ORIGINAL RESEARCH

Clinical evaluation of effect of intravenous clonidine, dexmedetomidine and normal saline premedication for prevention of tourniquet induced hypertension in surgeries under general anaesthesia

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ABSTRACT
Tourniquet induced hypertension occurs more frequently under general anaesthesia than regional anaesthesia and can be serious in patients with cardiopulmonary diseases, neurological disease and glaucoma. This study was a double-blinded randomized Control trial designed to investigate the effects of Clonidine, Dexmedetomidine and normal saline on prolonged tourniquet inflation. **Material and Methods:** Ninety patients scheduled for elective orthopaedic surgery of the upper limb under general anaesthesia were recruited. They were randomly assigned to receive intravenous Clonidine (1.0 mcg/kg; n=30) intravenous dexmedetomidine (0.5 mcg/kg; n=30), intravenous normal saline(n=30) 10 ml infused over a period of 10 min before tourniquet inflation. Arterial blood pressure and heart rate were recorded every 10 minutes until 90 minutes after the start of tourniquet inflation and again immediately after deflation. **Result:** In the Clonidine group, arterial pressure was not significantly changed, but in the Dexmedetomidine group arterial pressure was significantly increased at 20, 30, and 60 and 90 minutes after the start of tourniquet inflation. in the NS group arterial pressure was significantly increased at 40, 50, and 60 minutes after the start of tourniquet inflation. Development of more than 30% increase in arterial pressure during tourniquet inflation was more frequent in the group D and group NS than in the Clonidine group. **Conclusion:** Preoperative intravenous clonidine could therefore prevent tourniquet-induced hypertension in patients undergoing general anaesthesia.
Keywords: clonidine; Dexmedetomidine; General anaesthesia; Hypertension; Tourniquet

INTRODUCTION

In 1873 Johann **Friederich August Von Esmarch** introduced the use of a flat rubber bandage wrapped repeatedly around a limb as a tourniquet.[1]

Tourniquets are mostly used during limb operations to minimize surgical bleeding and to maintain a relatively bloodless field. The limb should be exsanguinated by elevating [2]for emptying the blood vessels from the distal end to the proximal end prior to tourniquet inflation. This technique has numerous advantages including establishing a clear operating field, reducing overall blood loss, and reducing the risk of microemboli at the time of deflation.[4,5] This exsanguination results in autotransfusion of blood from the peripheral circulation into the central circulation.[4,6] Tourniquet application can cause cellular hypoxia, acidosis, cooling in the occluded limb and ischemic damage to muscle and nerve. Application of tourniquet may cause Complications, most commonly nerve injury. Other complications are tourniquet pain, intra operative bleeding, compartment syndrome, pressure sores, digital necrosis and deep vein thrombosis.[3,4] Pain develops after Tourniquet application is described as severe dull aching sensation

at the site of tourniquet or in the distal extremities with rise in arterial blood pressure.[7]

Exsanguination of the limb and inflation of the tourniquet produce an initial increase in systemic blood pressure. This increase has been attributed to expansion of central venous blood in association with a theoretical increase in peripheral vascular resistance and delayed hypertension, accompanied by ischemia and pain due to tourniquet compression. [8-11]

The tourniquet pain and increase in arterial blood pressure are frequently observed 30-60 min after tourniquet inflation in spite of adequate level of anesthesia and they are often resistant to profound depth of anesthesia and analgesic drugs. [12]

Tourniquet-induced hypertension (TIH) is generally defined as a progressive increase of more than 30% in arterial blood pressure after tourniquet inflation under general anesthesia.[10,13-15]

Tourniquet induced hypertension occurs more frequently under general anesthesia than regional anesthesia and more with lower limb tourniquet than with upper limb tourniquet .[12]

The mechanism of TIH is unknown, but possibility of involvement of the autonomic nervous system and rise in plasma catecholamine concentration continuously in parallel to arterial blood pressure during tourniquet inflation has been documented.[13,14,17,18]

Once tourniquet induced hypertension develops, it's treatment is difficult and often ineffective, even with increased doses of anesthetics and antihypertensive drugs.[13,16] Many drugs like ketamine,[19] magnesium,[20] intravenous opioids (Remifentanil),[8] dextromethorphan,[22] and stellate ganglion block,[23] have been used prophylactically to prevent TIH. [13,14,18,21]

