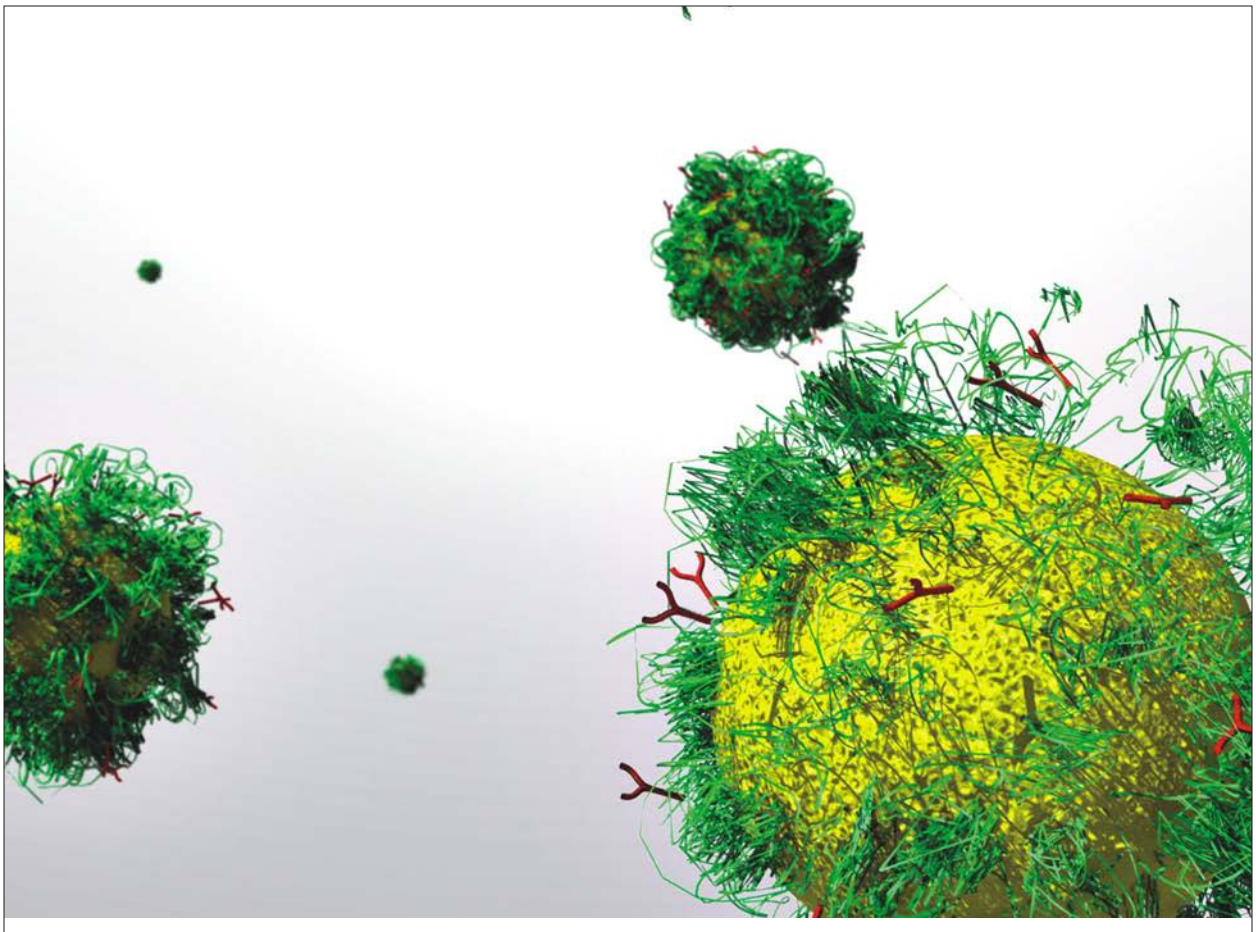

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Research Article
Comparison Between the Effect of the Intravenous Dexmedetomidine with Fentanyl on the Propofol Induction Dose Requirement and the Hemodynamic Response Due to Laryngoscopy and Tracheal Intubation

[1]Syafri Kamsul Arif, [1]Imtihanah Amri and [2]Anwar Mallongi

[1]Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Hasanuddin University, Hospital 5 Floor Building A, Jalan Perintis Kemerdekaan 11, Tamalanrea, 90245 Makassar, Indonesia
[2]Department of Environmental Health, Faculty of Public Health, Hasanuddin University, Jalan Perintis Kemerdekaan, Tamalanrea, 90245 Makassar, Indonesia

Abstract

Background: Laryngoscopy and endotracheal intubation can cause increase in sympathetic activity and simpatoadrenal reflex, associated with increased blood pressure and heart rate. The objective of this study was to compare the effects of dexmedetomidine 0.75 μg kg^{-1} b.wt., and fentanyl 2 μg kg^{-1} b.wt., to propofol induction dose requirement and hemodynamic response due to laryngoscopy and endotrakheal intubation. **Materials and Methods:** Randomized, single-blind controlled study, involving 48 patients with ASA physical status I and II planned for elective surgery with general anesthesia in DR (Wahidin Sudirohusodo hospital). Subjects are divided into two groups and each group is given dexmedetomidine (D) 0.75 μg kg^{-1} b.wt. or fentanyl (F) 2 μg kg^{-1} b.wt. intravenously before induction of propofol (50 mg kg^{-1} h^{-1}) until the BIS reached 48±2, continued administration of atracurium 0.5 mg kg^{-1} and maintenance with 1.0 vol% isoflurane in oxygen 60%. Systolic and diastolic blood pressure, mean arterial pressure and heart rate are recorded at 1, 3 and 5 min after intubation as well as side effects. **Results:** Induction dose requirement in D group was less than the F group ($p<0.05$). In the 1st min, there is a 16.32% increase in average MAP and 18.88% in mean heart rate in F group, whereas a 2.90% increase in average MAP and 3.37% decrease of average heart rate was observed in D group. In the 3rd and 5th min, both groups were able to prevent increase in blood pressure but the F group has not been able to prevent an increase in average heart rate at the 3rd min (3.99% increase). The incidence of hypertension and tachycardia were significantly different ($p<0.05$) between the two groups. **Conclusion:** Induction dose requirement in dexmedetomidine group is less than the fentanyl group ($p<0.05$). Hemodynamic response on dexmedetomidine 0.75 μg kg^{-1} b.wt., is more stable than fentanyl 2 μg kg^{-1} b.wt., at 1st min after intubation but at 3rd and 5th min after intubation both groups can maintain stable hemodynamic response with a lower mean heart rate achieved by dexmedetomidine.

