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EFFECT OF LOW DOSE KETAMINE HYDROCHLORIDE ON TOURNIQUET INDUCED HYPERTENSION IN LOWER LIMB SURGERIES

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ABSTRACT

Aim:-There is a constant increase in hemodynamic parameters during prolonged tourniquet inflation .We had investigated the effect of low dose 0.5mg/kg bolus ketamine on hemodynamic changes during tourniquet application in lower limb orthopaedic surgeries under general Anesthesia. Method:-100 patients posted for lower limb surgeries under standard general anesthesia using tourniquet were randomly assigned to one of two groups in double blind study. The Group C (control group) received 10 ml saline IV and Group K (study group) received 0.5mg/kg diluted in 10ml 0.9% saline IV given 10 minutes before tourniquet inflation. We had recorded hemodynamic changes, EtCO2 and Et Sevoflurane at 5 minutes interval up to 20 minutes of tourniquet deflation. Inj. Fentanyl 1mcg/kg supplemented if Systolic BP or heart rate raised more than 30% of base line. Results: - Hemodynamic stability was seen statically significant in Group K (p value, < 0.05) at 40, 50 and 60 minutes. Less number of patients needed supplemental fentanyl intra operatively in Group K than in Group C (3 V/s.18 p value <0.05). Conclusion: - Low dose bolus Ketamine 0.5mg/kg prevents tourniquet induced hypertension in lower limb surgery done under general anesthesia.

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INTRODUCTION

Tourniquets are widely used in limb surgery to get bloodless field and easy dissection. However tourniquet use is not as safe as thought, its use is also associated with appreciable morbidity and mortality.

Tourniquet induced hypertension defined as more than 30% increase in either systolic or diastolic arterial pressure with tachycardia in patients with the tourniquet inflated for at least an hour [1], may develop despite of adequate anaesthesia depth for surgical procedure. It is more common under general anaesthesia (53%-67%) than spinal anaesthesia[2]. And occurs more often in lower limb surgery than in upper limb surgery [3].

Pathogenesis behind this increased blood pressure has been due to an expansion of central venous blood in association with theoretical increase in peripheral vascular resistance and delayed hypertension, accompanied by ischemia and pain due to tourniquet compression.

There are few reports on the relationship between ketamine and tourniquet pain or tourniquet-induced arterial pressure increase. Tourniquet inflation activates C-fibres [4].

N-methyl-D-aspartic acid (NMDA) receptor activation is involved in the mechanism of Central sensitization induced by repeated nociceptive C-fiber afferent input[5].

It is hypothesized that tourniquet induced systemic arterial pressure increase might be related to NMDA receptor activation by the peripheral noxious input from the affected limb and that ketamine, an NMDA receptor antagonist, might mask the hypertensive effects.

We investigated the effect of preoperative 0.5 mg/kg IV ketamine given before 10 minutes of tourniquet inflation and noticed systemic arterial pressure and heart rate changes in patients under general anaesthesia undergoing lower limb surgery with tourniquet application [6].

METHOD

Ethical approval was obtained from the institutional ethics review committee and informed consent was taken from each patient included in the study. We included patients aged 18 years to 60 years belonging to ASA grade I and II undergoing elective lower limb surgery under general anaesthesia with application of tourniquet for 60 to 150 minutes.

We had excluded patients with known hypertension, ischemic heart disease, diabetes mellitus, renal impairment, asthma, chronic obstructive pulmonary disease and patients weighing <30 kg. Patients in whom epidural or spinal anaesthesia or analgesics other than this study used were also excluded from the study.

All patients had premedication with Lorazepam one milligram at previous night. All patients were induced with 2 mg/kg fentanyl, 0.1mg/kg vecuronium and 2mg/kg propofol, and maintained with 1mg/kg/min vecuronium after tracheal intubation. Anaesthesia was maintained with 40% oxygen in 60% nitrous oxide and sevoflurane 1% to 2.5%. The end tidal sevoflurane concentration (1MAC) was maintained steady during the study period.

Ventilation was adjusted to obtain an end-tidal carbon dioxide partial pressure between 30 and 35 mm Hg starting 10 minutes after anaesthesia induction and for the duration of study. No patient had spinal or epidural anaesthesia.

Total of 100 patients were recruited and randomly assigned to ketamine group (0.5mg/kg in 5mL) and control group (5mL saline) using sealed opaque envelope technique. The study drug was administered by the primary anesthesiologist who was blinded to the grouping.

Before inflation the limb is exsanguinated by elevation for 1 minute. A pneumatic thigh tourniquet was applied as proximal as possible to limb radix and the tourniquet was inflated to a pressure 100 mm of Hg about systolic arterial blood pressure for the entire surgical time. Surgical procedure was started after tourniquet inflation. Tourniquet was inflated 10 minutes after the administration of the study drug. The tourniquet was applied on the thigh of the surgical side and was inflated to a pressure of 100 mm of Hg about patient's baseline systolic blood pressure. Baseline systolic blood pressure and diastolic blood pressure were calculated as an average of two readings taken 5 minutes apart before induction of anaesthesia. Blood pressure was recorded at 10 minutes interval till 20 minutes of tourniquet deflation.

