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Original research article

Comparative evaluation of pre-medication with intravenous clonidine and dexmedetomidine for prevention of tourniquet-induced hypertension in upper limb orthopaedic surgeries under general anaesthesia

[1]Dr. Kamal raj singh baghel, [2]Dr. Anivesh Jain, [3]Dr. Vishwanath mohire, [4]Dr Anurag Dubey

[1,2]Assistant Professor, Department of Anaesthesiology, Super speciality hospital, NSCB Medical College, Jabalpur, Madhya Pradesh, India

[3]Associate professor, Department of Anaesthesiology, Super speciality hospital, NSCB Medical College, Jabalpur, Madhya Pradesh, India

[4]Assistant Professor, Department of Urology, Super speciality hospital, NSCB Medical College, Jabalpur, Madhya Pradesh, India

Corresponding Author:
Dr. Anurag Dubey

Abstract

The use of tourniquets goes back to early Roman times when various constricting bandages were used to control haemorrhage during limb amputation. Tourniquets are widely used during limb operations to minimize surgical bleeding and to maintain a relatively bloodless field. Tourniquet-induced hypertension occurs more frequently under general anaesthesia than spinal anaesthesia and can be serious in patients with cardiopulmonary diseases, neurological diseases and glaucoma. This study was designed to investigate the hemodynamic effects of Clonidine and Dexmedetomidine on prolonged tourniquet inflation.This study was a double-blinded randomized control trial designed to investigate the hemodynamic effects of Clonidine and Dexmedetomidine on prolonged tourniquet inflation.

Material and Methods: Sixty 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 Z=30) intravenous dexmedetomidine (0.5 mcg/kg; n=30) 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. Development of more than 30% increase in arterial pressure during tourniquet inflation was more frequent in the control group 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

The use of tourniquets goes back to early Roman times when various constricting bandages were used to control haemorrhage during limb amputation. Tourniquets are widely used during upper and lower limb operations to minimize surgical bleeding and to maintain a relatively bloodless field. The limb should be exsanguinated by elevating and using tourniquet exsanguination (S-MART) [1] for emptying the blood vessels from the distal end to the proximal end prior to tourniquet inflation. There are numerous advantages of this, including establishing a clear operating field, reducing overall blood loss, and reducing the risk of micro emboli at the time of deflation [2, 4]. This exsanguinations results in auto transfusion of blood from the peripheral circulation into the central circulation [2, 5]. Tourniquet application can cause cellular hypoxia, acidosis, and cooling in the occluded limb. Muscle is more susceptible to ischemic damage than nerve. The most common complication of tourniquet inflation is nerve injury. Other complications are tourniquet pain; intraoperative bleeding, compartment syndrome, pressure sores, digital necrosis, and deep vein thrombosis [2]. Exsanguination of the limb and inflation of the tourniquet produce an initial increase in systemic arterial pressure. This increase has been attributed to several factors, including an 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 [6-9]. The tourniquet pain and increase in arterial blood pressure are frequently observed 30-60 min after tourniquet inflation in spite of an adequate level of anesthesia and

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they are often resistant to the profound depth of anesthesia and analgesic drugs [10]. 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 [8, 11-13]. Tourniquet-induced hypertension occurs more frequently under general anesthesia than spinal anesthesia [10]. Although the mechanism of TIH is unknown, the possibility of involvement of the autonomic nervous system and increased plasma catecholamine concentration continuously in parallel to arterial blood pressure during tourniquet inflation has been documented [11, 12, 15, 16]. Once tourniquet-induced hypertension develops, its treatment is difficult and often ineffective, even with increased doses of anesthetics and antihypertensive drugs [11, 14]. Many drugs like ketamine [17], magnesium [18], intravenous opioid (Remifentanil) [6], dextromethorphan [19], and stellate ganglion block [20], have been used prophylactically to prevent TIH [11, 12, 16].