Key words: Dexmedetomidine, fentanyl, propofol induction, hemodynamic response, intravenous, laryngoscopy, tracheal intubation

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Corresponding Author: Anwar Mallongi, Department of Environmental Health, Faculty of Public Health, Hasanuddin University, Jalan Perintis Kemerdekaan, Tamalanrea, 90245 Makassar, Indonesia

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The airway management is absolutely controlled by all the expert's anesthesia. One of action airway management is mostly done in the practice of anesthesia is laryngoscopy and intubation trakhea. From observations and the existing show that most of the operations or surgical procedures performed under general anesthesia. Most of general anesthesia were accompanied by action laryngoscopy and intubation trakhea[1,2].

Action laryngoscopy and intubation were performed immediately after induction of anesthesia with standard doses can often lead to reflex sympathetic and simpatoadrenal excessive, resulting in increased blood pressure, increased heart rate and arrhythmia. The increased blood pressure ranges from 40-50% and an increase in heart rate ranges from 20%. This response even only temporary, may be in a healthy person, it was not dangerous but in patients who have had previous risk factors such as hypertension, Coronary Artery Disease (CAD), cerebrovasculer disease (CVD) and intracranial aneurysm it may be dangerous[1-4].

Various ways or techniques have been used to prevent or reduce the hemodynamic response at the time of laryngoscopy and intubation[5]. The ways or techniques, such as: Deepening of anesthesia, local anesthetic (lidocaine) intravenous or topical, opioids (fentanyl and alfentanil), β-adrenergic blockers, vasodilators (nitroglycerin and sodium nitroprusside), calcium channel antagonist (diltiazem) and α2-adrenergic agonists (clonidine). Every ways have advantages and disadvantages[2,3,6,7].

Fentanyl is a synthetic opioid agonist phenyl pyridine derivatives were often used as an effective addition to reducing the hemodynamic response to the act of laryngoscopy and intubation, also has several other advantages namely as intraoperative analgesics. However, the procurement of fentanyl was not without problems, opioids are classified as narcotic drugs. As a consequence, they are regulated by international treaties and national drug control policy and in Indonesia the availability of opioids was limited. Therefore, to overcome the limitations of the amount of fentanyl, it can be used other medications that can reduce the hemodynamic response due to the actions laryngoscopy and intubation, one of them was dexmedetomidine.

Dexmedetomidine is the drug of the class of α2-adrenergic agonist that has an affinity to the α2-adrenoceptor 8 times stronger when compared with clonidine, which can reduce catecholamine levels in plasma and to withhold the release of catecholamines, which have properties sympatholytic, anxiolytics, sedatives and analgesia relative more potent and selective than α2-adrenergic earlier. Dexmedetomidine such as clonidine has been reported to reduce the stress response simpatoadrenal effectively, minimizing the hemodynamic response after laryngoscopy and intubation and raise the hemodynamic stabilization during operation. It is also able to suppress and lower the intraocular pressure increase caused by the actions of laryngoscopy and intubation[7,8].

Besides having sympatholytic effects, anxiolytic, sedative and analgesia, dexmedetomidine also have the effect of saving anestesik (anesthetic sparing effect) where it can reduce the need for opioid intraoperatively. Sedation and analgesia produced were achieved without affecting the respiratory and hemodynamic significance[7-9].

Dexmedetomidine has been studied the use for premedication with a dose of 0.3-0.6 μg kg^{-1} b.wt., intravenously and 1.0 μg kg^{-1} b.wt., intramuscularly and it was obtained the optimum effect. At a dose of 0.6 μg kg^{-1} b.wt., intravenously can reduce the hemodynamic response due to intubation and at a dose of 1.0 μg kg^{-1} b.wt., intramuscularly can reduce catecholamine and lower pentotal needs as much as 17%[10].

The aim of this study to demonstrate the effectiveness of dexmedetomidine in reducing the need for propofol induction dose and lower the hemodynamic response due to laryngoscopy and intubation endotrakhea.

MATERIALS AND METHODS

This study was conducted at the Installation Surgery Center Dr. Wahidin Sudirohusodo Hospital, Makassar from December, 2015 until the samples were met. This study was a clinical trial by a single-blind randomized controled trial, with the shape of the experimental design (pre and post-test control group design). Variables consisted of independent variables (dexmedetomidine 0.75 μg kg^{-1}, fentanyl 2 μg kg^{-1}), the dependent variable (Needs induction doses, the hemodynamic response (TDS, TDD, TAR, LJ)), moderating variable n (general anesthesia with laryngoscopy and intubation) and the control variables (age, BMI, ASA PS, Mallampati).

The study was conducted on 48 people who have had an explanation and agree to follow all study procedures, measured systolic blood pressure (TDS), diastolic blood pressure (TDD), mean arterial pressure (TAR) and heart rate (LJ) as the basic data then further divided into 2 groups: dexmedetomidine (0.75 mg kg^{-1}) dissolved in NaCl 0.9% up to 20 mL and given over 10 min and group (F) fentanyl

(2 mg kg^{-1}) in a solution of NaCl 0.9% administered over 2 min via syringe pump. Induction of anesthesia was using propofol (50 mg kg^{-1} $days^{-1}$) via syringe pump until the BIS value of 48±2 (calculated amount of propofol). Then given muscle relaxants atracurium 0.5 mg kg^{-1} as facilities intubation and 3 min after administration of atracurium action laryngoscopy and intubation endotrakhea made up for 30 sec, then measuring and recording hemodynamic 1, 3 and 5 min after intubation.

