Original Research Article

Low dose of intravenous ketamine for prevention of hypotension after subarachnoid block

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Abstract

Objectives and background: The study was conducted to know the efficacy of low dose i.v. ketamine for prevention of hypotension and to compare the hemodynamic changes following subarachnoid block with intrathecal bupivacaine heavy with or without low dose i.v. ketamine.**Materials and Methods:** 100 patients belonging to ASA-1 of both the sex (each group 50 patients n =50) undergoing General surgical and orthopaedic operations were randomly selected for the study.**Results:** The pulse rate in test group showed a slight increase at 20 minutes followed by a insignificant decrease during the subsequent one hour period. But in control group the pulse rate decreased to about 12% below the preoperative level showing a statistically very highly significant change. Systolic blood pressure in test group fell by a maximum of 7.29% when compared to control group where it fell to a maximum of 19.18% and diastolic blood pressure in test group fell by a maximum of 3.69% as compared to control group where the decrease was 12.28%. Thus the difference was statistically very highly significant.**Conclusion:** Low dose i.v. ketamine in doses of 0.3 mg/kg offers superior cardiovascular stability, and low dose i.v. ketamine in combination with midazolam, has good sedative and analgesic properties, reduces the volume of crystalloids required to maintain hemodynamic stability.

Keywords: Intrathecal; ketamine; midazolam; pulse rate; blood pressure; hypotension.

Introduction

A reduction in blood pressure is an accompaniment of spinal anaesthesia. Sympathetic blockade is the major determinant of physiological responses to subarachnoid anaesthesia. Paralysis of the sympathetic vasoconstrictor fibres occurs in the arterioles, capillaries and veins at the preganglionic level of block and thereby produces various dramatic, indirect physiologic effects[1]. This sympathetic blockade causes venous dilatation, venous pooling, fall in cardiac output and blood pressure.

Hypotension during spinal anaesthesia can be partially controlled by administration of intravenous fluids and vasopressor therapy. But infusion of a large volume of crystalloids over a short period of time carries risk of pulmonary edema and postoperative urinary retention. Among vasopressors, various drugs like ephedrine, mephenteramine etc. have been tried, but they may cause deleterious effects like overshoot of hypertension, impaired tissue perfusion and marked vasoconstriction especially in renal and coronary vessels[2-3].

Consciousness, prolonged posture maintenance and awareness during spinal anaesthesia always cause apprehension to the patient. Thus supplementary sedation is always needed during regional blocks. Quite a few agents have been tried for this purpose. But all these methods lead to depression of respiratory and cardiovascular system thus aggravating the side effects produced during spinal block like hypotension and bradycardia[4].

Ketamine induces activation of sympathetic nervous system and increases catecholamine levels in blood thereby increasing pulse rate and blood pressure. Cardiovascular stability is far better with low dose ketamine supplementation because it has cardiotonic effects.

Respiratory depression is not seen with low doses of ketamine. The incidence of psychological disturbances and unpleasant emergence sequelae is significantly reduced with benzodiazepine premedication [5].

This study was conducted to evaluate the role of low dose intravenous ketamine in prevention of hypotension and to assess the utility of low dose ketamine in combination with midazolam as supplementary sedation during spinal anaesthesia.

Aim& Objectives

To study the efficacy of low dose intravenous ketamine for prevention of hypotension after subarachnoid block.

To compare the hemodynamic changes following spinal anaesthesia with intrathecal bupivacaine heavy and with or without low dose intravenous ketamine.

To compare the volume of crystalloid infusion required to maintain hemodynamic stability in test and control groups.

To study the incidence of adverse effects and complications following low dose intravenous ketamine administration.

Materials and Methods

Source of data

100 patients undergoing general surgical and orthopaedic operations under spinal anaesthesia at Princess Esra Hospital and Owaisi Hospital , DCMS , were only included for the study.The study was approved by the hospitals ethics committee.

