Research Article

Non-opioid analgesia with Regional block: The effect of ketamine as adjuvant with 0.5% bupivacaine in infraclavicular brachial plexus block

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Abstract

Aims: To determine the effect of the addition of 25 µg/kg body weight ketamine to 0.5% bupivacaine in infra-clavicular brachial plexus block.
Patients and Methods: In a randomized double blinded, placebo controlled clinical trial, Forty patients, from the age of 20-60 years, with ASA I, II and III, undergoing upper limb (below elbow) surgery, had been chosen to be enrolled in the study. They had been divided randomly, into 2 groups. Group 1 will receive 30 ml of solution 1 (25 ml of 0.5% bupivacaine with 5 ml of normal saline) as placebo or control group. Group 2 will receive 30 ml of solution 2 (25 ml of 0.5% bupivacaine with 25 µg/kg body weight ketamine) as ketamine group. A nerve stimulator (B/Braun Stimuplex® HNS 11) had been connected to 22G-10 cm length insulated needle. Time of motor impairment was assessed by lack of muscular coordination and heaviness feeling of the limb. Time of parasthesia was assessed by loss of pin brick sensation.
Results: There was a quite noticeable prolonged time of analgesia in the ketamine group. The mean ± SD was 698 ± 139 minutes in ketamine group while the mean ± SD in placebo group was 140 ± 40 minutes ($p<0.05$). Twelve patients out of 20 had recorded 800 minutes of analgesia (60%) in ketamine group. There were no other clinical differences in side effects or motoric latency in between both groups.
Conclusions: Low dose of ketamine added as an adjuvant to 0.5% bupivacaine in infra-clavicular brachial plexus block, will prolong the time of post-operative analgesia without any side effects.

Keywords: non-opioid analgesia, infra-clavecular block, bupivacaine 0.5%, ketamine

INTRODUCTION

Infra-clavicular approach for brachial plexus block is under used but effective technique.[1] This kind of approach will minimize the risk of Horner syndrome and pneumothorax as in inter-scalene and supraclavicular approaches, and the escape of musculo-cutaneous nerve in axillary approach.[1, 2] The two main approaches in this technique were the medial approach (mid-clavicle) and the lateral approach (around the coracoid process).[2] The coracoid approach had gained popularity with the presence of consistent bony landmark, less chance of vascular puncture, less chance of pneumothorax and adequate neural blockade.[3, 4] The infra-clavicular brachial plexus block is designed for surgery in the distal arm; elbow, forearm, wrist and hand surgery. The block meets the axillary and musculo-cutaneous nerve at the level of the cords before it leaves the brachial plexus sheath.[5] The use of regional anesthesia, with infra-clavicular brachial plexus block had shown a more acceptance by the patients in hand surgery, especially in day cases.[6] Even with the use of short acting local

analgesic agents, the patients had shown better analgesia and fewer side effects than general anesthesia.[7]

Bupivacaine is a long-acting amide local anesthetic agent when used in 0.5% concentration.[7] The effect of 0.5% bupivacaine may persist for 2-3 hours if administered alone.[8] The addition of opiates as adjuvants to bupivacaine shows weak additive effects on the post-operative analgesia, while the addition of clonidine provides good analgesic effect but with adverse effects in doses more than 150 µg.[9] The addition of non-opiate as adjuvants to local anesthetic agents will prolong the analgesic effect.[10, 11]

Ketamine is a well-known anesthetic agent with potent local effect on peripheral nerves.[12] This local effect of ketamine is most probably by blocking the voltage-operated sodium channels.[13] The effect of ketamine on (NMDA) N-methyl-D-aspartate antagonism abolishes peripheral afferent noxious stimulation.[14, 15] The use of 0.5 mg/kg body weight ketamine as an adjuvant to local anesthetic agent in caudal anesthesia will double or triple the analgesic period and reduces the need of analgesia.[16, 17] Some of the studies had shown that the local effect of ketamine as an adjuvant to bupivacaine may persist for longer time. The analgesia may persist for 7 days, while other studies show the effect may persist for 20 minutes only, but no clinical evidence of analgesia if administered locally alone.[18]

Aim of the study

To determine the effect of the addition of 25 µg/kg body weight ketamine to 0.5% bupivacaine in infra-clavicular brachial plexus block on the time of onset, sedation, nausea and vomiting, headache, motoric latency and postoperative analgesia time.

