# EFFECT OF REMIFENTANIL BOLUS VS FENTANYL IN ATTENUATING HEMODYNAMIC RESPONSE IN VIDEOLARYNGOSCOPIC ENDOTRACHEAL INTUBATION

Shakho Jamal Jalal [a], and Amir Murad Khudadad [b]

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## ABSTRACT

### *Background*

Elevation of blood pressure and pulse rate are hemodynamic changes that occur during general anesthesia as a consequence of laryngoscopy and endotracheal intubation ETI, different laryngoscopies and many drugs have been tried to reduce these changes.

### *Objectives*

To evaluate and compare the efficacy of minimum dose of fentanyl and comparable remifentanil bolus dose during videolaryngoscopic ETI.

### *Patients and Methods*

A triple blind randomized clinical trial implemented on 224 patients of age group between 16-65 years of either sex (ASA I and ASA II) scheduled for elective operation under general anesthesia with endotracheal intubation, they are randomly assigned into two groups, group A and group B representing both fentanyl and remifentanil as the drug preparation was unknown neither by the patient nor by the researcher and nor by the data analyser, in addition propofol two mg/kg and rocuronium 0.8 mg/kg were given then systolic blood pressure SBP, diastolic blood pressure DBP, mean arterial blood pressure MAP and heart rate HR were recorded in five different occasions as (T0) for baseline preinduction, (T1) one minute before ETI, (T2) one minute after ETI, (T3) three minutes after ETI and (T4) five minutes after ETI.

### *Results*

There was a significant difference in the mean value of HR, SBP, DBP, MAP in both groups before, one, three and five minutes after endotracheal intubation with King vision videolaryngoscope KVVL and one µg/kg remifentanil bolus administration (group B) effectively showed substantial reduction in all hemodynamic parameters with significant statistical result ($P < 0.05$) when compared to intravenous IV fentanyl one µg/kg (group A).

### *Conclusion*

Remifentanil bolus of one µg/kg is better than intravenous fentanyl one µg/kg in attenuating hemodynamic response to ETI when KVVL used.

**Keywords:** *Remifentanil, fentanyl, hemodynamic change, videolaryngoscope, tracheal intubation.*

[a]Shorsh Teaching Hospital,Sulaimani, Kurdistan Region, Iraq.
Correspondence: shaxojamal@gmail.com
[b]College of Medicine, University of Sulaimani, Kurdistan Region, Iraq.

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## INTRODUCTION

Loss of airway patency, loss of protective airway reflexes, hypoventilation, and apnea are all possible impact of general anesthesia on respiratory system, therefore one of the fundamental aim of a safe anesthesia technique is maintaining a secure airway [1]. Although endotracheal tube remain the gold standard airway device, but its placement is known to elicit stress response [2].

Hemodynamic response during induction of general anesthesia first described by Reid and Braise in 1940 [3]. It occurs as a result of stimulation of sensory receptors in the supraglottic region by laryngoscopic blade and irritation of trachea by passage of endotracheal tube and inflation of its cuff [4]. This mechanical stimulation eventually leads to transient but marked elevation of plasm catecholamine level as a result of provocation of sympathetic nervous system, which accompanied by increase in heart rate, blood pressure and cardiac dysrhythmias for about 5 minutes [3,5].

After laryngoscopy, blood pressure and heart rate will start to rise within 5 seconds and peak after 30-45 seconds. These alterations are usually temporary and well tolerated by healthy people, but they can be disastrous in people with high blood pressure, coronary artery disease, or cerebrovascular illness and may trigger pulmonary edema, acute left ventricular failure, intraoperative myocardial infarction [6].

The degree of the response to laryngoscopy and intubation varies greatly and several parameters play role such as anaesthetic depth, use of an agent that reduce sympathetic nervous system activation, ease and time of intubation. A variety of strategies have been added into current safe anesthetic practice to lessen these negative consequences, with varying degrees of success, these include both pharmacological and non-pharmacological method [7], with more focus being on pharmacological approach that encompass volatile anaesthetics, topical and IV lidocaine, vasodilators as Sodium nitroprusside ,Nitroglycerine, opioids, Beta blockers, Calcium channel blockers, and alpha 2 agonist [8].