Clonidine and Dexmedetomidine both are alpha 2 agonist[25,27]. dexmedetotmidene is more selective for alpha 2 receptors compared to clonidine.[11] They produces sedation, analgesia and anxiolysis after intravenous administration, thus decreases perioperative requirement of inhaled anaesthetic.[24-26] This property of attenuation of hyperadrenergic response could be of therapeutic or prophylactic value in reduction of tourniquet induced hypertension.[11,22-23]

In this study, we investigated the effect of preoperative intravenous Clonidine and dexmedetomidine on the tourniquet induced rise in arterial blood pressure and heart rate and to find out the better effective drug for prevention of tourniquet induced hypertension in patients undergoing orthopaedic surgery under general anaesthesia.

MATERIAL & METHOD

This study was randomized, double-blinded, and placebo controlled. After obtaining approval from the institutional ethical committee, the study was conducted on 90 patients of ASA grade I and II scheduled for orthopaedic operation requiring tourniquet inflation under general anaesthesia were enrolled in the Department of anaesthesiology, J.A Group of Hospital Gwalior (M.P) after obtaining written informed consent. Patients with known contraindications to dexmedetomidine/clonidiine who had ischemic heart disease, hypertension, kidney dysfunction, or diabetes mellitus; and with expected tourniquet inflation time shorter than 60 minutes were excluded. Patients were premedicated with Inj. Pentazocine 0.5 mg/kg BW followed by preoxygenation with 100% oxygen for 3 minutes by facemask.

Induction of General Anaesthesia was done with i.v. inj. Thiopentone Sodium 5 mg/kg BW. Endotracheal intubation was facilitated with i.v. inj. Succinylcholine 1.5 mg/kg BW followed by IPPV done with 100% oxygen for 90 seconds.General anaesthesia was maintained with nitrous oxide & oxygen in the ratio of (66:33), Loading (0.25mg/kg BW) and intermittent dosage (0.1mg/kg BW) of non-depolarizing muscle relaxant and Isoflurane (1-1.5%) on Bain's anaesthetic circuit. Selected 90 patients were randomly allocated into three groups (n=30 each) depending upon the drug given after intubation:

1.Group 'NS' (n=30)	10 ml NS infused over a period of 10 min, before tourniquet inflation
2.Group 'C' (n=30)	Inj.Clonidine (1.0mcg/kg) diluted in 10 ml N/S infused over a period of 10 min, before tourniquet inflation.
3.Group 'D' (n=30)	Inj. Dexmedetomidine (0.5mcg/kg) in 10ml N/S infused over a period of 10 min, before tourniquet inflation.

The infusions were prepared by a nurse anesthetist not involved with the case according to a computer-generated sequence. All the haemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) , mean arterial pressure (MAP) and Oxygen saturation (SpO2) were be recorded ,before induction (Bo), after endotracheal intubation(AETI), before study drug administration (Do), after inflation of tourniquet(AI) and then at 10, 20, 30, 60, 90 min (A10, A20, A30, A60, A90) and 5 min after deflation (AD_5) of tourniquet. Throughout the procedure for any 20% rise in MAP above the basal MAP, Isoflurane concentration was increased to maintain the basal MAP. For fall in MAP more than 20% of the basal MAP, Isoflurane was decreased or stopped. Heart rate less than 50 bpm was treated with Atropine 0.6 mg intravenously.

The number of patients who developed TIH, was recorded. The patients were extubated at the end of surgery after reversal with Inj. Glycopyrrolate (0.005-0.01 mg/kg) and Neostigmine (0.04-0.08mg/kg) intravenously.

The observations recorded in all the groups were tabulated and statistical analysis carried out by using appropriate statistical software SPSS 17. Student 't'test for inter group comparison was used. P-value >0.05 was taken to be statistically insignificant & P-value <0.05 was taken statistically significant whereas

P-value <0.01 taken to be statistically highly significant.

There were no statistically significant difference between the groups with respect to the patients' demographic characteristics (Table 1).

