV: intravenously; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean arterial blood pressure;

Key words: Endotracheal intubation; Hemodynamic insult; Remifentanil

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1. Introduction

Laryngoscopy and endotracheal intubation are one of the most painful stimuli as an integral part of general anesthesia.^{1,2} The response to laryngoscopy and intubation is a sympathetic reflex associated with an acute hemodynamic response that may last for approximately 10 min,^{2,3} with a potential to cause morbidity and mortality.⁴⁻⁷ Patients with hypertension and cardiovascular disease may experience myocardial ischemia, acute heart failure, pulmonary edema, arrhythmias, or cerebrovascular hemorrhage.^{1-3,4,8}

Therefore, preventive measures to reduce sympathoadrenal response caused by laryngoscopy and endotracheal intubation are important in general anesthesia. Opioids are the most widely used drugs to prevent hemodynamic spikes during intubation with satisfactory results.^{1,3,8-10} Remifentanil has rapid onset of action, short duration of action, constant context-sensitive half-life, rapid metabolism, and drug elimination.¹¹⁻¹³ The recommended dose range of remifentanil required to blunt cardiovascular response to intubation is 3–4 µg/kg without muscle relaxants and 0.5–2 µg/kg with muscle relaxants.¹⁰ Maintenance use of remifentanil during general anesthesia requires an effect site (Cet) of 3–10 ng/ml or about 0.1–0.3 µg/kg/min. Maintenance is generally given to maintain the effective plasma concentration of remifentanil because of the context sensitive half time, which is around 3 min; therefore, a single bolus administration of remifentanil is unable to maintain effective blood concentrations and achieve hemodynamic stability for some time after intubation.^{5,13} Higher doses of remifentanil increase the risk of hypotension and bradycardia by up to 50%.⁵ The analgesic effect of remifentanil effectively reduces the hemodynamic response to laryngoscopy and endotracheal intubation. Remifentanil is also known to have an inhibitory effect on stress response by inhibiting the secretion of norepinephrine and glucocorticoids.¹⁴

Increasing remifentanil dose to more than 1 µg/kg conferred only minimal additional advantage but was associated with increased risk of hypotension and bradycardia.¹⁵ Another study showed that a bolus dose of remifentanil 0.5 µg/kg followed by maintenance dose of 0.1 µg/kg/min was effective in suppressing the hemodynamic response to laryngoscopy and intubation with the incidence of mild hypotensive side effects in almost 50% of patients.^{13,16} Subsequent studies showed that the incidence of hypotension was less in 0.5 µg/kg compared to higher dose but the pulse rate was higher.¹⁷

We aimed to compare the effect of two different doses of remifentanil on hemodynamic response to endotracheal intubation.

2. Methodology

The study was conducted at the Central Operating Theater of Hasan Sadikin General Hospital during March–July 2021, after obtaining approval from the Health Research Ethics Committee of Hasan Sadikin General Hospital (Number LB.02.01/X.6.5/006/2021). It was a double blind randomized controlled trial comparing the hemodynamic effects with two different doses of remifentanil associated with endotracheal intubation.

The inclusion criteria for this study were patients with American Society of Anesthesiologists (ASA) physical status categories I–II, aged 19–65 y, and had a body mass index (BMI) between 18.5 and 29.99 kg/m². The exclusion criteria for this study were pregnant ladies, patients suffering from cardiovascular disorders, those taking drugs that affect blood pressure and pulse rate, patients who received sedatives, opioids, and analgesics in the last 24 h, and patients with difficult airway assessed using the Mallampati score. The drop-out criteria for the study were patients requiring more than 1 attempt at laryngoscopy and endotracheal intubation, patients requiring more than 45 sec for successful laryngoscopy and intubation, and patients who showed symptoms of allergic reaction to drugs used during intubation.