Non pharmacological approach includes use of videolaryngoscope instead of conventional Macintosh, In the field of airway management, videolaryngoscopes are quickly gaining popularity, and a variety of devices with various design features are currently available. They are now recommended by numerous airway experts as the first-line method device for tracheal intubation in all patients not only for difficult airway conditions [9,10].

As videolarygoscopes do not require the alignment of the oral, pharyngeal, and laryngeal axes for glottic viewing & oropharyngeal stimulation may be lessened. Each videolaryngoscope has its own design features and application technique, which might result in a variation in the extent of oropharyngeal stimulation, King Vision video laryngoscope (KVVL) is an example of indirect laryngoscope [7]. The KVVL is made up of a reusable 2.4-inch display and a disposable rigid blade.

There are two types of blades: one is channeled, allowing the ET tube to be advanced through the glottis, and the other is non-channeled, allowing only glottis visualization. ET intubation is aided by a metal stylet [11]. Since introduction of modern anesthesia technique, many studies have been conducted on hemodynamic changes following endotracheal intubation comparing videolaryngoscope to conventional type with different results [12,13].

There are also several studies on hemodynamic response after endotracheal intubation with conventional laryngoscope comparing different types of opiod or different doses of same kind opioid with various outcome [14,15]. To the best of our knowledge, till now there is no any study comparing the effect of 1 μg/kg of fentanyl and remifentanil bolus in attenuating hemodynamic response using videolaryngoscope for endotracheal intubation.

## MATERIALS AND METHOD

This study is a triple-blind clinical trial where the anesthesiologist, the patients and the specialist who analyze the collected data were uninformed about the study groups and hence they had no idea about the groups in which fentanyl or remifentanil have been used, allocation of the group was done by an expert anesthesia nurse who didn't participated in data collection but prepared the drugs by diluting either fentanyl and remifentanil separately in 100 ml normal saline bottle in a way each ml of the solution contains 10 μg /ml of the diluted drug and labelled them as A and B.

At the end of the study and accomplishing data analysis the nurse revealing that A was for fentanyl and B was for remifentanil. The study conducted in Shorsh general teaching hospital and Zhyan private hospital over a period of 8 monthes from December 2021 to July of 2022. After obtaining permission from Sulaimani

university research ethics committee (Date:29/11/2021, No: 7/5/13527) and patient written consent, the study done on two hundred twenty-four adult patients with inclusion criteria of 18-55 years old age, American Society of Anesthesiologist ASA I and II physical status and those who scheduled for elective surgical procedure under general anesthesia with endotracheal intubation.

Exclusion criteria were patient's refusal, ASA physical status more than II, expected difficult airway in which the patient has more than 2 criteria of difficult airway, operations with double lumen or nasal endotracheal intubation, body mass index BMI equal to or greater than 30 , pregnancy, patients on medications that affect hemodynamic stability like beta blockers, patients on steroid, addiction to opioids, patients with duration of laryngoscopy more than 30 seconds and those who needed second attempt of laryngoscopy and intubation. The pre-anesthetic evaluation of patients were done one day prior to the planned surgery with airway assessment which include mouth opening, neck mobility, thyromental distance, inter-incisor distance, modified Mallampatti grade, Upper lip bite test and protruded upper incisors, they were not received any premedication and asked to fast 8 hours for heavy and fatty solid food, 6 hours for light solid food and 2 hours for water and clear fluids, on the day of surgery before patients entry to operation theatre intravenous cannula was put on the dorsum of nondominant hand then in operation room standard monitoring applied as electrocardiography, noninvasive blood pressure and pulse oximetry then SBP, DBP, MAP and HR were measured and recorded as baseline (T0).