RESULTS

From the analysis in Table 1 and 2, it was not found significant differences in baseline characteristics in both study groups. Therefore, 48 characteristics of research subjects can be expressed statistically homogeneous ($p \geq 0.05$). Gender, ASA PS and Mallampati analyzed by chi-square test, whereas age and Body Mass Index (BMI) were analyzed using the Mann Whitney test, in which the value of $p<0.05$ revealed significant statistically.

The initial clinical characteristics of the sample in this study were comprised of TDS, TDD, TAR and heart rate before induction, which can be seen in Table 3. From the results it shows that, there was no significant difference in initial clinical hemodynamic characteristics from both study groups, so that it can be expressed homogeneous statistically ($p \geq 0.05$).

Needs of propofol induction dose: Results of a study of the needs of propofol induction in both groups depicted in Table 4 and Fig. 1.

From the analysis of Table 4, there was a significant difference for the needs dose of propofol induction in both study groups ($p<0.05$). The initial clinical characteristics were analyzed using Mann Whitney test, in which the value of $p<0.05$ were significant statistically.

Hemodynamic: The study of hemodynamics in each group for each measurement time were described in Table 5 and 6. From results, it was shown in Table 5 that there was a change in the TAR in both groups. There was a rise TAR in both groups 1 min after intubation, where the greater increase occur in the fentanyl group and the comparison between the two groups was significant statistically ($p<0.05$). Further decline again at 3rd and 5th min after intubation, the average mean arterial pressure (TAR) was lower than the average mean arterial pressure (TAR) basal in both groups. There was a larger increase in the fentanyl group 1 min after intubation, although it has fallen back on the observation of 3 min after intubation, TAR was remained higher in the fentanyl group than dexmedetomidine group and was different significantly ($p<0.05$). There was no mean arterial pressure (TAR) difference significance found significance ($p>0.05$) between the two groups at 5 min after intubation.

Table 1: Comparison of proportions of gender, ASA PS and mallampati at the second group

	Groups				
	Dexmedetomidine (n = 24)		Fentanyl (n = 24)		
Variables	n	%	n	%	p-value
Gender					
Male	9	37.5	12	50	0.561
Female	15	62.5	12	50	
ASA PS					
I	12	50	13	54.2	1.000
II	12	50	11	45.8	
Mallampati					
1	16	66.7	11	45.8	0.244
2	8	33.3	13	54.2	

Data was presented as a percentage (%). Tested with chi-square test, $p<0.05$ was significant. Group D: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group F: Fentanyl 2 μg kg^{-1} b.wt.

Table 2: Comparison distribution of age and IMT at both of the groups

	Groups								
	Dexmedetomidine (n = 24)				Fentanyl (n = 24)				
Variables	Min	Max	Mean	SD	Min	Max	Mean	SD	p-value
Age (year)	18	54	35.04	10.06	17	50	38.62	11.36	0.253
IMT (kg m^{-2})	18.73	24	21.79	1.40	17.44	23.90	21.62	1.80	0.710

Data was presented as a percentage (%). Tested with chi-square test, significant difference at $p<0.05$. Group D: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group F: Fentanyl 2 μg kg^{-1} b.wt.

Table 3: Characteristics of the initial clinical hemodynamic both for dexmedetomidine and fentanyl

	Groups								
	KD (n = 24)				KF (n = 24)				
Variables	Minimum	Maximum	Mean	SD	Minimum	Maximum	Mean	SD	p-value
TDS (mmHg)	107	138	123.4	7.6	108	138	127.3	7.8	0.086
TDD (mmHg)	66	84	74.1	5.5	60	90	75.9	6.7	0.327
TAR (mmHg)	83	103	93.6	5.8	80	107	96.8	7.0	0.098
LJ (x/min)	68	92	83.3	7.4	62	95	79.5	9.3	0.357

Data was presented in the form of Mean±SD (standard deviation). Tested with Mann Whitney test, $p<0.05$ was signifincant. Group D: Dexmedetomidine 0.75 mg kg^{-1} b.wt., group F: Fentanyl 2 mg kg^{-1} b.wt., TDS: Systolic blood pressure, TDD: Diastolic blood pressure, TAR: Average of arterial pressure, LJ: Heart rate

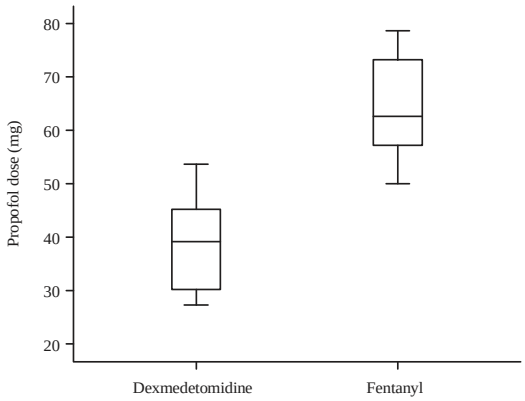

Fig. 1: Comparison of mean at needs induction propofol dose in both groups. Data was presented in Mean±SD (standard deviation). Dexmedetomidine group KD = 0.75 μg kg^{-1} b.wt., KF: Group fentanyl 2 μg kg^{-1} b.wt.

