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ORIGINAL RESEARCH

Dexmedetomidine 0.6 mcg/kg versus Magnesium Sulphate 50% 30 mg/kg for attenuation of Intubation Response

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ABSTRACT

Background: Direct laryngoscopy followed by endotracheal intubation is prone to haemodynamic fluctuations which may be detrimental in subjects with coronary artery disease, hypertension, and cerebral vascular disease. The aim is we wanted to compare Dexmedetomidine with Magnesium sulphate to determine the better drug with regard to attenuation of the haemodynamic responses during laryngoscopy and endotracheal intubation.

Materials and Methods: This study was conducted among 80 subjects aged between 18 and 55 years belonging to ASA grade 1 or 2posted for elective surgeries under general anaesthesia. The study subjects were included randomly in 2 groups of 40 each.Group D received intravenous Dexmedetomidine 0.6µg/kg body weight and Group M received intravenous Magnesium sulphate 50%, 30 mg/kg body weight, both diluted in 100 ml of normal saline.Both were administered intravenously over 10 minutes.They were then induced with intravenous Thiopentone 5mg/kg, and intravenous Vecuronium Bromide 0.1mg/kg body weight 3 minutes before laryngoscopy and intubation. Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR) were noted at basal, 2^{nd} minute, 5^{th} minute, 8^{th} minute after study drug infusion, before and after induction, 1^{st}, 2^{nd}, 3^{rd}, 5^{th}, 10^{th}, 15^{th}minute from laryngoscopy and intubation.

Results: The reduction was significant statistically (P <0.05) in SBP, DBP, MAP and HR at all the time points in the Dexmedetomidine group as compared with that ofMagnesium sulphate group.

Conclusion: One intravenous dose of Dexmedetomidine 0.6µg/kg body weight given over a period of 10 minutes, just 10 minutes before induction was far more superior to intravenous Magnesium sulphate 50% at a dose of 30mg/kg body weight administered over a period of 10 minutes just 10minutes before induction, with regard to attenuation of the haemodynamic response during laryngoscopy and endotracheal intubation without any significant side effects.

Keywords: Dexmedetomidine; Magnesium Sulphate; Haemodynamic Response; Laryngoscopy; Endotracheal Intubation.

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INTRODUCTION

Alpha- 2 agonists are involved in the regulation ofautonomic and cardiovascular system. Their activation results in a reduction in tonic levels of sympathetic out flow and hence they are used for attenuation of the sympathetic response."Both Clonidine and Dexmedetomidine act on α1 and α2 receptors, Dexmedetomidine is a highly specific and selective α2 agonist with α2:α1 binding ratio of 1620:1 as compared to Clonidine with 220:1."[1-5] Dexmedetomidine, has analgesic, sympatholytic, and sedative properties. Also, it is effective in maintaining haemodynamic stability during intubation and extubation and does not prolong recovery. "It has been known to attenuate airway reflexessecondary to endotracheal extubation."[6] The fact that it reduces the opioid dosage requirements, the stress response during surgical events and provides a stable haemodynamic state makes it a very attractive option. It has a distribution half-life of approximately 6-8 minutes so that it could be successfully used for attenuation of the stress response during laryngoscopy and intubation. "Both 0.6µg/kg and 1µg/kg were found to be effective in blunting the intubation response".[7,8]

Magnesium sulphate (MgSO4) functions by inhibiting the release of catecholamine from adrenal glands and reducing the serum epinephrine levels and thereby causing a reduction in the cardiac force of contraction, reduction in the HR, and vasodilatation. "Doses of Magnesium sulphate in the range of 30 to 50 mg/kg were found to be effective in the attenuation of the intubation response."[1,9,10]

Objectives

1. To compare intravenous Dexmedetomidine 0.6µg/kg body weight with intravenous Magnesium sulphate 50% 30mg/kg body weight with regard to attenuation of haemodynamic response such as systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate secondary to laryngoscopy and endotracheal intubation.
2. To study their side effects including bradycardia, sedation, hypotension, and others.

