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ORIGINAL ARTICLE

A Comparison between Magnesium Sulfate and Two Doses of Dexmedetomidine to Attenuate the Hemodynamic Response to Laryngoscopy and Tracheal Intubation

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ABSTRACT

Background: Laryngoscopy and endotracheal intubation are stressful for patients, as these procedures can produce tachycardia, hypertension, and arrhythmias. **Aim of work:** The aim of the current study was to compare the effect of magnesium sulphate and two doses of dexmedetomidine on hemodynamic response to laryngoscopy and tracheal intubation. **Patients and methods:** This comparative prospective randomized controlled (single-blind) clinical study was carried out in Zagazig University hospitals on 80 patients during the period from May 2019 to February 2020. Patients were divided randomly into four groups each is 20 patients: Group Da: 20 Patients received dexmedetomidine 0.5mcg/kg in 20 ml normal saline intravenous infusion over 10 min. Group Db: 20 Patients received dexmedetomidine 1mcg/kg in 20 ml normal saline intravenous infusion. Group M: 20 Patients received magnesium sulphate 30mg/kg in 20 ml normal saline intravenous in fusion over 10 min. Group C: 20 Patients received 20 ml 0.9% in 20 ml normal saline intravenous infusion over 10 min**. Results:** The heart rate in Db group was statistically lower than other groups, Heart rate in the Da group were statistically significantly lower compared to group M and group C. Systolic blood pressure was statistically significantly lower in group Db compared to another group. **Conclusions:** Through this study, we can conclude that Dexmedetomidine 1mcg/kg is more effective than dexmedetomidine 0.5mcg/kg and magnesium sulphate 30mg/kg in decreasing the hemodynamic response to laryngoscopy and tracheal intubation.

Keywords: Dexmedetomidine, magnesium sulphate, stress response, laryngoscopy, hemodynamic parameters

INTRODUCTION

Direct laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response due to reflex sympathetic stimulation. This response may be hazardous in patients with hypertension, coronary artery disease, myocardial disease, and cerebrovascular disease. Numerous agents have therefore been utilized to blunt this response [1].

Magnesium sulphate is used to decrease the hemodynamic response to airway management, with proven effectiveness. It blocks the release of catecholamines from adrenergic nerve terminals and the adrenal gland, has cardioprotective and antiarrhythmic action, and induces coronary and systemic vasodilation by antagonizing calcium ions in vascular smooth muscle [2].

Dexmedetomidine is a potent highly selective alpha-2 adrenergic agonist. Alpha-2 adrenergic agonists have been widely used as adjuncts in the preoperative period for their analgesic, sedative, hypnotic, anxiolytic and sympatholytic properties. It has been used and found to be more effective to attenuate the stress response to laryngoscopy when compared with agents like esmolol, fentanyl, and clonidine [3].

Currently, dexmedetomidine is considered very useful in blunting the hemodynamic effects of laryngoscopy and intubation. Many authors studied different doses of dexmedetomidine, but the effective dose which blunts the stress response with minimal side effects is yet to be established [4].

The aim of the current study was to compare the effect of magnesium sulphate and two doses of dexmedetomidine in hemodynamic response to laryngoscopy and tracheal intubation.

PATIENTS AND METHODS

This comparative prospective randomized placebo-controlled clinical study was carried out in Zagazig University hospitals on 80 patients during the period from May 2019 to February 2020.

Written informed consent was taken from all patients and the study was approved by the research ethical committee of the Faculty of Medicine, Zagazig University. The study was done according to the ethical code of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Patient acceptance, Body Mass Index (BMI) <35kg/m^2. Patient undergoing elective surgery under general anesthesia. Age between 21-60 years old. Both sexes (male and female). Physical status: American Society of Anesthesiologists (ASA) physical status I and II.

Exclusion criteria: Risk index of El-Ganzouri score for difficult tracheal intubation ≥4 [5]**.** Patients with hypersensitivity to one of the studied drugs. Altered mental status. Cardiac arrhythmias, Ischemic heart diseases. Liver and kidney impairment. Pregnant female. Uncontrolled hypertension. Postural hypotension. Anticipated Sever blood loss during surgery. Patients on sedation

Sample size:

A sample size of 80 American Society of Anesthesiologists (ASA) physical status I and II patients [6] undergoing elective surgery were enrolled in the study. Patients were divided to four groups, 20 in each group at 80% power and 95% CI (confidance interval) using open EPI.

ASA 1: A normal healthy patient. Example: Fit, nonobese (BMI under 30), a nonsmoking patient with good exercise tolerance.