Table 4: Comparison of propofol induction dose requirement in both groups

	Dose of propofol induction (mg)					
Groups	Minimum	Maximum	Mean	SD	IK (95%)	p-value
1 (n = 24)	36	58	45.58	7.30	42.50-48.67	<0.001
2 (n = 24)	55	79	66.96	7.21	63.70-70.22	<0.001

Data was presented in Mean±SD (standard deviation). Tested by Mann Whitney test, p<0.05 revealed significant difference. Group 1: Dexmedetomidine μg kg^{-1} b.wt., group 2: Fentanyl 2 μg kg^{-1} b.wt.

Figure 2 shows that first there was an increase mean arterial pressure (TAR) at 1 min after intubation, then decreases to the observation of 3 and 5 min after intubation and lower than the mean arterial pressure (TAR) basal value. The increase in fentanyl group was higher than in the group of dexmedetomidine 1 min after intubation. Although, mean arterial pressure (TAR) decreased in both groups during the 3 min after intubation but the chart mean arterial pressure (TAR) of fentanyl group located above the graph dexmedetomidine during 3 min after intubation. Then 5 min after intubation chart mean arterial pressure (TAR) of both groups coincide.

From the results, it was shown in Table 6 that there was a change in both of the groups. There was heart rate (LJ) increasing trend in the fentanyl group 1 min after intubation and then fell back at 3rd and 5th min after intubation, whereas in the group dexmedetomidine there was no increase and even tends lower than heart rate (LJ) basal and more decreased at 3rd and 5th min after intubation. There were significant difference (p<0.05) after intubation at the both of the groups. Rate of heart at fentanyl group was higher than dexmedetomidine group at each time of observation.

Figure 3 shows that first there was an increase mean arterial pressure (TAR) 1 min after intubation in the fentanyl group and then decline steeply up to the observation of 3 min and remained decreased 5 min after intubation with ramps

Table 5: Comparison of the mean arterial pressure at the both of the groups in time of measurement

Time of		Mean arterial pressure (mmHg)					
measurement	Groups	Minimum	Maximum	Mean	SD	IK (95%)	p-value
To	1 (n = 24)	83	103	93.6	5.8	91.2-96.1	0.098
	2 (n = 24)	80	107	96.8	7.0	93.8-99.7	
T1	1 (n = 24)	85	103	96.2	5.2	94.0-98.4	<0.001
	2 (n = 24)	98	137	112.2	10.2	107.9-116.5	
T2	1 (n = 24)	80	100	89.3	5.4	87.0-91.5	0.005
	2 (n = 24)	80	108	94.5	7.0	91.6-97.5	
T3	1 (n = 24)	77	96	84.7	4.7	82.7-86.7	0.714
	2 (n = 24)	76	96	85.3	6.2	82.6-87.9	

Data was presented in Mean±SD (standard deviation). Tested by Mann Whitney test, p<0.05 revealed significant difference. Group 1: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group 2: Fentanyl 2 μg kg^{-1} b.wt.. To: Measurement time before grouped, T1: Measurement time of 1 minute after intubation, T2: Measurement time 3 min after intubation, T3: Measurement time 5 min after intubation

Table 6: Comparison heart rate at both of the groups in time of measurement

Time of		Heart rate (x/min)					
measurement	Groups	Minimum	Maximum	Mean	SD	IK 95(%)	p-value
To	1 (n = 24)	68	92	83.3	7.4	79.2-85.5	0.357
	2 (n = 24)	62	95	79.5	9.3	75.6-83.5	
T1	1 (n = 24)	68	86	79.3	5.2	77.1-81.5	<0.001
	2 (n = 24)	82	119	93.7	8.7	90.0-97.3	
T2	1 (n = 24)	64	77	70.5	3.6	87.0-91.5	<0.001
	2 (n = 24)	70	104	82.2	8.3	78.7-85.7	
T3	1 (n = 24)	59	72	64.5	3.6	82.7-86.7	<0.001
	2 (n = 24)	65	98	77.7	7.6	74.4-80.9	

Data was presented in Mean±SD (standard deviation). Tested by Mann Whitney test, p<0.05 revealed significant difference. Group 1: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group 2: Fentanyl 2 μg kg^{-1} b.wt. To: Measurement time before grouped, T1: Measurement time of 1 min after intubation, T2: Measurement time 3 min after intubation, T3: Measurement time 5 min after intubation

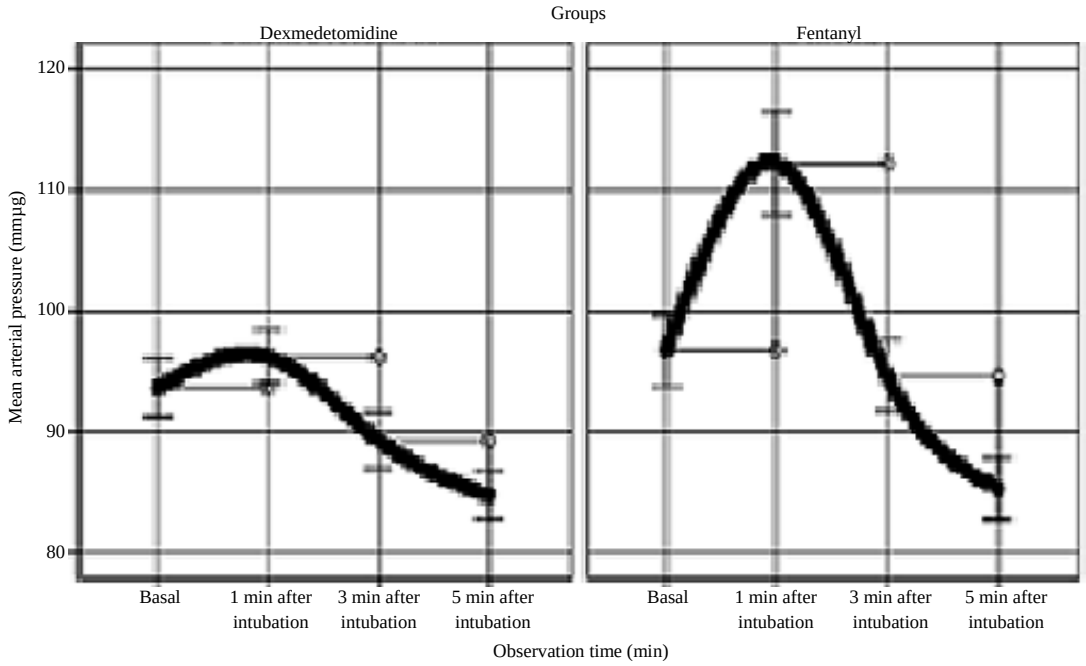

Fig. 2: Dynamics of mean arterial pressure (TAR) in both groups. Data was presented in Mean±SD (standard deviation). Group D: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group F: Fentanyl 2 μg kg^{-1} b.wt.

