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RESEARCH ARTICLE

A COMPARATIVE STUDY BETWEEN MAGNESIUM SULPHATE AND DEXMEDETOMIDINE FOR ATTENUATION OF HAEMODYNAMIC PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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Abstract

Backround: 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

Objectives:

1. To study the effects of magnesium sulphate and dexmedetomidine in attenuation of haemodynamic response to laryngoscopy and intubation .\
2. To study the side effects of the above drugs

Methodology: This study was conducted among 60 subjects aged between 20 and 60 years belonging to ASA grade IandII, posted for elective surgeries under general anaesthesia. The study subjects were included randomly in 2 groups of 30 each. Group A received intravenous Dexmedetomidine 0.75µg/kg body weight and Group B received intravenous Magnesium sulphate 50%, 25 mg/kg body weight, both diluted in 20 ml of normal saline. Both were administered intravenously over 10 minutes. Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR) were noted at baseline, after study drug infusion, before induction, before intubation,1,2,3,4,6,8,10 and 15^{th} min after intubation. If any sideeffects present, were also noted and treated.

Result: Data was compared using paired t-test,chi-square test,Fisher exact probability test and the reduction in the heart rate was found to be statistically significant ($p<0.05$) at all intervals. There was also significant decrease in systolic,diastolic and MAP during the immediate post intubation period.

Conclusion: Dexmedetomidine 0.75 µg/kg IV infusion is more effective than Magnesium sulphate 25mg/kg IV infusion for attenuating

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the haemodynamic response to laryngoscopy and intubation in elective general surgical patients.

Introduction:-

Increase in heart rate and blood pressure are well documented sequelae of direct laryngoscopy and endotracheal intubation in normotensive individuals[1].

The effect is transient, occurring immediately after intubation and lasting for 5-10 minutes. Intubation response may be well tolerated by normal, fit, ASA (American Society of Anaesthesiologist) physical status-I patients, but can be deleterious in patients with poor cardiovascular reserve. In patients with coronary artery disease (CAD), hypertension, raised intra-cranial pressure it may be associated with myocardial infarction, arrhythmias, cardiac failure or cerebral haemorrhage[2].

Various anaestheticagents and agents acting on the sympathetic system have been used to attenuate this sympathetic response to direct laryngoscopy and tracheal intubation, such as opioids, calcium channel blockers, local anaesthetics, beta-blockers, dexmedetomidine, esmolol, magnesium sulphate etc[3].

Dexmedetomidine, an ideal α_2 adrenergic agonist possess anxiolytic, sedative, analgesic and sympatholytic properties with minimal respiratory depression. It is effective in attenuation of haemodynamic stability and sympathoadrenal responses during laryngoscopy and endotracheal intubation[4].

Magnesium Sulphate (MgSO4) is well known to block the release of catecholamine from both adrenergic nerve terminals and the adrenal gland. Moreover, Magnesium produces vasodilator effect by acting directly on blood vessels, and high-dose Magnesium attenuates vasopressin-stimulated vasoconstriction[5].Magnesium also exerts its analgesic action as a non-competitive NMDA receptor antagonist, blocking ion channels in a voltage dependent manner. Intravenous (IV) magnesium sulphate has also been shown to reduce the haemodynamic changes associated with laryngoscopy and intubation[6].

Single anaesthetic technique produces undesirable side effects or are partially effective. Hence the present study will be undertaken to compare the efficacy of Magnesium sulphate and Dexmedetomidine in attenuating the stress response to laryngoscopy and intubation[7].

Materials And Methods:-

The study population consist of 60cases of age group of 20 years to 60 years, undergoing elective surgery under general anaesthesia at Basaveshwara Teaching and General Hospital ,Kalaburagi, After obtaining written informed consent from each patient ,the study was conducted

Study Design:
Prospective randomized Control study

Source of Data:
Hospital:Basaveshwar teaching and general hospital, Kalaburgi

Sample Size:
Total -60
• Group A patients will receive Inj. Dexmeditomedine 0.75 mcg/kg intravenously.
• Group B patients will receive Inj. Magnesium sulphate 25mg/kg intravenously.