Inclusion criteria: Patients of either sex Patients with ASA grade 1 Patients aged between 18-69 years the cases where blood loss would be minimal and spinal hypotension would not be accounted due to blood loss were selected.

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Exclusion criterion: Patients with severe systemic disease, neurological, congenital or cardiovascular disease.
Mode of selection: Random
Preoperative period: A day before surgery all the patients were visited and detailed preanaesthetic examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous system and examination of spine for deformity, infection was carried out.
The anaesthetic procedure was briefly explained to the patient
An informed and written consent was obtained from the patient or his/her guardian.
Patients weight and height were recorded.
Preoperative preparation: Includes a period of overnight fasting i.e. for 6-8 hours before surgery.
Intra operative period: Once the patient was shifted to the operating room, the patient was connected to the routine monitors which include sphygmomanometer, pulse oximeter and ECG.
All resuscitation equipment's like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephenteramine, adrenaline were kept ready. The anaesthesia machine was checked along with the oxygen delivery system.
Patients were divided randomly into two groups of 50 patients each. One group was called the Test Group in whom iv ketamine was given and the other Control Group.
Base line pulse rate, blood pressure, respiratory rate and SPO2 were recorded. An intravenous infusion was started with ringers lactate solution and all the patients were preloaded with 7ml/kg over 20 minutes prior to anaesthesia.
Premedication with injection Midazolam 0.01mg/kg and injection Atropine 0.01 mg/kg was given to all the patients intravenously. Injection Ketamine 0.3 mg/kg iv was given before giving spinal anaesthesia prophylactically.
Under strict aseptic precautions, subarachnoid block was performed in all the patients in left lateral position with 3-3.5 ml of 0.5% bupivacaine heavy by 23-25 G Quincke lumbar puncture spinal needle at L3-L4 intervertebral space.
After securing supine position and confirming the level of spinal anaesthesia, the patients belonging to test group were given ketamine in doses of 0.3 mg/kg iv at 15min and 30min after Subarachanoid block, the use of vasopressors to treat hypotension became significantly low and this is of paramount information observed in this study.
Pulse rate and blood pressure changes were measured every minute for the first five minutes and then every 5 minutes for 40 minutes and then every 15 minutes till the end of surgery. Intraoperative complications like severe hypotension, bradycardia, nausea, vomiting, nystagmus and hallucinations were recorded and treated appropriately.
The pulse rate, blood pressure changes, i.v fluid requirement to maintain haemodynamic stability were noted and these results were subjected to statistical analysis using Fischer's 'f' test, Bonferroni 't' test, unpaired student 't' test and Guassian test (Z).

Observations and Results

100 ASA-1 patients were included in the study. The age and sex distribution of patients in both the groups is shown in table-1.

Table 1:Age and sex distribution

	Test group		Control Group	
Age group (in years)	**Male**	**Female**	**Male**	**Female**
16-25	7	4	7	6
26-35	8	6	8	6
36-45	5	5	6	5
46-55	3	3	3	2
56-65	3	2	2	3
66-75	2	2	1	1
76-80	28	22	27	23

Mean age± SD 37.4 ± 12.12mean age ± SD 38.4 ±12.79
The age distribution of patients in both the groups was similar and the difference of age between the two groups was statistically not significant (P> 0.05).