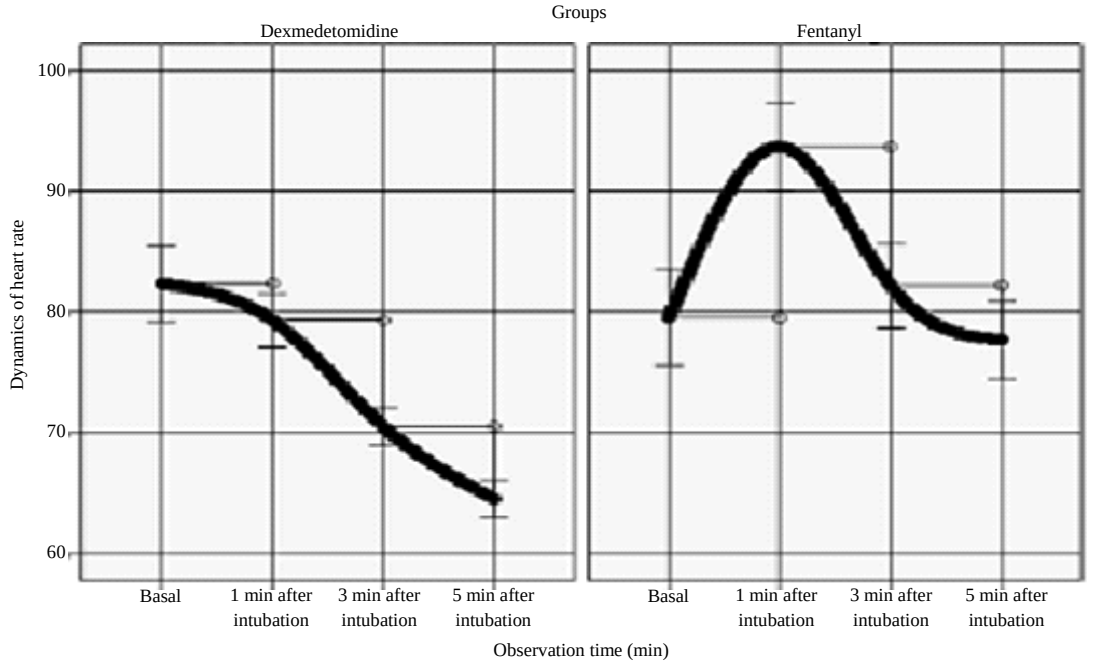

Fig. 3: Dynamics of heart rate (LJ) in both groups. Data was presented in Mean±SD (standard deviation). Group D: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group F: Fentanyl 2 μg kg^{-1} b.wt.

and slightly lower than the basal value. In the group of dexmedetomidine there was no increase and even tends to decrease at 1 min after intubation and decreased more steeply 3 min after intubation and remained decreased to 5 min after intubation.

From the analysis, it can be seen from Table 7, at 1 min after intubation obtained percentage increase mean arterial pressure (TAR) in the fentanyl group (16.32%) was higher than the percentage increase mean arterial pressure (TAR) at the dexmedetomidine group (2.90%) and it shows the difference

Table 7: Comparison changes percentages mean arterial pressure (TAR) to basal mean arterial pressure (TAR)

Time of measurement	Groups	Average changes of TAR (%) Minimum	Maximum	Mean	Standard deviation	IK (95%)	p-value
T1	1 (n = 24)	-7.29	12.05	2.90	5.49	0.58-5.220	<0.001
	2 (n = 24)	4.04	38.37	16.32	10.90	11.71-20.92	
T2	1 (n = 24)	-13.98	9.64	-4.47	6.36	-7.15-(-1.38)	0.261
	2 (n = 24)	-20.00	21.18	-1.81	9.82	-5.96-2.330	
T3	1 (n = 24)	-19.79	0.00	-9.46	3.80	-11.06-(-7.85)	0.103
	2 (n = 24)	-28.04	12.94	-11.40	9.56	-15.43-(-7.36)	

Data was presented in of Mean±SD (standard deviation). Tested by Mann Whitney test, p<0.05 revealed significantly difference. Group 1: Dexmedetomidine 0.75 75 μg kg^{-1} b.wt., group 2: Fentanyl 75 μg kg^{-1} b.wt., To: Measurement time before grouped, T1: Measurement time of 1 min after intubation, T2: Measurement time 3 min after intubation, T3: Measurement time 5 min after intubation

Table 8: Comparison of percentage heart rate (LJ) changes to heart rate (LJ) basal

Time of measurement	Groups	Changes of heart rate (%) Minimum	Maximum	Mean	SD	IK (95%)	p-value
T1	1 (n = 24)	-11.76	5.26	-3.37	5.11	-5.53-1.21	<0.001
	2 (n = 24)	2.47	57.58	18.88	14.41	12.79-24.96	
T2	1 (n = 24)	-25.58	5.88	-13.87	7.00	-16.82-(-10.91)	<0.001
	2 (n = 24)	-13.58	35.48	3.99	10.43	-0.41-8.39	
T3	1 (n = 24)	-31.03	-7.25	-21.22	6.35	-23.90-(-18.53)	<0.001
	2 (n = 24)	-14.77	25.81	-1.64	10.36	-6.01-2.73	

