VOLUME-7, ISSUE-4, APRIL-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Anesthesiology

PREOPERATIVE DEXMEDETOMIDINE PREVENTS TOURNIQUET INDUCED HYPERTENSION IN UPPER LIMB ORTHOPAEDIC SURGERIES DURING GENERAL ANAESTHESIA

Dr. Kamal Raj Singh Ex-Resident, Department of Anaesthesiology G.R. Medical College, Gwalior 474009 (M.P.).

Dr. Jitendra Agrawal* Associate Professor, Department of Anaesthesiology G.R. Medical College, Gwalior 474009 (M.P.). *Corresponding Author

Dr Bhanu Choudhary Prof. & Head, Department of Anaesthesiology G.R. Medical College, Gwalior 474009 (M.P.).

ABSTRACT

Introduction: During limb operations tourniquets are widely used 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 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 dexmedetomidine (0.5 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 dexmedetomidine group, arterial pressure was not significantly changed, but in the Control group arterial pressure was significantly increased at 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 dexmedetomidine group.

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

KEYWORDS : dexmedetomidine; General anaesthesia; Hypertension; Tourniquet

INTRODUCTION:-

During limb operations tourniquets are widely used. Advantages of tourniquet inflation include establishing a clear operating field, reducing overall blood loss, and reducing the risk of micro emboli at the time of deflation.[1,2] 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] 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 ischemia and pain due to tourniquet compression.[3-5]

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.[5-8] 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.[6,7,9,10] Once tourniquet induced hypertension develops, it's treatment is difficult and often ineffective, even with increased doses of anaesthetics and antihypertensive drugs.[6,11] Many drugs like ketamine,[12] magnesium,[13] intravenous opioids (Remifentanil),[3] dextromethorphan,[14] and stellate ganglion block,[15] have been used prophylactically to prevent TIH. [6,7,10] 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.[16]

Dexmedetomidine is a centrally acting 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. It also produces attenuation of haemodynamic response to tracheal intubation and decreases plasma catecholamines as well.[17-20] This property of attenuation of hyperadrenergic response could be of therapeutic or prophylactic value in the reduction of tourniquet induced hypertension.[21-23]

In this study, we investigated the effect of preoperative intravenous dexmedetomidine on the tourniquet induced rise in arterial blood pressure and heart rate 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 instituitional ethical committee, the study was conducted on 60 patients of ASA grade I and II scheduled for orthopedic operation requiring tourniquet inflation of the upper limbs under general anesthesia 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 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 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. After intubation, patients in group 'D'(n=30) received the infusion of study drug Inj.dexmedetomidine (0.5mcg/kg) 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 anesthetist~~ junior Resident 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

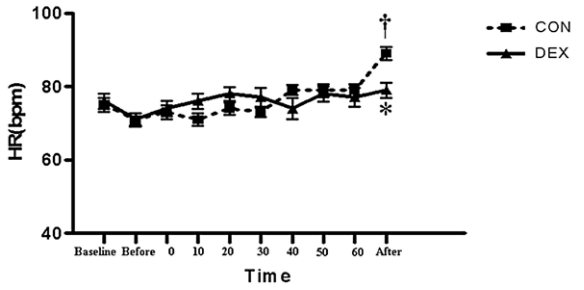
arterial pressure (MAP) and Oxygen saturation (SpO2) were ~~be~~ recorded ,before induction (Bo), after endotracheal intubation (AETI), before study drug administration (Do), after inflation of tourniquet(AI) and then at 10, 20, 30, 60, 90 min (A10, A20, A30, A60, A90) and 5 min after deflation (AD_5) 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 inj. 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.

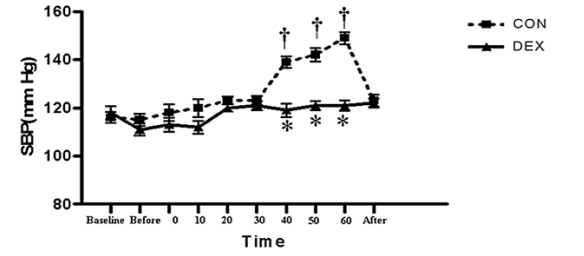
Table–1: Demographic data, of Control and Dexmedetomidine group

Variable	Group 'NS' (n = 30)	Group 'D' (n = 30)
Age (years)	34.6±14.3	39.1±14.4
Sex (m/f)	22/8	21/9
Weight (kg)	61±7.07	61.4±7.11