The sample size was calculated to test the difference between the two means of blood pressure and pulse rates by selecting the 95% confidence level ($\alpha = 0.05$) and the 80% power of the test; considered significant if the $P < 0.05$. The minimum sample size calculated was 17 subjects per group with a total of at least 34 subjects for two groups. The selection of research subjects was based on convenient sampling. The patients were allocated to the groups based on randomization table.

Informed consent was obtained from every patient. The study subjects were divided into 2 groups, namely the group receiving a bolus dose of remifentanil 0.5 µg/kg followed by remifentanil 0.1 µg/kg/min (Group R1), and the group receiving a bolus dose of remifentanil 1 µg/kg followed by 0.1 µg/kg/min maintenance (Group R2). The demographic characteristics of the patients were collected including age, body mass index and ASA physical status.

Drug preparation was carried out in the pharmacy section of the Center Operating Theater. Each drug was divided into 2 preparations, namely bolus and maintenance in 50 ml syringes. The bolus preparation of remifentanil 0.5 µg/kg was diluted in a 50 ml syringe into a 2.5 µg/ml concentration and administered at a dose of 0.2 ml/kg in 1 min using a syringe pump. The bolus preparation of remifentanil 1 µg/kg was diluted in a 50 ml syringe into a 5 µg/ml preparation and administered at a dose of 0.2

ml/kg in 1 min using a syringe pump. The maintenance preparation of remifentanil 0.1 µg/kg/min was diluted in a 50 ml syringe into a 5 µg/ml preparation and administered at a dose of 0.02 ml/kg/min using a syringe pump.

All patients were fasted for at least 6 h prior to surgery, had an IV line installed and received maintenance fluids before entering the operating room. The patients were infused with fasting fluid replacement and brought to the operating room. Routine noninvasive hemodynamic monitoring, e.g., non-invasive blood pressure, ECG, and oximeter were installed and systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and pulse rate were recorded as baseline data (T₀).

The patient was preoxygenated with a face mask, using 100% oxygen for 5 min. Then the study drugs were injected. The loading dose of remifentanil in both groups were injected in 60 sec, followed by a maintenance dose using a syringe pump. It was followed by a bolus of propofol 2 mg/kg body weight in 30 sec. After the patient lost consciousness and we managed to control the airway, atracurium 0.5 mg/kg body weight was given IV.

Direct laryngoscopy and endotracheal intubation were performed by an experienced anesthesiologist using a Macintosh laryngoscope blade and an appropriately sized endotracheal tube in one attempt. If the pulse rate fell to < 40 beats/min, atropine sulfate 0.5 mg IV was given. If blood pressure fell for more than 30%, a vasopressor (ephedrine 5–10 mg) was given. Anesthesia was maintained using isoflurane and 50% oxygen in air at a flow rate of 3 L/min.

Hemodynamic measurements were performed 2 min after induction (T₁), 1 min after intubation (T₂), and continued at 3 and 5 min after intubation (T₃ and T₄). Then the surgery was initiated.

Statistical analysis

An independent T test was performed on numerical data to compare the mean difference of two treatment groups if the data were normally distributed. Otherwise Chi-square test was performed on categorical data. Mann-Whitney U test was performed if these conditions were not met. The Kolmogorov-Smirnov test was performed by comparing the distribution of normally distributed data. Calculations and statistical analyses were carried

Table 1: Comparison of the subjects' characteristics between two groups

Variable	Group R1 Remifentanil 0.5 µg/kg (n = 17)	Group R2 Remifentanil 1 µg/kg (n = 18)	P
Age	35.82 ± 10.99	36.11 ± 9.41	0.934
Weight (kg)	57.47 ± 6.59	54.28 ± 7.63	0.284
Height (cm)	157.35 ± 6.15	155.50 ± 9.01	0.284
BMI (kg/m ²)	23.22 ± 2.33	22.40 ± 2.12	0.219
Mallampati score			
1	4 (23.5)	6 (33.3)	0.711
2	13 (76.5)	12 (66.7)	
ASA			
1	9 (52.9)	11 (61.1)	0.625
2	8 (47.1)	7 (38.9)	
Time for laryngoscopy and intubation (sec)	29.59 ± 8.993	28.06 ± 8.815	0.614