PATIENTS AND METHODS

After the ethical approval and a full consent form describing the trial had been signed by the patient. Forty patients, from the age of 20-60 years, with ASA I, II and III, undergoing upper limb below elbow surgery, had been chosen to be enrolled in the study. They had been divided randomly according to a random allocation table, into 2 groups. Group 1 will receive 30 ml of solution 1 (25 ml of 0.5% bupivacaine with 5 ml of normal saline) as placebo or control group. Group 2 will receive 30 ml of solution 2 (25 ml of 0.5% bupivacaine with 5 ml of fluid containing 25 µg/kg body weight ketamine) as ketamine group. Any patient refusal, history of drug sensitivity to the used agents and bleeding tendency, considered as exclusion criteria. Both of the patients and the orthopedic surgeon who operated the patient and who is responsible for data collection and the patient's follow up had been blinded from the drug mixture that had been given to the patient.

At admission to the induction room, patient's age, sex, weight, habits (smoker, drinking alcohol), any medication had been recorded. An open vein had been applied, 5% glucose infusion started with 5 mg diazepam given IV as a sedative agent. Blood pressure, pulse rate, respiratory rate, ECG and SpO_2 had been monitored from the beginning to the end of the operation.

Sedation was scored according to the level of consciousness with the patient's response to oral command as Conscious (0), Open his eyes for call (2) and Asleep (3) when there is no response to oral command. Additional sedation was given to the patient as 5 mg diazepam IV when the patient feels distressed or discomfort.

While the patient is lying supine, the mid-clavicular and the coracoid process were identified. The area was stained with 20% bovidone iodine. A wheel raised with 2 ml 2% lidocaine at the site of entry of the needle. The point of entry was cited as 2 cm below the mid-clavicular line and 2 cm medial to the coracoid process. A nerve stimulator (B/Braun Stimuplex® HNS 11) had been connected to G22-10 cm length insulated needle. The nerve stimulator was set on 1.2 mA with 0.1m second impulse rate. The needle advanced perpendicularly until a brisk movement at the wrist or flexion of the digits had been detected. The current of the nerve stimulator reduced to 0.3-0.5 mA. If the brisk movement of the wrist or flexion of the digits remains, slow injection of the local anesthetic agent started. The brisk movement will abolish immediately after the first few milliliters injection of the solution, which is an indication that the needle in the proper position of the brachial plexus sheath and the block will be successful. During injection of the local anesthetic agent, aspiration from time to time to was done to avoid accidental intravascular injection.

Time of motor impairment was assessed by lack of muscular coordination and heaviness feeling of the limb. Time of parasthesia was assessed by loss of pin brick sensation. The time tourniquet application had been recorded, as the tourniquet applied 5 minutes after parasthesia. After the end of the operation, the patient discharged to the ward. A data collection sheath was filled by the orthopedic surgeon in the ward. This orthopedic surgeon was blinded for the type of solution given to the patient. The time of the motor regaining

activity and the time for the first rescue dose of analgesia were recorded. If the patient did not ask for any analgesic need for over-night, until 8 am of the next day, the time was stated as 800 minutes. Once the patient will feels in mild pain, 75 mg diclofenac IM and 100 mg tramadol given IV as a rescue analgesic dose.

All of the parametric data was analyzed using Student's t test and the non-parametric data by Man-Whitney U test.

RESULTS

The demographic data of both groups is shown in table (1), showing almost no differences between both groups. The time of onset of parasthesia, motor function loss and application of tourniquet is demonstrated in graph (1). The graph shows that there is some delay in the time of parasthesia and application of tourniquet in the placebo group. This difference has no statistical value ($p > 0.05$) as shown in table (2).