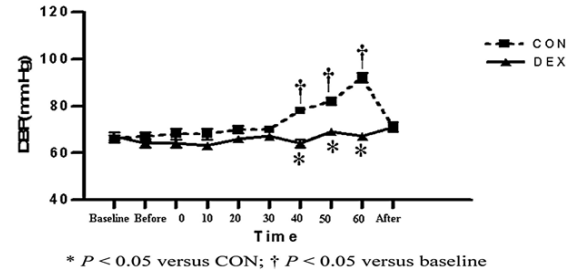
Values are presented as mean ± SD. There were no significant differences between groups. Group NS = group receiving normal saline; Group "D"= receiving dexmedetomidine



Figure–1: Statistical analysis of Mean Pulse rate (bpm) in 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; group 'D'= receiving dexmedetomidine)



Figure–2: Statistical analysis of Mean Arterial Pressure (mmHg) in study groups.



* $P < 0.05$ versus CON; † $P < 0.05$ versus baseline

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

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

Result

There were no statistically significant differences between the groups with respect to the patients' demographic characteristics (Table 1). As compared to dexmedetomidine group there was highly significant increase ($p<0.01$) in HR occour in control group patients at 60 and 90 minutes after tourniquet inflation and change was also highly significant immediately after tourniquet deflation.(Fig.1) In the dexmedetomidine group, systolic and diastolic arterial pressures were not changed during the study period, but in the control group, systolic arterial pressure was highly significantly increased at 90 minutes after the start of tourniquet inflation.(Fig.2) The control group had a greater percentage of patients who developed TIH when compared with the dexmedetomidine group (Fig. 3).

Discussion

The results from this study showed that preoperative intravenous dexmedetomidine 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. The intraoperative hypertension induced by prolonged tourniquet inflation of the lower limbs is often unresponsive to increased doses of anaesthetics and antihypertensive drugs. Once tourniquet-induced arterial pressure increase develops, it is often difficult to Control. In these patients, intravenous dexmedetomidine before tourniquet inflation may have a role in attenuating these blood pressure increases. An increase in plasma norepinephrine levels was related to the tourniquet induced arterial pressure increase under general anaesthesia. Catecholamine release after the activation of the sympathetic nervous system may contribute to the increase in systemic arterial pressure during prolonged tourniquet inflation. Dexmedetomidine is an alpha2-receptor agonist with both sedative and analgesic properties that reduce the sedation, anxiolytic, and analgesic requirements in the perioperative setting. [1,2,3]

Dexmedetomidine 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. Dexmedetomidine has been reported to be useful in attenuating hemodynamic stress secondary to hyperadrenergic over-reactivity. In awake patients, the addition of dexmedetomidine to the local anaesthetic solution in intravenous regional anesthesia decreases tourniquet pain .[4,5,6]

JC, Sehlhorst CS did work on response to maintenance of tourniquet inflation in a primate model Several theories have been proposed, but the etiology and pathway of neural transmission for the sensation of tourniquet pain remain unknown. So this study was designed to observe the circulatory response and to measure the stress response markers associated with maintenance of tourniquet inflation in an anesthetized primate model. An increase in serum cortisol and plasma norepinephrine was demonstrated to correlate with the circulatory response in this model. The results of this study suggest that the circulatory response to maintenance of tourniquet inflation in this animal model may be mediated by a neurohumoral response to tourniquet pain and that an animal model may be appropriate for further studies into the etiology and neural pathways associated with the sensation of tourniquet pain.[7,8,9]

Preoperative intravenous dexmedetomidine blunts both the increase in sympathetic out flow and arterial hypertension

associated with tourniquet inflation under general anaesthesia. In this study, we have shown that preoperative intravenous dexmedetomidine could also prevent TIH. The use of 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. Dexmedetomidine decreases the incidence and frequency of delirium in children and adults . Dyck JB et al, Belleville JP et al, Bhana N et al all authors studied the pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers and effects of intravenous dexmedetomidine in humans. Itseffect on Sedation, ventilation and metabolic rate. [10,11,12]

Valli H, Rosenberg PH. Effects of three anaesthesia methods on haemodynamic responses connected with the use of thigh tourniquet in orthopaedic patients. They also did a similar study on arterial hypertension associated with the use of a tourniquet with either general or regional anaesthesiaThere was a higher frequency of the occurrence of "tourniquet hypertension" with older age, longer operations and the operation site being the lower rather than the upper limb. Tourniquet hypertension rarely occurred in patients with spinal anaesthesia (2.7%) and brachial plexus blockade (2.5%), while those with intravenous regional anaesthesia had a higher incidence (19%) of hypertension [13,14]