To ensure patients' safety, if systolic blood pressure rose to 200 mm Hg or higher fentanyl 100 mcg IV would be administered and any further step required to manage hypertension would be left to the discretion of the primary anesthesiologist. Such patients would be excluded from the study. The anesthesiologist who charted the blood pressure did not have knowledge of the study protocol. At the end of surgery the patient was extubated after reversal of neuromuscular blockade.

Noninvasive arterial pressure, heart rate, end tidal CO_2 partial pressure and peripheral oxygen saturation were continuously monitored.

Data were collected 7 times during general anaesthesia as follows :T0, T10, T20, T30, T40, T50, T60 - during tourniquet inflation and D10, D20 - After tourniquet deflation.

RESULTS & DISCUSSION

Despite randomisation the two groups of patients were well matched in terms of age, gender. Patients' mean age was 32.34+/-22.05yr in control group and 33.12+/-21.89yr in ketamine group. The average duration of INF (Tin) was 76+/-10min in control group and 80+/-10
in ketamine group. A bloodless surgical field was obtained in all cases.

	GROUP Control	GROUP Ketamine
AGE	32.34+/-22.05	33.12+/-21.89
WEIGHT	38.12+/-20.33 Kg	37.86+/-21.67 Kg
MALE / FEMALE	57/43	55/45
TYPE OF SURGERY	Ortho Plastic	Ortho Plastic
DURATION OF SURGERY	100+/-18	105+/-20
TOURNIQUET TIME	76+/-10	80+/-10

Baseline arterial pressure and heart rate were not different among the two groups. In the Ketamine group, systolic and diastolic arterial pressure was not changed during the study period. But in the control group, systolic arterial pressure was significantly increased at 40, 50, 60 minutes and diastolic arterial pressure was significantly increased at 30, 40, 50 and 60minutes after the start of tourniquet inflation. ($P<0.05$). In all groups, heart rate was not changed significantly during tourniquet inflation.

During tourniquet inflation, heart rate did not change whereas SAP was higher than at T0 by approximately 27%. Thereafter, it increased in all patients to a mean value 18% higher than at T0.

No patient was excluded from the study because of an increased systolic arterial pressure of 200mmhg or more during tourniquet inflation.

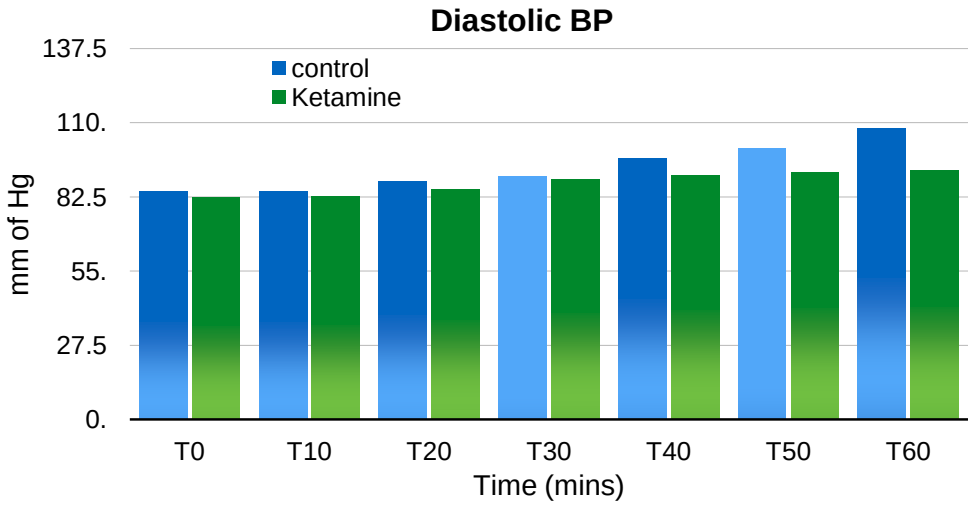
The results of this study showed that IV ketamine 0.5mg/kg administered before 10 minutes of inflation of tourniquet was significantly prevents tourniquet-induced rise in systolic arterial blood pressure compared in patients undergoing lower limb surgery under general anaesthesia. In control group, both systolic and diastolic blood pressure was higher as compared to the ketamine group from 30 minutes onwards and the difference was significant from 40 to 60 minutes after tourniquet inflation.