MATERIALS & METHODS

A comparative study between intravenous Dexmedetomidine 0.6µg/kg body weight and intravenous Magnesium sulphate 50%, 30mg/kg body weight to attenuate the haemodynamic response duringendotracheal intubation in adult subjects posted for elective surgeries under general anaesthesia and it was conducted on 80 subjects. Ethical committee clearance was obtained before the study was started. Informed consent was obtained from all the study participants. Data thus collected was entered into predesigned proforma and then the results were analysed

Inclusion Criteria

All subjects aged between 18 to 55 years of either sex belonging to ASA Class 1 and 2 with Mallampatti Grades of 1 and 2 posted for elective surgeries under general anaesthesia.

Exclusion Criteria

Study participants with pre-existing renal, hepatic, cardiac, cerebral or peripheral vascular disease, participants having a HR < 60 bpm or presence of 1st, 2nd, 3rd degree heart block or having endocrinal diseases like hyper/hypothyroidism, hypertension, diabetes mellitus or

having a known allergy to Dexmedetomidine or Magnesium sulphate, pregnant and lactating mothers or obese participants with difficult airway and cervical spine injuries were excluded from the study.

The study participants were randomly divided into 2 groups with 40 subjects in each group. It was done using opaque sealed covers containing the name of the group which were shuffled. Each study participant was asked to select a cover. An external senior anaesthesiologist opened the envelopes and prepared the study drugs.

Group D –Dexmedetomidine group – received intravenous Dexmedetomidine 0.6 µg/kg body weight diluted in 100ml of Normal saline as slow infusion over10minutes.

Group M – Magnesium sulphate group – received intravenous Magnesium sulphate 50%30mg/kg body weight diluted in 100 ml of normal saline as slow infusion over10 minutes.

Pre-anaesthetic evaluation was done for all the subjects participating in the study onthe evening before the surgery.All those subjects who were included in the study withinformed consent were given Alprazolam 0.5mg orally at bed time the night before surgery as our institute protocol. After transferring the subjects into the operation theatre the following morning, an intravenous line was secured using an 18 G intravenous cannula on the non-dominant hand and infusion of Ringer's Lactate was started. All study participants were monitored with non-invasive pulse-oximetry, electrocardiogram, and non-invasive blood pressure with a multi-monitor (EDAN iM80). The systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate at baseline were recorded. After recording the baseline readings, subjects in group D received injection Dexmedetomidine 0.6 µg/kg body weight diluted to 100 ml of Normal saline intravenously as a slow infusion over 10minutes. Subjects in group M received injection Magnesium sulphate 50%30 mg/kg body weight diluted to 100 ml of normal saline intravenously as slow infusion over 10minutes.

An external senior anaesthesiologist prepared the study drugs. Patients did not know which drug they were administered with.Midazolam 0.02mg/kg body weight and injection Ondansetron 0.1mg/kg bodyweight were used for premedication after testing them for sensitivity. Pre-oxygenation was done with 100% oxygen given for 3 minutes. Induction of anaesthesia was done with injection Thiopentone 5mg/kg body weight along with injection Vecuronium Bromide 0.1mg/kg body weight 3 minutes before laryngoscopy and intubation.Patients were ventilated with 50% Nitrous oxide, 50 % Oxygen, and 0.6% Isoflurane for 3 minutes. Then laryngoscopy and endotracheal intubation were performed. Bilateral equal air entry was checked by auscultatory method and also with ETCO2. Endotracheal tube was fixed. Ventilator was connected.

50% Nitrous oxide, 50% Oxygen and 0.6% Isoflurane were given for maintenance of anaesthesia. After the procedure was complete, all the subjects were given intravenous Neostigmine 0.05 mg/kg body weight, and intravenous Glycopyrrolate 0.01mg/kg body weight for reversing the anaesthesia.

Comparison of the haemodynamic response was done in all the groups, before the study drug, 2nd min, 5th min, 8th min after the completion of 10ml of infusion of study drug (the study drugs were infused over 10 minutes as a slow intravenous infusion), before induction, after induction, 1st min, 2nd min, 3rd min, 5th min, 8th min, 10th min and 15th min after laryngoscopy and intubation. Side effects of the study drug if any (hypotension, bradycardia, sedation etc.) were recorded. Ramsay Sedation Score was used to assess the level of sedation.