Table 1. Distribution of demographic date for both groups.

		Group					
		Ketamine			Placebo		
		Mean	SD	Count	Mean	SD	Count
Age		46	14		48	12	
Sex	F			14			13
	M			6			7
Weight		78	14		78	10	
Systolic blood pressure		136	16		132	13	
Pulse rate		97	12		100	11	

Table 2. Shows the statistics of the time of tourniquet application, onset of parasthesia and motor function loss.

	Group	N	Mean	Std. Deviation	Std. Error Mean	Significance
Onset of parasthesia	Ketamine	20	8.05	2.605	0.583	0.129
	Placebo	20	11.05	5.916	1.323	
Onset of motoric loss	Ketamine	20	8.00	2.847	0.637	0.552
	Placebo	20	7.70	4.462	0.998	
Time of onset of tourniquet application	Ketamine	20	12.60	2.873	0.642	0.107
	Placebo	20	15.25	6.859	1.534	

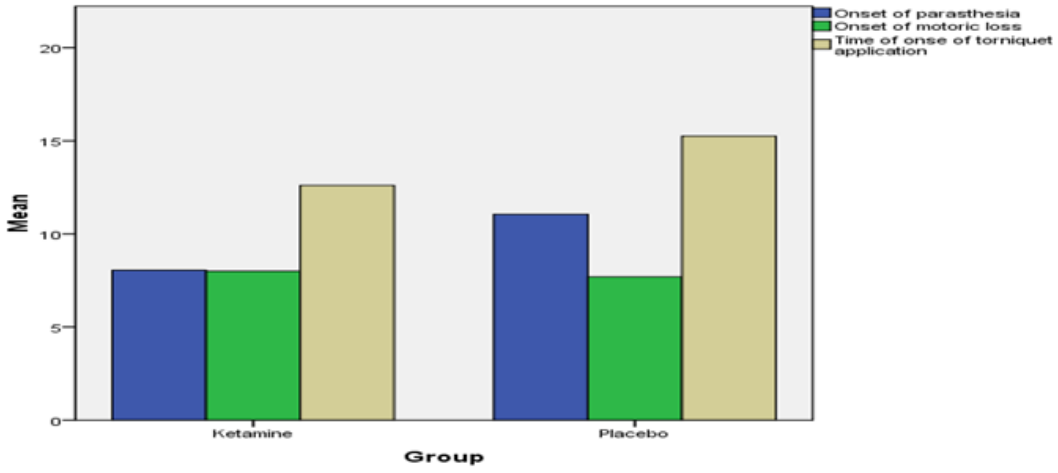

Figure 1. Shows the time of onset of parasthesia, motor function loss and time of application of tourniquet.

graphs (2) and (3) showing the stability in systolic blood pressure and pulse rate for the first 60 minutes after the application of the regional anesthesia in both groups respectively. Table (3) is showing the level of sedation, side effects and extra-sedatives rate given for both groups. The table shows there is no statistical significance in between the two groups as $p > 0.05$ as in table (4).

Table 3. Mann-Whitney U Test Statistics.

	Sedation	Headache	Nausea	Extra sedative
Mann-Whitney U	180.000	200.000	200.000	180.000
Wilcoxon W	390.000	410.000	410.000	390.000
Z	-0.655	0.000	0.000	-0.721
Asymp. Sig. (2-tailed)	0.513	1.000	1.000	0.471
Exact Sig. [2*(1-tailed Sig.)]	0.602[a]	1.000[a]	1.000[a]	0.602[a]

Table 4. Shows the frequency of side effects and extra- sedatives given for both groups.