ASA 2: A patient with mild systemic disease. Example: Patient with no functional limitations and a well-controlled disease (e.g., treated hypertension, obesity with BMI under 35, frequent social drinker, or cigarette smoker).

Patients have been divided randomly by computer generated randomization table into four groups each is 20 patients :

Group (Da) (n=20): Patients have been received dexmedetomidine 0.5mcg/kg according to patient's body weight and dilute the drug in normal saline to make the volume 20 cc then infused over 10 min. before intubation.

Group (Db) (n=20): Patients have been received dexmedetomidine1mcg/kg in 20 ml normal saline intravenous infusion over 10 min.

Group (M) (n=20): Patients have been received magnesium sulphate 30mg/kg in 20 ml normal saline intravenous infusion over 10 min .

Group (c): Control group (n=20): Patients have been received 20ml 0.9% normal saline intravenous infusion over 10 min.

Steps of performance:

Parameters of the study included:

Full history has been taken. General and local examinations have been done for all patients, also routine laboratory investigations. On arrival to the operating room, standard monitoring has been applied to all patients, including pulse oximeter, electrocardiogram (ECG), non-invasive arterial blood pressure (NIBP), and basal values of heart rate, systolic blood pressure,e and diastolic blood pressure have been recorded.

After securing an IV line, The infusion has been done by a syringe pump at rate 120ml/hr over 10 min. The sedation score has been assessed after completion of the infusion of the drugs and just before the induction of anesthesia using AVPU scale (A=alert ,V=verbal ,P=pain , U=unresponsive.)AVPU assessments were extracted from the eye component of the Glasgow coma scale ."A" was assigned to a Glasgow coma scale eye score of 4(opens eyes spontaneously),"V" to a score of 3(opens eyes in response to voice),"P" to a score of 2 (opens eyes in response to painful stimuli)and "U" to a score of 1(does not open eyes)[7].

All patients have been preoxygenated with 100% oxygen for 3 minutes. All patients received propofol 2mg/kg IV and fentanyl 1 mcg/kg IV. Endotracheal all patients received propofol (2mg/kg), fentanyl (1mcg/kg) and the intubation has been facilitated by 0.5 mg/kg cisatracurium, anesthesia given after completion of studied drugs. Heart rate, systolic blood pressure and diastolic blood pressure have been recorded at 0 (at intubation) 1,3,5,10 and 15 minutes after intubation. Anesthesia has been maintained by isoflurane 1.5 MAC (mean alveolar concentration) in 100% oxygen. Ventilation has been controlled mechanically, tidal volume =8ml/kg, respiratory rate is adjusted to maintain ETCO2 at range of 30-35mmHg and muscle relaxation has been maintained with intravenous cis-atracium 20% of initial dose when needed.At

the end of surgery, neostigmine methylsulphate 0.05mg/kg and atropine 0.01mg/kg was administered for antagonism of neuromuscular block, and the patient extubated.

Data collected as follows:

Heart rate (bpm) was recorded before infusion of the studied drug (basal) then at 0(at intubation), 1, 3, 5, 10 and 15 minutes after intubation.

Systolic blood pressure (mmHg) was recorded before infusion of studied drug(basal)then at 0 (at intubation), 1, 3, 5, 10, and 15 minutes after intubation.

Diastolic blood pressure (mmHg) was recorded before infusion of the studied drug(basal) then at 0(at intubation),1, 3, 5, 10, and 15 minutes after intubation.

During surgery, any fall in the MAP more than 20% from the baseline was treated with phenylephrine 20 mg IV, and bradycardia (decreased heart rate 20% from the baseline) was treated with atropine 0.5mg IV [8].

The incidence of hypotension, bradycardia, and any changes in the heart rhythm rather than sinus rhythm have been recorded.

STATISTICAL ANALYSIS

All data were statistically analyzed using SPSS 20.0 for windows. According to the type of data qualitative as number and percentage represented by mean ± SD, the following tests were used; t test for differences for significance, Chi-square test (X^2) for difference and association of qualitative variable, ANOVA test was used for the differences between quantitative independent multiple and Pearson's correlation for correlation. P value was set at <0.05 for significant results & <0.001 for highly significant result