Sampling method:Simple random sampling

Inclusion Criteria:
1. Patient scheduled for elective surgery
2. Age between 20-60 years of both gender

3. Patient with ASA gradeI or II
4. Mallampati airway assessment grade I and II

Exclusion Criteria
1. Emergency surgery
2. Anticipated difficult intubation
3. Patients with cardiovascular diseases
4. Patient on beta blockers or calcium channel blockers or other alpha 1 agonist

All patients were examined the day before surgery and anaesthetic counselling was done. All patients recieved tab Alprazolam 0.5 mg orally on the night before surgery. On the day of surgery IV line was secured with 18G cannula and following premedication wasgiven 10 min before induction.
1. Inj ondansetron 0.1 mg /kg IV
2. Inj Ranitidine 1mg/kg IV

Patients were monitored by pulse oximeter, noninvasive blood pressure and ECG monitoring.

After the patients were shifted to the operation theatre, standard monitors like NIBP, SPO2and ECG were connected and baseline parameters were recorded. A preinduction heart rate, systolic,diastolic and mean arterial pressure and pulse pressure were recorded. Intravenous infusion of RL solution started.

Loading doseof the study drug was infused as per group allotted . Group A was infused with intravenous inj Dexmedetomidine(0.75mcg/kg body wt.) diluted in 20 ml normal saline over 10 minutes before inducing general anaesthesia. Group B was given IV infusion of inj Magnesium sulphate at dose of 25 mg/kg diluted in 20ml NS over 10 min before induction. Patients were preoxygenated during infusion of the study drug after which general anaesthesia was induced with IV inj thiopentone sodium (5mg /kg body wt.) and paralyzed for intubation using IV injsuccinylcholine (1.5 mg / kg body wt.). Laryngoscopy was attempted 90 seconds after the administration of inj succinylcholine using appropriate sized Macintosh curved blade and trachea was intubated with appropriate size cuffed disposable oral Endotracheal tube. Laryngoscopy and intubation time was limited to 15-20 sec in all patients and patient with failure to intubate within this period with single attempt was excluded from the study. After confirming the ETT position, anaesthesia was maintained with 66% N2O in 33% oxygen. Paralysis was maintained withinj Vecuronium bolus IV dose of 0.08mg/kg body weight followed by intermittent doses of 0.02 mg/kg body weight. Vital parameters such as HR, SBP, DBP and MAP, SPO2 were recorded at baseline, after study drug infusion, before induction, before intubation and at 1,2,3,4,6,8, 10 and 15th min after intubation. No surgical intervention was allowed throughout the study period of 10 min.

Side effects of the drugs if any (hypotension,bradycardia,sedation etc) were recorded.

Statastical Analysis:
Data was analyzed by IBM SPSS 25.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis of descriptive statistics were done mean, standard deviation initially; independent samples "t-" test was used to compare the mean values between two variables for statistical significant. For quantitative data analysis chi-square test and Fisher exact probability tests were applied for statistically significant. $P \leq 0.05$ was considered statistically significant for all comparisons

Results:-

Table No.1:- Age wise distribution of cases.

Age in years	Group A (0.75mcg/kg body wt. of Dexmedetomidine)		Group B (25mg/kg body wt. of Magnesium sulphate)		Total	
	No.	%	No.	%	No.	%
21—30	8	26.7	9	30.0	17	28.3
31—40	7	23.3	8	26.7	15	25.0

41—50	8	26.7	4	13.3	12	20.0
51—60	7	23.3	9	30.0	16	26.7
Total	30	100.0	30	100.0	60	100.0
Mean ± SD	**40.60 ± 12.12**		**40.63 ± 13.38**		**40.62 ± 12.25**	
t-test value P-value	**t = 0.010 P = 0.992 NS**					

NS= not significant, S=significant, HS=highly significant

Study observes that, maximum number of cases in the both the groups 17 (28.3%) were belongs to the age group of 21-30 years, followed by 16 (26.7%) cases were belongs to the age groups of 51-60 year. Minimum age of patient was 21 years and maximum 60 years in both the groups. But there was no statistical significant difference of age between the group-A and group-B (P>0.05)

Table No.2:- Gender wise distribution of cases in the groups.

Gender	**Group-A**		**Group-B**	
	No.	**%**	**No.**	**%**
Males	16	53.3	17	56.7
Females	14	46.7	13	43.3
Total	30	100.0	30	100.0
χ2–Test value, P-value	**χ2 = 0.135, P = 0.921, NS**			

NS= not significant, S=significant, HS=highly significant

Study observed that; in the group-A Male cases were 16 (53.3%) and in Group-B male cases were 17 (56.7%) and Female cases in Group-A 14 (46.7%) and Group-B 13 (43.3%).There was no statistical significant difference of distribution of gender between the Groups A and Group B (P>0.05)

Table No.3:- Body Height and weight wise distribution of cases in the groups.