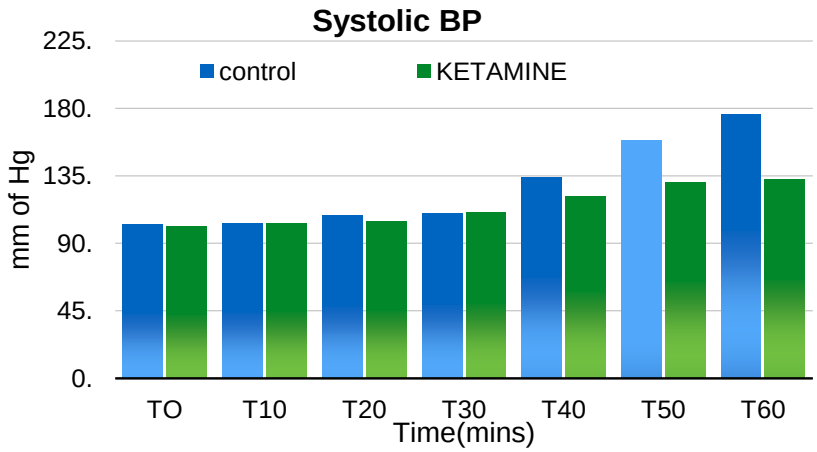
Perioperative hypertension may be associated with serious cardiac complications [8,9]. A progressive increase in systemic arterial pressure was observed during tourniquet inflation [6]. These changes are related to the sudden increase in blood volume (up to 15%) combined with a reduction in the capacitance of vascular bed. The autonomic nervous system is involved and plasma catecholamine concentrations are increased.

A tourniquet can induce significant physiological changes depending on the duration of inflation and general status of the patient [10,11].

An expansion of central venous blood by exsanguination of limb before inflation and pain sensation by tourniquet compression and ischemia are the two formal mechanisms are responsible for the increase of MAP occurring immediately after inflation.

The precise mechanism of tourniquet hypertension is unknown. However, a few hypotheses have been discussed. Satsumae et al recently ar gued that tourniquet hypertension might be related to N-methyl d-aspartic acid (NMDA) receptor activation by peripheral noxious stimuli from the extremities and that ketamine, as NMDA receptor antagonist, might attenuate tourniquet hypertension. They showed that systemic arterial blood pressure was significantly reduced during tourniquet inflation in the two ketamine treated groups compared with the control group. Although our study results seem to support their hypothesis, In fact, the tourniquet-induced increase in arterial blood pressure is continuous[12]. This has been confirmed again in our study.





The end tidal sevoflurane concentrations were similar in both groups at all points of time. Although we had not used BIS monitoring this may be a limitation of our study design.

Another hypothesis on tourniquet induced hypertension regards the correlation with autonomic nervous system changes, which was also the working hypothesis of this study. On the basis of power spectral heart rate analysis, Tetzlaff [13] et al showed that tourniquet hypertension is associated with the activation of sympathetic nervous system. Heropoulos [14] et al demonstrated that tourniquet hypertension is associated with an increase in plasma catecholamines.

Other researchers have demonstrated that ketamine prevents tourniquet induced arterial pressure increase. Satsumae [4] et al found that preoperative administration of 0.25mg/kg or more IV ketamine to patients undergoing knee surgery significantly prevented tourniquet induced increases in arterial pressure under general anaesthesia. They compared this dose of ketamine with a higher dose of 1mg/kg which also prevented increase in arterial pressure with no psychological problems after anaesthesia. Park[7] et al, obtain similar results in a placebo-controlled study with even a smaller dose of ketamine that is, 0.1mg/kg given 10 minutes after induction of anaesthesia. Takada [15] et al, found that low dose ketamine attenuates tourniquet pain and arterial pressure increase during high pressure tourniquet inflation in healthy volunteers. Lee et al, compared two NMDA antagonists, magnesium sulphate and ketamine, and found them to be equally effective in suppression of tourniquet induced hypertension. They suggested that this suppression may be due to reduced pain transmission associated with administration of magnesium and ketamine.

We observed that tourniquet induced hypertension occurred in 36% of patients in the control group as compared to 10% of those in the ketamine group ($P<0.001$). The exact mechanism for tourniquet induced hypertension is not known.

Although ketamine is an NMDA receptor antagonist and has been shown to be effective in preventing tourniquet induced hypertension there is a possibility that this effect could be due to relief in tourniquet induced pain rather than antagonism of NMDA receptors.

Tourniquet induced arterial pressure increase and pain subside within a few minutes after tourniquet deflation. Perhaps tourniquet induced hypertension and pain can be caused by acute onset hyperesthesia via Central neuronal plasticity but more confirmation is needed.

Sevofluranecoadministered with remifentanil inhibits NMDA receptors in a dose dependent manner,therebyneutralising remifentanil stimulation of these receptors [16].

A limitation of a study is that we did not use the bispectral index or electroencephalogram to ensure similar anesthetic depth in all patients because of unavailability of equipment. However, to overcome this issue we closely monitored anaesthetic gases, including sevoflurane and maintained MAC value of 1.0 throughout the study period.

Another limitation is that we did not assess the patient for postoperative psychological issues associated with Ketamine. However, Satsuae [4] et al did not find any psychological adverse effects even with higher doses than ourdoses of ketamine.

Our research population consisted of patient belonging to ASA physical status I and II while the risk related to tourniquet induced hypertension would be potentially more harmful in patients with preexisting cardiovascular disease especially ischemic heart disease. We, therefore, recommend that future research should include this patient population so as to assess the degree of attenuation of tourniquet induced hypertension in patients who would truly benefit from this effect.

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