*Data presented as Mean ± SD or n (%) For numerical data, the P-value was obtained from unpaired T-test because the data were normally distributed. While for categorical data, P-value was calculated based on the Chi-Square test with Kolmogorov Smirnov test and Fisher's Exact alternatively if the requirements for Chi-Square were not met. The data was considered significant if P < 0.05. * sign indicates P < 0.05, which means statistically significant.*

out with the help of Statistical Product and Service Solution (SPSS) version 20.0 for Windows with a significance level of 5% and was considered significant if P < 0.05.

3. Results

The study was conducted on 35 patients who underwent elective surgery. General characteristics of the study subjects between group R1 and R2 did not show significant differences (Table 1). Therefore, the study subjects were homogeneous and comparable.

There was no difference in the mean SBP between two groups initially. Then in both groups a decrease in SBP was observed after induction (T₁), with a significant difference between Group R1 and R2 (P < 0.05; Table 2). Significant differences between the two groups were found at the time points T₁ and T₃.

There was not a significant difference of DBP between two groups initially. Then both groups experienced a decrease in DBP after induction (T₁), with a significant

Table 2: Comparative hemodynamic parameters between the groups

Variables	Group R1 Remifentanil 0.5 µg/kg (n = 17)	Group R2 Remifentanil 1 µg/kg (n = 18)	p-value
SBP (mmHg)			
T0	132.71 ± 4.28	133.89 ± 3.74	0.386
T1	113.35 ± 4.66	107.83 ± 6.37	0.008*
T2	127.88 ± 5.84	127.56 ± 3.96	0.847
T3	118.18 ± 5.88	112.11 ± 10.08	0.038*
T4	111.35 ± 7.70	108.17 ± 8.79	0.263
DBP (mmHg)			
T0	79.76 ± 4.83	81.33 ± 7.31	0.462
T1	68.88 ± 5.80	61.83 ± 7.66	0.004*
T2	77.59 ± 5.92	76.56 ± 7.71	0.661
T3	70.47 ± 8.32	68.78 ± 10.13	0.369
T4	69.41 ± 7.64	65.06 ± 9.63	0.149
MAP (mmHg)			
T0	97.41 ± 3.52	98.83 ± 5.37	0.364
T1	83.76 ± 4.29	77.28 ± 5.84	0.001*
T2	94.29 ± 5.29	93.72 ± 6.06	0.768
T3	86.35 ± 6.86	83.17 ± 9.50	0.266
T4	83.41 ± 7.32	79.44 ± 8.79	0.157
Heart rate (Beats/min)			
T0	89.71 ± 7.07	88.67 ± 7.97	0.987
T1	83.71 ± 8.20	76.11 ± 9.70	0.013*
T2	87.71 ± 6.91	85.72 ± 9.48	0.660
T3	87.06 ± 13.92	77.17 ± 12.45	0.034*
T4	80.76 ± 13.93	73.06 ± 12.68	0.096

Note: The data analyzed using Mann-Whitney U test if it was not normally distributed and T-test if it was normally distributed. The data was considered significant if $P < 0.05$. The * sign indicates $P < 0.05$, which means statistically significant. T0: initial data; T1: data after induction; T2: 1 min after intubation; T3: 3 min after intubation; T4: 5 min after intubation.

difference between Group R1 and R2 ($P < 0.05$; Table 2).

MAP of Group R1 and R2 did not show any significant difference initially. Then a decrease in MAP occurred in both groups after induction (T1), with a significant difference between group R1 and R2 ($P < 0.05$; Table 2).