Variable	**Group A**	**Group B**	**t –test value**	**P- value & Significance**
	Mean ± SD	**Mean ± SD**		
Weight In kg	58.86 ± 5.88	57.06 ± 8.09	t = 0.887	P = 0.379 NS
Height In cms	157.73 ± 5.88	156.43 ± 5.45	t = 0.894	P = 0.375 NS

NS= not significant, S=significant, HS=highly significant,

The mean weight of Group-A was 58.86 and group-B was 57.06,difference in mean weight was not statistically significant between Group-A and Group-B (P>0.05) The mean height of Group-A was 157.73 and group-B was 156.43, difference in mean height was not statistical significant between Group A and Group B (P>0.05).

Table No.4:- ASA status wise distribution of cases in the groups.

ASA status	**Group-A**		**Group-B**	
	No.	**%**	**No.**	**%**
I	22	73.3	24	80.0
II	8	26.7	6	20.0
Total	30	100.0	30	100.0
χ2–Test value, P-value	**χ2 = 0.375, P = 0.823, NS**			

NS= not significant, S=significant, HS=highly significant

ASA status I in Group-A were 22 (73.3%) cases in Group-B were 24 (80.0%) cases. There was no statistically significant difference in the distribution of ASA status between Group-A and Group-B

Table No.5:- Comparison of heart rate between the Groups.

Time interval	Group-A		Group-B		t-test value, P-value & Significance
	Mean ± SD		Mean ± SD		
Baseline	82.00	9.43	80.80	8.45	t = 0.519 P = 0.606 NS
After drug Infusion	80.00	9.05	79.73	8.53	t = 0.117 P = 0.907 NS
Before Induction	78.10	9.39	79.26	8.88	t = 0.498 P = 0.623 NS
Before Intubation	77.60	9.15	78.43	8.16	t = 0.372 P = 0.711 NS
1 minute	85.63	9.67	90.20	8.30	t = 1.861 P = 0.071 NS
2 minutes	83.70	9.76	89.76	8.44	t = 2.573 P = 0.013 S
3 minutes	81.30	10.35	87.63	8.25	t = 2.619 P = 0.015 S
4 minutes	80.40	10.50	87.23	8.28	t = 2.797 P = 0.007 HS
6 minutes	78.93	10.38	86.76	8.16	t = 3.248 P = 0.002 HS
8 minutes	77.76	10.50	86.56	8.04	t = 3.642 P = 0.001 HS
10 minutes	75.93	10.89	86.13	7.93	t = 4.145 P = 0.000 HS
15 minutes	75.43	10.77	85.40	8.19	t = 4.003 P = 0.000 HS

NS= not significant, S=significant, HS=highly significant

The association between the intervention groups and heart rate at the time intervals - baseline, after drug infusion, before induction, before intubation and at 1minute after intubation were considered to be statistically not significant (P>0.05). Whereas the association between the intervention groups and heart rate at the time intervals 2 minutes, 3minutes, 4 minutes, 6 minutes, 8 minutes, 10 minutes and 15 minutes after intubation were considered to be statistically significant (P <0.05), (P<0.01) and (P<0.001). Though there was decrease in heart rate in both the study groups after infusion of study drugs, we found a relative increase in heart rate in the Magnesium sulphate group (10bpm) when compared to the Dexmedetomidine group (3bpm) at 1 min after intubation from the baseline. Heart rate reached baseline values by 3 min in Group A and also dropped below baseline (maximum drop by at 10 min) while it took more than 15 min to reach baseline in Group B. (Graph 5, table no 6)

Graph 1:- Line diagram represent comparison of heart rate between the Groups.