		Group	
		Ketamine	Placebo
		Count	Count
Sedation	Awake	8	6
	Arose-able	12	14
	Asleep	0	0
Headache	None	20	20
	Present	0	0
Nausea	None	20	20
	Nausea	0	0
	Vomiting	0	0
Extra sedatives	Basic	16	14
	Extra sedative	4	6

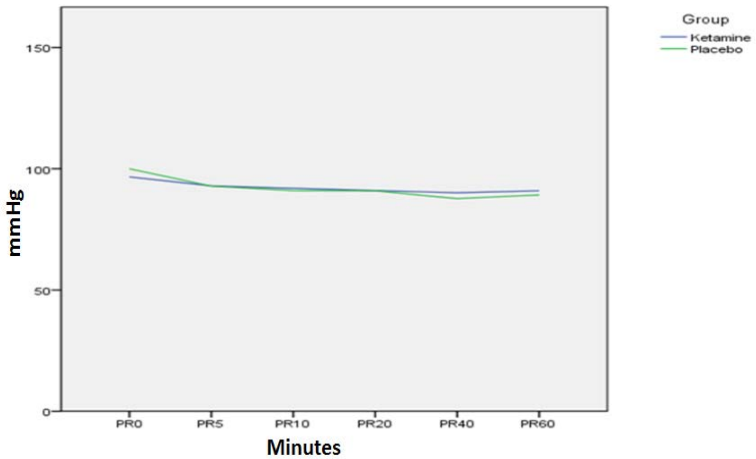

Figure 2. Shows the changes in systolic blood pressure.

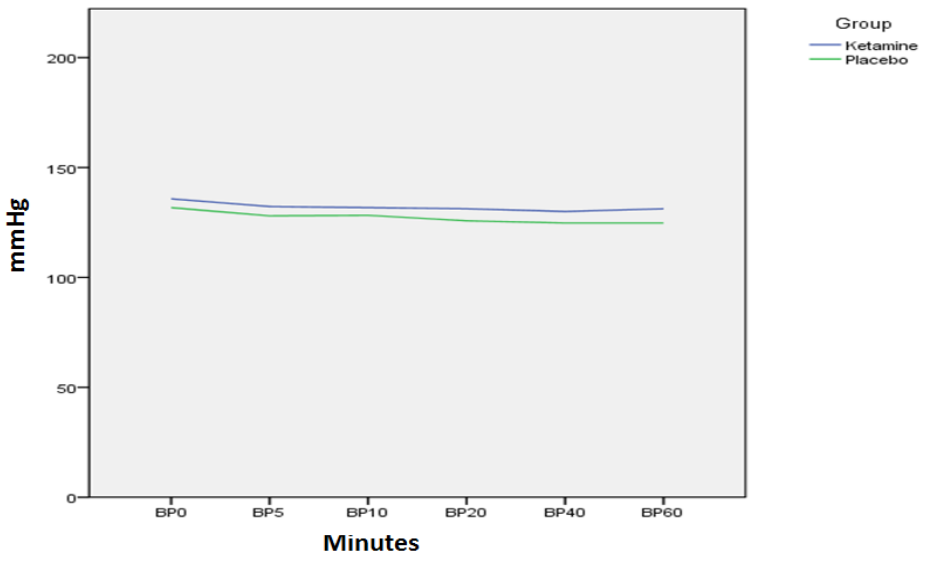

Figure 3. Showing the changes in pulse rate during the first hour after anesthesia.

Table 5. Onset of postoperative pain.

Group	minutes	Freq.	%	Valid %	Cumulative %
Ketamine	400	1	5.0	5.0	5.0
Valid	480	2	10.0	10.0	15.0
	560	2	10.0	10.0	25.0
	580	1	5.0	5.0	30.0
	650	2	10.0	10.0	40.0
	800	12	60.0	60.0	100.0
	Total	20	100.0	100.0	
Placebo	90	1	5.0	5.0	5.0
Valid	100	1	5.0	5.0	10.0
	110	2	10.0	10.0	20.0
	115	1	5.0	5.0	25.0
	120	4	20.0	20.0	45.0
	125	2	10.0	10.0	55.0
	130	1	5.0	5.0	60.0
	135	2	10.0	10.0	70.0
	150	2	10.0	10.0	80.0
	200	1	5.0	5.0	85.0
	210	2	10.0	10.0	95.0
	230	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

Table 6. Onset of postoperative motor activity.