Table (1) showed there was no statistically significant difference regarding demographic data between studied groups. Table (2) showed that basal heart rate were nearly similar between the studied groups. Heart rate in Db group at and after intubation was statistically significant ower than other studied groups. Heart rate in Da group was statistically significant lower than group M and group C at and after intubation. There was a statistically significant difference among the studied groups regarding heart rate all over the measured time points. Table (3), showed that basal systolic blood pressure was comparable between all studied groups p>0.05. Systolic blood pressure in Db group were statistically significant lower than other groups. Systolic blood pressure in M group was statistically significant lower than in group Da and group C. There was statistically significant difference among the studied groups regarding systolic blood pressure at the measured time points. Table (4), showed that basal diastolic blood pressure were comparable among the studied groups p>0.05. Diastolic blood pressure in Db group were statistically significant lower than other groups after intubation. Diastolic blood pressure in M group was statistically significant lower than in group Da and group C .There were statistically significant difference among all studied groups regarding diastolic blood pressure all over the measured time points. Table (5), showed that group Db were more sedated compared to other groups with a statistical significant difference. Table (6), showed that there was no statistical significant difference of adverse effects among the studied groups (p>0.05).

Table 1: Demographic characteristics, type and duration of operation among the studied groups (each group n = 20)

Demographic items	Studied groups				F	p
	Da group	**Db group**	**M group**	**C group**		
Age per years Mean ±SD	30.6±5	32.5±6.39	33.1±4.97	29.95±5.98	1.43	0.24
Sex n(%)					χ^2 =2.4	0.49
Females	4(20)	5(25)	3(15)	7(35)		
Males	16(80)	15(75)	17(85)	13(65)		
ASA	15(75)	16(80)	16(80)	17(85)		0.89
I	5(25)	4(20)	4(20)	3(15)	χ^2 =.62	
II						
Type of surgery :					2.74	0.99
Lap cholecysteomy	10(50)	9 (45)	11 (55)	10 (50)		
Herniorraphy	5 (25)	6 (30)	3 (15)	4 (20)		
Appendicectomy	2 (10)	3 (15)	3 (15)	2 (10)		
Adenotonsillectomy	1 (5)	1 (5)	1 (5)	2 (10)		

Demographic items	Studied groups				F	p
Tonsillectomy	2 (10)	1 (5)	2(10)	2 (10)		
Operation Duration(min) Mean ±SD	40.45±6.76	42.9±6.87	38.85±7.47	38.35±5.96	1.35	0.26

Da group (Dex= 0.5mic/kg) Db group (Dex= 1 mic/kg) M group (Mg sulfate = 30mg/kg) C group (C= 20ml N/S). Data were expressed as mean ± SD or number (percentage) F = One Way ANOVA test, χ^2 =Chi square test, ASA= American society of anesthesia,

Table 2: Comparison of Heart rate (HR) (b\m) among the studied groups at measured time points (each group n = 20)

Variables	Studied groups				F	P	Post hoc (P)			
	Da group	**Db group**	**M group**	**C group**			Da &M	Da &C	Db &M	Db&C
Basal Heart rate	78.45±7.56	76.95±9.59	73.5±7.06	74.8±7.4	1.53	.21	-	-	-	-
Heart rate at intubation	67.6±6.77	61.95±9.59	73.15±6.7	72.8±7.4	9.3	<.001	.026	.036	<.001	<.001
	*P=0.023		**P=0.88							
Heart rate after intubation	66.6±6.77	60.95±9.59	72.95±5.73	72.45±7.06	11.5	<.001	.008	.015	<.001	<.001
	*P=.019		**P=.83							
Heart rate1min	68±6.54	61.7±9.15	74.7±5.47	73.45±7.1	13.6	<.001	.004	.019	<.001	<.001
	*P=.007		**P=.58							
Heart rate3min	66.9±6.54	60.75±9.23	74.05±4.22	73.1±6.09	16.6	<.001	.001	.005	<.001	<.001
	*P=.005		**P=.66							
Heart rate5min	68.5±5.83	62.2±8.44	75.2±5.7	74.55±6.18	16.8	<.001	.002	.005	<.001	<.001
	*P=.004		**P=.76							
Heart rate10min	67.2±6.29	61.55±9.48	73.85±6.03	73.55±6.08	13.5	<.001	.004	.006	<.001	<.001
	*P=.014		**P=.89							
Heart rate15 min	67.9±5.21	62.65±8.15	74.7±4.26	74.4±5.82	18.3	<.001	.007	.001	<.001	<.001
	*P=.007		**P=.87							

Table 3: Comparison of Systolic blood pressure among the studied groups at measured time points (each group n = 20)

