

ORIGINAL RESEARCH

PERIOPERATIVE MEDICINE

Comparison of 2 µg/kg of fentanyl and 150 µg/kg oxycodone during induction on post-intubation hemodynamics: a randomized clinical trial

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Abstract

Context: Endotracheal intubation may cause increased blood pressure and heart rate. The use of fentanyl as pre-intubation medication may blunt the hemodynamic changes. However, fentanyl has side effects of sedation and respiratory depression. Oxycodone is an opioid similar to fentanyl that may be used as preintubation medication with less effects on sedation and respiratory depression.

Aims: This study aimed to compare the effect of 150 µg/kg oxycodone and 2 µg/kg fentanyl during induction on post-intubation blood pressure and heart rate changes.

Methodology: The study was a double-blind, randomized clinical trial in 40 patients ASA I-II aged between 19-65 years old undergoing elective surgery under general anesthesia.

The patients were divided into 2 groups, one receiving 150 µg/kg oxycodone and one receiving 2 µg/kg fentanyl during induction. Blood pressure and heart rate were recorded before induction (T0), before intubation (T1), just after intubation (T2), 3 min after intubation (T3) and 5 min after intubation (T4).

Statistical data was analyzed using unpaired t-test and Mann-Whitney test, where $p < 0.05$ was considered significant.

Results: The results showed significant differences ($p < 0.05$) in MAP (and #61508;MAP) in every time points assessed (12.15 ± 6.753 , 13.40 ± 6.143 , and 17.59 ± 7.715 in oxycodone group versus 3.65 ± 3.746 , 6.05 ± 4.186 , and 9.40 ± 6.484 in fentanyl group, consecutively). This study also showed significant differences ($p < 0.05$) in heart rate in every time points assessed ($3,40 \pm 4.212$, $8.35 \pm 4,891$ and 10.45 ± 6.253 in oxycodone group versus -4.80 ± 6.477 , -2.15 ± 4.671 , and -1.20 ± 6.978 in fentanyl group, consecutively).

Conclusions: Administration of 150 µg/kg oxycodone during induction causes smaller increase in post-endotracheal intubation blood pressure and heart rate compared to 2 µg/kg fentanyl.

Key words: Blood pressure; Fentanyl; Heart rate; Intubation; Oxycodone; Post-intubation hemodynamic

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1. Introduction

Endotracheal intubation is usually accompanied by elevations in blood pressure and heart rate as a result

of sympathetic nervous system activation. In certain patients, the hemodynamic response may be fatal enough to cause myocardial ischemia, ventricular arrhythmia, heart failure, and intracerebral hemorrhage especially those with minimum tolerance

such as patients with increased intracranial pressure, aorta aneurysm, uncontrolled hypertension, heart failure, and arrhythmia with 1.7-23% incidence of emergent endotracheal intubation cardiac arrest. This sympathetic activation may be suppressed by pre-intubation administration of strong analgesic.¹⁻²

Fentanyl is an opioid that is commonly used to blunt sympathetic stimulation during intubation.⁴⁻⁵

Oxycodone is a semisynthetic opioid that binds to μ -opioid receptor, just like fentanyl. However, oxycodone's receptor binding is not as strong as fentanyl, so it causes less sedation and respiratory depression. Oxycodone also binds to κ -opioid receptor which has antagonist effect on respiratory depression induced by μ -opioid receptor. The potency ratio between oxycodone and fentanyl is 75 μ g:1 μ g.⁶⁻⁸ The optimal dose of oxycodone to attenuate hemodynamic response to endotracheal intubation is 0.15 mg/kg.⁹

These findings from the previous literature cause oxycodone to have a comparable analgesic effect as fentanyl with less complications of respiratory depression and sedation. However, there are no studies comparing oxycodone and fentanyl on postintubation hemodynamic, especially in Indonesia. The present study was aimed to confirm the hypothesis in which the administration of 150 μ g/kg intravenous oxycodone during induction may cause less increase of post-intubation blood pressure and heart rate changes, when compared to 2 μ g/kg intravenous fentanyl.

2. Methodology

This study is a randomized clinical trial regarding the effectiveness of oxycodone compared to fentanyl on suppressing post-intubation hemodynamic changes including forty patients of American Society of Anesthesiology (ASA) grade I-II aged between 20-60 years undergoing elective surgical procedures that required endotracheal intubation in Hasan Sadikin General Hospital from January to July 2020. Patients with history of drug allergy, anticipated difficult intubation, history of malignancy, and patients who had been taking routine opioid and beta-blocker medications were excluded from the study. Sample size was obtained using a formula for unpaired categorical-numerical variables analysis with 95% confidence interval and permuted block randomization

was applied to divide the 40 patients into two groups based on the independent variables: Group I (oxycodone group): patient received 150 μ g/kg oxycodone before induction and Group II (fentanyl group): patient received 2 μ g/kg fentanyl before induction. The dependent variables observed were heart rate (beats per-minute) and mean arterial pressure (mmHg).

