

## Effect of Ketamine on Tourniquet Induced Hypertension

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### ABSTRACT

**Objective:** To compare the frequency of tourniquet induced hypertension in patients undergoing limb surgeries under general anesthesia with intravenous infusion of ketamine and placebo (saline infusion).

**Study Design:** Comparative prospective study.

**Place and Duration of Study:** Anaesthesia Department, Combined Military Hospital, Rawalpindi Pakistan, from May to Nov 2018.

**Methodology:** Total 80 patients undergoing upper and lower limb surgeries with tourniquet application under general anesthesia were randomly assigned into two equivalent groups. Group A (n=40) received intravenous ketamine 0.1 mg/kg bolus followed by infusion at a rate of 2ug/kg/min while Group B (n=40) received intravenous bolus of normal saline followed by its infusion via infusion pump. Systolic blood pressures were recorded by non-invasive method 30 seconds prior to tourniquet inflation and at 60 mins interval after its inflation. Results were characterized using the descriptive statistics. Mean and standard deviation (SD) were used for quantitative variables while frequency and percentages for qualitative variables. The *p*-value <0.05 was considered as significant.

**Results:** Tourniquet induced hypertension was found in 2 (5.0%) group A patients and 11 (27.50%) group B patients with statistically significant *p*-value of <0.05. Visual analogue scale score was slightly higher in the Saline group, but the result was statistically not significant (*p*=0.32).

**Conclusion:** Ketamine infusion reduces the occurrence of tourniquet induced hypertension in patients undergoing surgeries with tourniquet application.

**Keywords:** General anaesthesia, Ketamine infusion, Tourniquet induced hypertension.

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## INTRODUCTION

Haemodynamic variations occurring from pain due to prolonged tourniquet inflation remains one of the major worries for anaesthetists. Application of pneumatic tourniquets in orthopaedic surgeries of upper and lower limbs is of great significance and frequently executed, however, one of the most frequent complication with prolonged tourniquet inflation is the pain and associated rise in the arterial blood pressure generally 30-60 minutes following tourniquet inflation.<sup>1</sup> Tourniquet induced hypertension is described as the elevation of systolic or diastolic blood pressure of more than 30% in patients 30-60 minutes after the tourniquet inflation.<sup>2</sup> This tourniquet induced hypertension is usually resistant to the analgesics and increasing depth of anaesthesia. Additionally, patients with cardiovascular compromise may not tolerate this abrupt rise in blood pressure very well.<sup>1</sup>

Prolonged inflation of tourniquet may result in compression and injury to soft tissues including

muscles, skin, arteries and most importantly the peripheral nerves.<sup>3</sup> The exact mechanism of this tourniquet associated rise in blood pressure is ambiguous and not fully understood but a proposed cause is the N-methyl-D-aspartic acid (NMDA) receptor activation via C fibers causing central sensitization which in turn causes rise in blood pressure through sympathetic nervous system response to pain. Different drugs are utilized to control these haemodynamic changes (pain induced) secondary to tourniquet inflation especially for prolonged procedures. These drugs include opioids (Remifentanyl), Magnesium sulfate, ketamine, ketorolac, clonidine and dexmedetomidine.<sup>1,3,4,5</sup> Ketamine, an NMDA receptor antagonist, has been found quite effective in this respect by many researchers.<sup>6</sup>

Ongaya *et al*, compared ketamine with saline for study of frequency of tourniquet induced hypertension. They reported reduced frequency of hypertension in ketamine group (4.6%) versus the saline group (26%); *p*-value <0.05.<sup>7</sup>

According to literature review, no single technique/medication has been shown to completely prevent tourniquet induced hypertension. Rationale of

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this study was that currently, at our local institutes, no drug is used for prevention of tourniquet induced hypertension, however, tourniquet induced hypertension is treated with injection Glyceryl trinitrate, increasing the depth of anaesthesia and analgesia.<sup>8,9</sup> In this study we have compared the frequency of tourniquet induced hypertension between intravenous ketamine infusion and placebo secondary to tourniquet inflation in patients undergoing limb surgeries under general anaesthesia with the aim that, in future, evidence-based recommendations can be made on use of ketamine to avoid such haemodynamic disturbances associated with tourniquet inflation.

Our research was based on that whether intravenous ketamine infusion considerably reduces the occurrence of tourniquet induced hypertension. Our null hypothesis stated no variability in the frequency of tourniquet induced hypertension in patients receiving either ketamine infusion or the placebo. Our secondary objective was to evaluate the effect of ketamine on post operative tourniquet pain.

## METHODOLOGY

Following permission of ethical review committee (03A/02/18) of the Hospital, this study was carried out in the Anaesthesia Department, Combined Military Hospital Rawalpindi Pakistan. The total study duration was six months (May 2018 to November 2018).

