Original Article

PROPHYLACTIC USE OF KETAMINE HYDROCHLORIDE FOR PREVENTION OF POST OPERATIVE SHIVERING

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SUMMARY:

Postoperative shivering is one of the recognized complications following general, regional anaesthesia and also effect of some surgical procedure specially in the recovery room[1]. Shivering increases the muscular activity, O_2 consumption, CO_2 production and may result in hypoxaemia, hypercarbia and lactic acidosis[2]. It is not only uncomfortable but also cold sensation which is even worse feeling than pain sensation. As a result preventing the symptoms is clearly desirable and beneficial for the patient. Different methods are suggested for prevention of postoperative shivering including biogenic monoamines, cholinomimetcis, cations, endogenous peptides, opioids, GA agents, NMDA antagonists [3].

The present study was designed to compare the efficacy of ketamine on the patients undergoing elective surgery for prevention of postoperative shivering. The study was also done to deffect incidence of shivering, haemodynamic status, untoward effects of drug used (hallucination, unpurposeful movement, restlessness).

A total number of 60 patients of ASA I and II grade of both sex, age range 30-60 yrs, weight 50-70 kg, undergoing elective gynaecological surgery was randomly selected into two groups Gr K and Gr P and received ketamine 5mg. kg^{-1} and placebo (normal saline) respectively at 20 minutes before the end of the operation. In the postoperative period, incidences of shivering were 80% & 50% in group "K" and "P" which are highly significant between the groups P<001. Cardiovascular parameters SAP, DAP, MAP and SpO_2 between the groups were not significant P> .05. The study showed that patients of group 'K' were less shivering with good recovery.

Key words: Postoperative shivering, ketamine.

INTRODUCTION:

Post anaesthetic shivering is remarkably uncomfortable, some patients find cold sensation worse than surgical pain. Shivering aggravates post-operative pain by stretching surgical incision[5]. Shivering interferes with monitoring technique, increases intracranial and intraocular pressure, can double or triple O_2 consumption and CO_2 production. The incidence of post-operative shivering is 6-65% in GA and 30% in regional anaesthesia. Etiology of Post operative shivering in multifactorial. Different methods are available for prevention of Post operative shivering. Multimodal approaches like warming, O_2 therapy, correction of metabolic abnormalities, drugs opioids, benzodiazepine, clonidine, corticosteroids, ketamine, nefopam, doxapram, are used to prevent and for management of postoperative shivering[6]. Among which drugs are more popular mode. Intravenous ketamine .5mg/kg 20 min before completion of surgery will abolish shivery in most subjects [7]. NMDA receptor agonists increase the firing rate of neuron in the preoptic anterior hypothalamus, modulate noradrenergic and serotonergic neuron in brain. NMDA receptor antagonists modulate shivering by interfering central thermoregulatory control mechanism[8], Ketamine is cheaper and easily available in our country. The objective of current study was to evaluate effectiveness of ketamine in prevention of postoperative shivering in low dose without major side effects.

Material & Methods

In the preoperative period patients were fasted at least 6 hrs. and on arrival at OT I/V line was inserted; pulse, BP respiratory rate and SpO_2 were recorded. After 3 minutes preoxygenation induction was facilitated by suxamethonium 1.5 mg. kg^{-1},

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General anaesthesia was maintained by halothane. 5%, N_2o 70 % in O_2. Muscle relaxation was maintained by intermittent vecuroneum. Hartmann's solution was used for proper hydration and patients were covered with sheets as usual. Neostigmine 40 ug. kg^{-1}, atropine 20 ug. kg^{-1} were given for reversal from muscle relaxant. (At the end of operation 'K' & P Gr. were given .5mg kg^{-1} ketamine and IO cc normal saline respectively.)

The severity of postanaesthetic shivering was assessed according to a 4 point scale by wrench et al[4]

O = no shivering

1= piloerection, peripheral vasoconstrictrion, peripheral cyanosis without other cause but without visible muscular activity.

2- Visible muscular activity confined to one muscle group.

3- Visible muscular activity in more than one muscle group

4- gross muscular activity involving the entire body.