Arai YC et al gave preoperative stellate ganglion blockade to prevent tourniquet-induced hypertension during general anesthesia. Prolonged and excessive inflation of pneumatic tourniquets leads to a hyperdynamic circulatory response. Sympathomimetic activity is an important factor in tourniquet-induced hypertension. Stellate ganglion block specifically blunts sympathetic efferent nerves and prevents hypertension induced by sympathomimetic stimulation. The present study was performed to investigate the effects of stellate ganglion block (SGB) on arterial pressure and heart rate during prolonged tourniquet use under general anesthesia.They concluded that ipsilateral SGB attenuated the hyperdynamic response mediated by prolonged tourniquet inflation during knee arthroscopy.[15]

Jun-Young Jung et al did work on remifentanil and found that it prevents tourniquet-induced arterial pressure increase in elderly orthopedic patients under sevoflurane/n2o general anesthesia Prolonged tourniquet inflation produces a hyperdynamic cardiovascular response.They investigated the effect of continuous remifentanil infusion on systemic arterial pressure, heart rate, and cardiac output changes during prolonged tourniquet use in elderly patients under sevoflurane/N_2O general anesthesia and demonstrated that infusion with remifentanil prevented an increase in hemodynamic pressure during tourniquet inflation in elderly patients under sevoflurane/N_2O general anesthesia.[16,17]

This study is similar to the study done by Lu Y, Zhang Yet al .It was a double-blinded randomized control trial designed to investigate the hemodynamic effects of dexmedetomidine on prolonged tourniquet inflation. Thirty-seven patients scheduled for elective orthopedic surgery of the lower limb under general anesthesia were recruited. They were randomly assigned to receive intravenous dexmedetomidine (DEX, 0.5 μg/kg; n = 18) or normal saline (CON; n = 19) before tourniquet inflation. Arterial blood pressure and heart rate were recorded every 10 minutes until 60 minutes after the start of tourniquet inflation and again immediately after deflation. In the DEX group, arterial pressure was not significantly changed, but in the CON 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 CON group than in the DEX group. They also concluded that preoperative intravenous dexmedetomidine could therefore prevent tourniquet-induced hypertension in patients undergoing general anesthesia.[18,19]
Zalunardo MP et al in a similar study found that preoperative clonidine blunts hyperadrenergic and hyperdynamic responses to prolonged tourniquet pressure during general anesthesia Although the mechanism of tourniquet-induced hypertension is still unclear, plasma norepinephrine concentrations continuously increase in parallel to arterial blood pressure during tourniquet inflation. Clonidine attenuates hyperadrenergic and hyperdynamic responses. In conclusion, preoperative IV clonidine blunts hyperadrenergic and hyperdynamic responses resulting from prolonged tourniquet inflation under general anesthesia in ASA class I–II patients.[20,21]

Lee DH et al studied that magnesium sulphate attenuates tourniquet-induced hypertension and spinal c-fos mRNA expression and did a comparison with ketamine. The aim of this study was to determine whether magnesium, in comparison with ketamine, attenuates tourniquet-induced hypertension and spinal *c-fos* mRNA expression. Magnesium and ketamine are equally effective in attenuating tourniquet-induced hypertension and spinal *c-fos* mRNA expression, suggesting that this effect may be due to reduced pain transmission. Yamashita S et al gave preoperative oral dextromethorphan and attenuated tourniquet-induced arterial blood pressure and heart rate which increases in knee cruciate ligament reconstruction patients under general anesthesia.[22,23]

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 dexmedetomidine 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 anesthesia 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,

preoperative intravenous dexmedetomidine significantly prevents hemodynamic responses to prolonged tourniquet inflation of the upper limbs under general anesthesia 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 dexmedetomidine treatment.

