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Original research article

DEXMEDETOMIDINE VS. MAGNESIUM SULPHATE IN ADULT PATIENTS UNDERGOING MAXILLECTOMY/MANDIBULECTOMY SURGERY: CHANGES IN INTRAOPERATIVE MAP

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Abstract

Dexmedetomidine can result in cardiovascular depression, i.e., bradycardia and hypotension due to central presynaptic alpha 2A stimulation, with decreased norepinephrine. The incidence of postoperative bradycardia has been reported to be as high as 40% in healthy surgical patients who received Dexmedetomidine, especially high doses. After obtaining approval from the ethics committee, data was collected from patients coming to Oncology department for elective mandibulectomy/maxillectomy surgeries performed under General Anaesthesia. Patients fulfilling the inclusion criteria were briefed about the procedure and written informed consent taken. Patient demographic details noted. Comparison of MAP between Groups by Unpaired t-test were BL, BI shows no statistical significance difference at $p > 0.05$ level, whereas in 15 AI, 30 AI, 45AI, 60AI, 90AI, 120 AI, 150AI, 180 AI, 5BE shows highly statistical significance difference at $p<0.01$ level respectively.

Keywords: MAP, Dexmedetomidine, magnesium sulphate

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Introduction

Oral and maxillofacial surgeries involve surgical manipulation of facial skeletal elements and thus have marked impact on the cardiovascular stress response, which can result in a significant increase in the MAP and HR. To blunt such haemodynamic stress response, frequent adjustments in the depth of anaesthesia and analgesia are required [1]. Controlled hypotension is of utmost importance in such surgeries to reduce bleeding in the surgical field and thereby facilitate the surgery [2].

Dexmedetomidine compared to clonidine is a much more selective alpha-2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha 1-receptors. After abrupt cessation of clonidine infusion for sedation, rebound hypertension occurs [4].

This is not seen with Dexmedetomidine after discontinuation of infusion, even when it was given for more than 24 hours. In addition, Dexmedetomidine is shorter-acting drug than clonidine and has a reversal drug for its sedative effect, as Atipamezole. These properties render Dexmedetomidine suitable for sedation and analgesia during the whole perioperative period.

Dexmedetomidine does not appear to have any direct effect on the heart. The basic effects of Dexmedetomidine on the cardiovascular system are decreased heart rate, decreased systemic vascular resistance and indirectly decreased myocardial contractility, cardiac output and systemic blood pressure [5]. Dexmedetomidine can result in cardiovascular depression, i.e. bradycardia and hypotension due to central pre-synaptic alpha 2A stimulation, with decreased norepinephrine. The incidence of postoperative bradycardia has been reported to be as high as 40% in healthy surgical patients who received Dexmedetomidine, especially high doses. Usually, these temporary effects were successfully treated with atropine or ephedrine and volume infusions [6].

Magnesium is an important component of many physiologic processes. It has long been used in the field of anaesthesia and pain medicine. Magnesium is 4th most common cation after sodium, potassium and phosphorus. Normal plasma range is 1.4-2.2 mEq/L (0.7-1.1 mmol/L). Most important action of magnesium is blockade of NMDA receptors and calcium channels [7, 8].

Methodology

Inclusion Criteria

- Patients aged > 18 and <65 years.
- ASA class I and II.
- Patients undergoing elective mandibulectomy/maxillectomy surgeries.

Exclusion Criteria

- Patient refusal.
- History of Allergy to study drug.
- Patients on calcium channel blockers, beta Blockers, ACE inhibitors, anticoagulants.
- H/O cerebrovascular accident, ischemic heart disease, chronic obstructive lung disease.

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- Impaired renal function test, Impaired liver function test.
- Preoperative heart rate of <45 beats/min, second or third degree heart block.

Sample Size

The sample size and power were calculated based on the following formulae,

$n=(z\alpha/2+z\beta)2 \times z\sigma2/d2$

Where,

- n is sample size.
- $\sigma2$ is population variance.
- $z\alpha/2$ is the critical value at normal distribution $\alpha/2$.