RESULT

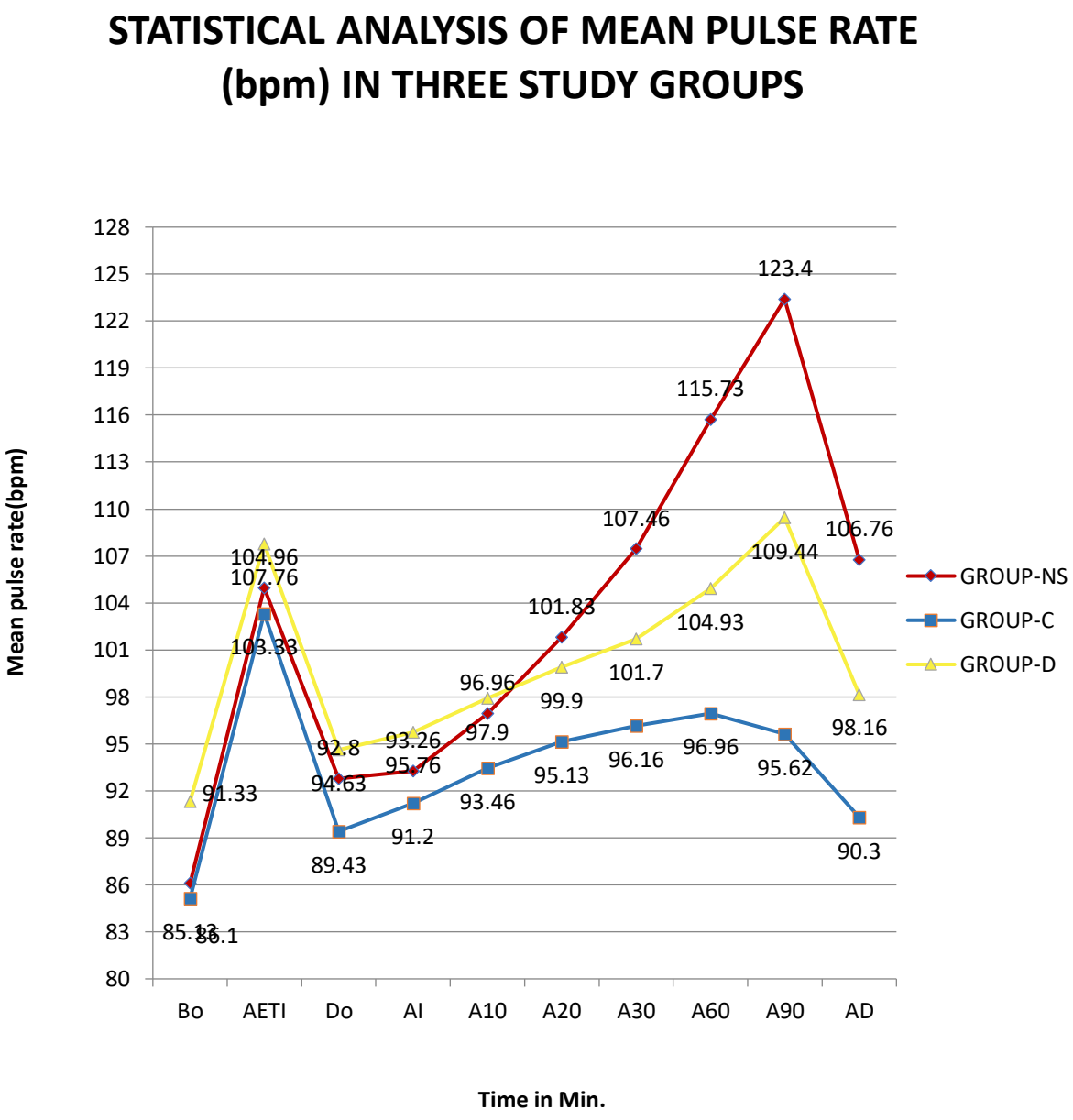
Table - 1

Variable	Group 'NS' (n = 30)	Group 'D' (n = 30)	CLONIDINE group (*n* = 18)
Age (years)	34.6±14.3	39.1±14.4	37.2±13.1
Sex (m/f)	22/8	21/9	23/7
Weight (kg)	61±7.07	61.4±7.11	61.3 ±7. 16

Values are presented as mean ± SD. There were no significant differences between groups.