On arrival at the operating theatre, baseline HR (heart rate) and MAP (mean arterial pressure) were recorded. The study drug was injected before laryngoscopy and endotracheal intubation and the patients were carefully monitored. Vital signs including HR and MAP were recorded before administration of the study drug (T0), before intubation (T1), just after intubation (T2), 3 min after intubation (T3) and five min after intubation (T4).

Statistical analysis: The results were statistically analyzed by Statistical Packages for Social Science (SPSS) version 16 for windows. The parametric data was presented as mean \pm standard deviation (mean \pm SD), median, and range. Normality test using Saphiro-Wilk test was performed, then normally distributed data was analyzed using unpaired T-test and abnormally distributed data was analyzed using Mann-Whitney test. $P < 0.05$ were considered statistically significant.

3. Results

Forty patients participated in the study. There was no significant difference in the demographic profile amongst the regarding age, sex, weight, height, and BMI of the subjects (Table 1).

In this study, the mean difference in MAP (Δ MAP) on T2, T3, and T4, compared with baseline in oxycodone group were 12.15 ± 6.753 , 13.40 ± 6.143 , and 17.59 ± 7.715 consecutively. Meanwhile, the Δ MAP on T2, T3, and T4 in fentanyl group were 3.65 ± 3.746 , 6.05 ± 4.186 , and 9.40 ± 6.484 , consecutively. There were significant differences in both groups in every time points: T2 ($p = 0.0001$), T3 ($p = 0.0001$) and T4 ($p = 0.0005$) (Figure 1). In this study, the mean difference in heart rate on T2, T3, and T4 in oxycodone group were 3.40 ± 4.212 , 8.35 ± 4.891 and 10.45 ± 6.253 , consecutively. Meanwhile, the difference in heart rate on T2, T3, and T4 in fentanyl

Table 1. Demographic data on 40 patients in oxycodone and fentanyl groups

Variable	Oxycodone Group N=20	Fentanyl Group N=20	P value
Age			
Mean ± SD	40.35 ± 13.027	46.20 ± 12.530	0.156
Median	40.00	48.50	
Range	21.00-63.00	21.00-65.00	
Sex			
Male	8 (40.0%)	10 (50.0%)	0.525
Female	12 (60.0%)	10 (50.0%)	
Height (cm)			
Mean ± SD	158.35 ± 6.808	157.80 ± 9.111	0.830
Median	160.00	160.00	
Range	144.00-170.00	140.00-173.00	
Weight (kg)			
Mean ± SD	56.40 ± 9.960	55.60 ± 7.563	0.776
Median	56.00	54.50	
Range	40.00-78.00	45.00-70.00	
BMI (kg/cm²)			
Mean ± SD	22.39 ± 2.945	22.43 ± 3.165	0.963
Median	21.84	22.86	
Range	17.58-27.64	15.57-27.55	

group were -4.80 ± 6.477 , -2.15 ± 4.671 , and -1.20 ± 6.978 , consecutively. There were significant differences between oxycodone and fentanyl group in every time points: T2 ($p = 0.0001$), T3 ($p = 0.0001$) and T4 ($p = 0.0001$) (Figure 2).

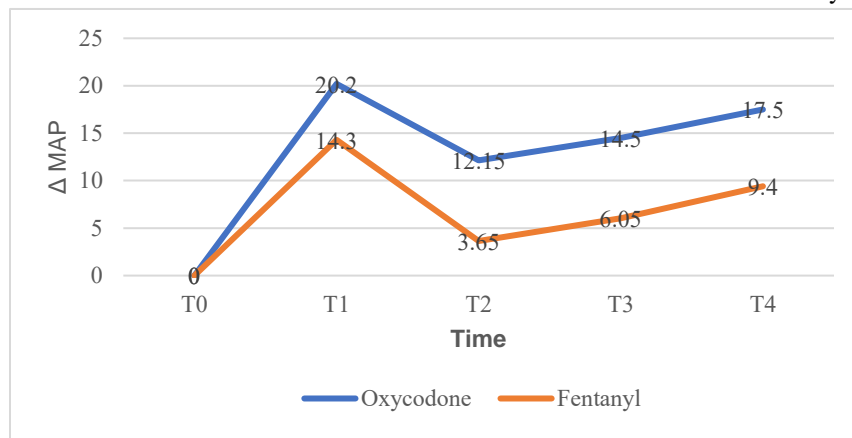


Figure 1: Comparison of Δ MAP between oxycodone and fentanyl groups

4. Discussion

Fentanyl is the opioid of choice for intubation due to its rapid onset of action.¹⁵ Oxycodone has similar onset as fentanyl (2-3 min after intravenous injection)