The evaluation of shivering was carried out by independent anaesthesiologist who is unaware of grouping. If a score>2, 25mg ketamine was given intravenously as rescue medication. BP, Pulse rate, SpO_2 were measured during induction and 10, 20, 30 & 60 min after extubation. All patients received diclofenac suppository rectally at the end of operation. Post anaesthetic recovery score was graded by using Aldrete score and Patients were carefully observed for adverse effects like hallucinations, restlessness, drowsiness and dream.

Results:

Demographic data concerning the patient age, weight as well as duration of anaesthesia and type of surgery were comparable in two groups (Table I & II) which are fairly matched. In preoperative situation in group P mean pulse rate was 78 ± 2.30, in Gr-k 81 ± 1.04 , mean anterial pressure 91.71 ± 1.04 (Gr P), 93.o1 ± 1.12 (Gr K), SpO_2 98 ± .55 Gr P, 97 ± 0.25 (Gr K) which showed no significant difference between the groups (Table III). There were no clinically relevant differences in measured results as regards to blood pressure and heart rate between the study group (group K) through out the study period (table IV & table V). Except 20 minutes before the end of surgery when ketamine was administered the heart rate in group 'P' was 96.7 ± 1.85 and in group 'K' was 101.0 ± 1.22 MAP (mean arterial pressure) in group 'P' was 105.80 ± 1.32 and in group 'K' was 110.97 ± 1.20. But after 30 minutes and onwards of ketamine given, the blood pressure and the heart rate both came down to normal range and even to lower level than the initial pre-anesthetic states though it was not significant only two are significant. Before induction in group 'P' arterial oxygen saturation was 98.28 ± 0.72, and in group 'K' was 99.35 ± 0.78. But 20 minutes after the end of surgery SpO_2 in group 'P' 98.94 ± 0.48 and in group 'K' 98.82 ± 0.08, P> 0.05, so pulse oximetry showed no such significant difference between the two groups (table VI). The incidence of post operative shivering was 80% in group-P, 50% in group-K. Analysis was done by "Z" test; p< 0.001. The difference between the two groups was highly significant (table VII)

Shivering score 60 minutes after the end of surgery varies at the post operative period for both the groups. Severity of shivering is expressed by using four-point scale. In patients treated with placebo 0.5 $mg.kg^{-1}$, 06 of 30 (20%) have no symptoms of shivering (shivering score grade 0) but twelve patients (40%) showed signs of piloerection, peripheral vasoconstriction or peripheral cyanosis (shivering score grade 1). In grade (2-4) patients from four-point scale revealed shivering of 20%, 16.66 %, 3.33% respectively. They also showed visible gross muscular activity. In patients treated with ketamine 0.5 $mg.kg^{-1}$, 15 of 30 (50%) have no symptoms of shivering but eleven patients (33.33%A) showed signs of piloerection, peripheral vasoconstriction or peripheral cyanosis (shivering score grade 1). In grade (2-4), patients from four –point scale revealed shivering of 6.66 %, 3.33%, 32.33% respectively. Analysis done by "Z" test: p<0.001-highly significant, p>0.05-not significant. Analyzing the shivering score we found a significant higher grading in the placebo group compared to ketamine group (tableVIII). Table IX: — In placebo group there was no untoward effects such as (hallucinations, unpurposeful movements, restlessness, drowsiness) but in ketamine group 2 of 30 patients (6.66%), 3 of 30 (10 %), 1 of 30 (3.33%) p<0.001 highly significant.

Table-I

Demographic Data of the Patients.

Parameter	Group – P N = 30	Group – P N = 30
Age in years	36.3(30-60)	37.4(30-60)
Sex, M : F	14 : 16	15 : 15
Body weight in Kg	52.3(50 – 70)	54 (50-70)
Duration of Surgery in minutes	85 min(60 – 120)	80 min(50 – 115)

Values are expressed in mean (Range)
Results : fairly matched

Table II

Types of operation :

Operation	Group – P N = 30	Group – P N = 30
Gynaecological Laparotomy, Hysterectomy.	120309	110308
Surgical Cholecystectomy	120804	130805
Urological.Nephrolithotmy.NephrectomyPyeloplasty	06030201	06030201
Total	30	30

Table III

Comparison of the control states of the study population :

Parameter	Group – P N = 30	Group K N=30	P – Value (unpaired student's t-test)
Pulse/minute	78 ± 2.3	81 ± 2.3	> 0.05
MAP (mm of Hg)	91.71 ± 1.04	93.01 ± 1.12	> 0.05
SpO_2	98 ± 0.55	97 ± 0.25	> 0.05

Values are expressed in mean ± SEM
unpaired students t-test, P-> 0.05 not significant
MAP = mean arterial of pressure, SpO_2 = Arterial oxygen saturation.