Mean heart rates did not show any significant difference between two groups initially. Then it decreased after

induction (T1), with significant differences between Group R1 and R2 at T1 and T3 ($P < 0.05$; Table 2).

4. Discussion

This study was conducted on 35 patients who underwent general anesthesia, and divided into two groups. The subjects' general characteristics including age, weight, height, BMI, Mallampati score, ASA, and time for laryngoscopy and intubation did not have significant differences between the groups initially.

Laryngoscopy and endotracheal intubation are one of the most painful stimuli as an integral part of general anesthesia.^{1,2} The response to laryngoscopy and intubation is a sympathetic reflex associated with an acute hemodynamic response that may last for approximately 10 min.^{2,3} Laryngoscopy and intubation can also cause undesirable pathophysiological effects such as increased intraocular pressure, intracranial pressure, cardiac rhythm disturbances and bronchoconstriction.^{1-3,8} At the time of intubation, several measures can be undertaken to blunt the intubation related hemodynamic response. Opioids are the most widely used drugs in general anesthesia in preventing hemodynamic spikes during intubation with satisfactory results.^{2,3,8-10} The ideal anesthetic drug for obtunding the pressor response should have a rapid onset of action, be safe and easily administered, and have a relatively short duration of action.⁷ Remifentanil is a fast-acting opioid with favorable pharmacokinetic and pharmacodynamic profiles for attenuating pain stimuli and transient and brief hemodynamic responses during laryngoscopy and intubation. Its pharmacokinetic

properties may allow a greater margin of safety given the large individual variability in the amount of drug required to suppress the response to a given stimulus.^{11,12}

Based on the results of the analysis in this study, there was a greater decrease in SBP in remifentanil 1 µg/kg group compared to the 0.5 µg/kg group. These results are consistent with previous study by Park et al. which reported a greater reduction in SBP in administration of remifentanil 1 µg/kg compared to remifentanil 0.5 µg/kg.¹⁸

This study is also in accordance with another study comparing loading doses of remifentanil of 0.5 µg/kg, 1 µg/kg and 2 µg/kg on hemodynamic response during laryngoscopy and intubation, which reported that remifentanil 0.5 µg/kg effectively attenuated the hemodynamic response with lower rates of hypotension compared to remifentanil 1 and 2 µg/kg.¹⁷

In this study, we reported a greater decrease in systolic, diastolic, and MAP in the remifentanil 1 µg/kg group compared to remifentanil 0.5 µg/kg group. This result is similar with previous study comparing placebo and different doses of remifentanil (0.5, 1, and 1.25 µg/kg) which stated that there was a greater decrease in blood pressure at higher remifentanil dose.¹⁵ Another study also reported that the use of remifentanil 1 µg/kg followed by 0.5 µg/kg/min can attenuate hemodynamic response during endotracheal intubation, but with a significant incidence of hypotension.¹⁹

This study showed a greater decrease in heart rate in the remifentanil 1 µg/kg group compared to remifentanil 0.5 µg/kg group. Previous studies stated that administration of a loading dose of remifentanil 1 µg/kg followed by maintenance of 0.5 µg/kg/min could reduce hemodynamic response during endotracheal intubation, but with significant incidence of bradycardia compared to a loading dose of 0.5 µg/kg, followed by maintenance of 0.25 µg/kg/min.¹⁹

Another study that compared control group with remifentanil bolus of 0.5, 1, and 1.25 µg/kg towards hemodynamic response during laryngoscopy and intubation reported that remifentanil bolus of 0.5 µg/kg was effective in attenuating cardiovascular response during laryngoscopy and intubation with lower incidence of bradycardia compared to remifentanil bolus of 1 and 2 µg/kg.¹⁷ This study is also in agreement to another study which showed that bolus of remifentanil at 1 and 1.25 µg/kg can reduce heart rate greater than 0.5 µg/kg at the time of induction and endotracheal intubation.¹⁵

5. Conclusion

Administration of remifentanil 1 µg/kg followed by maintenance of 0.1 g/kg/min can cause a statistically significant decrease in blood pressure and heart rate compared to remifentanil 0.5 µg/kg followed by maintenance of 0.1 µg/kg/min. Remifentanil 0.5 µg/kg followed by maintenance of 0.1 µg/kg/min can be a good choice during induction to attenuate the sympathetic response during laryngoscopy and intubation because it provides hemodynamic stability without causing an excessive drop in blood pressure and pulse rate.

