Preoperative Clonidine Prevents Tourniquet Induced Hypertension in upper Limb Orthopaedic Operation during General Anaesthesia

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ABSTRACT

Introduction: 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 more with lower limb tourniquet than with upper limb tourniquet and can be serious in patients with cardiopulmonary diseases, neurological disease and glaucoma. This study was designed to investigate the hemodynamic effects of Clonidine 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=30) or normal saline (NS group; 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 Control 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 Control group than in the Clonidine group.

Conclusion: Preoperative intravenous Clonidine could therefore prevent tourniquet-induced hypertension in patients undergoing general anaesthesia.

Keywords: Clonidine; General anaesthesia; Hypertension; Tourniquet

INTRODUCTION

Tourniquets are widely used during limb operations to minimize surgical bleeding and to maintain a relatively bloodless field.[1,2] Tourniquet application can cause cellular hypoxia, acidosis and cooling in the occluded limb. The most common Complication of tourniquet inflation is nerve injury. Others are tourniquet pain, intra operative bleeding, compartment syndrome, pressure sores, digital necrosis and deep vein thrombosis.[1] The tourniquet pain and increase in arterial blood pressure are frequently observed 30-60 min after tourniquet inflation inspite of adequate level of anaesthesia and they are often resistant to profound depth of anaesthesia and analgesic drugs.[3] 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.[4-6] Tourniquet induced hypertension occurs more frequently under general anaesthesia than spinal anaesthesia and more with lower limb tourniquet than with upper limb tourniquet and can be serious in patients with cardiopulmonary diseases, neurological disease and glaucoma.[3] Although the mechanism of TIH is unknown, but possibility of involvement of the autonomic nervous system and increase in plasma catecholamine concentration continuously in parallel to arterial blood pressure during tourniquet inflation has been documented.[5,7-9] Once tourniquet induced hypertension develops, it's treatment is difficult and often ineffective, even with increased doses of anaesthetics and antihypertensive drugs.[5,10] Many drugs like ketamine,[11] magnesium,[12] intravenous opioids (Remifentanil),[13] dextromethorphan,[14] and stellate ganglion block,[15] have been used prophylactically to prevent TIH.[5,7,9] Clonidine is a centrally acting selective partial alpha 2 agonist, known to induce sedation, decrease anaesthetic drug requirement improved perioperative haemodynamics by altering blood pressure and heart rate responses to surgical stimulation, and protection against perioperative myocardial ischemia.[16-18] In this study, we investigated the effect of preoperative intravenous Clonidine on arterial blood pressure and heart rate in patients undergoing general anaesthesia for orthopaedic surgery of the upper limbs with a tourniquet.

MATERIAL AND METHODS

This study was randomized, double-blinded, and placebo controlled. After obtaining approval from the institutional ethical committee, the study was 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; 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 and 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. After intubation, patients in Clonidine group (n=30) received the infusion of study drug Inj.Clonidine (1.0mcg/kg)

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diluted in 10 ml normal saline over a period of 10 min, Patients in the normal saline Group (NS; n =30) received the same volume of normal saline infused 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 haemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and Oxygen saturation (SpO_2) 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, 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 (0.005-0.01mg/kg) and Neostigmine (0.04-0.08mg/kg) intravenously.

STATISTICAL ANALYSIS

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 and P-value <0.05 was taken statistically significant whereas P-value <0.01 taken to be statistically highly significant.

RESULTS

There were no statistically significant differences between the groups with respect to the patients' demographic characteristics (Table-1). In the Clonidine group, Mean arterial pressures were not changed during the study period, but in the Control group, mean arterial pressure were significantly increased at 40, 50, and 60 minutes after the start of tourniquet inflation (Figure-2). In all patients of Clonidine group, the heart rate did not change significantly during tourniquet inflation, but there was a significant increase in HR in patients of NS group after 30 minute of tourniquet inflation and change was also significant immediately after deflation of tourniquet in the Control group (Figure-1). The Control group had a greater percentage of patients who developed TIH when compared with the Clonidine group (Figure-3).