Sample Size Estimation

Sample size was determined based on the observations of the pilot study. It was noted that each group had 33 patients for ensuring a power of study of 0.80 to detect a clinically meaningful difference by 15% in mean arterial blood pressure and heart rate. It was assumed

that the dropout rate would be 5%. And hence it was finally decided to have a sample size of 40 patients in each one of the groups, after allowing a type 1 alpha error of 0.05, a type 2 error of beta=0.2 and power of 0.8.

Statistical Methods

Descriptive statistics and inferential statistics i.e., cross tabs and students t-test were used to compare the data from the two groups. A 'P' value of < 0.05 was considered to be significant statistically and a 'P" value < 0.01 was considered to be highly significant. Data was analysed using Microsoft Excel and SPSS for Windows (version 2.0).

RESULTS

Table 1: Weight wise (kg) distribution of patients among the two groups

Age group (years)	**Group D**		**Group M**	
	No	**Percentage**	**No**	**Percentage**
<20	4	10.0	5	12.5
21-30	13	32.5	14	35.0
31-40	14	35.0	14	35.0
41-50	7	17.5	6	15
51-55	2	5.0	1	2.5
Total	40	100	40	100
Mean+/-SD	32.9250+/-9.47165		31.3500+/-9.35771	
P-value	0.457(NS)			
Age wise distribution of patients among the two groups (NS–Not significant (P>0.05); Group D–Dexmedetomidine group; Group M–Magnesium sulphate group.)				
Sex	**Group D**		**Group M**	
	No	**Percentage**	**No**	**Percentage**
Male	15	37.5	18	45
Female	25	62.5	22	55
Total	40	100	40	100
P value	0.496(NS)			
Sex wise distribution of patients among the two groups. NS– Not significant (P >0.05)				

Weight (kg)			
	No.	**Mean**	**SD**
Group D	40	54.5500	6.19326
Group M	40	54.0000	8.77058
Total	80		
P value	0.747		
(NS–Not significant (P >0.05);SD –Standard Deviation.)			

The difference was not significant statistically (P = 0 .457) in age wise distribution of the patients between Group D and Group M nor it was significant statistically (P=0.496) in sex-wise distribution of the patients between Group D and Group M nor it was significant statistically (P=0.747) in weight wise distribution of the patients among Group D and Group M.

The difference was not significant statistically (P=0.088) in laryngoscopy and intubation duration between Group D and Group M nor it was significant statistically (P =0.509) in the mean duration of surgery among Group D and Group M.

Table 2:Distribution of mean baseline parameters - Heart Rate (bpm), Systolic BP (mmHg), Diastolic BP (mmHg) and Mean Arterial Pressure (mmHg) among the two groups

Base Line Parameters	Group	No.	Mean	SD	P value
HR (bpm)	Group D	40	86.1500	8.08782	0.248(NS)
	Group M	40	87.5000	9.57025	
SBP (mmHg)	Group D	40	123.5750	6.03786	0.397(NS)
	Group M	40	123.9750	7.07284	
DBP (mmHg)	Group D	40	77.5500	5.46293	0.171(NS)
	Group M	40	78.7500	5.80782	
MAP (mmHg)	Group D	40	93.1750	4.68980	0.291(NS)
	Group M	40	93.7750	4.92762	
NS: Not significant; SD: Standard deviation; HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure.					

The difference was not significant between Group D and Group M with regard to basal mean HR (P=0.248), basal mean SBP (P=0.397), basal mean DBP (P=0.171), basal MAP (P=0.291).

The basal mean heart rate was comparable between the two groups and the difference was not significant statistically (P=0.248).However there was a significant statistical fall (P=0.031/0.041/0.017) in mean heart rate in Group D compared to Group M at the 2nd, 5th, 8th minute after study drug infusion and before induction. The fall in mean heart rate in Group D as compared to Group M was significant statistically (P – 0.000) after induction at 1^{st}, 2^{nd}, 3^{rd}, 5^{th}, 8^{th}, 10^{th}, 15^{th} minute after laryngoscopy and intubation.

The HR increased by approximately 8 units within 1 min in Group D after intubation while the same with Group M was 15 units. It has to be noted that in both the groups by about 15 minutes the heart rate settled down. With Dexmedetomidine (Group D) the heart rate never crossed the basal value while with Magnesium sulphate (Group M) there was an increase more than the baseline which later settled down below it.