$z\beta$ is the critical value at normal distribution at β.

By considering 80% power and 5% level of significance (α), the sample size 30 in each group is enough to compare two means i.e. 60.

Study Design: A Prospective Randomized Comparative study.

Methods

After obtaining approval from the ethics committee, data was collected from patients coming to Oncology department for elective mandibulectomy/maxillectomy surgeries performed under General Anaesthesia. Patients fulfilling the inclusion criteria were briefed about the procedure and written informed consent taken. Patient demographic details noted.

- Patients were kept nil per oral 8 hours prior to the surgery, pre-medicated with Tab Pantoprazole 40 mg and Tab Alprazolam 0.5 mg on the night prior to the surgery.
- All the patients were then randomly allocated to one of the following two groups using computer generated random sequence.

Group D: Patients were given IV Dexmedetomidine 1mcg/kg as loading dose over 10 mins before induction, and maintained as an IV Infusion at 0.5mcg/kg/hr till the end of the surgery.

Group M: Patients were given IV Magnesium sulphate 50mg/kg IV over 10mins before induction and maintained as an IV Infusion at 15mg/kg/hr till the end of the surgery.

- In the operation theatre, patients were connected to monitors and baseline hemodynamic parameters such as Electrocardiography, pulse oximetry and non-invasive blood pressure were noted. An intravenous line secured and patients were given intravenous Fluids, and infusion of study drugs started.
- Group D patients were given IV Dexmedetomidine 1mcg/kg over 10mins as loading dose and IV dexmedetomidine infusion continued at 0.5mcg/kg/hr.
- Group M patients were given IV Magnesium sulphate 50mg/kg over 10mins as loading dose and IV Magnesium sulphate infusion continued at 15mg/kg/hr.
- Patient were then preoxygenated with 100% oxygen with O2 flow rate at 5L/min for a period of 3 mins.

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- Patients were then induced with intravenous Fentanyl 1mcg/kg and Propofol 1-1.5 mg/kg. Patients once check ventilated and confirmed HR then muscle relaxant Succinylcholine 2mg/kg was given prior to laryngoscopy and intubation for muscle relaxation. Patients were intubated with appropriate sized cuffed endotracheal tube. Bilateral equal air entry checked and endotracheal tube placement was confirmed by capnography. The endotracheal tube is then fixed, and then patients were connected to a closed-circuit system. The mechanical ventilator set to achieve an end tidal CO_2 of 35-45 mm Hg.
- Maintenance was by 40% O2, 60% N2O and Isoflurane (0.8 to 1 MAC). 0.02 mg/kg Vecuronium bromide every 30 to 40 mins administered to maintain surgical relaxation. During the maintenance of anaesthesia study drug infusion was continued.
- Intraoperatively hemodynamics were assessed at regular time intervals.
- Patients with heart rate below 50bpm (i.e. decrease in HR more than 20% of baseline) was managed with Inj. Glycopyrrolate 0.01mg/kg.
- If Mean Arterial Blood pressure (MAP) decreased below 50mmHg, it was managed with IV fluids bolus over 5-10min according to response and a bolus dose of inj. Ephedrine (5-10mg) if needed. Inotropes (NorAdrenaline 0.1-3mcg/kg/min) was added in cases where hypotension not managed by IV fluids and inj Ephedrine.
- Inj. Nitroglycerin (5mcg/min max upto 20mcg/min) was added if Diastolic Blood Pressure above 100mmHg, to control hypertension.
- The secondary outcome, Adverse effects of the study drug such as bradycardia, hypotension and the postoperative sedation assessment done using Ramsay sedation score.
- At the end of surgery study medications stopped and neuromuscular blockade was reversed with injection Neostigmine 0.04mg/kg and injection Glycopyrollate 0.01mg/kg. All patients were shifted to post-anaesthesia care unit with Endotracheal tube *in situ*.
- In post-operative unit patients were assessed for sedation according to Ramsay sedation score.
- Adverse effects of the study drugs such as bradycardia, hypotension, respiratory depression and hyporeflexia were assessed perioperatively.