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7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of Interest

No conflict of interest declared by the authors.

9. Authors contribution

All authors took part in the concept, conduction of the study, manuscript writing and editing. All authors have read the manuscript and confirm.

10. References

1. Kanchi M, Banakal S, Murugesan C, Nair H, Murthy K. Haemodynamic response to endotracheal intubation in coronary artery disease: Direct versus video laryngoscopy. *Indian J Anaesth.* 2011;55(3):260. [PubMed] DOI: [10.4103/0019-5049.82673](https://doi.org/10.4103/0019-5049.82673)
2. Valeshabad AK, Nabavian O, Nourijelyani K, Kord H, Vafainejad H, Kord Valeshabad R, et al. Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation: Propacetamol versus lidocaine-A randomized clinical trial. *Anesthesiol Res Pract.* 2014;2014. [PubMed] DOI: [10.1155/2014/170247](https://doi.org/10.1155/2014/170247)
3. Sener EB, Ustun E, Ustun B, Sarihasan B. Hemodynamic responses and upper airway morbidity following tracheal intubation in patients with hypertension: Conventional laryngoscopy versus an intubating laryngeal mask airway. *Clinics.* 2012;67(1):49–54. [PubMed] DOI: [10.6061/clinics/2012\(01\)08](https://doi.org/10.6061/clinics/2012(01)08)
4. Lee SK, Jeong MA, Sung JM, Yeon HJ, Chang JH, Lim H. Effect of remifentanil infusion on the hemodynamic response during induction of anesthesia in hypertensive and normotensive patients: a prospective observational study. *J Int Med Res.* 2019;47(12):6254–67. [PubMed] DOI: [10.1177/0300060519883568](https://doi.org/10.1177/0300060519883568)
5. Park SJ, Shim YH, Yoo JH, Nam SH, Lee JW. Low-dose remifentanil to modify hemodynamic responses to tracheal intubation: Comparison in normotensive and untreated/treated hypertensive Korean patients. *Korean J Anesthesiol.* 2012;62(2):135–41. [PubMed] DOI: [10.4097/kjae.2012.62.2.135](https://doi.org/10.4097/kjae.2012.62.2.135)
6. Kwon SY, Chung SW, Joo JD. Optimal neuromuscular blocking effects of remifentanil during tracheal intubation under general anesthesia. *J Int Med Res.* 2018;46(8):3097–103. [PubMed] DOI: [10.1177/0300060518772227](https://doi.org/10.1177/0300060518772227)
7. Özütürk B, Ersoy A, Altan A, Uygur LM. Comparison of the Effects of Remifentanil and Dexmedetomidine Infusions on Hemodynamic Parameters and Thyroid Hormones. *Turk J Anaesthesiol Reanim.* 2013;41(6):206–10. [PubMed] DOI: [10.5152/TJAR.2013.39](https://doi.org/10.5152/TJAR.2013.39)
8. Altun D, Ali A, Camci E, Ozonur A, Ozkan Seyhan T. Haemodynamic Response to Four Different Laryngoscopes.