Using computer-generated random selection, the engaged patients were divided into two equal groups A and B each with 112 patients, preoxygenation with 100% oxygen done for 3 minutes then induction started with 2 mg/kg propofol, 0.8mg/kg rocuronium and 1 µg/kg from 100cc normal saline prepared solution that contain either 10µg/ml fentanyl or remifentanil, then 3 minutes after the start of induction, ETI done with suitable size 35 degree bended (Hockey stick) endotracheal tube via stylet using KVVL by the same expert anesthesiologist, if the duration of laryngoscopy lasting more than 30 seconds or second attempt was required for ET intubation the procedure regarded as failure and the patient was excluded from the study, anesthesia maintained with isoflurane using close circuit mechanical ventilation circle absorber with the aim maintaining end tidal $CO_2$ between 35-40, then muscle relaxation maintained with intermittent dose of rocuronium as per requirement of the surgery.

All surgical interventions like bladder catheteriazation, nasogastric tube insertion and position change or additional cannulation were advised not to done in first five minutes after ETI in order not to affect patient's hemodynamic changes. Then the study parameters as HR, SBP, DBP and MAP were measured 1 minute before ETI (T1) and one, three, five minutes after ETI (T2), (T3) and (T4) respectively. At the end of the surgery the neuromuscular blocking agent was reversed with combination of neostigmine 0.05mg/kg and atropine 0.02mg/kg then extubation done after fulfilling its criteria then the patient been transferred to post anesthesia care unit (PACU).

### *Statistical analysis*

After data collection and prior to data entry and analysis, the questions of study were coded. Data entry performed using an excel spreadsheet then the statistical analysis was performed by SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences).

Compliance of quantitative random variables with Gaussian curve (normal distribution) was analysed using Kolmogorov-smirnov and Shapiro-Wilk test.

The data presented in tabular forms showing the frequency and relative frequency distribution of different variables among the both groups. Chi-square tests were used to compare the categorical data between these two groups of patients (A group and B group) in respect to different variables.

Variables which showed to be normally distributed quantitative continuous variables and described by mean and SD (standard deviation). The statistical significance of difference in mean between two groups were assessed using independent sample t-test, while between more than two groups ANOVA test was used and P value of 0.05 and less were used as a cut off point for significance of statistical tests.

## RESULTS

Both groups were comparable in demographic parameters as age (P = 0.33), gender (P = 0.47), ASA physical status (P = 0.81), mallampati grade (P = 0.65), BMI (P = 0.27) and also baseline hemodynamic variables before induction including mean of HR (P = 0.21), SBP (P = 0.12), DBP (P = 0.37), MAP (P = 0.24)

and statistically no significant difference were found between the two groups (P > 0.05). (Table 1 & 2).

Increase in the HR after laryngoscopy and intubation were occurred in both groups and was maximum at T2, then gradually decreasing at T3 and T4. The remifentanil (group B) showed lower values at all time intervals than fentanyl (group A) and the differences were statistically significant (P < 0.05). (Table 3), (Fig.1)

Attenuation of SBP after laryngoscopy and intubation was more in remifentanil group at T2, T3, T4 when compared to fentanyl group, although the difference in lowering of SBP at T4 between both groups was statistically not significant (P > 0.05) possibly due to the end of the drug's duration of action but at T2 and T3 were statistically significant (P < 0.05). (Table 4), (Fig.2) Attenuation of DBP after laryngoscopy and intubation at T2, T3 and T4 were more in remifentanil than fentanyl group and when the difference compared it was statistically significant (P < 0.05) in all time intervals. (Table 5), (Fig.3)

Attenuation of MAP after laryngoscopy and intubation was more in remifentanil than fentanyl group at all recorded time intervals (Table 6) and when the difference was compared it was statistically significant (P < 0.05).