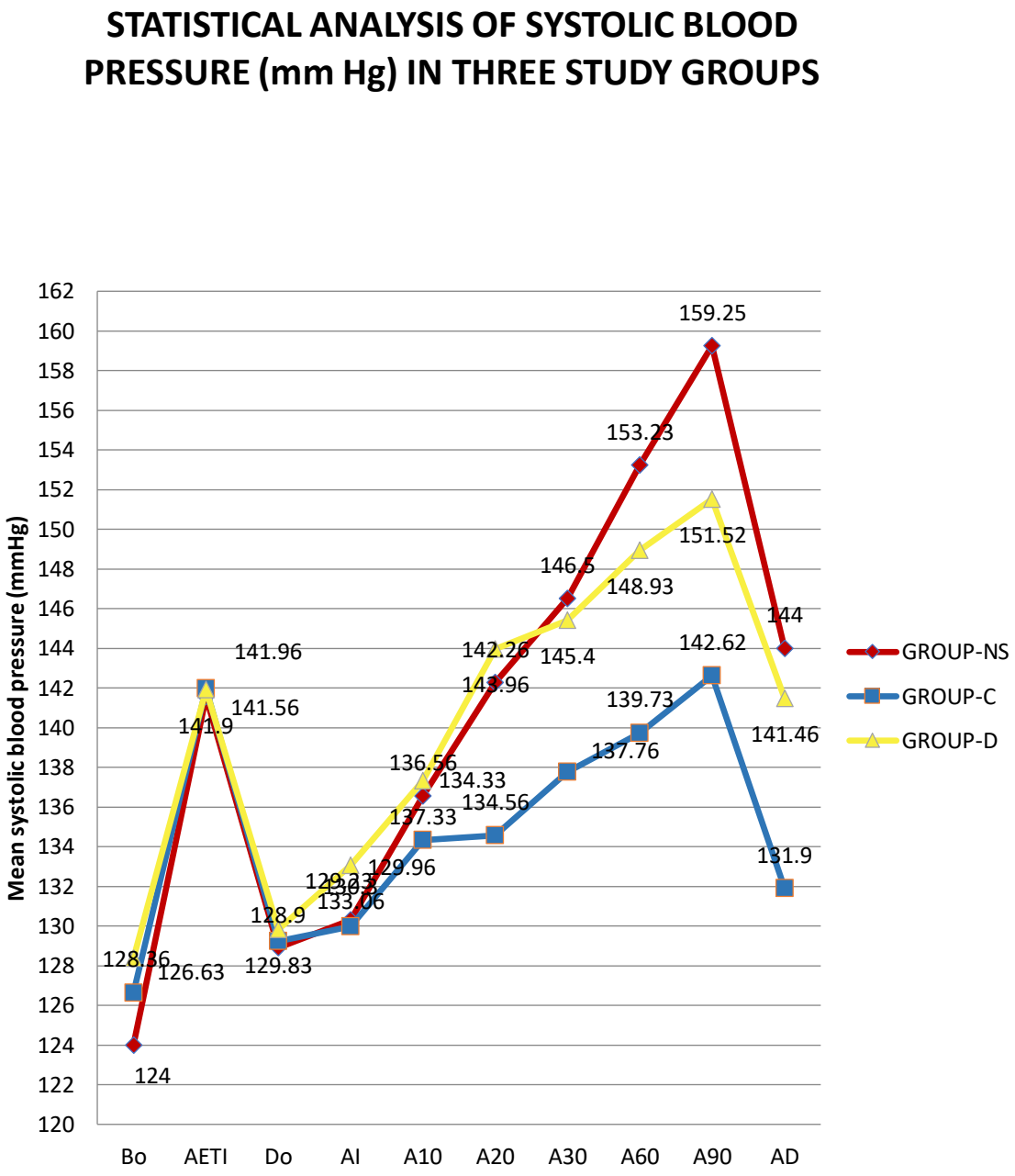
As compared to group C there was significant increase ($p \leq 0.05$) in pulse rate (bpm) in group D and group NS at different time interval after tourniquet inflation and after deflation of tourniquet and highly significant increase ($p<0.01$) at 90 minutes after start of tourniquet inflation. (Fig-1)

Figure – 1 Comparison of mean pulse rate in study groups.



