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RESEARCH ARTICLE
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DEXMEDETOMIDINE VERSUS MAGNESIUM SULFATE FOR BLUNTING CARDIOVASCULAR RESPONSE TO LARYNGOS COPY AND ENDOTRACHEAL INTUBATION IN GENERAL ANAESTHESIA.

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Introduction:
Direct laryngoscopy and endotracheal intubation frequently induce cardiovascular stress response in form of tachycardia and hypertension due to reflex sympathetic stimulation which in turn leads to increased plasma norepinephrine concentration. Numerous drugs like opioids, calcium channel blockers, alpha2 agonists, magnesium sulphate, local anesthetics used to blunt the stress response. Magnesium sulphate, as the physiological calcium antagonist for membrane calcium channels can modify many calcium mediated response. The ability of Mg2+ ions to inhibit the release of catecholamines from both the adrenal glands and peripheral adrenergic nerve terminals has been known and is now well established. Dexmedetomidine is an alpha2 agonist stimulate alpha2 receptor in lateral reticular nucleus result in reduce central sympathetic outflow and blunting hemodynamics response to unpleasant stimulation. Pretreatment with dexmedetomidine provides sedation and analgesia also reduces sympathetic tone and attenuate the stress response to anesthesia and surgery.

Subjects and Methods:
A randomized, prospective, double blind study of patients' undergoing elective abdominal surgeries that requires general anaesthesia with endotracheal intubation was taken after institutional approval. Sample size of 60 was calculated by using OpenEpi software. We included patients of 18-65years of age, both sexes, ASA-I/II having mallampatti grading-I/II for the study and randomly divided into two groups of 30 each (Group-D(Dexmedetomidine) and Group-M(Magnesium sulphate)) by coin toss method. Pregnant and lactating women, patient having pre-existing cardiac, respiratory, renal and hepatic disease, patient having heart rate <60/min, patient with history of drug allergy and if attempt for intubation takes >20 seconds were excluded. After pre-anaesthestic checkup, patients

were kept fasting from previous night. Procedure of general anaesthesia and the endotracheal intubation were explained and informed written consent was obtained. Patients' baseline parameters were recorded and 20G cannula taken and IV Ringer Lactate started. All patients were premedicated with inj.Glycopyrrolate 0.004mg/kg, inj.Ondansetron 0.15mg/kg, inj.Midazolam 0.01mg/kg. Group-D patients received Dexmedetomidine 1mcg/kg slowly IV infusion over a period of 10minutes, 10minutes before induction of anesthesia and Group-M patients received Magnesium Sulphate 30mg/kg slowly IV infusion over a period of 10minutes, 10minutes before induction of anesthesia. Hemodynamic parameters were recorded again at the end of 5min after giving the study drug infusion. Patients were induced with Inj.

Fentanyl 1mcg/kg, inj. Thiopentone sodium 4-7mg/kg IV, inj.Suxamethonium 1.5mg/kg. Followed by laryngoscopy and intubation were accomplished within 15 and 20seconds by an expert anesthesiologist. Only one attempt of intubation lasting for not more than 10seconds was accepted in the study. Heart rate, systolic blood pressure, diastolic blood pressure was noted at 1, 3, 5 and 10minutes after intubation. Anesthesia was maintained with O2, N2O, Sevoflurane and Vecuronium. At the end of surgery patient were reversed with Neostigmine 0.05mg/kg IV and inj.Glycopyrrolate 0.008 mg/kg IV and extubated. Side effects like hypotension, bradycardia and respiratory depression were noted. Hypotension was treated with bolus dose of 6mg mephentermine IV. Bradycardia was treated with 0.6mg atropine IV. Incidence of respiratory depression defined as respiratory rate<9/min and SpO2<90% on room air was noted.

Observation and Results:

The present study included 60 adult patients aged 18-65 years schedules for elective abdominal surgeries, belonging to ASA class I and II having mallampatti class I or II schedules for elective surgical procedure under general anesthesia with endotracheal intubation.

Patients were randomly assigned into two groups of 30 patients each. Demographic data in terms of age, sex, height, weight, mean duration of surgery were comparable in both groups.

Table: 1 Demographic Data:

Parameters	Group: D	Group: M	P value	Result
Age (years)	35.62 ± 12.89	39 ± 13.96	0.333	NS
Weight (kg)	55.06 ± 5.37	57.51 ± 6.98	0.133	NS
Male: Female	13:17	17:13	_	_
ASA status (I/II)	12/18	14/16	_	_
Mallampatti grade (I/II)	11/19	9/21	_	_

(Data expressed as Mean ± SD, p value < 0.05 was considered as significant).
NS – Non significant.

Table:1 Compared the demographic profile of patients and there was no significant difference in age and weight between the group (p value > 0.05).