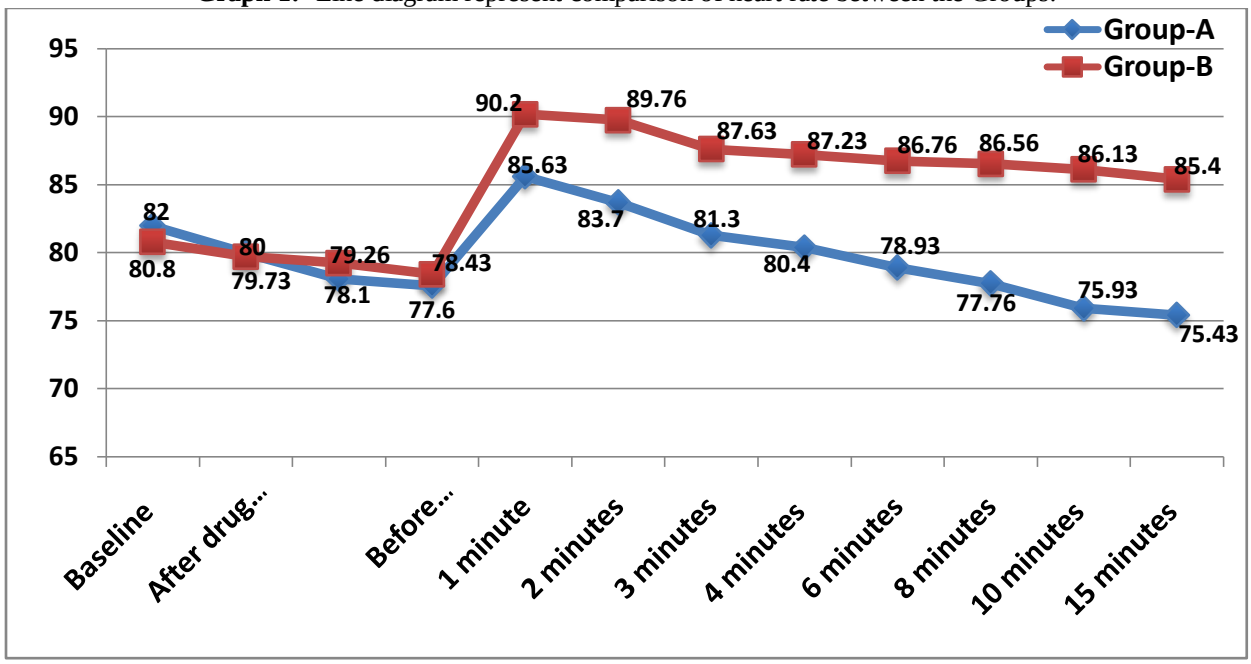


Table No.6:- Comparison of systolic blood pressure between the Groups.

Time interval	Group-A		Group-B		t-test value, P-value & Significance
	Mean ± SD		Mean ± SD		
Baseline	121.67	10.19	126.83	13.37	t = 1.683 P = 0.098 NS
After drug Infusion	119.53	9.89	125.36	13.12	t = 1.810 P = 0.075 NS
Before Induction	118.50	9.45	124.60	12.91	t = 1.912 P = 0.059 NS
Before Intubation	117.56	9.56	124.40	13.29	t = 2.258 P = 0.026 S
1 minute	133.26	11.48	153.13	13.30	t = 6.191 P = 0.000 HS
2 minutes	132.53	10.88	145.60	12.69	t = 4.281 P = 0.000 HS
3 minutes	127.20	18.71	137.06	12.71	t = 2.438 P = 0.018 S
4 minutes	129.30	10.34	134.40	13.22	t = 1.664 P = 0.112 NS
6 minutes	126.06	11.38	131.36	12.84	t = 1.692 P = 0.102 NS
8 minutes	123.26	11.11	127.20	12.69	t = 1.504 P = 0.138 NS
10 minutes	118.70	10.79	125.20	12.30	t = 2.175 P = 0.034 S
15 minutes	117.13	10.04	124.91	12.17	t = 2.484 P = 0.018 S

NS= not significant, S=significant, HS=highly significant

The association between the intervention groups and systolic blood pressure at the time intervals - baseline, after drug infusion, before induction and at 4minutes, 6 minutes and 8 minutes were considered to be statistically not significant (P>0.05). Whereas the association between the intervention groups and SBP at the time intervals before intubation, 1 minutes, 2 minutes, 3minutes and 10 minutes and 15 minutes were considered to be statistically significant (P <0.05) and (P<0.001). We also found that both drugs could not completely abolish rise in SBP soon after intubation. There was 10.8% rise in SBP in Group A compared to 20.1% rise in Group B immediately after laryngoscopy and intubation. (Graph 6, Table 7)

Graph 2:- Line diagram shows comparison of systolic blood pressure between the Groups.