Clonidine and Dexmedetomidine both are alpha 2 agonist [25, 30]. Dexmedetomidine is eight times more selective for alpha 2 receptors compared to clonidine [11]. They produce sedation, analgesia, and anxiolysis after intravenous administration, thus decreasing the perioperative requirement of inhaled anaesthetic [24-26]. It is known to produce attenuation of hemodynamic response to tracheal intubation and decreases plasma catecholamines as well [22, 23]. This property of attenuation of hyperadrenergic response could be of therapeutic or prophylactic value in the reduction of tourniquet-induced hypertension [11].

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 of the upper limbs under general anaesthesia.

Material and Methods

This study was randomized, double-blinded, and placebo controlled. After obtaining approval from the institutional ethical committee, the studywas conducted on 60 patients of ASA grade I and II scheduled for orthopaedic operation requiring tourniquet inflation of the upper limbs under general anaesthesia were enrolled in the Department of anaesthesiology, J.A Group of Hospital, G.R. Medical College, Gwalior (M.P) after obtaining written informed consent. Patients with known contraindications to clonidine/dexmedetomidine, 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 pre-medicated with Inj. Pentazocine 0.5 mg/kg BW followed by pre-oxygenation with 100% oxygen for 3 minutes by facemask.

Induction of General Anaesthesia was done with intravenous injection of Thiopentone Sodium 5 mg/kg BW. Endotracheal intubation was facilitated with an intravenous injection of 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 anesthetic circuit. After intubation, patients in group 'C' (n=30) received the infusion of the study drug Inj. Clonidine (1.0 mcg/kg) diluted in 10 ml normal saline over a period of 10 min, patients in group 'D' (n=30) received the infusion of study drug Inj. dexmedetomidine (0.5mcg/kg) diluted in 10 ml normal saline over the same period. The infusions were prepared by a nurse anaesthetist not involved with the case according to a computer-generated sequence. All the hemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and Oxygen saturation (SpO2) were 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 a tourniquet. Throughout the procedure for any 20% rise in MAP above the basal MAP, Isoflurane concentration was increased to maintain the basal MAP. For a fall in MAP more than 20% of the basal MAP, Isoflurane was decreased or stopped. A heart rate less than 50 bpm was treated with Atropine 0.6 mg intravenously. The number of patients, who developed TIH, as defined by an increase in arterial blood pressure greater than 30% of the baseline value, 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.

Statistical analysis

The observations recorded in all the groups were tabulated and statistical analysis was carried out by using the appropriate statistical software SPSS 17. Student's 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 was taken to be statistically highly significant

Result

There were no statistically significant differences between the groups with respect to the patient's demographic characteristics (Table 1).

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Table 1: Demographic data, of Clonidine and Dexmedetomidine group

Variable	Group 'C' (n=30)	Group 'D'(n = 30)
Age (years)	37.2±13.1	39.1±14.4
Sex (m/f)	23/7	21/9
Weight (kg)	61.3 ±7. 16	61.4±7.11

Values are presented as mean ± SD. There were no significant differences between the groups. Group 'C' = group receiving Clonidine; Group "D"= receiving dexmedetomidine.

As compared to group C there was a significant increase ($p \leq 0.05$) in pulse rate (bpm) occur in group D at 60 minutes after tourniquet inflation and after deflation of the tourniquet and a highly significant increase ($p < 0.01$) at 90 minutes after the start of tourniquet inflation.(Fig-1).

