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A COMPARATIVE STUDY ON THE EFFICACY OF KETAMINE AND PETHIDINE IN THE TREATMENT OF POST OPERATIVE SHIVERING IN PATIENTS UNDERGOING GENERAL ANESTHESIA.

Anaesthesiology

Surgeon Captain Urvashi Tandon — Professor, Department of Anesthesia, SGT Medical Collage, Gurugram, Haryana, India.

Surgeon Captain Milind Y Dharmamer* — Assistant Professor, Department of Anesthesia, INHS Asvini, Mumbai-400005, India. *Corresponding Author

Dr.Pritha Raj — Senior Resident, Department of Anesthesia, PSG Institute of Medical Sciences and Research, Coimbatore, India

ABSTRACT

Background: - Postoperative shivering is a known complication following exposure to anesthesia. It is seen in approximately 5-65% patients after general anesthesia and 33% patients after regional anesthesia.

Methods: - Evaluate the effects of a single dose of IV Ketamine (0.3 mg/kg) and IV Pethidine (0.3mg/kg) in treating post-operative shivering by studying the following: (a) effect on grade of shivering (b) time taken for resolution of shivering (c) the hemodynamic, percentage saturation of oxygen and temperature changes (d) occurrence of adverse effects, if any.

Results:- (a) Effect on grade of shivering – The percentage of shivering with grade of shivering = 0 at T_1 was 93.3% in group K in comparison to 0% in group P.

(b) Time taken for resolution of shivering –In group K, the mean time taken for resolution of shivering was 47.80 sec while in group P it was 102.50 sec.

(c) Hemodynamic changes- Heart Rate - The variation in the heart rate prior to beginning of the surgery (baseline), intra operative and post-operative period after drug administration for a period 10 min every minute was not found to be statistically significant.

MAP – The MAP variation was insignificant till T_5.After that MAP was higher in group K than group P. The difference was statistically significant but not clinically significant.

Pulse Oximetry- None of the patients in both groups had any episode of desaturation.

Temperature- Comparison of core temperature measured preoperatively, intraoperatively, postoperatively at T_0, T_5, T_{10}, in both groups was statistically insignificant ($p>0.005$) All patients had temperature > 36^0C

(d) Adverse effects- In group P no adverse effects were seen. In group K ,05 out of 30 (16.7%) had adverse effects.

KEYWORDS

Postoperative shivering Pethidine Ketamine

Introduction

Post anesthetic shivering is a known complication following exposure to anesthesia. It is seen in approximately 5-65% patients after general anesthesia and 33% patients after regional anaesthesia[1]. It is defined as detected tremor or fasciculation of the face, jaw, head, trunk or extremities lasting longer than 15 sec. [2,3.]

Pethidine 25mgIV is remarkably effective in treating postoperative shivering[4,5].Its antishivering action is partially mediated by K opioid receptors[6,7]Ketamine, a competitive NMDA receptor antagonist also inhibits post operative shivering[8].It is likely that NMDA receptor antagonists modulate thermoregulation at multiple levels. These areas are preoptic anterior hypothalamus[9] and locus coerulus[10].

Material and methods

A total of 60 patients of ASA Gd-I and II, 30 patients in each group, undergoing elective surgical procedures under general anesthesia were included in the study. Patients were allotted by simple randomization to both groups. Written informed consent was obtained from every patient.

After receiving approval from the hospital ethics committee, patients of both genders aged 20-60 yrs, who had undergone surgery under general anesthesia for duration of 120-180min with observed post operative shivering were enrolled into the study.

Preoperative Monitoring – Baseline HR, MAP, SpO2 were recorded.

Intraoperative Monitoring and Medication- Anesthesia was induced with Thiopentone Sodium 4-6mg/kg IV , Fentanyl 1- 2mcg /kg IV and Vecuronium 0.1mg/kg IV for orotracheal intubation. Maintenance of anesthesia was done with oxygen (0.6)/Air/Isofluorane . Warm IV fluids were used intraoperatively. Intraoperative HR , MAP, SpO_2 and core temperature were recorded.

Postoperative Monitoring and Medication (Study Period)- After surgery all patients were observed in the postoperative recovery area. All patients were administered oxygen by face mask at 6ltr/min and were covered with a blanket.

Patients with observed shivering and meeting the study criteria were recruited in to the study. The presence of shivering was accessed using the following scale.

0= No Shivering
1= No visible muscular activity but pilo erection, peripheral vasoconstriction or both are present(other causes excluded).
2= Muscular activity in only one muscle group
3= Moderate muscular activity in more than one muscle group but no generalized shaking.
4= Violent muscular activity that involves the whole body.