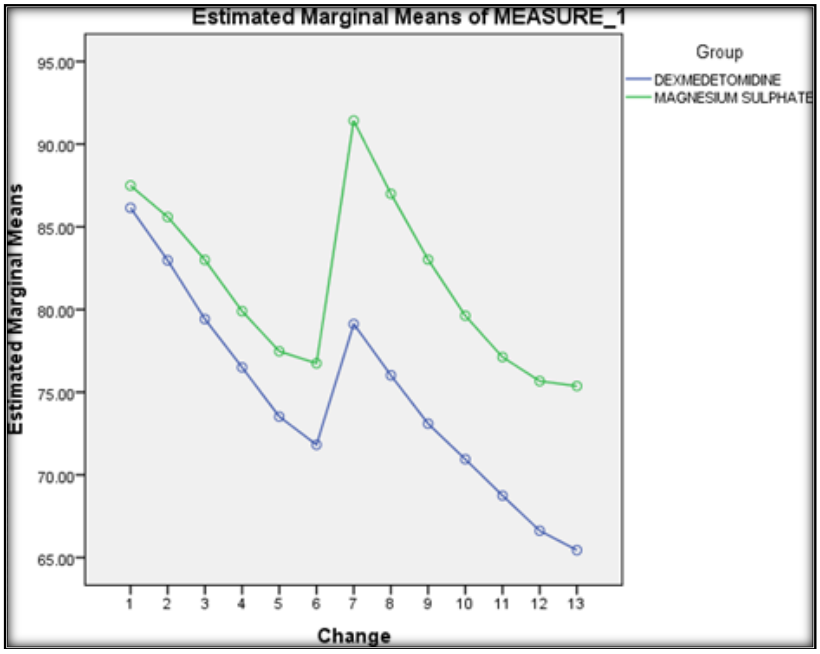

Figure 1: Plot of HR (y-axis) at various time intervals (x-axis) between the two groups