**Table 1. Demographic parameters of the two studied groups.**

| Items | | Groups | | P value |
|---|---|---|---|---|
| | | A | B | |
| **Age ( Years)** | **Mean ± SD** | 28.3 ± 7.8 | 29.4 ± 9.0 | 0.33 |
| | **18 - 25** | 52 | 48 | |
| | **26 - 35** | 40 | 37 | |
| | **36 - 45** | 16 | 21 | 0.72 |
| | **46 - 55** | 4 | 6 | |
| **Gender** | **Male** | 37 | 32 | 0.47 |
| | **Female** | 75 | 80 | |
| **American Society of Anesthesiologist** | **I** | 102 | 103 | 0.81 |
| | **II** | 10 | 9 | |
| **Mallampati grade** | **I** | 80 | 83 | 0.65 |
| | **II** | 32 | 29 | |
| **BMI** | **Mean ± SD** | 23.9 ± 3.4 | 24.4 ± 3.4 | 0.27 |
| | **16 - 18.49** | 8 | 6 | |
| | **18.5 - 24.9** | 64 | 64 | 0.85 |
| | **25 - 29.9** | 40 | 42 | |
| **Total** | | **112** | **112** | |

**Table 2. Baseline hemodynamic variables including HR, SBP, DBP and MAP before induction of general anesthesia.**

| Baseline hemodynamic variables (T0) | Groups ( mean ± SD) | | P value |
|---|---|---|---|
| | A | B | |
| **Systolic blood pr. baseline (mm Hg)** | 122.5 ± 8.9 | 124.3 ± 8.8 | **0.13** |
| **Diastolic blood pressure baseline** | 77.1 ± 8.2 | 78.2 ± 7.5 | **0.31** |
| **Heart rate baseline** | 89.1 ± 15.8 | 91.6 ± 14.2 | **0.21** |
| **Mean arterial pressure baseline** | 92.3 ± 7.5 | 93.6 ± 6.9 | **0.17** |

**Table 3 .Changes in the mean of HR per minute with statistical comparison in the two studied groups.**

| Heart rate | Groups ( mean ± SD) | | P value |
|---|---|---|---|
| | A | B | |
| **Before laryngoscopy (T1)** | 82.2 ± 15.4 | 79.0 ± 12.7 | **0.03** |
| **One minute after laryngoscopy (T2)** | 102.0 ± 15.9 | 92.1 ± 12.4 | **< 0.001** |
| **Three minutes after laryngoscopy (T3)** | 96.8 ± 14.4 | 90.1 ± 12.0 | **< 0.001** |
| **Five minutes after laryngoscopy (T4)** | 93.5 ± 15.3 | 88.5 ± 13.5 | **0.01** |

**Table 4. Mean SBP in mmHg with statistical comparison in the two studied groups.**

| Systolic Blood pressure ( mmHg) | Groups ( mean ± SD) | | P value |
|---|---|---|---|
| | A | B | |
| **Before laryngoscopy (T1)** | 105.5 ± 9.9 | 98.2 ± 15.0 | **< 0.001** |
| **One minute after laryngoscopy (T2)** | 126.9 ± 13.2 | 110.9 ± 17.2 | **< 0.001** |
| **Three minutes after laryngoscopy (T3)** | 111.9 ± 12.8 | 102.5 ± 14.2 | **< 0.001** |
| **Five minutes after laryngoscopy (T4)** | 106.6 ± 12.5 | 103.7 ± 15.9 | **0.14** |

**Table 5. Mean DBP in mmHg with statistical comparison in the two studied group.**

| Diastolic Blood pressure | Groups ( mean ± SD) | | P value |
|---|---|---|---|
| | A | B | |
| **Before laryngoscopy (T1)** | 63.3 ± 8.5 | 56.3 ± 11.6 | **< 0.001** |
| **One minute after laryngoscopy (T2)** | 81.7 ± 10.6 | 69.5 ± 14.2 | **< 0.001** |
| **Three minutes after laryngoscopy T3)** | 69.8 ± 10.4 | 61.4 ± 11.2 | **< 0.001** |
| **Five minutes after laryngoscopy (T4)** | 65.7 ± 10.9 | 61.9 ± 12.8 | **0.02** |