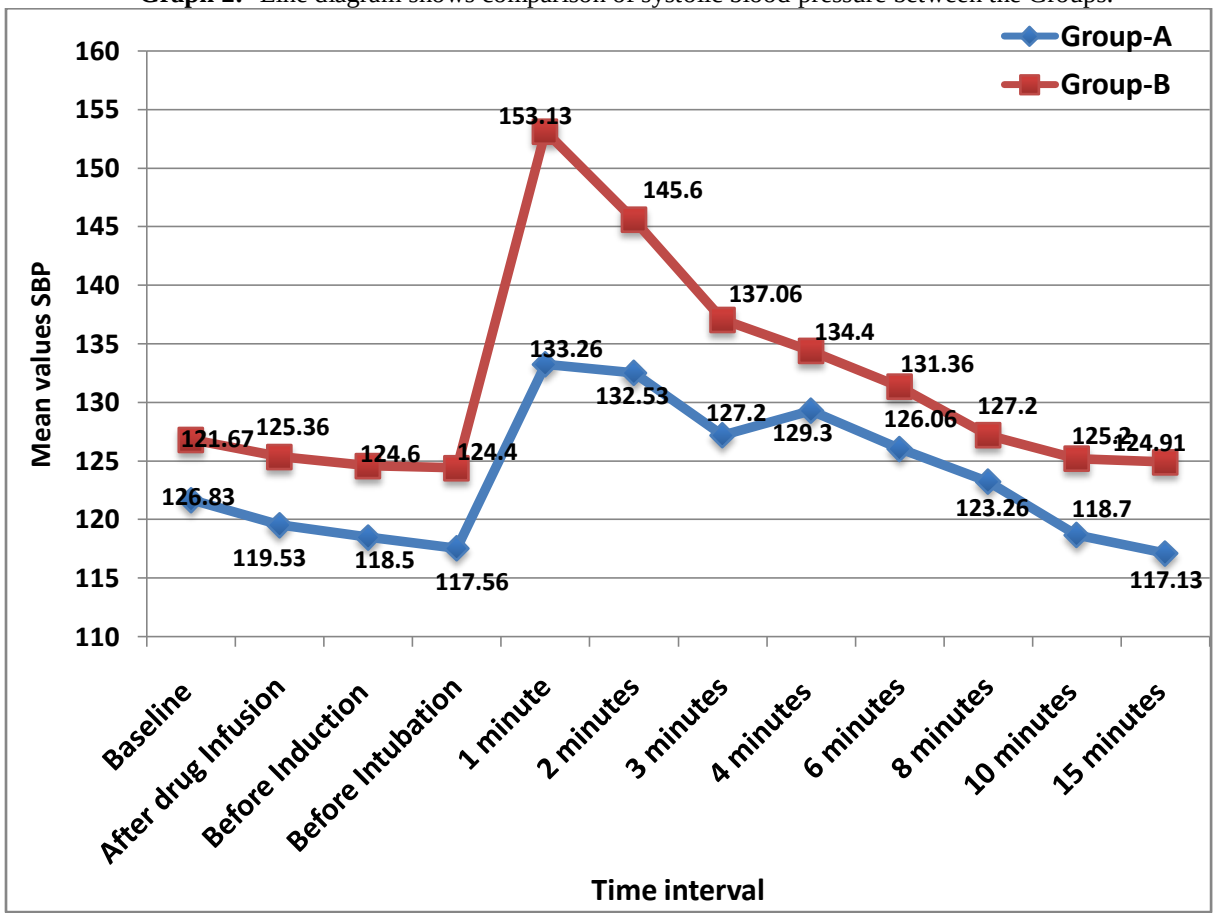


Table No.7:- Comparison of diastolic blood pressure between the Groups.

Time interval	Group-A		Group-B		t-test value, P-value & Significance
	Mean ± SD		Mean ± SD		
Baseline	79.20	6.88	80.66	7.31	t = 0.926 P = 0.358 NS
After drug Infusion	77.43	7.03	79.86	7.50	t = 1.296 P = 0.200 NS
Before Induction	76.43	7.23	79.30	7.40	t = 1.517 P = 0.135 NS
Before Intubation	75.70	6.94	78.70	7.48	t = 1.609 P = 0.113 NS
1 minute	85.20	8.63	101.70	8.32	t = 7.536 P = 0.000 HS
2 minutes	83.86	8.22	98.96	7.95	t = 7.225 P = 0.000 HS
3 minutes	82.41	8.30	91.10	8.88	t = 3.933 P = 0.000 HS
4 minutes	81.87	7.65	89.56	8.78	t = 3.625 P = 0.001 HS
6 minutes	81.26	7.51	88.26	8.69	t = 3.336 P = 0.001 HS
8 minutes	80.00	7.48	87.40	8.64	t = 3.545 P = 0.000 HS
10 minutes	75.73	7.79	86.16	8.89	t = 4.833 P = 0.000 HS
15 minutes	74.76	7.86	85.5	9.14	t = 5.010 P = 0.000 HS