with slightly longer duration of action ($t_{1/2}$: 4 hrs 52 min versus 3 hrs 39 min).^{16,17} Oxycodone has analgesic potential equivalent to fentanyl at a dose ratio of 1:75 μg and 1:100 μg (fentanyl; oxycodone). The current study implemented the dose ratio of 1:75 μg because it produced lower rate of complications of apnoea.⁷

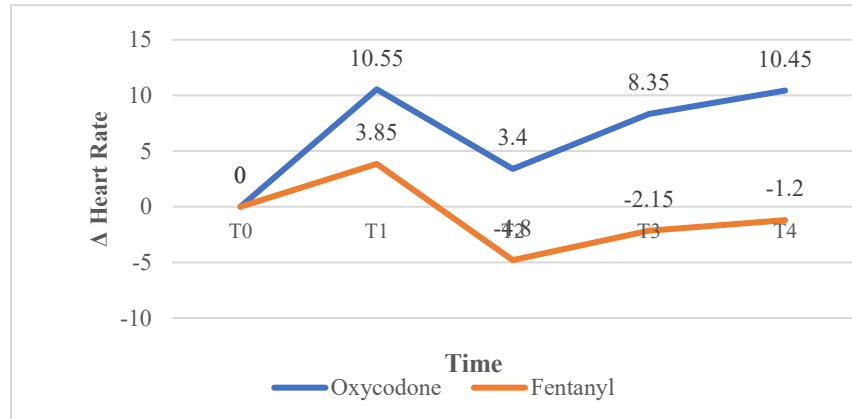


Figure 2: Comparison of difference in heart rate between oxycodone and fentanyl groups

The result of this study showed that the decrease in blood pressure and heart rate in oxycodone group was smaller than the decrease in fentanyl group. This indicated that the administration of oxycodone before intubation could reduce post-intubation hemodynamic changes which is marked by increased blood pressure and heart rate more than fentanyl.

Laryngoscopy and intubation can cause hemodynamic changes marked by increased blood pressure and heart rate as a result of sympathetic nerve stimulation. Sympathetic nerve stimulation will increase and reach its maximum effect within a minute and will last up to 5-10 min after intubation.⁷ The hemodynamic changes due to intubation can lead to fatal perioperative complications such as cerebral hemorrhage, cardiac arrhythmias, or heart failure in patients with prior histories of heart or cerebral diseases. There are various ways to blunt post-intubation hemodynamic changes. Medications that can be used are beta-blockers, local anesthetics such as lidocaine (either administered intravenously or via nebulization), acetaminophen, and magnesium sulphate.¹⁰⁻¹³ Opioids are also known as strong analgesics that can be used to suppress hemodynamic changes during intubation.¹⁴

In our study, the oxycodone group showed smaller increase in blood pressure compared to fentanyl group in T2, T3, and T4. Similar result has been shown by Park *et al.*⁷ whose study showed that oxycodone administration resulted in lower mean blood pressure than fentanyl. There are three possible explanations for the current result. First, the synergistic effect of propofol and oxycodone is greater than the synergistic effect of propofol and fentanyl in suppressing blood

pressure elevation. Second, unlike fentanyl, oxycodone releases histamine which might induce decreased MAP as a result of vasodilation.^{18,19} Third, oxycodone binds to κ -opioid receptors. Activation of these receptors dilate the superior mesenteric artery and might cause a decrease in MAP.^{5-7,20}

In this study, the increases in heart rate in T2, T3, and T4 were smaller in oxycodone group than in fentanyl group. This result is similar to studies by Park *et al.*⁷

and Park *et al.*⁹ which stated that a group of patients who received oxycodone before intubation showed lower heart rate than the other group of patients who received fentanyl before intubation.^{7,9}

5. Conclusion

From the present study, we conclude that administration of 150 $\mu\text{g}/\text{kg}$ oxycodone during induction can cause smaller increase in blood pressure and heart rate compared to administration of 2 $\mu\text{g}/\text{kg}$ fentanyl during induction.

6. Limitations

The limitation of this study is the limited scope of population because the study was only carried out in population groups with good physical and hemodynamic status, so it is necessary to conduct research on a wider population group.

7. Conflict of interest

None declared by the authors

8. Authors' contribution

SS, BR, RH: Concept, conduction of the study, manuscript writing and editing

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