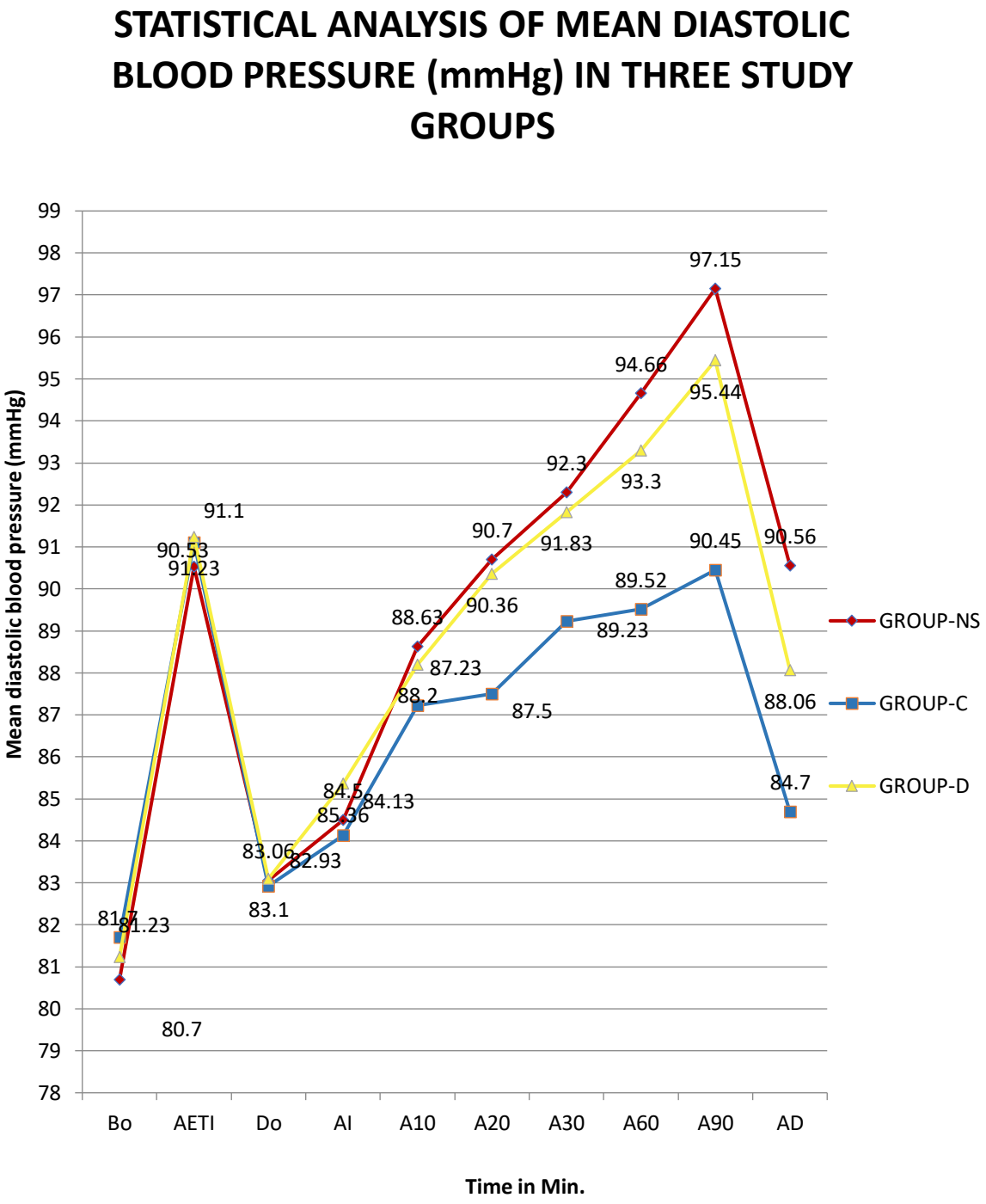
Group NS showed highly significant($p<0.01$) rise in systolic blood pressure as compared to group C and group D at 20,30,60,90 minutes after tourniquet inflation and after tourniquet deflation. (FIG-2)

Figure – 2 Comparison of Systolic blood pressure in study groups.