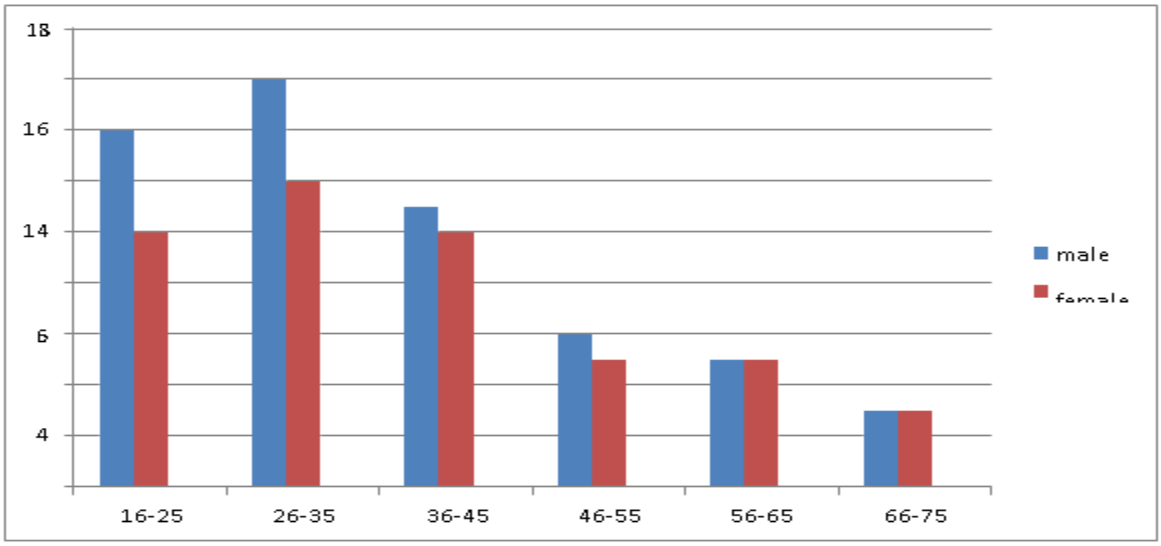

Fig 1:Age distribution

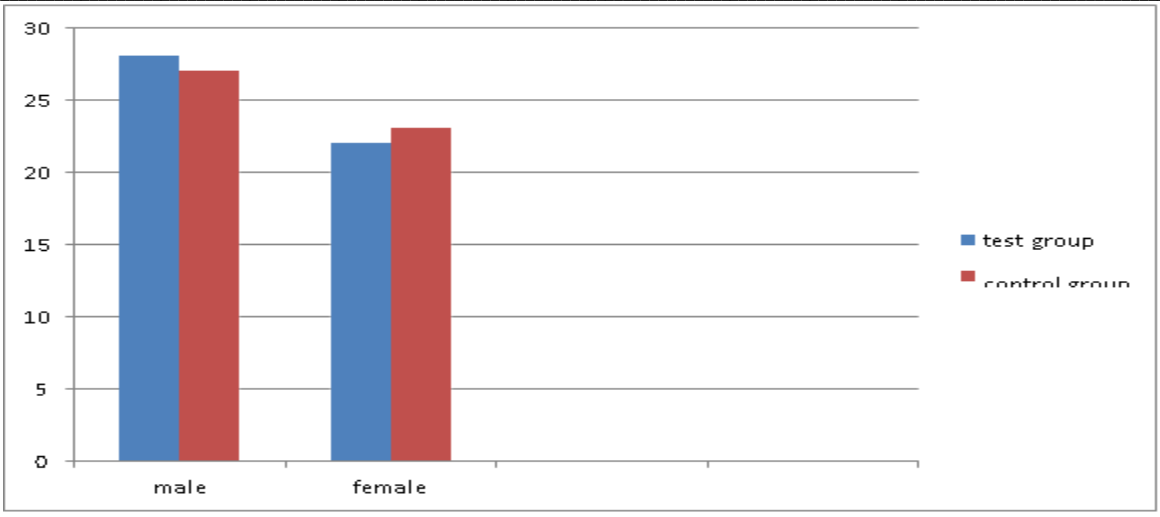

Fig 2: Sex distributioN

Table 2: Weight wise distribution of the patients scheduled for the study

Weight (Kgs)	Test Group		Control Group		Total
	Male	Female	Male	Female	
46-50	0	3	1	5	9
51-55	3	7	2	3	15
56-60	9	3	3	5	20
61-65	8	3	12	3	26
66-70	9	3	10	3	25
71-75	2	0	3	0	5

Table 3: Distribution of height

Height (ft-inches)	Test Group		Control Group		Total
	Male	Female	Male	Female	
4'9"-5'00"	0	1	0	2	3
5'1"-5'4"	6	18	7	17	48
5'5"-5'8"	24	0	22	0	46
>5'8"	1	0	2	0	3

