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Role of Low Dose Preoperative Dexmedetomidine in Preventing Tourniquet Induced Hypertension in Paediatric Orthopaedic upper Limb Surgeries during General Anaesthesia.

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ABSTRACT

Background: Pneumatic Tourniquets are commonly used in orthopaedic surgery of the extremities to reduce bleeding and to provide a clear field to the surgeon, but severe pain often complicates the tourniquet inflation. Although the mechanism of tourniquet induced hypertension (TIH)is not well understood, the autonomic nervous system plays an important role. Hence, Dexmedetomidine, a potent a_2-adrenoceptor agonist may prevent hyper adrenergic responses and can be of prophylactic value for tourniquet induced hypertension. **Methods:** Forty American Society of Anesthesiologists (ASA) physical status class I and II children, aged 5-12 years, posted for Orthopaedic surgery of upper limbs under general anaesthesia with tourniquet application were included in the study. They were randomly assigned to receive intravenous Dexmedetomidine (Group D; n=20) or normal saline (Group C; n=20) before tourniquet inflation. Incidence of TIH, Mean Arterial blood pressure and heart rate were recorded. **Results:** There were no significant differences between the baseline characteristics. The incidence of TIH in group D was significantly less than the group C (20%) as compared to group D (70%).There was significant increase in the heart rate of placebo group after 30 minutes of tourniquet inflation while there was minimal variability of heart rate in the group D. In the group D, arterial pressure was not significantly changed, but in the group C, the arterial pressure was significantly increased after 20 minutes of tourniquet inflation. No significant adverse effects were noted in any group. **Conclusion:** Preoperative low dose intravenous Dexmedetomidine prevents tourniquet-induced hypertension in paediatric patients undergoing general anaesthesia for upper limb surgeries.

Keywords: Dexmedetomidine, General anaesthesia, Tourniquet induced hypertension.

INTRODUCTION

Pneumatic Tourniquets are commonly used in orthopaedic surgery of the extremities to reduce bleeding from the site and to provide a clear, bloodless field to the surgeon, but inflation of tourniquet for long hours is not without adverse effects. There is severe pain often accompanied by a progressive increase in systemic arterial pressure.[1]

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Tourniquet-induced hypertension (TIH) is generally defined as a progressive increase of more than 30% in arterial blood pressure after tourniquet inflation under general anaesthesia.[2, 3] The onset of TIH is usually after 30-45mins of inflation, and is not controlled even after increasing doses of anaesthetic agents and use of antihypertensive drugs.[3] It has been seen in studies that the increase in blood pressure is more during lower limb surgeries taken under general anaesthesia.[4] This increase in blood pressure and heart rate could be deleterious in patients with cardiovascular disease.[5]

In the past various drugs have been used prophylactically to decrease TIH like Clonidine[6], ketamine [7], magnesium [8], and methods like stellate ganglion block have also been used for the same.[9] Although the mechanism of TIH is not well understood, the autonomic nervous system plays an important role.[10] Hence, dexmedetomidine, a potent a_2-adrenoceptor agonist may prevent hyper adrenergic responses and can be of prophylactic value for tourniquet induced hypertension.[11]

Tourniquet induced hypertension is a definite entity in children but there is no data regarding the use of dexmedetomidine in children for the prevention of TIH. Therefore, the present study was designed to evaluate the effects of low dose intravenous dexmedetomidine on the blood pressure and Heart

rate in children undergoing upper limb orthopaedic surgery under general anaesthesia.

MATERIAL AND METHODS

Following approval from institutional ethics committee and informed consent, this prospective, randomized, double-blinded, and placebo controlled study was conducted on 40 American Society of Anesthesiologists (ASA) physical status class I and II children, aged 5-12 years, posted for Orthopaedic surgery of upper limbs under General Anaesthesia with tourniquet application. The patients were randomly divided into two groups as per the computer-generated sequence (www.randomzation.com). Children with known cardiac, pulmonary, or renal disease, and patients with markedly reduced muscle mass and with tourniquet inflation time expected to be less than 60 minutes were excluded from this study [Figure 1]. Patients in the Dexmedetomidine group (D; n=20) received intravenous Dexmedetomidine (0.5 mg/kg) mixed in 10 mL normal saline infused over 10 minutes, immediately before induction of general anesthesia.