**Table 6.Mean of MAP in mmHg with statistical comparison in the two studied group.**

| Mean arterial pressure | Groups (mean ± SD) | | P value |
|---|---|---|---|
| | A | B | |
| **Before laryngoscopy (T1)** | 77.4 ± 8.3 | 70.3 ± 12.2 | **< 0.001** |
| **One minute after laryngoscopy (T2)** | 96.8 ± 10.7 | 83.3 ± 14.8 | **< 0.001** |
| **Three minutes after laryngoscopy (T3)** | 83.4 ± 10.7 | 75.1 ± 11.7 | **< 0.001** |
| **Five minutes after laryngoscopy (T4)** | 79.4 ± 10.6 | 75.9 ± 13.4 | **0.03** |

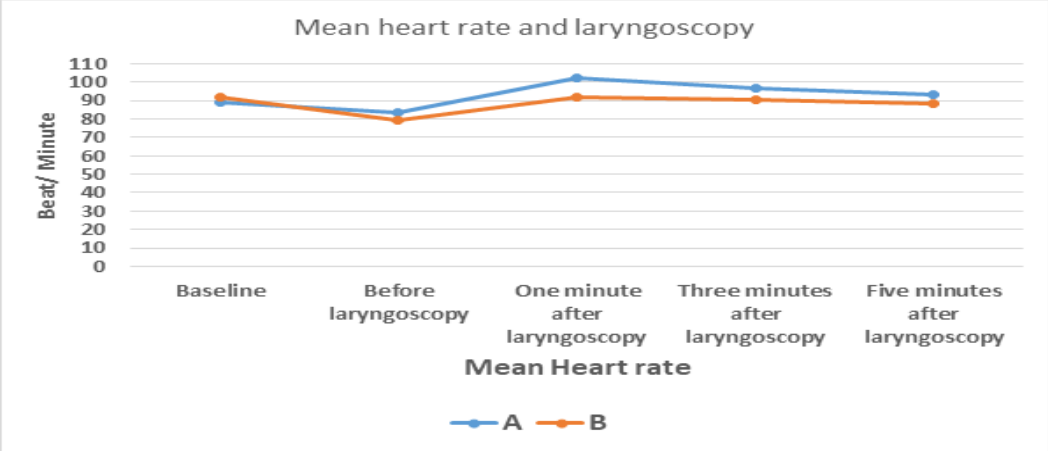


**Figure 1. Changes in HR at different time intervals in both groups.**

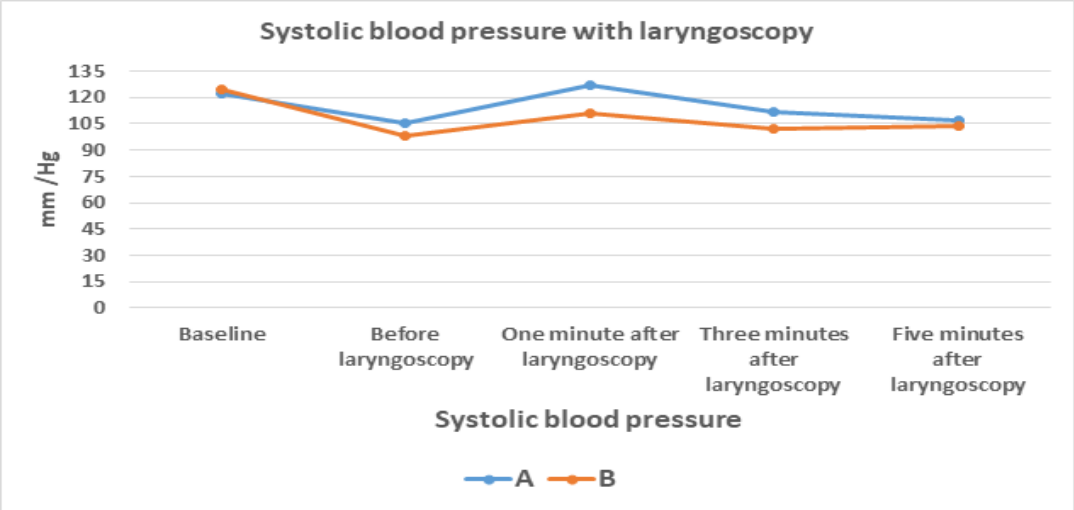


**Figure 2. Changes in SBP at different time intervals in both groups.**

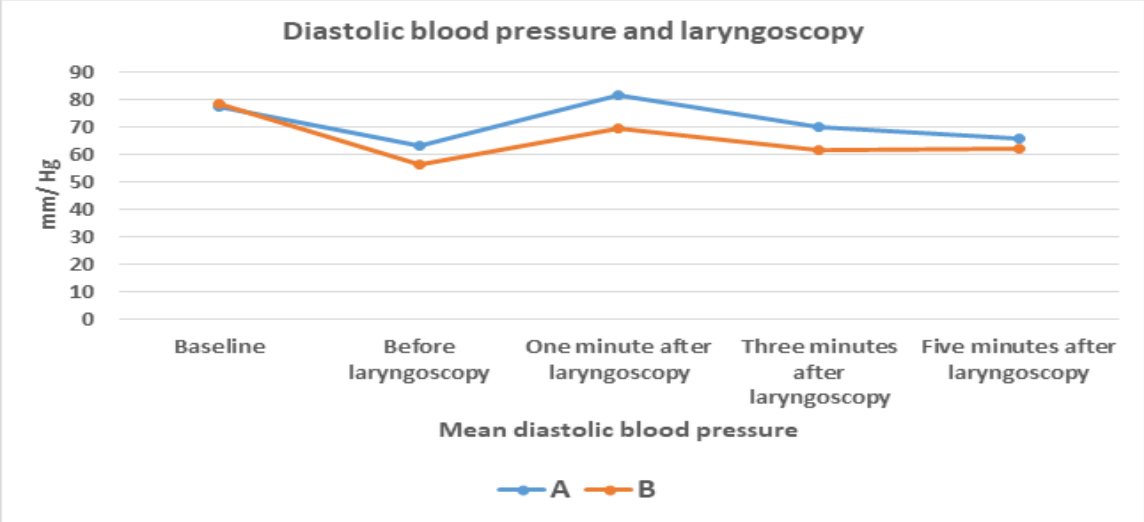


**Figure 3. Changes in DBP at different time intervals in both group.**

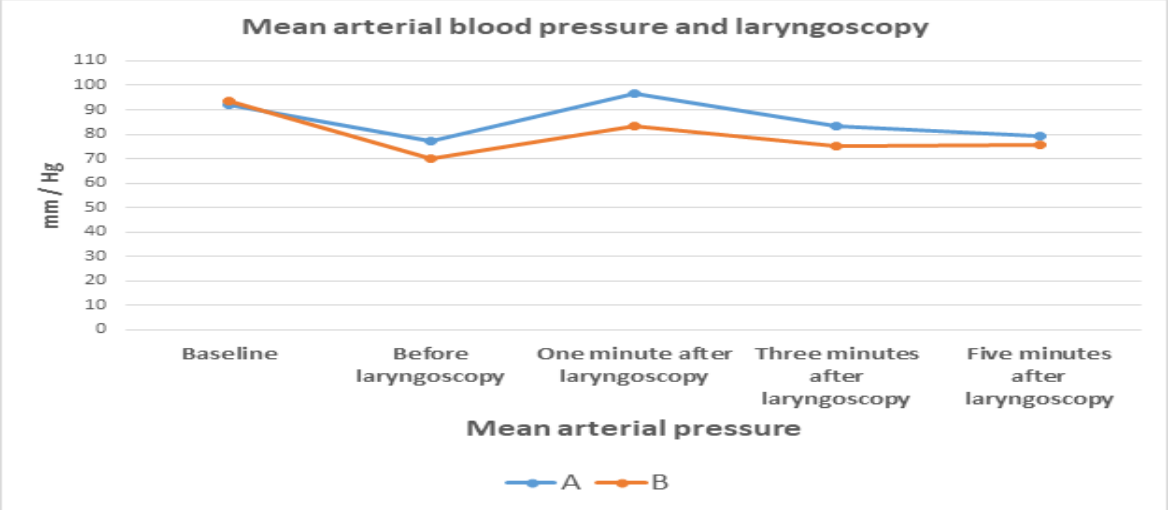


**Figure 4. Changes in MAP at different time intervals in both group.**

## DISCUSSION

Laryngoscopy and endotracheal intubation are both excruciatingly strong stimuli, resulting in a period of acute hemodynamic stress that is linked to an increase in sympathetic activity which manifests clinically as tachycardia and hypertension. Such sympatho adrenal activation, particularly in patients with coronary or cerebral atherosclerosis, may trigger LVF, myocardial ischemia and cerebral hemorrhage. Numerous pharmacological and non-pharmacological techniques have been tried to lessen or blunt this hemodynamic pressor response, with variable degrees of effectiveness [16].