Patients with clinically observed shivering were administered a single dose of IV Ketamine (0.3mg/kg) - Group K or IV Pethidine (0.3mg/Kg)- Group P . The shivering was accessed before treatment- T_0, and for every subsequent one minute after treatment with either Ketamine or Pethidine for the next 10 minutes. Core temperature was measured immediately before treatment –T_0 and at 5 and 10 minutes (T_5 and T_{10} respectively) after treatment was administered. Side effects attributable to the study drugs(i.e. nausea, vomiting, hypotension, hypertension, tachycardia, nystagmus, feeling like walking in space and hallucination) were recorded and specific treatment was given.

Results

The results of this study are as follows:

1. Comparison in the GOS(Grade Of Shivering) of patients in Group K and Group P showed statistically significant correlation at T1($p<0.005$). Differences in GOS were not statistically significant at any other given instant.
2. In Group K, the mean time taken for resolution of shivering to occur (GOS-0) was observed to be 47.80 seconds. In Group P, time for resolution of shivering (GOS=0) was found to be 102.50

seconds. This difference was found to be statistically significant ($p<0.005$).
3. The variations in heart rate between T0-T10 was not found to be statistically significant.
4. Variations in the MAP were not statistically significant in the first 4 minutes of the study period. However, from T5-T10, the variation in MAP was statistically significant ($p<0.005$), But this difference was not found to be clinically significant.
5. None of the patients in both the groups had any episode of desaturation in the study period. Hence, the variation in SpO2 was statistically insignificant.
6. Comparison of core temperatures measured preoperatively, intraoperatively and postoperatively in both the groups were found to be statistically insignificant.($p>0.005$)
7. In Group P no adverse effects were seen following treatment. In Group K , 5 out of 30(16.7%) had observed adverse effects.
8. Two patients out of the 5 had recurrence of shivering at T3,T4 with GOS=2 that responded to pethidine given i.v. 3 out of 5 patients had nausea which was treated with Inj Ondansetron 4mg i.v. Nausea in all 3 patients was not followed by emesis. No other adverse effects were noted.

Statistically significant difference was found based on the occurrence of adverse effects.($p=0.0195$)

Discussion

The mechanism of postoperative shivering is unclear. General anesthesia results in thermoregulatory impairment. Shivering can occur as a thermoregulatory response to hypothermia .However in the postoperative period, mechanisms other than heat loss may contribute to the development of shivering viz.- uninhibited spinal reflexes, postoperative pain, decreased sympathetic activity , pyrogen release , adrenal suppression and respiratory alkalosis[11]

Apart from being uncomfortable for the patients, shivering is associated with a number of potentially deleterious sequelae like, increased oxygen consumption and carbon di oxide production[12,13], catecholamine release , increased cardiac output , tachycardia and hypertension[14], increased IOP[15]and interference with monitoring[16,17].

Numerous pharmacological interventions have been proposed for the treatment of postoperative shivering. Potent antishivering properties have been attributed to numerous drugs. These drugs are substances of several classes including biogenic monoamines, cholinomimetics, cations, endogenous peptides and possibly N-methyl-D- aspartate (NMDA) receptor antagonists. However, the exact mechanism of action of each agent in amelioration of postoperative shivering remains unclear.

We designed a comparative study to compare the effects of ketamine and pethidine on the treatment of postoperative shivering.

The objectives of this study were to evaluate and compare the effects of single dose of I.V ketamine(0.3 mg kg^{-1}) and I.V pethidine(0.3mg kg^{-1}) in treating post-operative shivering by studying the following:

- Effect on grade of shivering
- Time taken for resolution of shivering
- The hemodynamic, Oxygen saturation, temperature changes
- Occurrence of adverse effect

EFFECT ON GRADE OF SHIVERING:

Table 1: Comparison of Postop GOS at T1 between Group K and Group P

PostOp T1-GOS		Group		Total
		K	P	
0	No.	28	0	28
	%	93.3%	0.0%	46.7%
1 ^	No.	0	14	14
	%	0.0%	46.7%	23.3%
2 ^	No.	1	13	14
	%	3.3%	43.3%	23.3%
3 ^	No.	1	3	4
	%	3.3%	10.0%	6.7%
Total	No.	30	30	60
	%	100.0%	100.0%	100.0%

The grade of shivering at the beginning of the study-T0, was similar in both the groups. The difference was not statistically significant.($p=0.072$) The percentage of patients with GOS=0 at T1 was 93.3%(28/30) in Group K, in comparison to 0% in Group P. Of the remaining two patients in Group K,one had GOS=2 and another had GOS=3.Patients in Group P had a higher GOS at T1 with 46.7%(14/30) having GOS=1,43.3%(13/30) having GOS=2 and 10%(3/30) had GOS=3 . This difference in GOS at T1 had a statistically significant correlation.{$p<0.005$}.