Group	minutes	Freq.	%	Valid %	Cumulative %
Ketamine	90	2	10.0	10.0	10.0
Valid	95	1	5.0	5.0	15.0
	98	1	5.0	5.0	20.0
	100	3	15.0	15.0	35.0
	110	3	15.0	15.0	50.0
	120	3	15.0	15.0	65.0
	123	1	5.0	5.0	70.0
	130	2	10.0	10.0	80.0
	135	1	5.0	5.0	85.0
	150	2	10.0	10.0	95.0
	180	1	5.0	5.0	100.0
	Total	20	100.0	100.0	
Placebo	85	2	10.0	10.0	10.0
Valid	90	2	10.0	10.0	20.0
	95	1	5.0	5.0	25.0
	98	3	15.0	15.0	40.0
	100	6	30.0	30.0	70.0
	110	2	10.0	10.0	80.0
	120	2	10.0	10.0	90.0
	130	1	5.0	5.0	95.0
	135	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

Tables (5) and (6) show the frequency distribution of the time of onset of postoperative pain and time of motor regaining activity respectively.

In table (5) it can be noticed that 60% of ketamine group (12 out of 20) had recorded 800 minutes (overnight pain free) delay in the postoperative pain. In placebo group only one case had recorded 230 minutes of analgesia and 20% was recoded 140 minutes. The mean ± SD in ketamine group was 698±138 minutes of pain free while the placebo group was 140±40 minutes. This difference is of statistical significance with $p < 0.05$ according to table (7).

Table (6) describes the motoric affect in both groups, showing the time, distribution and frequencies of distribution. The mean± SD of motor paralysis in ketamine group was 118±23 minutes while placebo group had recorded 103±13.7 minutes. This difference was carrying no statistical difference as the $p > 0.050$ according to table (7).

Table 7. Student's t test statistical results.

	Grp.	N	Mean	SD	SEM	Pvalue
Onset of postoperative pain	**Ketamine**	20	698	138.663	31.006	0.0001
	Placebo	20	140.25	40.016	8.948	
Onset of postoperative motor activity	**Ketamine**	20	118.05	23.132	5.173	
	Placebo	20	103.2	13.779	3.081	0.061

DISCUSSION

In this study, the addition of small dose of ketamine to the local anesthetic agent has no effect on the onset of parasthesia, motoric deficiency nor tourniquet application ($p > 0.05$). The prominent change is the time of postoperative analgesia ($p < 0.05$). The effect is well noticed in the whole ketamine group (n=20). The lowest registered time in ketamine group was 400 minutes, while 90 minutes in the control (placebo) group. Forty percent of the patients in ketamine group had registered 400-650 minutes time for analgesia. The other 60% (12 patients out of 20) had registered more than 12 hours of postoperative analgesia (800 minutes). This result goes with the study of Koining et al. about the effect of ketamine in caudal analgesia had recorded more than 15 hours. With that study the analgesia persisted more than one week in some of the cases.[17] Those results are contradicting to the study of Castro and Garcia, which had shown no effect, could be seen in the postoperative analgesia after adding ketamine to the epidural solution in abdominal hysterectomy.[19] In our study, the surgeons were well satisfied with the post-operative results, as the patients with ketamine had shown less peripheral edema in the second and the third post-operative day. The explanation could be the early movement of the limb due to the lack of pain at the site of surgery. It is a plan for next study to notice the promote effect of addition of ketamine on the postoperative complications.

The effect of analgesia by ketamine is prolonged when administered with the local anesthetic agents due to the higher concentration of ketamine in the pre-neural fat than in the systemic circulation. It exerts the effect on neuronal transmission by blocking the Na-K ion gates at the peripheral nerves.[12, 17, 19]

From this study we can conclude that the addition of small dose of ketamine to the local anesthetic agents in infraclavicular brachial plexus block will reduce the need of postoperative analgesia.

***Conflict of interest*:** none.

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