One drug that is used to diminish the laryngo-tracheal pressor response is fentanyl. By acting on two receptors, opioid receptors and μ receptors, it increases parasympathetic tone while decreasing sympathetic tone [17]. Fentanyl is found to blunt the sympathoadrenal response in a dose-dependant manner. The physiological hemodynamic response to conventional laryngoscopy and endotracheal intubation is considerably decreased when a dose of two μg/kg is administered as per study which is conducted by Splinter WM et al. [18].

Remifentanil is a potent ultra-short acting opioid with rapid onset of action, it provides pure mu-opioid receptor agonist action, effectively reduce hemodynamic response to laryngoscopy and tracheal intubation and has a wide usage in general anesthesia [15]. Remifentanil effect on hemodynamic response at multiple doses were researched. It was administered in three different doses during the induction of anesthesia by Hare et al. in order to control the hemodynamic response caused by conventional laryngoscopy and ETI. Likewise, they found that one μg/kg of remifentanil was an effective dose for producing suitable intubating conditions in children [19]. Yuan et al. used videolaryngoscope and remifentanil to significantly reduce stress response caused by tracheal intubation and they found that the most effective approach is to administer one μg/kg of remifentanil for anesthesia induction and 1.5 μg/kg of remifentanil for tracheal intubation [15].

Both remifentanil and fentanyl in a dose of one μg/kg were compared using conventional laryngoscopy in day case surgery by Whitten et al., they concluded that Remifentanil (1 μg/kg IV) was superior to a standard one μg /kg IV dose of fentanyl in controlling the early hemodynamic response to laryngoscopy and tracheal intubation in healthy outpatients [20]. As per some research, videolaryngoscopes apply less pressure to the upper airway structures during laryngoscopy, this could reduce oropharyngeal stimulation and lessen the resulting hemodynamic response [21, 22].