The pulse rate changes in the Test group over the test period are as shown in table – 4

Table 4: Test Group – Pulse Rate changes (in beats/minute)

Time	Mean ± D	% change from preop. Value
Pre-op	82.2± 8.45	-
10minutes	85.37±8.67	+3.86
20minutes	81.76± 8.3	-0.55
30minutes	80.44±8.16	-2.14
40minutes	9.18± 8.00	-3.69
60minutes	79.24±7.95	-3.60

The pulse rate changes in control group are as shown in table – 5

Table 5: Control group – Pulse rate changes (in beats/minute)

Time	Mean ± SD	% change from preop. Value
Pre-op	81.44 ± 7.41	-
10 minutes	78.96 ±6.40	-3.05
20 minutes	71.44 ±5.97	-12.28
30 minutes	72.96 ± 5.06	-10.41
40 minutes	72.08 ±4.78	-10.61
60 minutes	71.04 ±5.28	-12.77

$P < 0.001$ (very highly significant) The systolic blood pressure changes in test group are shown in table – 6

Table 6: Test group – Systolic blood pressure changes (in mm/Hg)

Time	Test Group	% change from preop. Value
Pre-op	122.88	-
10minutes	126.72	+3.125
20minutes	118.88	-3.26
30minutes	115.84	-5.73
40minutes	113.92	-7.29
60minutes	115.28	-6.185

F= 6.749 , P < 0.01 (Highly significant)

Table 7:The systolic blood pressure changes in control group

Time	Mean ± SD	% change from preop. Value
Pre-op	124.72 ± 8.38	-
10 minutes	116.88 ±9.89	-6.29
20 minutes	101.6 ±10.26	-18.54
30 minutes	100.8 ±7.53	-19.18
40 minutes	101.36 ±6.21	-18.73
60 minutes	102.72 ±6.14	-17.64

F= 30.63 , P <0.001 (very highly significant)

The diastolic blood pressure changes in Test group are shown in table – 8

Table 8: Test group – Diastolic blood pressure changes (in mm/Hg)

Time	Test Group	% change from preop. Value
Pre-op	79.12 ± 3.54	-
10minutes	82.72±5.06	+4.56
20minutes	78.72±5.85	-0.501
30minutes	76.88 ±4.77	-2.83
40minutes	76.4±4.27	-3.44
60minutes	77.12 ±4.19	-2.53

F=4.942 , P < 0.05 (significant)

The diastolic blood pressure changes in control group are shown in table – 9

Table 9: Diastolic blood pressure

Time	Mean ± SD	% change from preop. Value
Pre-op	80.24± 3.21	-
10 minutes	75.12±7.20	-6.38
20 minutes	65.6±7.44	-18.25
30 minutes	64.8±5.87	-19.24
40 minutes	65.04±5.60	-18.94
60 minutes	65.6 ±5.42	-18.25

F= 24.505 , P < 0.001 (very highly significant)

The statistical analysis of pulse rate and blood pressure changes in relation to pre operative values were done by BONFERRONI 't' TEST. The results are shown in table – 10, 11, 12 for pulse rate, systolic blood pressure and diastolic blood pressure respectively.

Table 10:Test group – Pulse Rate

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 1.33	P > 0.05 (NS)
Pre-op v/s 20 min	t =0.184	P > 0.05 (NS)
Pre-op v/s 30 min	t =0.738	P > 0.05 (NS)
Pre-op v/s 40 min	t =1.275	P > 0.05 (NS)
Pre-op v/s 60 min	t =1.242	P > 0.05 (NS)

Table 10 a. Control group – Pulse rate

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 1.327	P > 0.05 (NS)
Pre-op v/s 20 min	t =5.349	P < 0.001 (VHS)
Pre-op v/s 30 min	t =4.536	P < 0.001 (VHS)
Pre-op v/s 40 min	t =5.077	P < 0.001 (VHS)
Pre-op v/s 60 min	t =5.563	P < 0.001 (VHS)