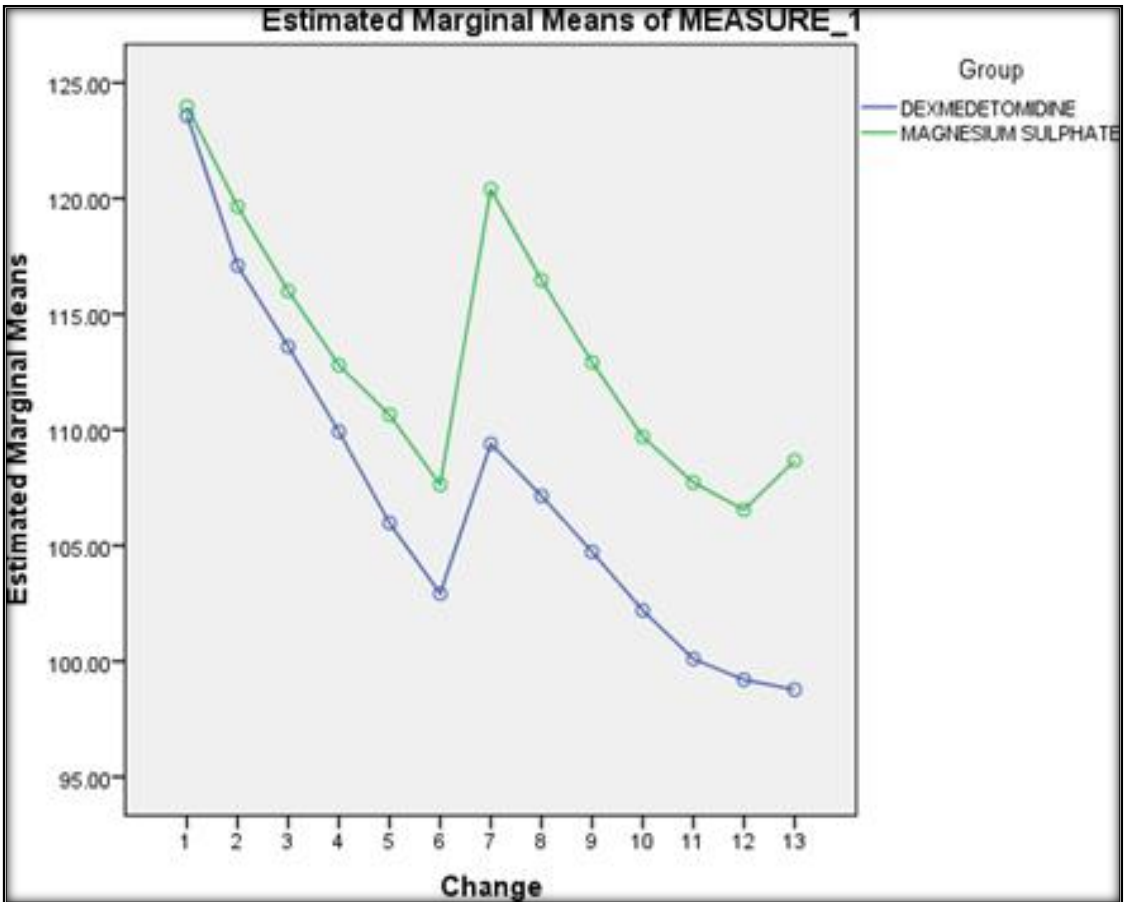

Figure 2: Plot of SBP (y-axis) at various time intervals (x-axis) between the two groups

The basal mean systolic blood pressure was comparable between the two groups. It was not significant statistically (P = 0.15).At 2^{nd}, 5^{th}, 8^{th} minute after drug infusion, before induction, after induction, 1^{st}, 2^{nd}, 3^{rd}, 5^{th}, 8^{th}, 10^{th} and 15^{th} minute after laryngoscopy and intubation in

Group D when compared to Group M, the reduction of mean systolic blood pressure was statistically very significant.

There was an increase in SBP by approximately 7 units within 1 min after intubation in Group D while the same with Group M was 13 units. It is to be noted that in both the groups by about 15 minutes the SBP settled down. With both Dexmedetomidine and Magnesium sulphate, the heart rate never crossed the basal value while in Group M there was a significant increase compared to Dexmedetomidine which almost approached the baseline and later settled down well below it.

The basal mean diastolic blood pressure and mean diastolic blood pressure at 2 minutes after drug infusion were comparable. The difference between Group D and Group M was statistically insignificant. At 5th minute after drug infusion, the reduction in mean diastolic blood pressure and the difference was significant statistically. The result was statistically highly significant after 8th minute of drug infusion, before induction, after induction,1st, 2nd, 3rd, 5th, 8th, 10th, and 15th minute after laryngoscopy and intubation in Group D as compared to Group M. There was an increase in DBP by approximately 4 units immediately 1 min after intubation in Group D while the same with Group M was 8 units. It is to be noted that in both the groups by about 15 min the DBP settled down. With both Dexmedetomidine and Magnesium sulphate, the DBP never crossed the basal value; but in Group M the increase was significant when compared with that of Dexmedetomidine which almost approached the baseline and later settled down well below it.