Table-2 Changes in Mean Heart Rate

Time Interval	Group-D	Group-M	P value	Result
Baseline	82.96 ± 7.75	81.83 ± 9.30	0.611	NS
After drug	75.51 ± 6.39	80.16 ± 10.71	0.045	SS
1 minutes	82.41 ± 6.21	87.3 ± 8.99	0.017	SS
3 minutes	80.96 ± 7.07	85.2 ± 7.65	0.029	SS
5 minutes	77.10 ± 8.01	83.96 ± 9.86	0.004	SS
10 minutes	75 ± 7.98	80.63 ± 7.72	0.007	SS

There was significant difference in Mean Heart Rate in Group-D compared to Group-M. (p<0.05)

Table-3 Changes in Systolic Blood Pressure

Time Interval	Group-D	Group-M	P value	Result
Baseline	129.58± 10.17	127.4 ± 5.94	0.341	NS
After drug	113.72 ± 6.55	117.0 ± 7.04	0.066	NS
1 minutes	118.82 ± 5.57	121.73 ± 6.09	0.058	NS
3 minutes	117.10 ± 7.28	120.33 ± 8.07	0.109	NS
5 minutes	110.82 ± 4.18	113.33 ± 7.59	0.118	NS
10 minutes	107.93 ± 4.15	109.86 ± 4.42	0.087	NS

There was no significant difference in Mean Systolic BP in both groups.

Table-4 Changes in Diastolic Blood Pressure

Time Interval	Group-D	Group-M	P value	Result
Baseline	81.10 ± 6.08	80 ± 8.86	0.612	NS
After Drug	70.20 ± 4.84	72.06 ± 7.43	0.255	NS
1 minutes	73.03 ± 4.12	75.76 ± 6.92	0.068	NS
3 minutes	72.48 ± 5.08	75 ± 6.27	0.092	NS
5 minutes	69.10 ± 4.80	71.33 ± 4.37	0.064	NS
10 minutes	64.20 ± 5.99	66.2 ± 4.24	0.140	NS

There was no significant difference in Mean Diastolic BP in both groups.
The incidence of bradycardia was 3 in Group-D and hypotension incidences was 3 in Group-D where as no cases of bradycardia or hypotension noted in Group-M. No side effects like Spo2 fall noted in any cases.

Discussion

Direct laryngoscopy and endotracheal intubation are stressful event during general anesthesia. These lead to transient but marked sympathetic stimulation response leading to tachycardia, hypertension and arrhythmias. This transient hypertension, tachycardia is well tolerated in healthy individual but in patients with hypertension, coronary artery disease, cerebrovascular disease maybe hazardous. Stimulate somatic and visceral nociceptic afferent fibers which induce reflex sympatho adrenal response with enhanced neuronal activity in cervical sympathetic fibers. Sympathetic stimulation causes a significant increase in plasma catecholamine concentration leading to tachycardia, hypertension and arrhythmias. Many drugs like beta blockers, α–2 agonist, lidocaine, magnesium sulphate, narcotics have been used to attenuate the stress response to laryngoscope and endotracheal intubation. In this study, we compared Dexmedetomidine and Magnesium Sulphate for attenuating stress response to laryngoscopy and tracheal intubation.
Magnesium sulphate is a noncompetitive inhibitor of inositol triphosphate gated calcium channels and thus functions as an endogenous calcium antagonist by affecting its uptake and distribution. At Neuromuscular junction it inhibits calcium mediated released of acetylcholine from the presynaptic nerve terminal. In central nervous system it exerts its depressant effect by inhibition of N- methyl-D- aspartate glutamate receptor in neurons and inhibition of catecholamine release. It also shows modulatory effect on Na^+ and K^+current thus influencing membrane potential. It stabilizes hemodynamic by inhibition of catecholamine release from adrenal medulla and peripheral adrenergic nerve endings and direct blockade of catecholamine receptors. Magnesium sulphate acts by slowing the atrial rate by inhibiting the Ca^{++} mediated depolarizing current in pacemaker tissue and therefore overall effect is the mild increase in heart rate.
Dexmedetomidine is a highly selective α2 agonist that has been shown to have sedative, analgesic, sympatholytic effects. Its α2: α1 binding selectivity ratio is 1620:1 compared to 220:1 for clonidine. It by activating pre and post synaptic α2 receptors of sympathetic system produces vasodilatation and by acting on post synaptic α2 receptors of vascular smooth muscle cell it produces vasoconstriction. Thus, it shows biphasic dose dependent response on blood pressure (BP) and heart rate (HR); characterized by initial short-term increase in blood pressure followed by a longer lasting

reduction in BP and HR. Dexmedetomidine produced sedation by inhibiting the pontine locus cerules which has highest densities of α2 receptors adrenergic neurons in medullary vasomotor center which is manifested as peripheral vasodilatation and decrease in systolic blood pressure, heart rate and cardiac output.