P > 0.05 – Not significant (NS) P >0.05 - Significant (S)

P > 0.01 – Highly significant (HS)

P > 0.001 – Very highly significant (VHS)

Table 11:Test group – Systolic blood pressure

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 1.415	P > 0.05 (NS)
Pre-op v/s 20 min	t =1.474	P < 0.05 (NS)
Pre-op v/s 30 min	t =2.594	P < 0.02 (HS)
Pre-op v/s 40 min	t =3.302	P < 0.01 (HS)
Pre-op v/s 60 min	t =2.801	P < 0.01 (HS)

Table 11a: Control group – Systolic blood pressure

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 2.999	P < 0.01 (HS)
Pre-op v/s 20 min	t =8.845	P < 0.001 (VHS)
Pre-op v/s 30 min	t =9.15	P < 0.001 (VHS)
Pre-op v/s 40 min	t =9.089	P < 0.001 (VHS)
Pre-op v/s 60 min	t =8.416	P < 0.001 (VHS)

Table 12:Test group – Diastolic blood pressure

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 2.427	P < 0.05 (S)
Pre-op v/s 20 min	t =0.270	P > 0.05 (NS)
Pre-op v/s 30 min	t =1.51	P > 0.05 (NS)
Pre-op v/s 40 min	t =1.84	P > 0.05 (NS)
Pre-op v/s 60 min	t =1.35	P > 0.05 (NS)

Table 12 a: Control group – Diastolic blood pressure

Time	Results of Bonferroni 't' test	
Pre-op v/s 10 min	t = 2.706	P < 0.05 (HS)
Pre-op v/s 20 min	t =7.738	P < 0.001 (VHS)
Pre-op v/s 30 min	t =8.161	P < 0.001 (VHS)
Pre-op v/s 40 min	t =8.034	P < 0.001 (VHS)
Pre-op v/s 60 min	t =7.738	P < 0.001 (VHS)

The pulse rate, systolic blood pressure, diastolic blood pressure of the test and control group were compared using Unpaired student 't'Test. The results shown are shown in table 13, 14 and 15 respectively.

Table 13: Test v/s Control group – pulse rate

Time	Results of student 't' test	
Pre-op	t = 0.478	P > 0.05 (NS)
10 minutes	t =10.04	P < 0.001 (VHS)
20 minutes	t =9.85	P < 0.001 (VHS)
30 minutes	t =8.503	P < 0.001 (VHS)
40 minutes	t =7.348	P < 0.001 (VHS)
60 minutes	t =8.241	P < 0.001 (VHS)

Table 14: Test v/s Control group – Systolic blood pressure

Time	Results of student 't' test	
Pre-op	t = 1.19	P > 0.05 (NS)
10 minutes	t =9.349	P < 0.001 (VHS)
20 minutes	t =11.237	P < 0.001 (VHS)
30 minutes	t =10.785	P < 0.001 (VHS)
40 minutes	t =9.562	P < 0.001 (VHS)
60 minutes	t =8.764	P < 0.001 (VHS)

Table 15: Test v/s Control group – Diastolic blood pressure

Time	Results of student 't' test	
Pre-op	t = 1.66	P > 0.05 (NS)
10 minutes	t =7.673	P < 0.001 (VHS)
20 minutes	t =12.41	P < 0.001 (VHS)
30 minutes	t =13.42	P < 0.001 (VHS)
40 minutes	t =12.85	P < 0.001 (VHS)
60 minutes	t =11.495	P < 0.001 (VHS)

It can be seen that in table 13,14 and 15 the difference between the pulse rate, systolic blood pressure , diastolic blood pressure in the test and control group was statistically not significant (P > 0.05) at the pre- operative time, but was statistically very highly significant (P < 0.001) at all other times during the study period.

The amount of i.v fluids required to maintain haemodynamic stability in both the groups is shown in table – 16.