Data was presented in of Mean±SD (standard deviation). Tested by Mann Whitney test, p<0.05 revealed significantly difference. Group 1: Dexmedetomidine 0.75 μg kg^{-1} b.wt., group 2: Fentanyl μg kg^{-1} b.wt., To: Measurement time before grouped, T1: Measurement time of 1 min after intubation, T2: Measurement time 3 min after intubation, T3: Measurement time 5 min after intubation

Table 9: Incidence of side effect of both of the groups for dexmedetomidine and fentanyl

	Groups				
	Dexmedetomidine (n = 24)		Fentanyl (n = 24)		
Incidences	n	%	n	%	*p-value
Hypertension	-	-	5	20.83	<0.001
Hypotension	-	-	-	-	
tachycardia	-	-	5	20.83	
Bradycardia	-	-	-	-	
Nauseous vomit	-	-	-	-	

Data was presented as a percentage (%). *Tested with chi-square test, p<0.05 revealed significantly difference. Dexmedetomidine group KD: μg kg^{-1} b.wt., KF: Group of fentanyl μg kg^{-1} b.wt.

significance (p<0.05). When viewed in the lowest and highest value column, on the fentanyl group all increases ranging from 4.04-38.37%, whereas in group of dexmedetomidine were ranging from -7.29 to 12.05%. It means that in this group, there are not all experiencing an increase, there was some decline. The highest increase is 12.05% and the highest decrease is 7.29%.

At 3 min after intubation obtained a percentage reduction mean arterial pressure (TAR) in fentanyl group (1.81%) and mean percentage reduction mean arterial pressure (TAR) in dexmedetomidine group (4.47%) and this difference indicates a significant difference (p>0.05).

At 5 min after intubation obtained a mean percentage reduction mean arterial pressure (TAR) in fentanyl group (11.40%) and a percentage reduction mean arterial pressure (TAR) in dexmedetomidine group (9.46%) and this difference indicates a significant difference (p>0.05).

From the analysis results, it was shown in Table 8, at 1 min after intubation percentage average of heart rate increase in the fentanyl group was higher (18.88%) of the average heart rate basal, while the average percentage of heart rate on dexmedetomidine group decreased (3.37%). At 3 min after intubation average of the percentage decreased from previously (3.99%) even though they increased from basal of heart rate, whereas the average percentage of heart rate on group of dexmedetomidine decrease (13.87%). At 5 min after intubation both group of dexmedetomidine and fentanyl group decrease heart rate mean, wherein the fentanyl group decreased (1.64%) and dexmedetomidine (21.22%).

Incidence of side effect: From the results in Table 9, in this study only found the incidence of side effects of hypertension and tachycardia. For group of dexmedetomidine was not encountered any adverse experiences, while in the fentanyl group there were 5 patients (20.83%) who had hypertension and 5 patients (20.83%) who experienced tachycardia. So statistically significant difference (p<0.05) for the incidence of adverse events in both groups in this study. Comparison of the incidence of adverse events in both groups were analyzed using chi-square test, in which the probability value p<0.05 revealed statistically significant.

DISCUSSION

The use of induction supplements drugs aim to reduce the hemodynamic response due to intubation laryngoscopy actions have been carried out by experts. Some medications that are often used include: local anesthetics (lidocaine) intravenous or topical opioids (fentanyl), β-adrenergic blockers, vasodilators (nitroglycerin, sodium nitroprusside), calcium channel antagonist (diltiazem), α_2-adrenergic agonists (Dexmedetomidine) and combinations of these drugs. Dexmedetomidine are new drugs that some experts have been used to suppress hemodynamic response due to the actions laryngoscopy and intubation, while fentanyl was the most commonly drug that used in the Hospital of Dr. Wahidin Sudirohusodo Makassar. The aim of the study was comparing the efficacy among of both of the drugs[11-16].

In the group of dexmedetomidine, it was seen that the needs of the propofol induction dose was significantly lower compared to the fentanyl group. This was caused dexmedetomidine has sedative effects that study on sureleuspontine locus, which is an important source of the sympathetic nervous system that innervate forebrain and vital modulator of vigilance system[17].

In the 1st min after intubation group of fentanyl was not able to prevent the increase in blood pressure and heart rate due to laryngoscopy and intubation action, otherwise the group dexmedetomidine was effective. Obtained in the fentanyl group, mean arterial pressure (TAR) rose as much as 16.32% of mean arterial pressure (TAR) basal and mean heart rate (LJ) increased by 18.88% from basal of heart rate (LJ), while the mean arterial pressure (TAR) at dexmedetomidine rose as much as 2.90% of the mean arterial pressure (TAR) basal and average heart rate (LJ) decreased by 3.37% of the basal of heart rate. This was consistent with study of Kallio *et al.*[11], which reported that dexmedetomidine as α_2-adrenoceptor agonists can be used to control perioperative hemodynamics, there was significant reduction in the blood pressure and heart rate, depending on the dose given. In the 3 min, both groups of dexmedetomidine and fentanyl group was able to prevent the increase in blood pressure, it seems that the mean arterial pressure (TAR) of fentanyl group decreased as much as 1.81% and the mean arterial pressure (TAR) of group dexmedetomidine decreased as much as 4.47% from the mean arterial pressure (TAR) basal but the fentanyl group has not been able to prevent an increase in heart rate which is still an increase in the average of heart rate 3.99% of basal of heart rate. In contrast to the average heart rate decline in the group of dexmedetomidine as much as 13.87% of heart rate basal[17-23].