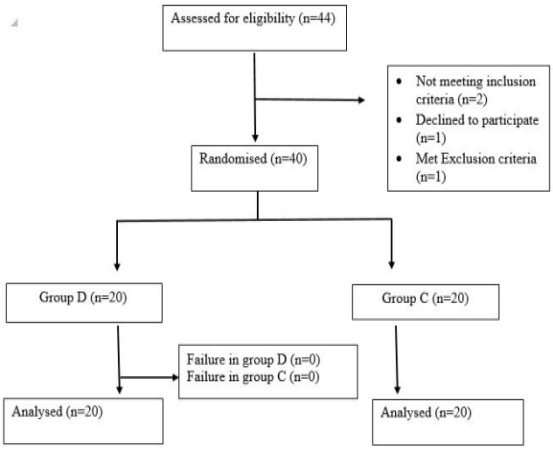
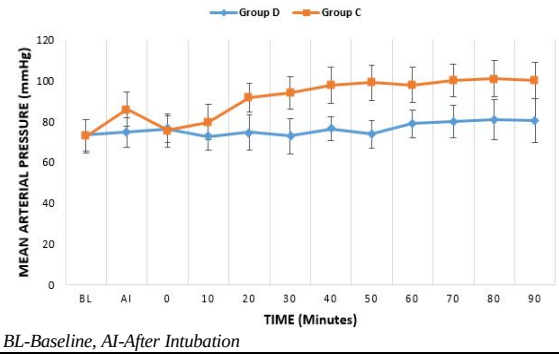


Figure 1: CONSORT diagram showing the flow of participants through each stage of a randomized trial.



BL-Baseline, AI-After Intubation

Figure 2: Showing the variation in mean arterial pressure (MAP) during the intraoperative period. Figure shows significant increase in the MAP in the dexmedetomidine group after tourniquet inflation.

Patients in the control group (C; n=20) received 10 ml of normal saline infused over 10 mins. The infusions were prepared by an anesthesiologist who was not involved in the study. In the study, patients were pre-medicated with midazolam 0.03 mg/kg, dexamethasone 0.1 mg/kg and fentanyl 2 microgram /kg intravenously. General anaesthesia was induced with Propofol 2 mg/kg, relaxation was achieved with Vecuronium bromide 0.1 mg/kg through intravenous route. Anaesthesia was maintained with oxygen, nitrous oxide (O2:N2O=40:60) and sevoflurane (0.5 MAC). Minute ventilation was adjusted to keep the end-tidal CO_2 concentration 35-45 mmHg. Intra operative Monitors included a continuous electro-cardiogram, a precordial stethoscope, a temperature probe, and non-invasive blood pressure and pulse oximeter. The extremity to be operated was exsanguinated with an Esmarch bandage and the pneumatic tourniquet inflated to a pressure 75-100 mm Hg higher than the child's systolic blood pressure. Blood pressure and heart rate were recorded at interval of 10 mins starting from 0, 10, 20, 30, 40, 50, 60, 70, 80, 90 minutes after the tourniquet was inflated and immediately after tourniquet was deflated. The number of patients who developed TIH was recorded. (TIH was defined by an increase in arterial blood pressure greater than 30% of the baseline value). The trachea was extubated at the end of surgery after reversal with Glycopyrrolate (0.01 mg/kg) and Neostigmine (0.05 mg/kg) given intravenously. It was proposed that for any increase in systolic blood pressure more than 160 mmHg additional Fentanyl 2ug/kg IV would be administered and any further treatment of hypertension would be as per the protocol of the institution. And these patients would be excluded from the study. Bradycardia was defined as pulse rate less 60 beats per min and hypotensions was defined as decrease in blood pressure of more than 20 % of baseline and were managed as per the protocol of institution.

Statistical Analysis: Data were analyzed using t-test and chi-square test and $p<0.05$ was taken as significant. All the values were expressed as mean±SD. Assuming α error of 0.05 and 40% decrease in proportion of patients with TIH (p_o= 80%, p_1=40%), it was found that a minimum of 20 patients were needed to obtain a power of 80%. So, we recruited a total of 40 patients for the study.