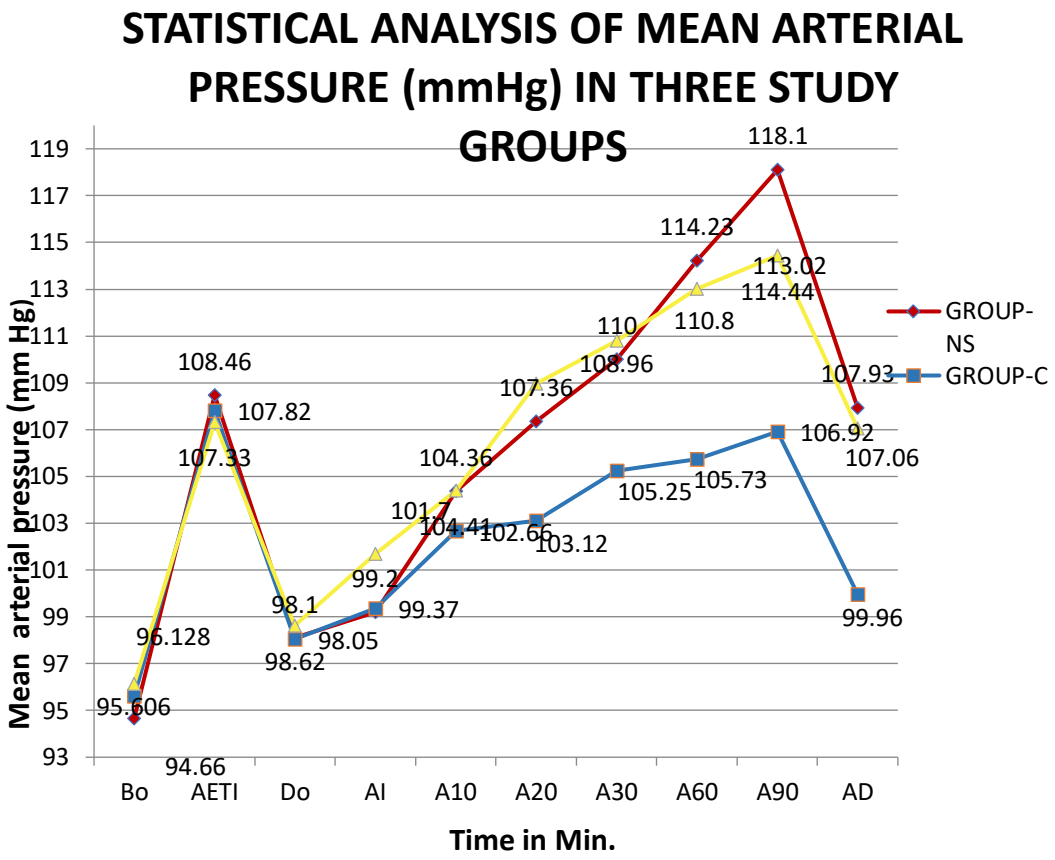
There was significant ($p\leq0.05$) difference in diastolic blood pressure at 20 minutes after tourniquet inflation and highly significant ($p<0.01$) difference at 30,60,90 minutes after tourniquet inflation and after deflation of tourniquet on comparing group NS with group C. While on comparing groups NS and D, there were no significant changes in diastolic blood pressure. On compairing group C with group D and group NS highly significant($p<0.01$) change in diastolic blood pressure were present at different time interval after tourniquet inflation and significant($p\leq0.05$) changes in diastolic blood pressure were present at 90 minutes after tourniquet inflation and after tourniquet deflation.(FIG-3)

Figure – 3 Comparison of Diastolic blood pressure in study groups.



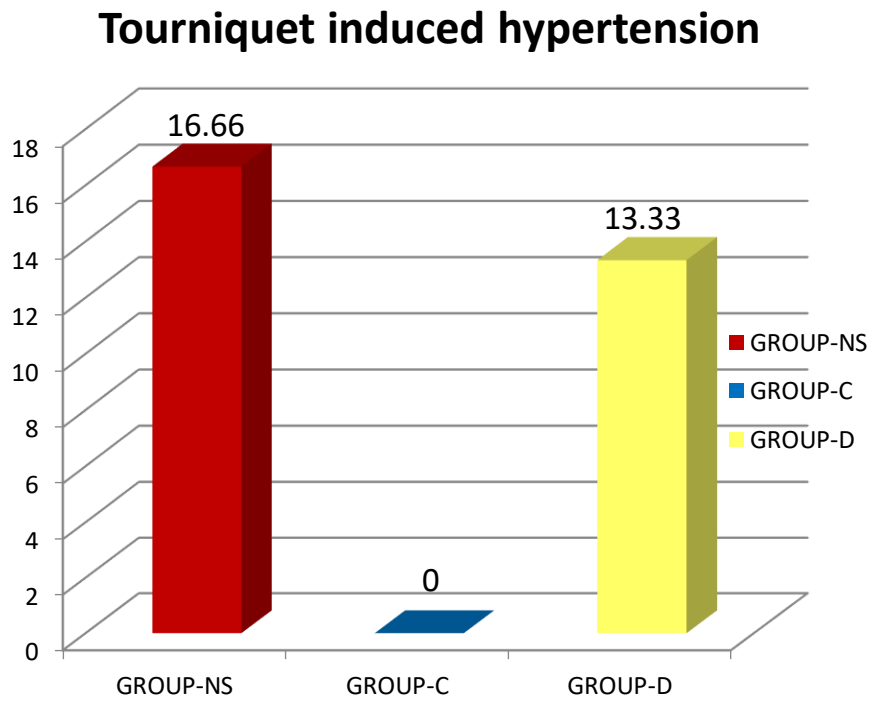
On comparing group C with group D and group NS, significant($p \leq 0.05$) change in mean arterial pressure were present at 20 minutes after tourniquet inflation and highly significant ($p<0.01$) changes in mean arterial pressure were present after 30, 60and 90 minutes after tourniquet inflation and after tourniquet deflation(AD). (FIG-4)