NS= not significant, S=significant, HS=highly significant

The association between the intervention groups and DBP at time intervals - baseline, after drug infusion, before induction and before intubation considered to be statistically not significant (P>0.05). Whereas the association between the intervention groups and DBP were at the time intervals 1 minutes, 2 minutes, 3minutes 4 minutes, 6minutes, 8minutes, 10 minutes and 15 minutes after intubation were considered to be statistically highly significant (P<0.001).There was 6% raise of DBP in group A and 21% raise of DBP in group B at 1 min soon after the intubation (Graph 7, Table 8)

Graph 3:- Line diagram shows comparison of diastolic blood pressure between the Groups.

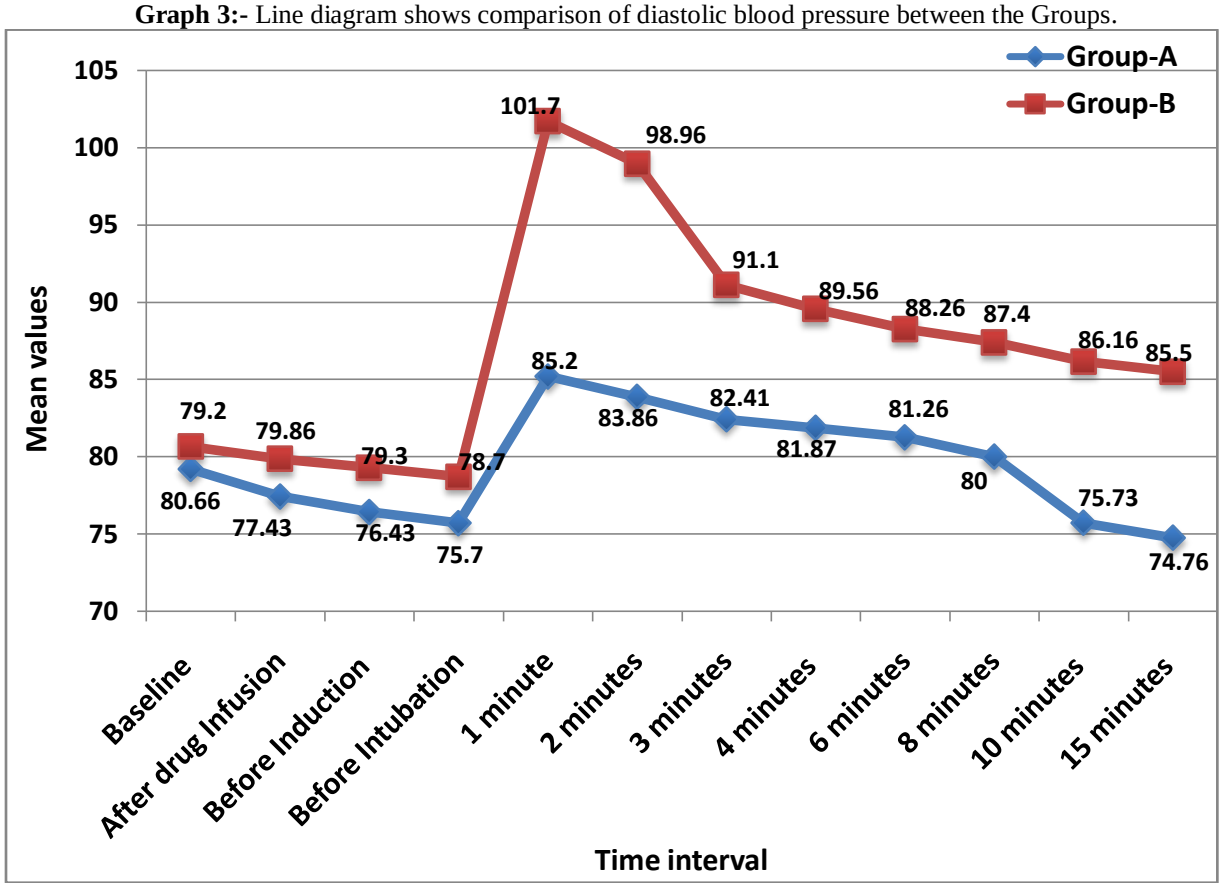


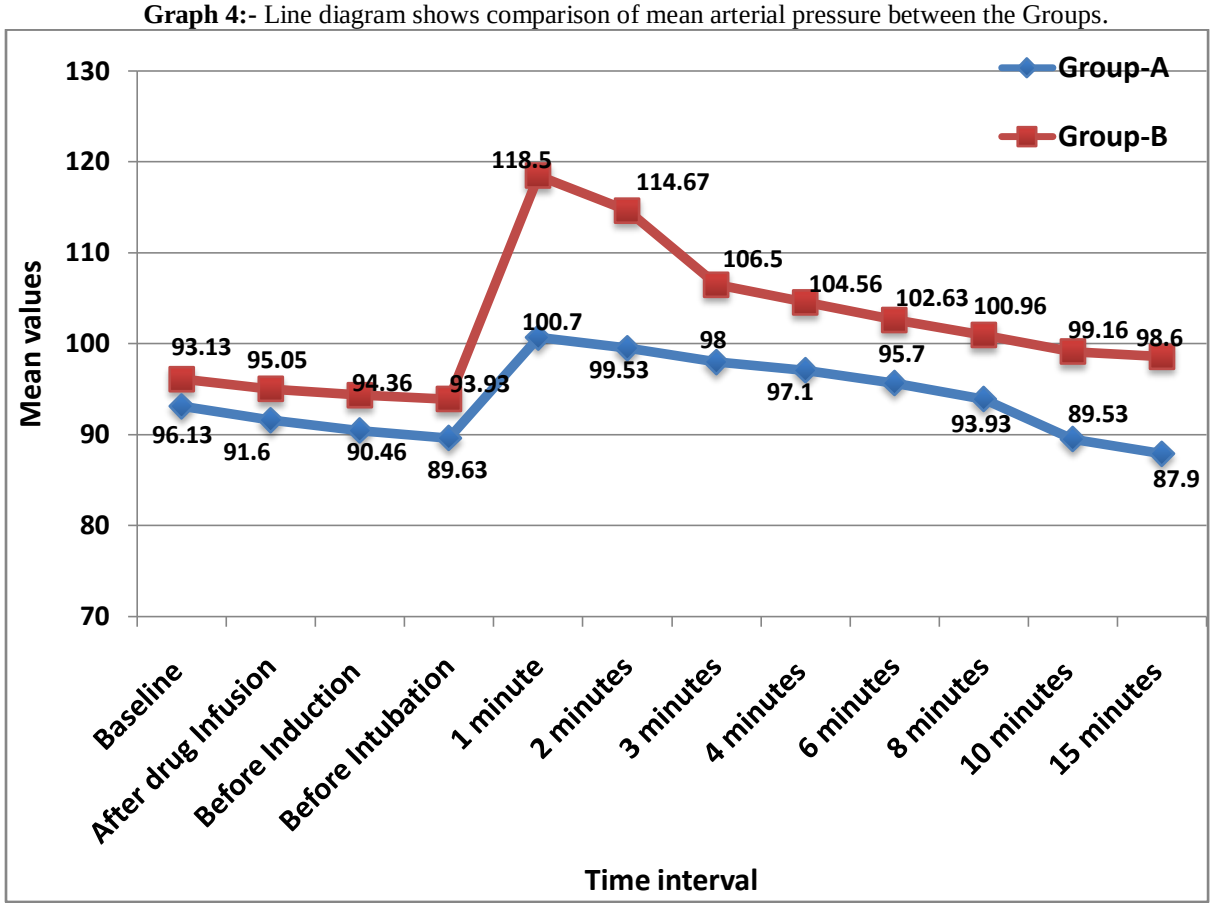
Table No.8:- Comparison of mean arterial pressure in min. between the Groups.