Table 16: i .v fluids required to maintain haemodynamic stability

I.V Fluids (in ml)	Test Group	Control Group
Mean ± SD(total in 1st hour)	764± 111.82	1474±183.36

The incidence of complications in both the groups was compared by using Gaussian Test (z)

Test group: 3 cases/out of 50 cases Control group: 9 cases/out of 50 cases Z = 2.128 , P < 0.05 (significant)

Table 17: Adverse effects

Adverse effects	Test Group	Control Group
Severehypotension	1	6
Bradycardia	0	4
Nausea	0	4
Vomiting	0	3
Nystagmus and Hallucinations	2	0

Discussion

Hypotension after spinal anaesthesia is one of the commonest complications. It is caused by physiological effects of spinal blockade leading to paralysis of preganglionic sympathetic nerves with arteriolar dilation and a fall in venous return due to this vasodilation. Majority of cases require immediate therapy for restoration of adequate circulation[6].

The other setbacks of regional anaesthesia are the fear amongst the patient while he is still awake, physical and psychological strains on the patient because of prolonged positioning and the limited duration of the effect of local anaesthetic. Thus the supplementary sedation is always needed during regional blocks[7].

In our study, 100 ASA class 1 patients were included. The age and sex distribution of patients in both the groups were comparable.

The cardiovascular stability was far better in test group compared to control group.

In the present study, pulse rate in test group showed a slight increase at 20 minutes followed by a insignificant decrease during the subsequent one hour period. But in control group the pulse rate decreased to about 12% below the preoperative level showing a statistically very highly significant change. The pulse rate changes of two group when compared by unpaired 't' test showed statistically very highly significant difference.

In the present study, Systolic blood pressure in test group fell by a maximum of 7.2% when compared to control group where it fell to maximum of 19.18% which was statistically very highly significant.

We found that Diastolic blood pressure in test group fell by a maximum of 3.69% as compared to control group where the decrease was 12.28%. Thus the difference was statistically very highly significant.

Thus it can be seen that the pulse rate was maintained close to preoperative levels in test group where as in control group there was significant decrease from preoperative levels.

In the present study, Although there was a slight decrease in systolic and diastolic blood pressure from the preoperative levels, but when the decrease was compared to the degree of fall in the control group, the fall in test group was statistically not significant.

The amount of i.v. fluids required to maintain hemodynamic stability in test group was 764 ± 111.82 ml when compared to control group 1474± 183.36 ml, thus the i.v. fluid requirement was significantly less.

In the present investigation, the incidence of side effects was less in test group (3/50) compared to control group (9/50). Two patients in test group experienced bad dreams and hallucinations (incidence of 4%). Thus the incidence of psychogenic emergence reactions was very less with the dose of ketamine given.

The incidence of severe hypotension, bradycardia, nausea, vomiting was very less in test group as compared to control group. The patients in test group were also better sedated and less apprehensive compared to control group.

Thus the results of our study are comparable to those conducted by Tripathi et al (1992)[8] and Dewoolkar et al (1995)[9].

In summary, ketamine in doses of 0.3 mg/kg i.v. given prophylactically before spinal anaesthesia with 0.5% bupivacaine heavy and therapeutically post spinal in incremental doses of 0.3 mg/kg. every 10 minutes, helps in reduction of i.v. fluid requirements and also a reduction in the incidence of fall in blood pressure and other adverse effects.

Another study was done to compare circulatory changes in patients who received either fentanyl or ketamine during spinal anaesthesia[10]. Thirty patients (ASA I-III) scheduled to undergo spinal anaesthesia for osteosynthesis of hip fractures were allocated to receive either ketamine or fentanyl intravenously during the procedure.

Immediately before anaesthesia, 7 ml/kg BW of an isotonic NaCl solution was administered i.v. Patients received either fentanyl 1.5 mg/kg BW i.v. before anaesthesia, or ketamine 0.7 mg/kg BW i.v. before anaesthesia, and 0.35 mg/kg BW 15 and 30 min after the first dose. No prophylactic vasopressor was used.