World Health Organization (WHO) sample size calculator was used to calculate the sample size. The total sample size of study was 80, (40 in each group) by keeping level of significance ( $\alpha$ ) 5%, Power of the test 80 % ( $1-\beta$ ), anticipated population proportion (P1) & (P2) were 4.6% and 26% respectively. Consecutive non probability technique was used for sampling.

**Inclusion Criteria:** Patients undergoing surgeries with tourniquet application under general anaesthesia from both genders of age group between 18-70 years, ASA status I or II, Haemodynamically stable with no known Ischemic heart disease, Hypertension or Peripheral vascular disease were included in this study.

**Exclusion Criteria:** Non-consenting patients, pregnant females, those allergic to the drugs being used in our study or with contraindication to the use of tourniquet were excluded.

Patients were randomly allocated in two groups (Group A and Group B) by lottery method on daily basis. Keeping the study protocol in view, the procedure was explained to all the patients included in the study and informed written consent was taken. Before

reporting to operation theatre, a detailed pre anaesthesia assessment was done in all patients and all necessary laboratory investigations were collected.

On the day of surgery, systolic blood pressure was recorded by noninvasive method. Pulse oximeter and ECG electrodes were attached and 18G IV cannula was passed under aseptic conditions. All the patients were pre medicated with intravenous injections of Nalbuphine 0.1 mg/kg, Paracetamol 15 mg/kg, Dexamethasone 0.08 mg/kg, Metoclopramide 0.1 mg/kg and Midazolam 0.07-0.15 mg/kg (used to reduce the psychotomimetic side effects of ketamine). Patients were Pre oxygenated with 100% oxygen for 3 mins. Induction was done with intravenous injection of propofol at a dose of 2mg/kg. Muscle relaxation was achieved with 0.5 mg/kg of intravenous injection atracurium followed by laryngoscopy and intubation by a qualified anaesthetist 3 minutes later. Tourniquet was applied to the limb undergoing surgery and inflated after exsanguination of that limb. Tourniquet pressure was kept 100 mm Hg above baseline systolic blood pressure in upper limb surgery; whereas it kept 150 mmHg above systolic blood pressure for lower limb surgery.<sup>8</sup>

Group A received Intravenous ketamine in a bolus dose of 0.1 mg/kg through 10ml syringe which was followed by its infusion at a rate of 2 ug/kg/min via infusion pump (ketamine group) starting immediately after induction and continuing till tourniquet deflation after which it was stopped.

Group B received intravenous bolus of normal saline in a 10ml syringe which was followed by an infusion of the same via infusion pump (saline group) starting immediately after induction and continuing till tourniquet deflation after which it was stopped.

Systolic blood pressure was recorded by non-invasive method 30 seconds prior to tourniquet inflation and at 60 mins interval following tourniquet inflation. Vitals documented on arrival to the post operative care unit (PACU) and pain severity was assessed on visual analogue scale one hour later.

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 20.0. Quantitative variables like age, weight and VAS score were measured in terms of mean and standard deviation. Qualitative variables like gender, ASA status and frequency of hypertension were measured in terms of frequency and percentages. Comparison of both groups in terms of systolic blood pressure was made by using chi square test.  $p$ -value  $\leq 0.05$  was considered significant.

**RESULTS**

Age range in this study was from 18-70 years with mean age of 40.78 ± 14.13 years. The mean age of patients in group A was 40.43 ± 14.01 years and in group B was 41.13 ± 14.31 years. Majority of the patients 52 (65.0%) were between 18 to 45 years of age as shown in Table-I. Out of these 80 patients, 49 (61.25%) were male and 31 (38.75%) were females with male to female ratio of ratio of 1.6:1. The mean weight of patients was 81.90 ± 9.47 kg. Distribution of patients according to ASA status is shown in Table-II. In my study, I have found tourniquet induced hypertension in 02 (5.0%) group A patients and in 11 (27.50%) group B patients (*p*-value =0.006) as shown in Table-III. Tourniquet Induced Hypertension with respect to age groups, gender and ASA status was shown in Table-IV.

None of the patients complained about ketamine induced psychotomimetic effects such as hallucinations probably due to the use of sub anaesthetic doses of ketamine and premedication with midazolam.