RESULTS

Patients in both the groups were comparable with regard to age, sex, weight, tourniquet and surgical time [Table 1]. There was significant increase in the heart rate of placebo group with respect to the baseline after 30 minutes of tourniquet inflation. On the other hand, in the group D, there was initial

significant drop in the heart rate after the drug administration followed by minimal variability during the intra-operative period. In the Dexmedetomidine group, there was no significant change in mean arterial pressure during the study period, but in the C group, mean arterial pressure were significantly increased from 20 minutes onwards after the tourniquet was inflated. There was significantly decreased incidence of TIH in the group D ($p>0.05$). 4 out of 20 patients (20%) developed TIH in group D during the intraoperative period. While, 14 (70%) patients in the group C developed TIH. There were no episodes of bradycardia or hypotension.

Table 1: Patient characteristics

Variable	Group D (n=20)	Group C(n=20)	P value
Age	8.78±3.26	8.10±2.76	0.48
Sex (M:F)	13:7	14:6	1.00
Weight	23.4±8.72	21.6±7.80	0.49
Tourniquet time (min)	60.36±7.46	62.46±6.66	0.35
Surgical time (min)	90.78±18.66	100.76±15.50	0.07

n=number, mean±SD, p≤0.05 statistically significant (Source: Authors)

Table 2: Heart rate variations during intraoperative period

Time	Group D(n=20)	Group C(n=20)	P value
Baseline (Pre-op)	**90.45±4.86**	**88.44±5.43**	**0.226**
After intubation	80.36±10.87(0.005)	99.20±12.73(.001)	0.04
0 min	71.00±9.93 (0.0001)	91.43±8.81(.20)	<0.05
10 min	75.19±8.87 (0.001)	90.68±10.64 (0.40)	<0.05
20 min	74.66±9.44 (0.001)	92.55±9.62 (0.14)	<0.05
30 min	74.74±9.77 (0.001)	103.65±9.47 (0.0001)	<0.05
40 min	72.84±10.87 (0.001)	109.46±10.74 (0.0001)	<0.05
50 min	76.86±9.87 (0.001)	110.56±11.76 (0.05)	<0.05
60 min	76.86±11.64 (0.001)	115.34±12.98 (<0.05)	<0.05
70 min	75.97±9.87 (0.001)	113.76±10.76 (<0.05)	<0.05
80 min	75.87±9.75 (0.001)	120.87±8.98 (<0.05)	<0.05
90 min	74.35±10.54 (0.001)	122.54±9.77 (<0.05)	<0.05

n=number, mean±SD, p≤0.05 statistically significant (Source: Authors)

Table 3: Mean arterial pressure (MAP) variation during intraoperative period

Time	Group D(n=20)	Group C(n=20)	P value
Baseline (Pre-op)	73.20±7.77	72.60±8.16/94	0.81
After intubation	74.68±7.16(0.53)	85.86±8.45 (<0.05)	<0.05
0 (Just before inflation)	76.41±6.57(0.17)	75.56±8.35(0.26)	0.73
10 min	72.64±6.47(0.81)	79.55±8.68 (0.01)	<0.05
20 min	74.65±8.76(0.58)	91.67±6.88(<0.05)	<0.05
30 min	72.85±8.75(0.89)	93.86±7.89(<0.05)	<0.05
40 min	76.36±5.78(0.15)	97.57±8.87(<0.05)	<0.05
50 min	73.73±6.66(0.82)	98.98±8.78(<0.05)	<0.05
60 min	78.83±6.96(0.02)	97.87±8.68(<0.05)	<0.05
70 min	79.87±7.86(0.01)	99.98±7.88(<0.05)	<0.05
80 min	80.97±9.80(0.008)	100.98±8.89(<0.05)	<0.05
90 min	80.47±10.78(0.01)	99.98±8.97(<0.05)	<0.05

n=number, mean±SD, p≤0.05 statistically significant (Source: Authors)

DISCUSSION

The results of this study showed that preoperative single low dose intravenous Dexmedetomidine 0.5 mcg/kg prevented tourniquet induced increase in systemic blood pressure (MAP) without significant adverse effects in children undergoing upper limb surgery under General Anaesthesia.