	Studied groups				F	P	Post hoc			
	Da group	**D b group**	**M group**	**C group**			Da & M	Da &C	Db & M	Db &C
Basal Systolic blood pressure	137±8.64	133.45±8.2	135.5±7.93	132.25±7.69	1	0.15	-	-	-	-
Systolic blood pressure Before intubation	134.1±8.14	117.5±8.18	124.5±7.93	130.1±7.37	16.6	<.001	<.001	.14	.006	<.001
	*P<.001		**P=.028							
Systolic blood pressure after	133.7±8.14	116.85±8.3	123.35±6.4	129.95±6.43	20.3	<.001	<.001	.11	.007	<.001
	*P=<.001		**P=.006							

	Studied groups				F	P	Post hoc			
	Da group	D b group	M group	C group			Da & M	Da &C	Db & M	Db &C
intubation										
Systolic blood pressure min1	133.15±7.5	115.2±6.39	122.4±6.1	130.15±6.39	29.7	<.001	<.001	.15	.001	<.001
	*P=<.001		**P=<.001							
Systolic blood pressure min3	132.9±7.52	106.1±9.17	112.8±8.56	129.1±7.35	49.3	<.001	<.001	.14	.012	<.001
	*P=<.001		**P=<.001							
Systolic blood pressure min5	133.35±6.87	106.6±8.34	112.6±8.37	129.45±7.1	56.4	<.001	<.001	.11	.015	<.001
	*P=<.001		**P=<.001							
Systolic blood pressure min10	127.85±5.07	106.1±7.99	112.15±8.3	128.9±6.47	51.9	<.001	<.001	.64	.008	<.001
	*P=<.001		**P=<.001							
Systolic blood pressure min15	129.8±4.68	110.95±6.5	117.9±5.64	131±5.56	58.7	<.001	<.001	.50	<.001	<.001
	*P=<.001		**P=<.001							

Table 4: Comparison of diastolic blood pressure among the studied groups at measured time points (each group n = 20)

Variables	Studied groups				F	P	Post hoc			
	Da group	Db group	M group	C group			Da & M	Da & C	Db &M	Db & C
Basal Diastolic blood pressure	78±6.25	74.5±9.54	75.15±8.9	72.65±8.87	1.36	.26				
Diastolic blood pressure Before intubation	77.15±5.19	54.7±6.97	61.45±8.21	75.35±7.32	48.1	<.001	<.001	.42	.003	<.001
	*P<.001		**P<.001							
Diastolic blood pressure after intubation	75.9±5.2	54.2±4.55	60.5±7.04	77.1±6.72	72.5	<.001	<.001	.53	.001	<.001
	*P<.001		**P<.001							
Diastolic blood pressuremin1	74.65±6.49	54.7±4.89	61±6.59	77.2±6.35	62.2	<.001	<.001	.19	.002	<.001
	*P<.001		**P<.001							
Diastolic blood pressuremin3	75.15±6.51	56.2±5.01	61.1±6.19	77.6±6.38	59.9	<.001	<.001	.20	.012	<.001
	*P<.001		**P<.001							
Diastolic blood pressuremin5	75.4±4.15	57.7±4.04	61.7±5.9	78.1±6.35	74.1	<.001	<.001	.11	.018	<.001
	*P<.001		**P<.001							
Diastolic blood pressuremin10	75.65±3.95	58.35±3.42	61.8±5.67	78.35±6.32	79.3	<.001	<.001	.09	.032	<.001
	*P<.001		**P<.001							
Diastolic blood pressuremin15	76.4±3.9	60.1±1.65	63.2±4.44	78.35±6.1	90.2	<.001	<.0	.16	.027	<.001
	*P<.001		**P<.001							

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Table 5: sedation level among the studied groups at measured time points (each group n = 20)

sedation level	Studied groups Da group	Db group	M group	C group	χ^2	P	Post hoc(P) Da & M	Da &C	Db &M	Db & C
Alert yes	18(90)	12(60)	19(95)	20(100)	16.3	<.001	0.99	0.48	.008	0.001
	*P=0.028		**P=0.99							
Verbal Yes	2(10)	8(40)	1(5)	0(0.0)	16.3	<.001	0.99	0.48	.008	0.001
	*P=0.028		**P=0.99							

Table 6: Adverse effects of the studied drugs among studied groups (each group n = 20)

Adverse effects of the studied drugs	Studied groups Da group	Db group	M group	C Group	χ^2	p
	N(%)	N(%)	N(%)	N(%)		
Bradycardia	3 (15)	2 (10)	0 (0)	0 (0)	5.7	0.124
Hypotension	4 (20)	1 (5)	2 (10)	2 (10)	2.4	0.49

DISCUSSION

Laryngoscopy and tracheal intubation cause catecholamine release due to the sympatho-adrenal stimulation. This effect can cause acute hemodynamic instabilities such as increasing in blood pressure, heart rate (HR), pulmonary artery capillary wedge pressure [9].