Figure – 4 Comparison of Mean arterial pressure in study groups



Above table showing that 16.66% patients in group NS and 13.33% patients in group D develops TIH (>30% rise in mean arterial pressure), and none of the patient develops TIH (>30% rise in mean arterial pressure) in group C.(FIG-6)

Figure – 5 Percentage of torniquet induced hypertension in the study group



DISCUSSION

The results from this study showed that preoperative intravenous Clonidine significantly prevented a systemic blood pressure increase and TIH during prolonged tourniquet inflation in patients under general anaesthesia. The intraoperative hypertension induced by prolonged tourniquet inflation of the lower limbs is often unresponsive to increased doses of anaesthetics and antihypertensive drugs[10]. Once increase in tourniquet-induced arterial pressure develops, it is often difficult to Control. In these patients, intravenous Clonidine and dexmedetomidine before tourniquet inflation may have a role in prevention of these blood pressure increases. Tetzlaff et al. showed that tourniquet induced arterial pressure increases correlate with the activation of the sympathetic nervous system, as measured by power spectral heart rate analysis[14]. Catecholamine release after the activation of the sympathetic nervous system may Contribute to the increase in systemic arterial pressure during prolonged tourniquet inflation[18,28]. Both the study drugs are alpha2-receptor agonist with both analgesic and sedative properties that reduce the sedation, anxiolytic, and analgesic requirements in the perioperative setting. They improve hemodynamic stability in the perioperative period by exerting sympatholytic effects via activation of the inhibitory a2-receptors both in the central nervous system and on peripheral sympathetic nerve endings, and reduces plasma epinephrine and norepinephrine levels. They have been reported to be useful in attenuating hemodynamic stress secondary to hyperadrenergic over-activity. intravenous clonidine and dexmedetomidine blunts both the increase in sympathetic out flow and arterial hypertension associated with tourniquet inflation under general anaesthesia [18]. In this study, we have shown that preoperative intravenous Clonidine is more effective than dexmedetomidine or normal saline for prevention of TIH. The use of Clonidine and Dexmedetomidine may have added benefits such as attenuating the cardiovascular and sympathoadrenal response to intubation and extubation and reducing opioid requirements during and after surgery[18,27].

There are several **limitations** in this study. First, we did not perform a dose response study having only used prefixed dose. Future studies could evaluate whether smaller doses can achieve the same benefit or whether larger doses can reduce TIH to a greater extent. Second, the depth of anaesthesia might have been different in the two groups as we did not use any depth of anaesthesia monitoring, Lastly, the effect of Clonidine and Dexmedetomidine on the relationship between tourniquet induced pain and hypertension was not evaluated, because this study was performed in patients receiving general anesthesia. however, there were no significant differences in induction and maintenace of anaesthesia during the study period and arterial pressure before tourniquet inflation between the groups.

CONCLUSION

Intravenous Clonidine is more effective than intravenous dexmedetomidine and intravenous NS in prevention of tourniquet induced hypertension and hemodynamic responses to prolonged tourniquet inflation under general anaesthesia. further investigations are needed to show whether perioperative outcome in patients with arterial hypertension or cardiovascular disease is improved by different doses of Clonidine and Dexmedetomidine treatment.

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