In the 5 min after intubation both dexmedetomidine group and fentanyl group decreased hemodynamic response in all variables. Where in the fentanyl group there was decrease mean arterial pressure (TAR) as much as 11.40% of the T mean arterial pressure (TAR) basal and decrease heart rate as much as 1.64% of the basal heartrate. While the decline mean arterial pressure (TAR) in the average group of dexmedetomidine as much as 9.46% of TAR basal and decrease the average of heart rate as much as 21.22% of heart rate basal[24,25].

Thus it can be said that dexmedetomidine was effective in reducing the increase in the hemodynamic response due to the actions laryngoscopy and intubation compared to fentanyl. Although less effective, fentanyl can also be used to reduce the increase in the hemodynamic response due to the actions laryngoscopy and intubation, because fentanyl was able to suppress hemodynamic response in the 3 and 5 min. Theory says that in healthy people there was an increase in blood pressure both systolic and diastolic occurred from 5 sec, reaching a peak in 1-2 min and again like before laryngoscopy in 5 min. The inceease of TDS mean more than 53 mmHg, TDD was more than 34 mmHg and heart rate[13, 26-28] more than 23 beats min^{-1}.

Hemodynamic response between the two groups differed significantly on all the variables in the 1 min. Statistically, dexmedetomidine was more effective than fentanyl in preventing an increase in the hemodynamic response to the laryngoscopy and intubation action. This was because dexmedetomidine α_2-adrenergic receptors activate presynaptic which will inhibit neurotransmitter release in the end of nerves and cause a decrease in plasma norepinephrine levels that produce cardiovascular stabilization. Fentanyl although less effective but it can also decrease the hemodynamic response with the procedure blocking pain stimuli, depressed central sympathetic tone and activation of vagal tone[29].

Previous studies either on dexmedetomidine or fentanyl generally produce the same results on the blood pressure response, where dexmedetomidine was effective, while fentanyl was less effective in reducing blood pressure due to laryngoscopy and intubation. Appropriate study of Kharwar *et al.*[12], which states that dexmedetomidine 1 μg kg^{-1} b.wt., was more effective in reducing the hemodynamic response due to the laryngoscopy and intubation compared with fentanyl 2 μg kg^{-1} b.wt., but side effects such as hypotension and bradycardia commonly occurst[12,30].

In the 5 min there were decreased hemodynamic response in both groups, which differ significantly decrease in

all variables except the variable of heart rate were not significantly different in the fentanyl group. The decline was bigger and stronger in dexmedetomidine group, even decline to below the initial value of all variables. Blood pressure and heart rate was more quickly descended on the group of dexmedetomidine caused by the effects of the central sympathetic tone depression from dexmedetomidine that produce vasodilation and decrease heart rate. Impairment to below the initial value occurs because until the 5 min the surgery have not been conducted, so in accordance with the theory that after the 1 min of the value will come down by itself and reach the initial value after the 5 min[17,18,31,32].

The incidence of hypertension and tachycardia obtained in the two groups was significantly different ($p<0.05$), in which 5 people (20.83%) hypertension and 5 people (20.83%) in the group of fentanyl experienced tachycardia occurring in the 1 min, whereas in the group of dexmedetomidine was not found. The incidence of hypotension and bradycardia in both groups were found.

CONCLUSION

The needs dose of profol induction was less on administration dexmedetomidine 0.75 μg kg^{-1} b.wt., compared to the administration of fentanyl 2 μg kg^{-1} b.wt., in patients who undergoing general anesthesia procedures.

Dexmedetomidine hemodynamic response in the administration of μg kg^{-1} b.wt., was more stable than administration offentanyl 2 μg kg^{-1} b.wt., at 1 min after intubation.

Both of dexmedetomidine 0.75 μg kg^{-1} b.wt. and fentanyl 2 μg kg^{-1} b.wt., can maintain stable response of hemodynamic at 3 and 5 min after intubation but the average heart rate at dexmedetomidine administration was lower.

SIGNIFICANCE STATEMENTS

In surgery procedure, laryngoscopy and endotracheal intubation can cause the increase of blood pressure and heart rate (hemodynamic indicators) due to the sympathetic activity and simpatoadrenal reflex. This study aimed to compare the capacity of dexmedetomidine and fentanyl in stabilize the hemodynamic status. Fourty eight patients, involved in this randomized, single-blind controlled study. Before induction with propofol and intubation, 14 patients in group D received dexmedetomidine 0.75 μg kg^{-1} b.wt. and the rest, group F, received fentanyl 2 μg kg^{-1} b.wt. The dose of propofol need to reach BIS as well as blood pressure, mean arterial pressure and heart rate were recorded at 1, 3 and 5 min after intubation. This study showed intravenous dexmedetomidine lowering induction dose of propofola, stabilize heart rate and blood pressure better than fentanyl. This study cloncluded that for patient who has heart problem, it is recommended to give dexmedetomidine as premedication.