Perioperative hypertension may be associated with serious cardiac complications in adults [12-14]. Despite of the fact that children typically do not suffer from systemic hypertension, CAD or congestive heart failure as in adults but there is always a possibility of perioperative complications in patients of undiagnosed cardiac disease. There are only few studies [15,16] reporting the perioperative complication rates in paediatric patients undergoing non-cardiac surgery. In a study by kakavouli et al cardiac complications accounted for 8.6% of all observed complications in children [15]. Similarly, Cravero et al reported a rate of cardiac complications (defined as change of more than 30% in heat rate, BP, or respiratory rate) of 60.8 events per 10,000 anaesthetic cases [16].

The intraoperative hypertension that develops after prolonged tourniquet inflation of the limbs is often difficult to control with increased doses of anesthetics and antihypertensive drugs. The mechanism of tourniquet pain is complex and multifactorial, and till date the exact cause is unknown. Ischemia as a result of mechanical compression blocks the fast conducting, myelinated, A delta fibers which usually inhibit the pain transmission through these c fibers [17,18]. The block

of A-delta fibres by mechanical compression of tourniquet usually takes about 30 minutes, while the C fibres continue to function even after 30 minutes. [19]. yet another cause of tourniquet pain is that during application of tourniquet there is an increase in spontaneous firing of the receptive fields (RF) of nociresponsive dorsal horn neurons in and around the area of tourniquet compression[20]. The painful stimuli of tourniquet inflation leads to activation of sympathetic nervous system. So, the intravenous Dexmedetomidine, is suggested to have a role in attenuating the sympathetic surge as well as the perioperative requirement of sedation and analgesia due to its intrinsic property[21-23]. It was Tetzlaff et al [22] who demonstrated the correlation between TIH and sympathetic system activation. Power spectral heart rate analysis was used to measure the nervous system activation. Under general anaesthesia the increase in systemic blood pressure was related to increase in plasma nor-adrenaline levels.[23] Hence, the sympathetic nervous system stimulation during prolonged tourniquet application may lead to an increase in the arterial pressures.

We in our study observed that Dexmedetomidine significantly prevented the increase in mean arterial pressure and heart rate as compared to the placebo group. It improves the hemodynamic stability in the perioperative period by causing sympatholysis via activation of the central inhibitory pathway [24-29]. Further, it was observed that patients who received Dexmedetomidine tolerated the deflation without significant changes in heart rate. Though there was significant fall in blood pressure which was comparable in both the groups. A study comparing systemic Responses to Tourniquet Release observed that children tolerated tourniquet release with less hemodynamic change as compared to adults where tourniquet deflation resulted in significant decreases in blood pressure [30]. In another study, Moncorge et al. [31], who studied 11 children, found that systolic blood pressure fell and pulse increased by 15 mm Hg and 12 beat per min, respectively. We also found similar hemodynamic changes on tourniquet deflation in either of the groups except two patients in placebo group who developed sinus tacchy-arrhythmias immediately after deflation. Few studies reported that the addition of Dexmedetomidine to the local anesthetic solution in bier's block decreased the tourniquet pain[32-34]. The use of Dexmedetomidine may have added benefits such as attenuating the cardiovascular and sympatho-adrenal response to intubation and extubation and reducing opioid requirements during and after surgery [35-38]. It also decreases the incidence and frequency of delirium in children [39]. Dexmedetomidine does result in adverse side effects like hypotension and bradycardia which increases with dosage along with its effects of sedation and anxiolysis, but 0.5mcg/kg seems safe optimal dose of Dexmedetomidine for preventing TIH in children[40] as we did not observed any significant adverse events.

There were few Limitations of the study. First a relatively small sample size. Second the children included in the study were all healthy. On the basis of the results of this study, further investigations are needed to show whether perioperative outcome in paediatric patients with congenital or acquired cardiovascular disease is improved by dexmedetomidine treatment.

In conclusion, preoperative low dose intravenous dexmedetomidine significantly prevents hemodynamic responses to prolonged inflation of tourniquet during surgery of the upper limbs under general anesthesia in paediatric patients.

CONCLUSION

The study shows that preoperative intravenous dexmedetomidine in low dose could prevent TIH in children without causing any serious side effects.

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