Various pharmacological and non-pharmacological methods have been tried to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation. The non-pharmacological methods like shorter duration of laryngoscopy, smooth and gentle intubation, whenever possible insertion of LMA in place of endotracheal intubation have been used to attenuate the cardiovascular response to laryngoscopy and endotracheal intubation [4].

This prospective, randomized controlled study was conducted to to compare the effect of magnesium sulphate and two doses of dexmedetomidine on hemodynamic response to laryngeoscopy and tracheal intubation.

We have not found study comparing dexmedetomidine 0.5mcg/kg to magnesium sulphate 30mg /kg which is included in our current study.

The studied groups in our study were comparable regarding the demographic data, type and duration of surgery which was statistically nonsignificant.

Regarding heart rate, our study showed the basal heart rate were comparable among the studied groups, heart rate in Db group were statistically significant lower compared to the other groups all over measured time points, the heart rate in Da group were statistically significant lower compared to group M and group C all over measured time points which was in agreement with Joshi et al., [10] who studied a sample size of 102 patients divided into two groups with 51 patients in each group, group D received dexmedetomidine 1mcg/kg, group M received magnesium sulphate 50 mg/kg IV infusion over 10 min. they reported that there were statistically highly significant decrease in HR in group D when compared to HR in group M.

Also Chaithanya et al., [11] published a study comparing between the effect of I.V Magnesium sulphate (30mg/kg) and Dexmedetomidine (1mcg/kg) for attenuation of cardiovascular stress response during laryngeoscopy and endotracheal intubation and they found that magnesium sulphate compared to dexmedetomidine was effective in controlling the rise in heart rate following intubation and this was in agreement with our results.

Regarding systolic blood pressure the current study showed statistically significant lower reading in group Db compared to other groups all over measured time points, also the systolic blood pressure were statistically significant lower in group M compared to group Da and group C all over measured time points. turquoise

Mahajan et al., [12] found that there were statistically significant decrease in SBP in group

DS and group MS when compared to NS group throughout the intraoperative period and group DS having the lowest SBP values, their study were conducted on one hundred and twenty patients divided into three groups, group DS received dexmedetomidine 1mcg/kg, group MS received magnesium sulphate 30mg/kg and group NS received normal saline their finding match our study.

Another study carried out by Gulabani et al.,[13] revealed that the maximum reduction in SBP was achieved in group D2 and was statistically significant, this study involve 90 patients divided into three groups, group D1 receive dexmedetomidine 0.5mcg/kg, group D2 receive dexmedetomidine 1ug/kg and group X receive lignocaine 1.5 mg/kg this study also match our study regarding SBP.

Regarding DBP our study showed statistically significant lower reading in group Db compared to other groups all over measured time points, whereas the diastolic blood pressure was statistically significantly lower in group M compared to group Da and group C all over measured time points.

A similar study conducted by Thapa and Gauchan [4] compared the effect of 0.5 mcg/kg and 1 mcg/kg of dexmedetomidine on the attenuation of hemodynamic effects of laryngoscopy and intubation and reported similar to the current results.

Joshi et al., [10] found the fall in DBP after intubation was statistically highly significant in group D compared to group M.

This dose dependant decrease in heart rate and blood pressure caused by dexmedetomidine can be explained by the inhibition of sympathetic release of catecholamine and increased vagal activity, while magnesium sulphate attenuates the release of catecholamines by adrenal glands and antagonize the action of calcium in smooth muscle cells of arterioles.

Our study showed that the patients in group Db were more sedative compared to other groups, otherwise the groups were comparable regarding sedation level just before intubation. which is match the study conducted by Sebastian et al., [14] who found that there was a statistically significant difference between the three studied groups in the sedation score where it was more in Group B and Group C when compared to Group A (Group A received normal saline, Group B received dexmedetomidine 0.5 mcg/kg, Group C received dexmedetomidine 0.75mcg/kg as an infusion over 10 min.).

Conclusions: Through this study, we can conclude that Dexmedetomidine 1mcg/kg is more effective than dexmedetomidine 0.5mcg/kg and magnesium sulphate 30mg/kg in decreasing the hemodynamic response to laryngoscopy and tracheal intubation..

Recommendations

Further studies should be done in high-risk hypertensive and cardiac patients. Dexmedetomidine and magnesium sulfate are a good choices in blunting the cardiovascular response resulting from laryngoscopy and tracheal intubation.

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