REFERENCES

1. Stone, D.J. and T.J. Gal, 2000. Airway Management. In: Anesthesia, Miller, R.D. (Ed.). 4th Edn., Churchill Livingstone, Philadelpia, pp: 1414-1448.
2. Burstein, C.L., F.J. Lopinto and W. Newman, 1950. Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine technics. J. Am. Soc. Anesthesiol., 11: 224-237.
3. Wycoff, C.C., 1960. Endotracheal intubation: Effects on blood pressure and pulse rate. Anasthesiology, 21: 153-158.
4. Forbes, A.M. and F.G. Dally, 1970. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br. J. Anaesth., 42: 618-624.
5. Shribman, A.J., G. Smith and K.J. Achola, 1987. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br. J. Anaesth., 59: 295-299.
6. Derbyshire, D.R., A. Chmielewski, D. Fell, M. Vater, K. Achola and G. Smith, 1983. Plasma catecholamine responses to tracheal intubation. Br. J. Anaesth., 55: 855-860.
7. Bruder, N., D. Ortega and C. Granthil, 1992. [Consequences and prevention methods of hemodynamic changes during laryngoscopy and intratracheal intubation]. Annales Francaises d'Anesthesie Reanimation, 11: 57-71, (In French).
8. Gertler, R., H.C. Brown, D.H. Mitchell and E.N. Silvius, 2001. Dexmedetomidine: A novel sedative-analgesic agent. Proc. Baylor Univ. Med. Center, 14: 13-21.
9. Savola, J.M., H. Ruskoaho, J. Puurunen, J.S. Salonen and N.T. Karki, 1986. Evidence for medetomidine as a selective and potent agonist α_2-adrenoreceptors. J. Auton. Pharmacol., 5: 275-284.
10. Hayashi, Y. and M. Maze, 1993. Alpha 2 adrenoceptor agonists and anaesthesia. Br. J. Anaesth., 71: 108-118.
11. Kallio, A., M. Scheinin, M. Koulu, R. Ponkilainen, H. Ruskoaho, O. Viinamaki and H. Scheinin, 1989. Effects of dexmedetomidine, a selective α_2-adrenoceptor agonist, on hemodynamic control mechanisms. Clin. Pharmacol. Therapeut., 46: 33-42.
12. Kharwar, R.K., M. Kumar, P.K. Tiwary, U. Suwalka and S. Prakash, 2014. A comparison of intravenous dexmedetomidine v/s inj. Fentanyl for attenuation of hemodynamic responses during laryngoscopy and intubation after propofol induction. Natl. J. Integrat. Res. Med., 5: 71-75.
13. Laito, I.P. and M. Rosen, 1985. Phatophysiological Effects of Tracheal Intubation. In: Difficulties in Tracheal Intubation, Latto, I.P. and R.S. Vaughan (Eds.). Elsevier Health Sciences, Philadelpia, ISBN-13: 9780702010965, pp: 12-31.

14. Chrysostomou, C. and C.G. Schmitt, 2008. Dexmedetomidine: Sedation, analgesia and beyond. Expert Opin. Drug Metab. Toxicol., 4: 619-627.
15. Thaib, M.R., 2002. Deksmedetomidin, α_2-adrenoseptor agonisbaru. 1st Indonesian Symposium on Obstetric Anesthesia, Bandung.
16. Ebert, T.J., J.E. Hall, J.A. Barney, T.D. Uhrich and M.D. Colinco, 2000. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology, 93: 382-394.
17. Kamibayashi, T. and M. Maze, 2000. Clinical uses of α^2-adrenergic agonists. Anesthesiology, 93: 1345-1349.
18. Bloor, B.C., D.S. Ward, J.P. Belleville and M. Maze, 1992. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology, 77: 1134-1142.
19. Hall, J.E., T.D. Uhrich, J.A. Barney, S.R. Arain and T.J. Ebert, 2000. Sedative, amnestic and analgesic properties of small-dose dexmedetomidine infusions. Anesth. Analg., 90: 699-705.
20. Yildiz, M., A. Tavlan, S. Tuncer, R. Reisli, A. Yosunkaya and S. Otelcioglu, 2006. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Perioperative haemodynamics and anaesthetic requirements. Drugs R and D, 7: 43-52.
21. Bovill, J.G., P.S. Sebel and T.H. Stanley, 1984. Opioid analgesics in anesthesia: With special reference to their use in cardiovascular anesthesia. Anesthesiology, 61: 731-755.
22. Grell, F.L., R.A. Koons and J.S. Denson, 1970. Fentanyl in anesthesia: A report of 500 cases. Anesth. Analg., 49: 523-532.
23. Reitan, J.A., K.B. Stengert, M.L. Wymore and R.W. Martucci, 1978. Central vagal control of fentanyl-induced bradycardia during halothane anesthesia. Anesth. Analg., 57: 31-36.
24. Aksu, R., A. Akin, C. Bicer, A. Esmaoglu, Z. Tosun and A. Boyaci, 2009. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Curr. Therapeut. Res., 70: 209-220.
25. Feld, J.M., W.E. Hoffman, M.M. Stechert, I.W. Hoffman and R.C. Ananda, 2006. Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. J. Clin. Anesth., 18: 24-28.
26. Morgan, G.E., M.S. Mikhail and M.J. Murray, 2002. Clinical Anesthesiology. 3rd Edn., McGraw-Hill, Philadelphia, pp: 218-219.
27. Struys, M.M.R.F., T. de Smet, L.F. Versichelen, S. van de Velde, R. van den Broecke and E.P. Mortier, 2001. Comparison of closed-loop controlled administration of propofol using Bispectral Index as the controlled variable versus standard practice controlled administration. Anesthesiology, 95: 6-17.
28. Sigl, J.C. and N.G. Chamoun, 1994. An introduction to bispectral analysis for the electroencephalogram. J. Clin. Monitor., 10: 392-404.
29. Pratiknya, A.W., 2001. Rancangan Penelitian Eksperimental I Polaumum. In: Dasar-Dasar Metodologi Penelitian Kedokteran dan Kesehatan, Pratiknya, A. (Ed.). PT Raja Grafindo Persada, Jakarta, pp: 117-143.
30. Harun, S.R., S.T. Putra and A.S. Wiharta, 1995. Chair I. Clinical Test. In: Fundamentals of Clinical Research Methodology, Sastroasmoro, S. and S. Ismael (Eds.). Binarupa Aksara, Jakarta, pp: 109-125.
31. Arif, S.K. and Firmansyah, 2016. The influence of lateral decubitus position in patients receiving unilateral spinal anesthesia on the sensory block, motoric block and hemodynamic stability in lower limb surgery. Pak. J. Nutr., 15: 474-479.
32. Arif, S.K., S. Gaus and R. Kasim, 2016. Use of base excess value and the blood lactate level in predicting organ disfunction measured by Sequential Organ Failure Assessment (SOFA) score system: Study in the post trepanation patients with severe traumatic brain injury. Trends Med. Res., 11: 101-106.