**DISCUSSION**

Pneumatic tourniquets are employed in Orthopaedic surgeries on upper and lower limbs to minimize to reduce the risk of surgical bleeding. Prolonged tourniquet inflation is accompanied with pain which causes a rise in arterial pressure generally noticed 30-60 min after inflation of the tourniquet.<sup>9</sup> Tourniquet induced hypertension is described as a rise in systolic or diastolic blood pressure of more than 30% usually when the tourniquet has been left inflated for more than 30-60 min.<sup>10</sup> The increase in blood pressure is more marked under general anaesthesia and during

**Table-I: Age distribution for both groups (n=80).**

Age (years)	Group A (n=40)		Group B (n=40)		Total (n=80)	
	No. of Patients	%Age	No. of Patients	%Age	No. of Patients	%Age
18-45	25	62.50	27	67.50	52	65.0
46-70	15	37.50	13	32.50	28	35.0
Mean ± SD	40.43 ± 14.01		41.13 ± 14.31		40.78 ± 14.13	

**Table-II: Distribution of patients according to ASA status (n=80).**

ASA Status	Group A (n=40)		Group B (n=40)		Total (n=80)	
	No. of patients	%Age	No. of patients	%Age	No. of patients	%Age
I	22	55.0	21	52.50	43	53.75
II	18	45.0	19	47.50	37	46.25

**Table III: Comparison of frequency of tourniquet induced hypertension in both Groups.**

		Group A (n=40)		Group B (n=40)		<i>p</i> value
		No.	%Age	No.	%Age	
Tourniquet Induced Hypertension	Yes	02	5.0	11	27.50	0.006
	No	38	95.0	29	72.50	

**Table-IV: Tourniquet Induced Hypertension with respect to age groups, gender and ASA status in both groups**

Patient Parameters		Group A (n=40)		Group B (n=40)		<i>p</i> -value
		Tourniquet Induced Hypertension		Tourniquet Induced Hypertension		
		Yes	No	Yes	No	
Age (years)	18-45	02	23	06	21	0.156
	46-70	00	15	05	08	0.008
Gender	Male	01	24	08	16	0.008
	Female	01	14	03	13	0.316
ASA Status	I	01	21	05	16	0.068
	II	01	17	06	13	0.043

VAS score showed slight difference between the two groups with Saline group having greater score, but this difference was statistically not significant (*p*=0.32) as shown in Table-V.

**Table-V: VAS scores at 01 hour in both groups.**

	Group A (Mean ± SD)	Group B (Mean ± SD)	<i>p</i> -value
VAS Score	3 ± 1	4 ± 1	0.32

lower limb surgeries.<sup>11</sup> This escalation in blood pressure can prove to be detrimental in patients with cardiovascular disorders.<sup>12</sup>

In our study, we found tourniquet induced hypertension in 2 (5.0%) group A patients (Ketamine group) and in 11 (27.50%) group B patients (saline group) with a *p*-value of 0.006. This was comparable to previous study by Ongaya *et al*, carried out at Aga

khan university, East Africa in 2017 which reported reduced frequency of hypertension in ketamine group (4.6%) versus the saline group (26%);  $p$ -value  $<0.05$ .<sup>7</sup>

Other researchers have described the reduction of tourniquet-induced arterial pressure increases with ketamine. Satsumae *et al*, demonstrated notable reduction in tourniquet-induced hypertension in patients going through knee procedures under general anaesthesia using 0.25 mg/.<sup>11</sup> They also compared it with a higher dose of 1 mg/kg ketamine, which showed comparable results with no psychological problems after anaesthesia. Park *et al*, obtained matching results with even a smaller dose of ketamine. They used 0.1 mg/kg given 10 min after induction of anaesthesia.<sup>13</sup> Takada *et al*, also found attenuation of tourniquet induced pain and rise in systolic blood pressure during high-pressure tourniquet inflation in healthy volunteers.<sup>14</sup> Lee *et al*, compared magnesium sulphate and ketamine, both of which are NMDA antagonists.<sup>15</sup> The results showed them to be equally effective in suppression of tourniquet induced hypertension. They suggested that this suppression may be the result of decreased pain transmission due to the administration of ketamine and magnesium.

VAS scores assessed 60 minutes post operatively were found to be a little elevated in saline group in comparison to those of ketamine group, but the difference was not statistically significant ( $p>0.05$ ). Various previous studies showed effectiveness of peri operative Ketamine use for acute pain control and decrease requirement of opioids in the post operative period, but they did not assess post operative tourniquet pain.<sup>16-18</sup>

#### LIMITATIONS OF STUDY

Study had few limitations as it was not double blinded. Moreover, it was performed on patients under general anaesthesia therefore the independent influence of ketamine on tourniquet induced hypertension could not be evaluated. Lastly, the anaesthetic depth might not have been equivalent among the patients due to lack of availability of Bispectral index (BIS) or Electroencephalogram (EEG) monitoring to ensure uniform anaesthetic depth.

#### CONCLUSION

This study concluded that ketamine infusion reduces the frequency of tourniquet induced hypertension as compared to saline infusion. So, we recommend that further studies should be done on this subject, such that, these strategies can be used routinely in patients undergoing procedures on the limbs under general anaesthesia in order to avoid such haemodynamic disturbances associated with tourniquet inflation.

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**Conflict of Interest:** None.

#### Authors' Contribution

MUH: Conception, data collection, research analysis and manuscript draft, MAS: Supervision of research, BMK: Data collection and analysis, SA: Data collection and analysis.

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