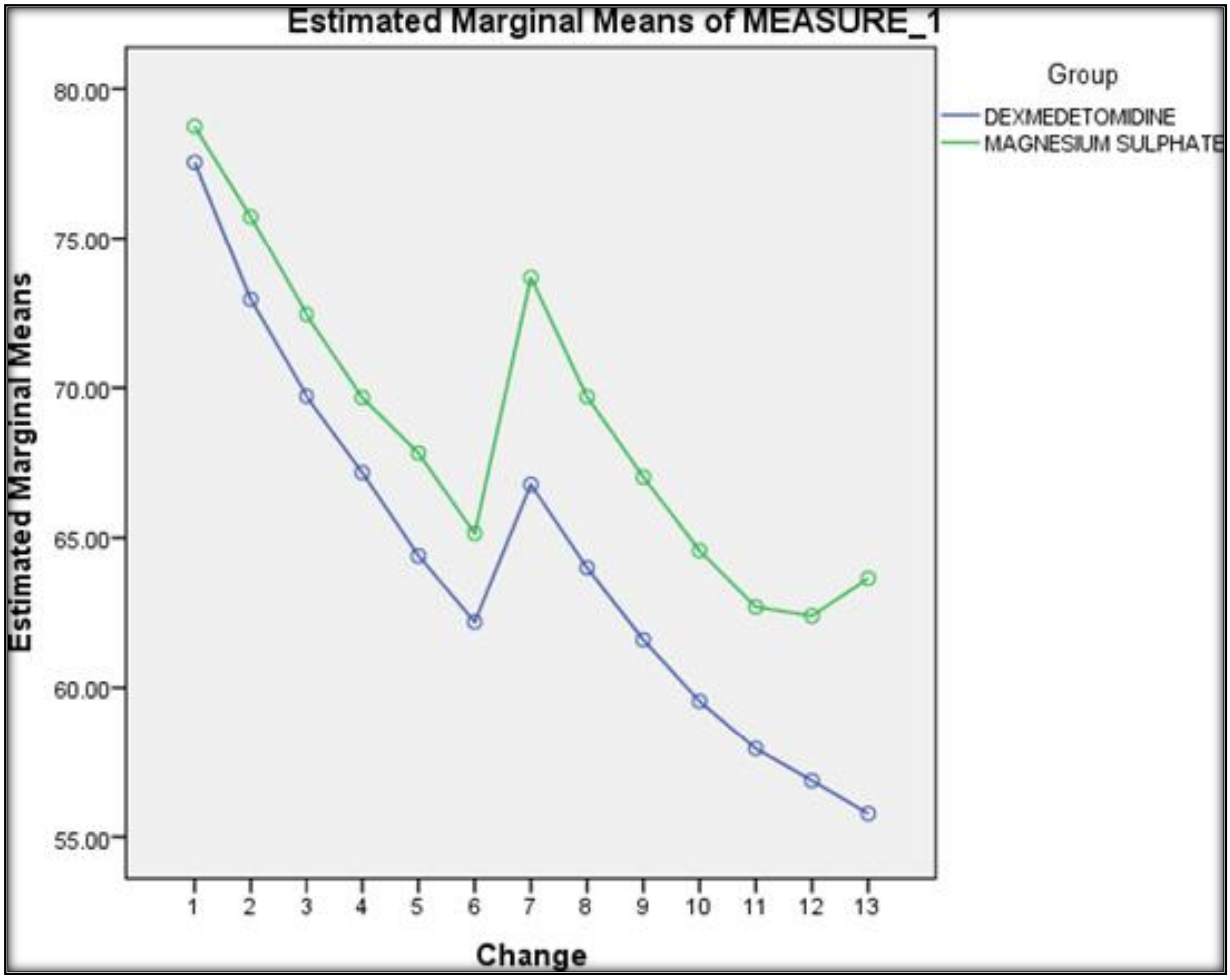

Figure 3: Plot of DBP (y-axis) at various time intervals (x-axis) between the two groups

Group D and Group M had comparable basal mean arterial pressure. The difference was statistically insignificant (P=0.292). Reduction in mean arterial pressure on the other hand was statistically very significant at 2^{nd} ,5^{th} ,8^{th}minute after drug infusion, before induction, after induction, 1^{st} ,2^{nd} ,3^{rd} ,5^{th} ,8^{th} ,10^{th} and 15^{th} minute after laryngoscopy and intubation in Group D as compared to that of Group M.

There was an increase in MAP by approximately 6 units immediately 1 min after intubation in Group D while the same with Group M was 10 units. It is to be noted that in both the groups by about 15 min the MAP settled down. With both Dexmedetomidine and Magnesium sulphate, the MAP never crossed the basal value while in Group M there was a significant increase compared to Dexmedetomidine which almost approached the baseline and later settled down well below it.

It was noted that there was greater sedation in the Dexmedetomidine group (Group D) which was significant statistically in the time intervals 0 hour (P = 0.012) which was immediately post-extubation, 1 hour (P = 0.021) and 2 hour (P = 0.038) compared to Magnesium sulphate group (Group M). The difference in the sedation scores between the two groups was not significant statistically from the 4^{th} hour onwards.