We had done our study in 60 ASA-I & II patients who underwent abdominal surgeries under General Anaesthesia, patients of Group-D were received I.V. Dexmedetomidine 1mcg/kg diluted to 10ml NS infused over 10mins and patients of Group–M received I.V. Magnesium sulphate 30mg/kg to 10ml of NS over 10mins before induction. Our study is comparable with Ghodki P. et al and Mahajan L. et al regarding dose and delivery method of the study drugs.

Mean age in Group-D 35.62±12.89years while in Group-M was 39±13.96years. Mean weight of patients in Group-D was 55.06±5.37kg while in Group-M was 57.51±6.98 kg. Male and female ratio in Group-D was 13/17 and Group-M was 17/13. ASA (I/II) status of patients in Group-D were 12/18 while in Group-M were 14/16. Mallampati grade (I/II) in Group-D were 11/19 while in Group-M were 9/21. These differences were found to be statistically non- significant. In our study both groups were comparable in form of demographic data. Our study was comparable with Ghodki P. et al[1], Mahajan L. et al[2], Kotwani D. et al[3] and Balata AA et al[4]. regarding demographic data in both the groups.

After injecting study drug, the mean HR in Group-D was 75.51±6.39bpm and Group-M was 80.16±10.71bpm. Mean HR at 1minute in Group-D was 82.41±6.21bpm and Group-M was 87.3±8.99bpm, at 3minutes mean HR in Group-D was 80.96±7.07bpm and in Group-M was 85.2±7.65bpm, at 5minutes mean HR in Group-D was 77.10±8.01bpm and Group-M was 83.96±9.86bpm, at 10minutes mean HR in Group-D was 75±7.98bpm and Group-M was 80.63±7.72bpm The difference in HR was statistically significant in both groups at 1, 3, 5 and 10 minutes. Group-D has maintained low HR compared to Group-M throughout the time period. It was statistically significant. In the study done by Chaithanya K. et al[5], there was a clinically and statistically significant decrease in HR in Group-D for 10minutes following study drug. Our study was comparable with the study of Chaitanya K. et al[5], Mahajan L. et al[2], Balata AA et al[4] regarding HR changes.

In our study, after study drug SBP was fall in both the groups which was statistically insignificant in both the groups. Group-D was 113.72±6.55mmHg and Group-M was 117.0±7.04mmHg. At the time of laryngoscopy and intubation SBP was rise in both the groups which was (118.82 ± 5.57 mm Hg) and (121.73 ± 6.09 mm Hg) in Group D and Group M respectively which was statistically insignificant. Then SBP was fall in both the group at 3minute (117.10 ± 7.28 mm Hg), (120.33 ± 8.07 mm Hg); at 5minute (110.82 ± 4.18), (113.33 ± 7.59) mm Hg and at 10minute (107.93 ± 4.15) and (109.86 ± 4.42) mm Hg in group D and group M respectively which were statistically insignificant in both the groups. In the study done by Ghodki P. et al[1] after laryngoscopy and intubation SBP was fall in both Group D and Group M at 2 min, 5min and 10min after laryngoscopy and intubation and there was not statistically significant difference between both the groups.

In the study done by Khan BA et al[6] they found both dexmedetomidine and magnesium sulphate have shown to effectively control the increase in systolic and diastolic blood pressure in response to laryngoscopy and intubation. There was no statistically significant difference between both the drug when compared at 0,1,3 and 5minute for blood pressure ($p > 0.05$). Our study was compared with the study done by Ghodki P.et al[1], Khan BA et al[6], Chaithanya k. et al[5], Balata AA et al[4] regarding SBP changes.

In our study, baseline DBP in both groups was comparable. After injecting drug, the DBP in Group D was (70.20 ±4.84) and group M was (72.06 ± 7.63) which was not significant in both groups. At the time of intubation DBP in both groups increase which was not statistically significant. After that there is fall in DBP at 3,5 and 10minute after intubation in both groups which was not significant. ($p>0.05$) In the study done by Khan BA et al[6], they found both dexmedetomidine and magnesium sulphate have shown to effectively control the increase in systolic and diastolic blood pressure in

response to laryngoscopy and intubation. There was no statistically significant difference between both the drugs when compared at 0,1,3 and 5minute for blood pressure ($p>0.05$). Our study was compared with the study done by Ghodki P. et al[1], Khan BA et al[6], Chaithanya K. et al[5], Balata AA et al[6] regarding DBP changes.

The incidence of bradycardia was 3 in Group-D and hypotension incidences was 3 in Group-D where as no cases of bradycardia or hypotension noted in Group-M. No side effects like Spo2 fall noted in any cases in both the groups.

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