During the first 40 min of anaesthesia a fluid load of 14 ml/kg BW was given i.v. If the mean arterial pressure (MAP) fell more than 20%, the infusion rate was increased. If the reduction in MAP exceeded 33% or if the systolic pressure decreased to less than 80 mmHg, patients were registered as haemodynamically unstable. In both groups the spinalanaesthesia caused a reduction in MAP. The MAP was lower in the fentanyl group than in the ketamine group at all times. In the fentanyl group six subjects developed a haemodynamically unstable condition, while only one subject in the ketamine group was registered as such (P less than 0.05). There was no significant change in heart rate in either group. We conclude that during spinal anaesthesia patients can be kept haemodynamically stable by intravenous administration of ketamine.

Hypotension is a common complication during spinal anesthesia.The elderly are at an increased risk of developing complications from hypotension due to reduced physiological reserves. Ketamine induces activation of the sympathetic nervous system, thus often increasing heart rate and blood pressure. The aim of their study was to determine protective effects of ketamine on hemodynamic changes under spinal anesthesia in the elderly patient.

Another study was conducted on Sixty patients (ASA I-III)[11] scheduled to undergo spinal anesthesia for transurethral resection. They were randomly allocated to receive either ketamine or placebo intravenously (i.v.) during the procedure. Immediately before spinal anesthesia, 500 ml of an isotonic NaCl solution was administered i.v. Patients received either placebo 2 cc NaCl solution i.v. before anesthesia or ketamine 1 mg/kg in 2 cc i.v. before spinal anesthesia[11].

In both groups, spinal anesthesia resulted in a reduction in Mean Arterial Pressure (MAP). MAP was lower in the placebo group than in the ketamine group at all times. There was a significant change in heart rate in placebo group compared to ketamine group. They concluded that ketamine 1 mg/kg i.v. given before spinal anesthesia resulted in greater hemodynamic stability in elderly patients undergoing transurethral resection compared with placebo.

Recent clinical applications of ketamine with moderate scientific evidence and based on a renewed interest in low dose ketamine regimes[12].Procedural sedation for adults and children: The literature is strongly supportive of the safety and efficacy of ketamine for emergencydepartment (ED) dissociative sedation for a variety of brief painful or emotionally disturbing procedures in both children and adults e.g.: Laceration repair, fracture reduction, abscess drainage, emergency cardioversion, amputation, chest tube insertion. It is useful for procedures in the mentally disabled who are often uncooperative[13].

This dissociative sedation can be readily achieved by administration of a single IV or IM loading dose of ketamine followed by titration. Intranasal ketamine is being used in a wide range of clinical doses for procedural sedation in children (0.5-9 mg/kg). It is used for sedation or general anesthesia for pediatric procedures like cardiac catheterization, radiation therapy, radiological studies such as magnetic resonance imaging, dressing changes, and dental work. Ketamine in low doses in combination with low doses of propofol provides effective and safe sedo-analgesia in pediatric emergency short surgical procedures and in adults undergoing colonoscopy and short gynecological procedures[13].

Conclusion

Based on the observation of results of this study, we concluded that low dose intravenous ketamine offers superior cardiovascular stability. In doses of 0.3 mg/kg i.v, it definitely offers protection against spinal hypotension. Low dose ketamine in combination with midazolam, has good sedative and analgesic properties, easy airway maintenance, reduces the incidence of severe hypotension, bradycardia, nausea, vomiting. It also reduces the volume of crystalloids required to maintain hemodynamic stability. The

requirement of vasopressors to treat hypotension was significantly low. This is of paramount information observed in this study.As a result avoidance of vasopressors in practice has many advantages like prevention of circulatory overload, overshoot hypertension and decrease in organ perfusion by vasoconstriction. The only drawback being a small incidence of minor unpleasant emergence sequelae. Thus it can be concluded that low doses of ketamine fulfils many of the requirements of an ideal supplementary medication during spinal anaesthesia.

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