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Results

Table 1: Comparison of MAP between the Groups by Unpaired sample t-test

MAP	Groups	N	Mean	SD	t-value	p-value
BL	Group D	30	103.90	10.80	0.258	0.797 #
	Group M	30	104.63	11.12		
BI	Group D	30	88.57	9.81	1.995	0.051 #
	Group M	30	93.23	8.23		
15 AI	Group D	30	80.37	8.65	4.769	0.0005 **
	Group M	30	91.33	9.16		
30 AI	Group D	30	79.60	10.00	3.839	0.0005 **
	Group M	30	89.47	9.91		
45 AI	Group D	30	78.23	10.63	3.959	0.0005 **
	Group M	30	90.70	13.58		
60 AI	Group D	30	76.07	8.15	4.225	0.0005 **
	Group M	30	86.27	10.42		
90 AI	Group D	30	73.87	7.44	4.663	0.0005 **
	Group M	30	83.40	8.37		
120 AI	Group D	30	73.43	7.87	5.214	0.0005 **
	Group M	29	84.10	7.84		
150 AI	Group D	29	74.24	7.43	3.821	0.0005 **
	Group M	29	82.31	8.61		
180 AI	Group D	27	74.52	10.45	3.973	0.0005 **
	Group M	28	84.32	7.69		
5BE	Group D	27	83.63	7.13	5.919	0.0005 **
	Group M	28	99.11	11.78		
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05						

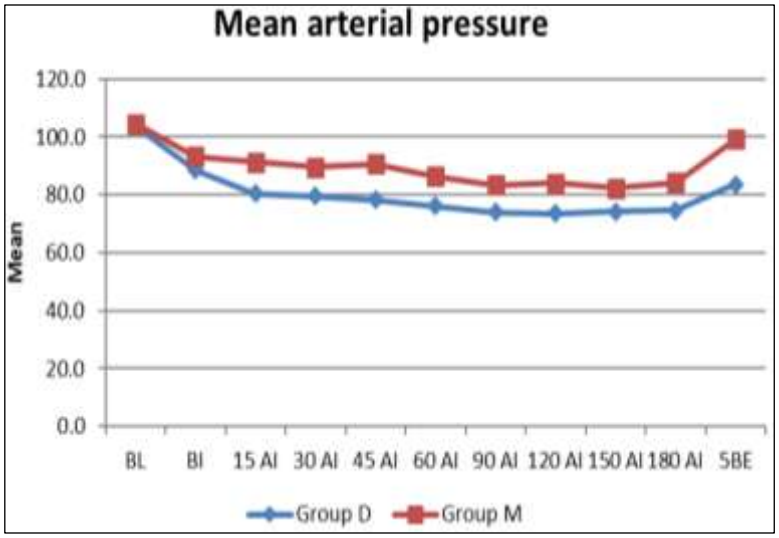

Fig 1: MAP

Difference in baseline MAP was not statistically significant. Hence the groups were comparable with regards to Baseline MAP.

Comparison of MAP between Groups by Unpaired t-test were BL, BI shows no statistical significance difference at p > 0.05 level, whereas in 15 AI, 30 AI, 45AI, 60AI, 90AI, 120 AI, 150AI, 180 AI, 5BE shows highly statistical significance difference at p<0.01 level respectively.

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Table 2: Comparison of Adverse effect (hypotension) between Groups by Fisher's exact test

			Groups		Total	□2 - value	p-value
			Group D	Group M			
Adverse effect	Nil	Count	23	30	53	7.925	0.011 *
		%	76.7%	100.0%	88.3%		
	Yes	Count	7	0	7		
		%	23.3%	0.0%	11.7%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		
* Statistical Significance at p < 0.05 level							