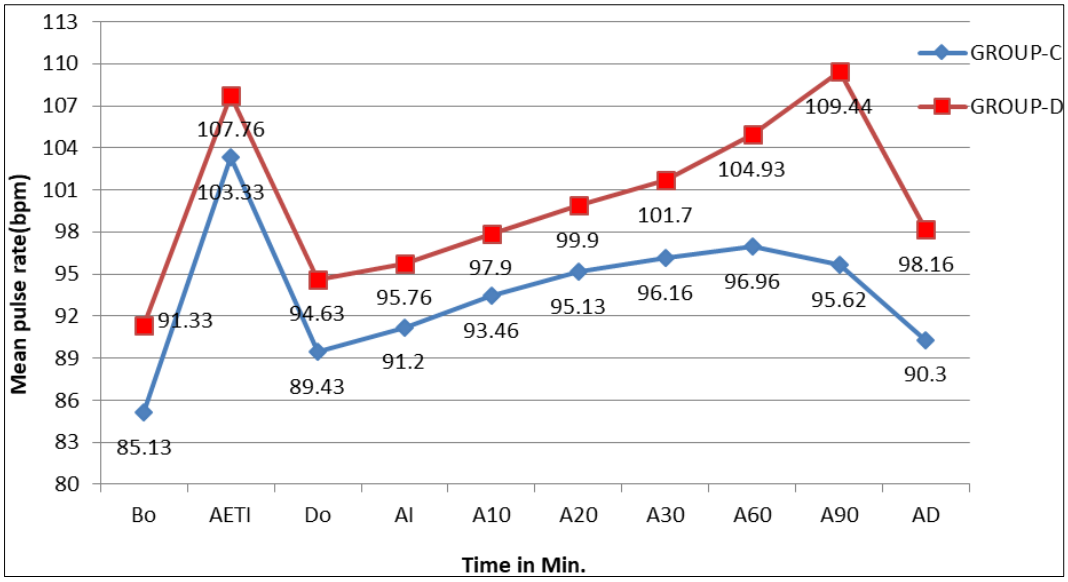

Fig 1: Statistical analysis of Mean Pulse Rate (bpm) in two study groups

As compared to group C there was significant ($p \leq 0.05$) increase in mean arterial pressure occur in group D at 20 minutes after tourniquet inflation and highly significant ($p < 0.01$) increase in mean arterial pressure were present after 30, 60 and 90 minutes after tourniquet inflation and after tourniquet deflation(AD). So In group C increase in mean arterial pressure was less marked in comparison to group D, (fig-2).

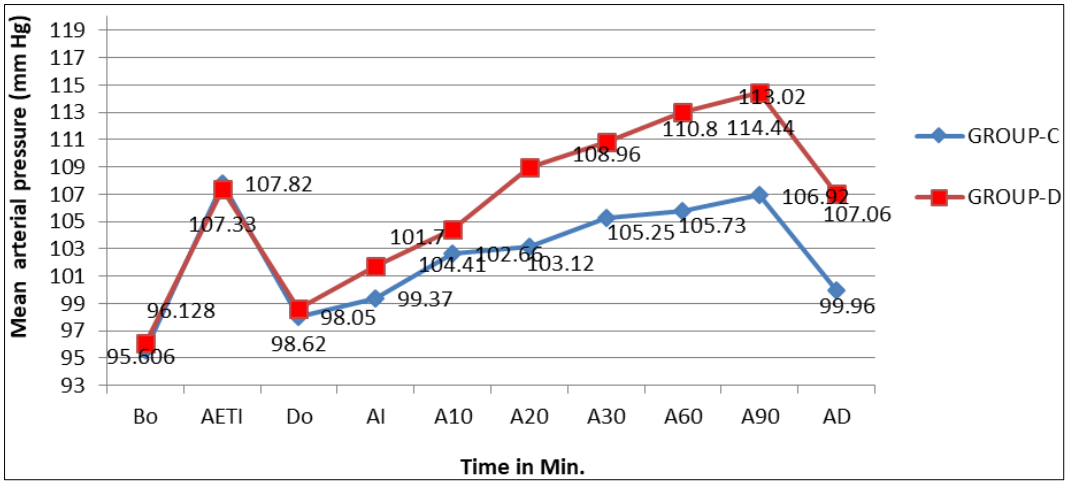

Fig 2: Statistical analysis of Mean Arterial Pressure (mmHg) in two study groups. (Values are presented as mean ± SD. Bo= base line value; AETI= after intubation; Do=before administration of drug; AI=immediately after tourniquet inflation; A10, A20, A30, A60, A90= After 10, 20,30,60,90 minutes of inflation; AD after tourniquet deflation.