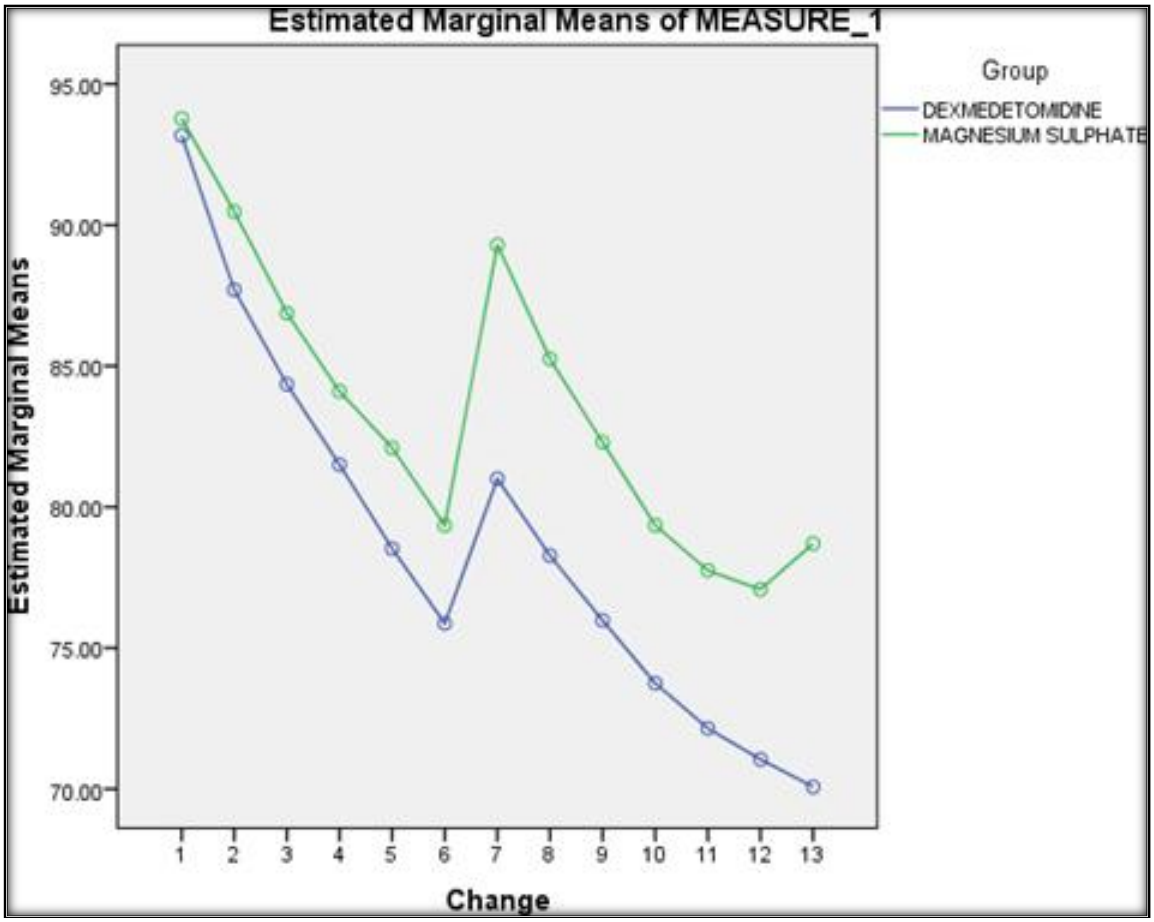

Figure 4: Plot of MAP (y-axis) at various time intervals (x-axis) between the two groups