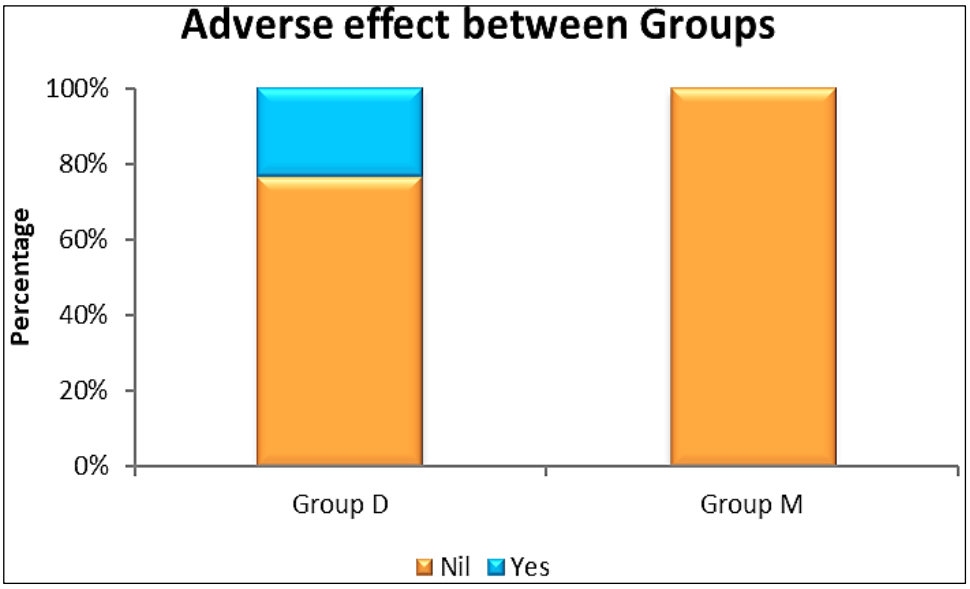

Fig 2: Comparison of Adverse effect

Comparison of Adverse effect (hypotension) between Groups by Fisher's Exact test were □2=7.925, p=0.011 <0.05 which shows statistically significant hypotension noted in dexmedetomidine group compared to magnesium sulphate group as p<0.05 (p=0.011).

Discussion

Ossama H. Aboushanab, Ahmed M. El-Shaarawy, Ahmed M. Omar, Hisham H. Abdelwahab [9]. "a comparative study between magnesium sulfate and dexmedetomidine for deliberate hypotension during middle ear surgery". They conducted the study in 88 patients and concluded that both magnesium sulfate and dexmedetomidine successfully induced deliberate hypotension and good surgical field visibility but magnesium sulfate was associated with shorter recovery time and earlier discharge from the PACU. But in our study we observed that dexmedetomidine was better than magnesium sulphate in inducing controlled hypotension and post-operative sedation in dexmedetomidine group was lasted for 90mins on average and 30 mins

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average in magnesium sulphate group.

Modir H *et al*. [10] conducted study comparing remifentanil, magnesium sulfate, and dexmedetomidine for intraoperative hypotension and bleeding and postoperative recovery in endoscopic sinus surgery found that dexmedetomidine is better to prevent bleeding than the others. Similar results observed in our study.

Hypotension with bradycardia was noticed in more patients who received dexmedetomidine 0.8 mcg/kg/hr compared to those who received magnesium sulphate 15mg/kg/hr, which was treated with IV fluid bolus and inj. Atropine 0.6 mg IV. Patients that had hypotension alone were treated with IV fluid bolus. The patients that received magnesium sulphate had hypertension, which was treated with IV nitroglycerine infusion. None of the above observations were statistically significant. Studies conducted by Manne GR *et al*., Jagadish V *et al*., Vaswani JP *et al*., and Luthra A *et al*., showed similar side effects [11, 12]. As these side effects were transient and responded well to treatment in the intraoperative period, they did not require postoperative follow-up.

As maxillofacial cancer surgeries require extensive resection and sometimes reconstruction leading to postoperative airway oedema, all the patients were shifted to ICU with nasal endotracheal tube and extubated during the first postoperative day as per institution protocol.

Conclusion

Mean arterial pressure were significantly lower in Group D than Group M at all points after induction and intubation ($p<0.05$).

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