The group 'D' had a greater percentage of patients who developed TIH when compared with the Clonidine group (Fig. 3).

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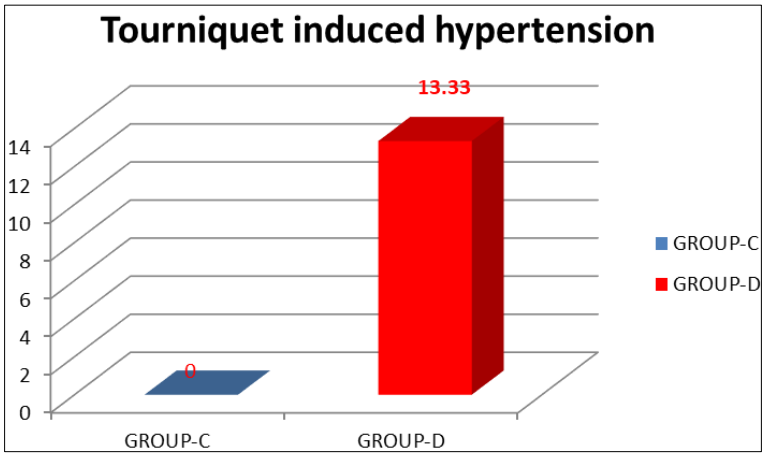

Fig 3: Statistical analysis of Tourniquet induced hypertension in two study groups

Discussion

The results from this study showed that preoperative intravenous Clonidine significantly prevented a systemic arterial pressure increase during prolonged tourniquet inflation in patients under general anaesthesia. Perioperative hypertension may be associated with serious cardiac complications. Furthermore, the level of hypertension is correlated with the occurrence of postoperative silent myocardial ischemia [24-27]. Intraoperative hypertension induced by prolonged tourniquet inflation of the lower limbs is often unresponsive to increased doses of anaesthetics and antihypertensive drugs [8]. Once tourniquet-induced arterial pressure increase develops, it is often difficult to Control. In these patients, intravenous Clonidine and dexmedetomidine before tourniquet inflation may have a role in attenuating 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. An increase in plasma norepinephrine levels was related to the tourniquet-induced arterial pressure increase under general anesthesia [16, 28]. Catecholamine release after the activation of the sympathetic nervous system may contribute to the increase in systemic arterial pressure during prolonged tourniquet inflation. Both the study drugs are alpha2-receptor agonists with both sedative and analgesic 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 reduce plasma epinephrine and norepinephrine levels. They have been reported to be useful in attenuating hemodynamic stress secondary to hyperadrenergic over-activity. In awake patients, the addition of Clonidine or dexmedetomidine to the local anesthetic solution in intravenous regional anaesthesia decreases tourniquet pain. Preoperative intravenous clonidine and dexmedetomidineblunt both the increase in sympathetic outflow and arterial hypertension associated with tourniquet inflation under general anesthesia [16]. In this study, we have shown that preoperative intravenous Clonidine is more effective than dexmedetomidine for the 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 [29, 31].

Limitations

In this study. First, we did not perform a dose-response study having only used one 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 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 anaesthesia.

Third and lastly, the depth of anaesthesia might have been different in the two groups as we did not use any depth of anaesthesia monitoring, however, there were no significant differences in induction and maintenance of anaesthesia during the study period and arterial pressure before tourniquet inflation between the groups.

Conclusion

As compared to preoperative intravenous Dexmedetomidine, intravenous Clonidine significantly prevents tourniquet-induced hypertension and hemodynamic responses to prolonged tourniquet inflation of the upper limbs under general anaesthesia in patients. On the basis of the results of this study, further investigations are needed to show whether the perioperative outcome in patients with arterial hypertension or cardiovascular disease is improved by Clonidine and Dexmedetomidine treatment.

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