Table IV. (a)

Pulse and mean arterial pressure at different point of observation of two groups:

60 minutes Parameters	20 minutes before the end of surgery	At recovery 10 minute	20 minutes	30 minutes	40 minutes	50 minutes	
Heart rate /minute	80.77 ± .20	91.0 ± .82	90.71 ± 1.01	82.28 ± 0.92	81 .25 ± .72	81 .05 ± .70	81.05 ± .70
MAP	97.72 ± 0.95	96.25 ± .72	94.15 ± 0.70	88.60 ± 0.96	87 .85 ± 0.80	87.85 ± 0.80	87.22 ± .73

Values are expressed in mean ± SEM

Table IV. (b)

60 minutes Parameters	20 minutes before the end of surgery	At recovery 10 minute	20 minutes	30 minutes	40 minutes	50 minutes	
Heart rate/	92.03	93.02	92.0	88.01	84 .32	81.90	79.91
minute	± 0.98	± .80	± 0.05	± 1.02	± 0.98	± 1.00	± 0.90
MAP	100.62	110.82	100.51	91 .34	88.14	87.34	87.01
	± 1.01	± 1.61	± 0.97	± .92	± 0.92	± 0.78	± 1.10

Values are expressed in mean ± SEM.

Table V

Comparison of changes produced in the mean values of the two groups

Observation Time	Parameters	Group-P	Group-K	P - Value
Before Induction	Pulse	84.56 ± 1.23	86.32 ± 1.20	> 0.05
	MAP	91.71 ± 1.04	94.68 ± 1.24	> 0.05
Start of drugs 20 minutes before the end of surgery	Pulse	96.71 ± 1.85	101.0 ± 1.22	<0.01
	MAP	105.80± 1.32	110.97 ± 1.20	<0.01
At recovery = 10 minutes	Pulse	91.00 ± 0.82	92 .03 ± 0.98	> 0.05
	MAP	97.22 ± 0.95	100.82 ± 1.61	< 0.01
20 minutes	Pulse	87.88 ± 0.93	90.01 ± 1.02	> 0.05
	MAP	90.71 ± 1.01	94.34 ± 0.92	,,
30 minutes	Pulse	84.71 ± 1.06	88.32 ± 0.98	,,
	MAP	88.60 ± 0.96	88.14 ± 0.97	,,
40 minutes	Pulse	82.28 ± 0.92	81.90 ± 1.00	,,
	MAP	87.85 ± 0.80	87.34 ± 0.78	,,
50 minutes	Pulse	80.77 ± 0.20	84.90 ± 0.90	,,
	MAP	87.22 ± 0.73	89.03 ± 1.25	,,
60 minutes	Pulse	84.26 ± 1.22	86.02± 0.98	,,
	MAP	92.65 ± 1.01	94.28 ± 1.21	,,

Values are expressed in mean SEM

Unpaired student's " t-test'

MAP = mean arterial pressure

P-Value > 0.05 not significant

P – Value < 0.01 significant

Table VI

Incidence of shivering in two groups

Observation time	Group-P	Group-K	P-Value
Before Induction	98.28 ± 0.72	99.35± 0.78	> 0.05
20 minutes before the end of surgery	98.97 ± 0.45	96.08 ± 0.78	,,
At recovery + 10 minutes	97.97 ± 0.52	97.29 ± 0.67	,,
20 minutes	98.94 ± 0.48	98.82 ± 0.08	,,
30 minutes	98.71 ± 0.57	97.05 ± 0.70	,,
40 minutes	98.80 ± 0.63	97.00 ± 0.63	,,
50 minutes	98.65 ± 0.63	98.01 ± 0.08	,,
60 minutes	98.70 ± 0.97	97.40 ± 0.83	,,