- Turk J Anaesthesiol Reanim. 2018;46(6):434–40. [PubMed] DOI: [10.5152/TJAR.2018.59265](https://doi.org/10.5152/TJAR.2018.59265)
9. Koswara Y, Pradian E, Redjeki IS. Perbandingan Pemberian Metoprolol Tartrat dengan Lidokain secara Intravena terhadap Perubahan Tekanan Darah dan Laju Nadi Akibat Tindakan Laringoskopi dan Intubasi. *Jurnal Anestesi Perioperatif*. 2014;2(2):2–31. [PubMed]
 10. Mireskandari SM, Abulahrar N, Darabi ME, Rahimi I, Haji-Mohamadi F, Movafegh A. Comparison of the effect of fentanyl, sufentanil, alfentanil and remifentanil on cardiovascular response to tracheal intubation in children. *Iran J Pediatr*. 2011;21(2):173–80. [PubMed]
 11. Devabhakthuni S. Efficacy and Safety of Remifentanil as an Alternative Labor Analgesic. *Clin Med Insights Womens Health*. 2013;6:37-49. [PubMed] DOI: [10.4137/CMWH.S8015](https://doi.org/10.4137/CMWH.S8015)
 12. Barclay K, Kluger MT. Effect of bolus dose of remifentanil on haemodynamic response to tracheal intubation. *Anaesth Intensive Care*. 2000;28(4):403–7. [PubMed]
 13. Ko BJ, Oh JN, Lee JH, Choi SR, Lee SC, Chung CJ. Comparison of effects of fentanyl and remifentanil on hemodynamic response to endotracheal intubation and myoclonus in elderly patients with etomidate induction. *Korean J Anesthesiol*. 2013;64(1):12–8. [PubMed] DOI: [10.4097/kjae.2013.64.1.12](https://doi.org/10.4097/kjae.2013.64.1.12)
 14. Yuan Y, Liu L, Feng S, Ma Y, Wang Q. Effects of different remifentanil doses on the stress reaction and bis value of video laryngoscope-guided tracheal intubation. *Trop J Pharm Res*. 2018;17(10):2025–30. DOI: [10.4314/tjpr.v17i10.19](https://doi.org/10.4314/tjpr.v17i10.19)
 15. O'Hare R, McAtamney D, Mirakhor RK, Hughes D, Carabine U. Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anaesthesia. *Br J Anaesth*. 1999;82(2):283–5. [PubMed] DOI: [10.1093/bja/82.2.283](https://doi.org/10.1093/bja/82.2.283)
 16. Habib AS, Parker JL, Maguire AM, Rowbotham DJ, Thompson JP. Effects of remifentanil and alfentanil on the cardiovascular responses to induction of anaesthesia and tracheal intubation in the elderly. *Br J Anaesth*. 2002;88(3):430–3. [PubMed] DOI: [10.1093/bja/88.3.430](https://doi.org/10.1093/bja/88.3.430)
 17. Cha JW, Kwak SH, Kim SJ, Choi J II, Kim CM, Jeong ST, et al. Optimal Dose of Remifentanil to Blunt Hemodynamic Response to Laryngoscopy and Endotracheal Intubation during Induction of Anesthesia with Propofol. *Korean J Anesthesiol*. 2006;51(3):292. DOI: [10.4097/kjae.2006.51.3.292](https://doi.org/10.4097/kjae.2006.51.3.292)
 18. Park BY, Jeong CW, Jang EA, Kim SJ, Jeong ST, Shin MH, et al. Dose-related attenuation of cardiovascular responses to tracheal intubation by intravenous remifentanil bolus in severe pre-eclamptic patients undergoing Caesarean delivery. *Br J Anaesth*. 2011;106(1):82–7. [PubMed] DOI: [10.1093/bja/aeq275](https://doi.org/10.1093/bja/aeq275)
 19. Hall AP, Thompson JP, Leslie NAP, Fox AJ, Kumar N, Rowbotham DJ. Comparison of different doses of remifentanil on the cardiovascular response to laryngoscopy and tracheal intubation. *Br J Anaesth*. 2000;84(1):100–2. [PubMed] DOI: [10.1093/oxfordjournals.bja.a013362](https://doi.org/10.1093/oxfordjournals.bja.a013362)