Time interval	Group-A		Group-B		t-test value, P-value & Significance
	Mean ± SD		Mean ± SD		
Baseline	93.13	6.93	96.13	8.33	t = 1.515 P = 0.135 NS
After drug Infusion	91.60	6.91	95.05	8.42	t = 1.726 P = 0.090 NS
Before Induction	90.46	6.80	94.36	8.34	t = 1.843 P = 0.063 NS
Before Intubation	89.63	6.77	93.93	8.27	t = 2.173 P = 0.034 S
1 minute	100.70	6.85	118.50	8.93	t = 8.490 P = 0.000 HS
2 minutes	99.53	6.88	114.67	8.83	t = 7.415 P = 0.000 HS
3 minutes	98.00	6.68	106.50	9.31	t = 4.018 P = 0.000 HS
4 minutes	97.10	6.94	104.56	9.25	t = 3.584 P = 0.001 HS
6 minutes	95.70	6.84	102.63	9.15	t = 3.321 P = 0.001 HS
8 minutes	93.93	6.92	100.96	8.93	t = 3.424 P = 0.000 HS
10 minutes	89.53	6.97	99.16	9.02	t = 4.638 P = 0.000 HS
15 minutes	87.90	6.97	98.60	9.10	t = 5.109 P = 0.000 HS

NS= not significant, S=significant, HS=highly significant

The association between the intervention groups and mean arterial pressure at baseline, after drug infusion, before induction time intervals were considered to be statistically not significant (P>0.05). Whereas the association between the intervention groups and mean arterial pressure at the time intervals of before intubation, 1 minutes, 2 minutes, 3minutes 4 minutes, 6minutes, 8minutes, 10 minutes and 15 minutes were considered to be statistically highly significant (P<0.001). In Group A MAP reaches baseline by 8 min and in Group B did not reach the baseline thoughout the observation

Graph 4:- Line diagram shows comparison of mean arterial pressure between the Groups.



Discussion:-

The pressor response to laryngoscopy and endotracheal intubation though transient, may be potentially hazardous due to reflex sympathetic discharge caused by pharyngeal stimulation. Transient hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular disease. These changes are the maximal at 1 minute after intubation and last for 5-10 minutes[2]. Prophylaxis include topical lignocaine sprays, deeper planes of anaesthesia by inhalational agents, narcotics, calcium channel blockers, vasodilators such as sodium nitroprusside,nitro-glycerineetc, but they have got side effects such as sedation, respiratory depression, hypotension and bradycardia[2].Various non pharmacological and pharmacological methods are in vogue to control this hemodynamic response.Opioids, local Anaesthetics, vasodilating agents and adrenergic blocking agents have been used to attenuate the pressor response[8-15]

Heart Rate:

In our present study, we found that there was significant statistically difference between the heart rate (HR) among the study groups, group A (Dexmedetomidine) and group B (Magnesium sulphate) after2min of intubation in either of them [P = >0.05 (NS)] more with group A. 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.[16-18]

Systolic Blood Pressure:

In the present study, basal mean systolic blood pressure in both group A(122 mmHg) and group B(127 mmHg) was comparable and statistically insignificant (P=>0.05).Before the intubation, Dexmedetomidine at a dose of 0.75µg/kg, in20 ml saline , the drop in SBP was statisticallysignificant when compared to that of group B (118 as compared with 124) [P=< 0.005 (S)], 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).[16-17]

Diastolic Blood Pressure:

In this study, basal mean diastolic blood pressure in both group A (79 mmHg) and group B(80mmHg) was comparable. It was statistically insignificant (P=>0.05).After starting the infusion of Dexmedetomidine at a dose of 0.75µg/kg, in20 ml saline , the drop in DBP was insignificant statistically when compared to that of group B (77 compared to 80) which were the post-induction values (P=>0.005). The fall in blood pressures in both the groups was gradual after the start of the drug infusions. It was highly significant statistically and lower value being achieved in Group A by about 1min after the intubation [P= 0.000 (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).[16,17]

Mean Arterial Pressure:

In this study, to begin with, the basal mean arterial blood pressure (MAP) in group A (93 mmHg) and group B (96 mmHg) was comparable and not found to have any statistical significance (P=>0.005).After the infusion of Dexmedetomidine at a dose of 0.75µg/kg, in 20 ml saline, the drop in the MAP was occured before the intubation and it is significant statistically when compared to that of group B (90 compared to 94) which were the post-induction values (P =>0.005).Such a relatable trend in MAP response was found in previous studies done by Balata AAH et al.(2018), Khan BA et al. (2017).[16-17]

Both the groups are not showing any significant adverse reaction during and after the infusion of study drugs.

Conclusion:-

Dexmedetomidine as an intravenous infusion (0.75µg/kg wt.) infused over 10 minutes is more effective than Magnesium sulphate infusion(25mg/kg) infused over 10 min for attenuation of haemodynamic response to laryngoscopy and endotracheal intubation with lesser side effects.

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