References:-

1. J.P. Sharma, R. Salhotra, Tourniquets in orthopaedic surgery. Indian J Orthop 2012;4 [46] : 377-382.
2. Tourniquet-A S-MART concept. Simon Axon. Accessed From http://usmorthopaedic.blogspot.in/2009/06/tourniquet-s-martconcept.html.
3. Kaufman RD, Walts LF. Tourniquet-induced hypertension. Br J Anaesth 1982; 54: 333-6.
4. Aantaa R, Scheinin M. Alpha2-adrenergic agents in anaesthesia. Acta Anaesthesiologica Scandinavica. 1993 Jul 1;37(5):433-48.
5. Aho M, Erkola O, Korttila K. Alpha2-adrenergic agonists in anaesthesia. Current Opinion in anaesthesiology1992; 5:481–7.
6. Schmelling W, Farber N. The effects of alpha-2 adrenergic agonists on cardiovascular system, Semin Cardiothor Vasc Anesth s1997;1:1-20.
7. Crews JC, Sehlhorst CS. Response to maintenance of tourniquet inflation in a primate model. Reg Anesth. 1991;16:195-8.
8. Tetzlaff JE, O'Hara J, Yoon HJ, Schubert A. Tourniquet induced hypertension correlates with autonomic nervous system changes detected by power spectral heart rate analysis. J ClinAnesth 1997;9 : 138-42.
9. Hagenouw RR, Bridenbaugh PO, van Egmond J, Stuebing R. Tourniquet pain: a volunteer study. AnesthAnalg 1986;65:1175-80.
10. Dyck JB, Maze M, Haack C, Vuorilehto L, Shafer SL. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology 1993;78:813-20.
11. Belleville JP, Ward DS, Blooor BC, Maze M. Effects of intravenous dexmedetomidine in humans. I. Sedation, ventilation and metabolic rate. Anesthesiology 1992;77:1125-33.
12. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000; 59: 263-8.
13. Valli H, Rosenberg PH. Effects of three anaesthesia methods on haemodynamic responses connected with the use of thigh tourniquet in orthopaedic patients. ActaAnaesthesiolScand 1985;29:142-7.
14. Valli H, Rosenberg PH, Kytta J, Nurminen M. Arterial hypertension associated with the use of a tourniquet with either general or regional anaesthesia. ActaAnaesthesiolScand 1987; 31: 279-83.
15. Arai YC,Ogata J, Matsumoto Y,Yonemura H, Kido K, Uchida T, et al. Preoperative stellate ganglion blockade prevents tourniquet-induced hypertension during

general anesthesia. ActaAnaesthesiolScand 2004; 48:613-8.
16. Elmawgood AA, Rashwan S, Rashwan D. Tourniquet-Induced cardiovascular responses in anterior cruciate ligament reconstruction surgery under general anaesthesia: Effect of preoperative oral Amantadine; Egypt J Anesth (2015);31(1):29-33.
17. Jun-Young Jung, Jin-Hee Han, Jae-Woo Yi, Jong-Man Kang*, Remifentanil Prevents Tourniquet-Induced Arterial Pressure Increase in Elderly Orthopedic Patients under Sevoflurane/N2O General Anesthesia, Intl Med. Sci. 2012; 9(4):311-315.
18. Lu Y, Zhang Y, Dong CS, Yu JM, Wong GT. Preoperative dexmedetomidine prevents tourniquet-induced hypertension in orthopedic operation during general anesthesia. Kaohsiung J Med Sci. 2013;29:271–4.
19. Lao HC, Tsai PS, Su JY, Kwok TG, Huang CJ. Dexmedetomidine attenuates tourniquate-induced hyperdynamic response in patients undergoing lower limb surgeries :a randomized controlled study. J SurgRes. 2013;179:99-106.
20. Zalunardo MP, Serafino D, Szelloe P, Weisser F, Zollinger A, Seifert B, et al. Preoperative clonidine blunts hyperadrenergic and hyperdynamic responses to prolonged tourniquet pressure during general anesthesia. AnesthAnalg 2002;94:615-8.
21. Satsumae T, Yamaguchi H, Sakaguchi M, Yasunaga T, Yamashita S, Yamamoto S, et al. Preoperative small-dose ketamine prevented tourniquet-induced arterial pressure increase in orthopedic patients under general anesthesia. AnesthAnalg 2001;92:1286-9.
22. Lee DH, Jee DL, Kim SY, Kim JM, Lee HM. Magnesium sulphate attenuates tourniquet-induced hypertension and spinal c-fos mRNA expression: a comparison with ketamine. J Int Med Res 2006;34:573-84.
23. Yamashita S, Yamaguchi H, Hisajima Y, Ijima K, Saito K, Chiba A, Yasunaga T. Preoperative oral dextromethorphan attenuated tourniquet-induced arterial blood pressure and heart rate increases in knee cruciate ligament reconstruction patients under general anesthesia. AnesthAnalg 2004; 98: 994-8.