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.[19-21] The intraoperative hypertension induced by prolonged tourniquet inflation of the lower limbs is often unresponsive to increased doses of

Variable	Control (NS) group (n = 30)	Clonidine group (n = 30)
Age (y)	34.6±14.3	37.2±13.1
Sex (m/f)	22/8	23/7
Weight (kg)	61 ± 7.07	61.3 ±7. 16
Values are presented as mean ± SD. There were no significant differences between groups. Group NS = group receiving normal saline; Clonidine = group receiving Clonidine		

Table–1: Demographic data, of Control and Clonidine group

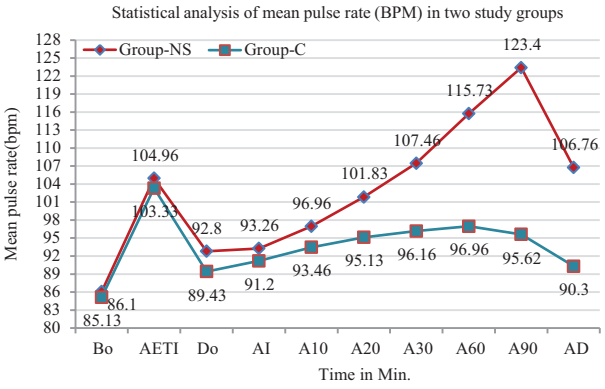
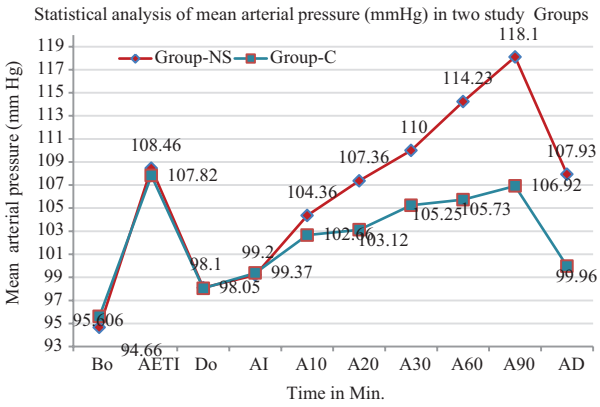


Figure-1: Statistical analysis of Mean Pulse Rate (bpm) in two study groups



Figure–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; NS group = receiving normal saline; DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure)

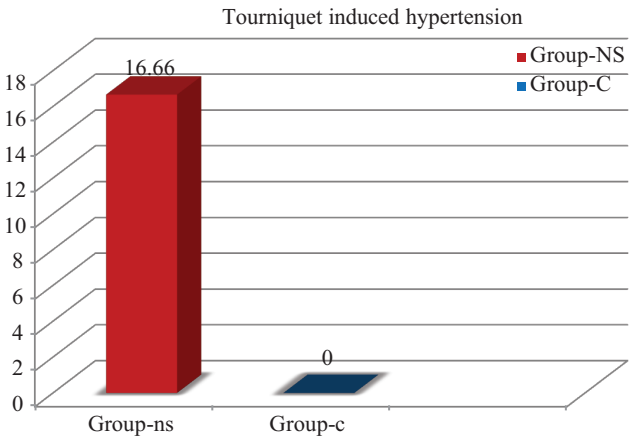


Figure-3: Statistical analysis of Tourniquet induced hypertension in two study groups

anaesthetics and antihypertensive drugs.[10] Once tourniquet-induced arterial pressure increase develops, it is often difficult to Control. In these patients, intravenous Clonidine 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 anaesthesia.[9,22] Catecholamine release after the activation of the sympathetic nervous system may contribute to the increase in systemic arterial pressure during prolonged tourniquet inflation. Clonidine is an alpha 2-receptor agonist with both sedative and analgesic properties that reduce the sedation, anxiolytic, and analgesic requirements in the perioperative setting. Clonidine improves 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. Clonidine has been reported to be useful in attenuating hemodynamic stress secondary to hyperadrenergic over-reactivity. In awake patients, the addition of Clonidine to the local anaesthetic solution in intravenous regional anaesthesia decreases tourniquet pain. Preoperative intravenous Clonidine blunts both the increase in sympathetic out flow and arterial hypertension associated with tourniquet inflation under general anaesthesia.[9] In this study, we have shown that preoperative intravenous Clonidine could also prevent TIH. The use of Clonidine may have added benefits such as attenuating the cardiovascular and sympathoadrenal response to intubation and extubation and reducing opioid requirements during and after surgery. Clonidine decreases the incidence and frequency of delirium in children and adults.[17,23]

There are several 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 on the relationship between tourniquet induced pain and hypertension was not evaluated, because this study was performed in patients receiving general anesthesia. Lastly, the depth of anesthesia 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 maintenace of anaesthesia during the study period and arterial pressure before tourniquet inflation between the groups.

CONCLUSION

Preoperative intravenous Clonidine significantly prevents 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 perioperative outcome in patients with arterial hypertension or cardiovascular disease is improved by Clonidine treatment.

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