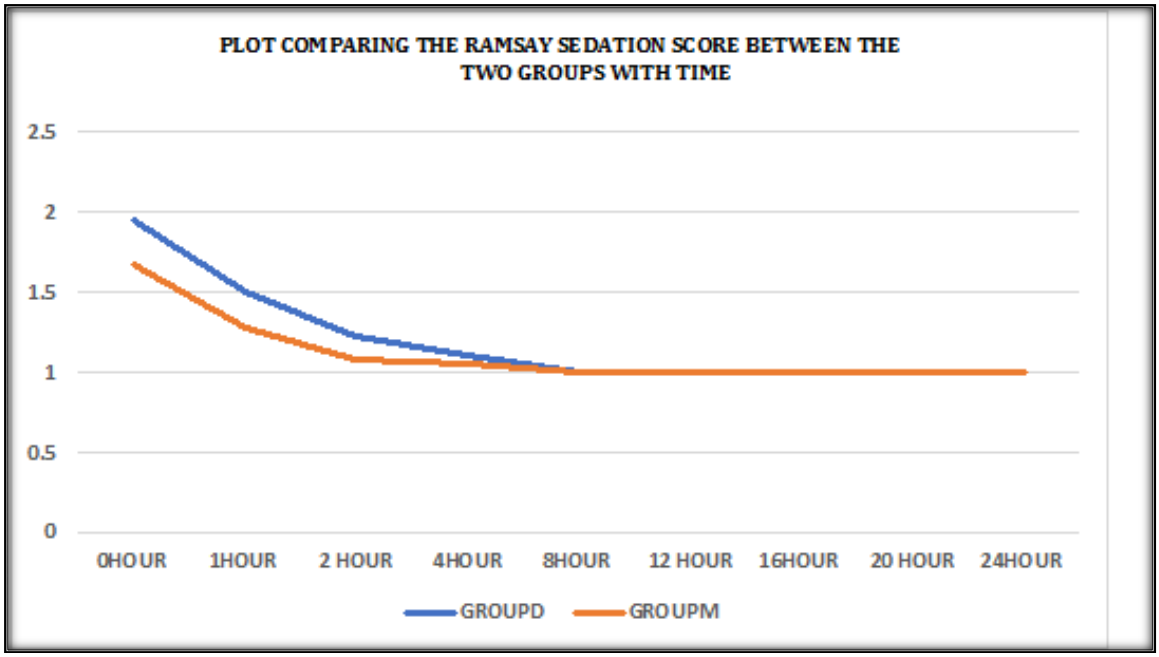

Figure 5: Plot comparing the Ramsay Sedation Score between the two groups with time

DISCUSSION

Heart Rate

In our present study, we found that the difference was not significant statistically between the heart rate (HR) among the study groups, group D (Dexmedetomidine) and group M (Magnesium sulphate) before the start of the study drug infusions in either of them [P = 0.248 (NS)].A similar trend in heart rate response was found in studies done by Balata AAH et al.(2018), Khan BA etal.(2017), Borah B et al.[11-13]

Systolic Blood Pressure

In the present study, basal mean systolic blood pressure in both group D (123 mmHg) and group M (124 mmHg) was comparable and statistically insignificant (P=0.393).After starting the infusion of Dexmedetomidine at a dose of 0.6µg/kg, in100 ml saline over 10 min, the drop in SBP was significant statistically when compared to that of group M (102 as compared with 107) [P= 0.000 (HS)], which were the post-induction values. Such a relatable trend in SBP response was found in previous studies done by Balata AAH etal.(2018),Khan BA et al. (2017).[11,12]

Diastolic Blood Pressure

In this study, basal mean diastolic blood pressure in both group D (77 mmHg) and group M (78mmHg) was comparable. It was statistically insignificant (P=0.171).After starting the infusion of Dexmedetomidine at a dose of 0.6µg/kg, in100 ml saline over 10 min, the drop in DBP was significant statistically when compared to that of group M (62 compared to 65) which were the post-induction values (P=0.006). The fall in blood pressures in both the groups was gradual after the start of the drug infusions. It was significant statistically and lower value being achieved in Group D by about 2ndmin into the drug infusion [P= 0.010 (S)] and this difference and significance were maintained from then on. Such a relatable trend in DBP responsewas found in studies done by Balata AAH etal. (2018), Khan BA et al. (2017).[11,12]

Mean Arterial Pressure

In this study, to begin with, the basal mean arterial blood pressure (MAP) in group D (93 mmHg) and group M (94 mmHg) was comparable and not found to have any statistical significance (P=0.292).After starting the infusion of Dexmedetomidine at a dose of 0.6µg/kg, in 100 ml saline over 10 min, the drop in the MAP was significant statistically when compared to that of group M (76 compared to 79) which were the post-induction values (P =0.001).Such a relatable trend in DBP response was found in previous studies done by Balata AAH et al.(2018), Khan BA et al. (2017).[11,12]

CONCLUSION

A single dose of intravenous Dexmedetomidine at a dose of 0.6µg/kg body weight given over 10 minutes just 10 minutes before induction was more superior on comparison with that of intravenous Magnesium Sulphate 50%at a dose of 30mg/kg body weight given over 10 minutes, 10 minutes before induction with regard to attenuation of haemodynamicresponses during laryngoscopy and endotracheal intubation with insignificant side effects.

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