In our study we compared a remifentanil bolus with fentanyl in a dose of one μg /kg for attenuation of hemodynamic response after ETI but with the use of KVVL , the major finding was that in comparison with the baseline value, remifentanil group showed more attenuation of HR, SBP, DBP and MAP at T2, T3, T4 after ETI with superior hemodynamic stability than fentanyl group and the difference was statistically significant with no substantial reduction in hemodynamic variables occurred in either groups, in contrast to our study and according to Hogue et al. [23]

remifentanil one µg /kg IV followed by an infusion of 0.5-1 µg /kg/min efficiently controlled hemodynamic reactions to tracheal intubation. However, during induction, 10%–15% of the patients in their research developed hypotension (defined as SBP < 80 mm Hg or MAP < 60 mm Hg), and 27%–30% had low MAP levels throughout the initial maintenance phase. Schuttler et al. [24] reported similar outcomes.

In our study, also there were no substantial airway complications or intubation failures. As per our results, Ali et al. noticed less airway trauma during KVVL use that may be attributed to the lack of an airway maneuver and the use of a soft blade. Jagannathan et al. [25]. compared the Miller laryngoscope and KVVL, in contrast to our findings, showed that complications were not statistically different between the two instruments.

In conclusion, based on our clinical study, bolus IV remifentanil one µg/kg provide better attenuation and effective control of hemodynamic response to endotracheal intubation than IV fentanyl one µg/kg when KVVL is used and remifentanil can be used as an alternative to fentanyl without producing sever hypotension in post intubation period.

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