Analysis done by Unpaired student's " t-test" Values are expressed in mean ± SEM
P-Value > 0.05 not significant

Table VII

Shivering score in post operative period in two groups

Incidence of post operative shivering	Group – P	Group –K	P-Value Z-test
	24	15	<0.001 (z>3)
	80%	50%	,,

Values are expressed in mean ± SEM Analysis done by "Z-test"
(P<0.001) highly significant

Table-VIII

Shivering score in post operative period in two groups

Shivering score	Group-P		Group-K		P-Value (z test)
0	06	20%	15	50%	0.001 (z value 3.3)
1	12	40%	11	33.33%	>0.05
2	06	20%	02	6.66%	<0.001
3.	05	16.66%	01	3.33%	< 0.001
4.	01	3.33%	01	3.33%	>0.05

4

Analysis done by "Z-test"
(P-<0.001) – highly significant
(P->0.05) – Not significant

Table IX
Untoward effects

Variable	Group-P	Group-K		P-Value(Z-test)
Hallucination	0	2	6.66%	<0.001
Unpurposeful	0	3	10%	<0.001
Movement of Face	0	1	3.33%	<0.001
Restlessness	0	6	20%	<0.001

DISCUSSION:

Postanaesthetic shivering is a frequent complication following surgery and anaesthesia and incidence about 5- 65% following GA and 33% under SAB. The frequency and severity has been reduced by identifying precipitating factors, improving surgical techniques, newer anaesthetic agents and technique and also by newer drugs. Despite these changes there is still an unacceptable frequency which need to be reduced for betterment of future surgery and anaesthesia.

The aetiology of post-operative shivering is multifactorial. Factors associated with an increased risk of post-operative shivering include age, sex, obesity, anxiety, pain, hypoxia, type of anesthetic, hypotension, type & duration of the surgical procedure. Patient undergoing gynecological surgery are at high risk for post-operative shivering. Because most of them are female & most of the surgery done in winter season.

D.Dal *et al* studied the efficiency of pethidine, ketamine with placebo[8]. S.N. Piper et al also have studied the effectiveness of three doses of Nefopam with clonidine & placebo in the prevention of post-operative shivering[11]. There was significantly greater number of asymptomatic patients in the ketamine, pathidine, clonidine and nefopam group 60 minutes after operation at PACU as compared to placebo ($p<0.01$). The average duration of anesthesia was 60 minutes. There was no significant difference between the groups respect to heart rate, MAP and $SpO_{2..}$

In our study, incidence of post operative shivering in group-P (those received placebo) were 80% and in group-k (those received ketamine) were 50% that means the data shows the incidence ($p<0.01$) of shivering is highly significant in placebo group. Heart rate differences between the groups at control states ($p>0.05$) and post operative period ($p>0.05$) were not significant. Mean arterial pressure and arterial oxygen saturation between the two groups were not ($p>0.05$) significant. The difference in the results of asymptomatic patients in our study 19% compared with those S. N. pi per et el 15 % may be explained by a small number of population and the meant duration of anesthesia was greater in our study.

Shivering score after one hour post-operatively varies from 0-4 (four-point scale) in both groups. In placebo-treated patients, it was 0 for 20%, 1 for 40%, 2 for 20%, 3 for 3.33% and 4 for 3.33% respectively and statistically significant ($p<0.001$). It may be explained that patients of group-k were less shivering with good recovery Aldrete score.

CONCLUSION:

On the basis of present, controlled, prospective clinical study it can be concluded that the post operative shivering are the most common complaints. The aetiology of postoperative shivering is multifactorial including anesthetic, patients and surgical factors. All surgical patients should be kept normothermic unless hypothermia is specifically indicated for putative protection against cerebral ischaemia. Antishivering prophylaxis may be justified in patients who are at great risk of developing post-operative shivering after general anaesthesia.

The incidence of major side effects is not significant in ketamine group and contributes to some extent to post operative analgesia with acceptable recovery score (Aldrete).

We can conclude that prophylactic use of ketamine hycholoride is effective in small doses without major side effects and some analgesic effects in preventing post operative shivering under general anaesthesia.

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