Table 2: Comparison of Postop GOS at T2 between Group K and Group P

PostOp T2-GOS		Group		Total
		K	P	
0	No.	30	27	57
	%	100.0%	90.0%	95.0%
1 ^	No.	0	2	2
	%	0.0%	6.7%	3.3%
2 ^	No.	0	1	1
	%	0.0%	3.3%	1.7%
Total	No.	30	30	60
	%	100.0%	100.0%	100.0%

At T2, the GOS was observed to be “0” in all 30 subjects in Group K while 27 in Group P had GOS=0.Out of three,two patients in Group P had GOS=1 and one had GOS=2 at T2. Analysis showed the association to be statistically insignificant.($p>0.005$)

At T3, all patients in Group P had GOS=0 while in Group K, 29 patients had GOS=0 and one patient was noted to have GOS=2. This finding was not statistically significant.($p>0.005$).

At T4, GOS in Group P was “0” in all the 30 patients. In Group K, 28 had GOS=0,with remaining patients having GOS of 1 and 2 respectively. This difference was not statistically significant.

At T5, Group P had GOS=0 in all patients. In Group K 29 patients had GOS=0 with one patient having GOS-1. The difference was not statistically significant.($p=0.313$). Comparison in the GOS of patients in Group K and Group P showed statistically significant correlation at T1($p<0.005$). Differences in GOS were not statistically significant at any other given instant.

Therefore, patients treated with ketamine were found to have lower GOS in comparison to those treated with pethidine. This observation had strongest statistical significance at T1. After this the correlation was insignificant. Recurrence of shivering was noted at T3,T4 in Group K which was treated with Inj pethidine given i.v(0.3mg/kg).

TIME TAKEN FOR RESOLUTION OF SHIVERING:

In this study,in Group K, the mean time taken for resolution of shivering to occur(GOS-0) was observed to be 47.80 seconds. In Group P, time for resolution of shivering (GOS=0) was found to be 102.50 seconds. This difference was found to be statistically significant ($p<0.005$). It was clinically observed too that patients treated with ketamine actually had faster resolution in shivering. This also correlated with lesser GOS at subsequent intervals in comparison to patients in Group P at the same time intervals denoting a slower onset of action with pethidine.

The changes in hemodynamics, temperature and Spo2:

HEMODYNAMIC CHANGES:

Heart rate: The variation in heart rate was studied prior to beginning of procedure (baseline), intraoperative and postoperative period after drug administration for a period of 10 minutes every minute. This variation was found to be statistically insignificant.

Mean arterial pressure:

In this study, the MAP variation was insignificant till T5. From T5 , a statistically significant difference in MAP was seen with higher MAP in Group K in comparison to Group P. However the difference detected was not clinically significant.

This difference may be attributable to the pharmacological effect of ketamine. It increases the heart rate, MAP,contractility and cardiac output. It potentiates the release of catecholamines from the adrenal medulla and also increases the sympathetic tone. In contrast,pethidine

resembles atropine in structure. It is associated with fall in blood pressure and can be associated with tachycardia.

PULSE OXIMETRY- SpO2:
In this study, none of the patients in both the groups had any episode of desaturation in the study period. Hence, the variation in SpO2 was statistically insignificant. However, in this study, supplementation with oxygen was done throughout the study period at the rate of 6L/min.

TEMPERATURE:
In this study, comparison of core temperatures measured preoperatively, intraoperatively and postoperatively at T0,T5,T10 in both the groups were found to be statistically insignificant. ($p>0.005$). All patients had temperatures greater than 36^0C

ADVERSE EFFECTS:
In Group P no adverse effects were seen. In Group K, 5 out of 30(16.7%) had observed adverse effects. 2 patients out of the 5 had recurrence of shivering at T3,T4 with GOS=2 that responded to pethidine given I.V. 3 out of 5 patients had nausea which was treated with Inj Ondansetron 4mg I.V. Nausea in all 3 patients was not followed by emesis. No other adverse effects were noted.

Statistically significant difference was found based on the occurrence of adverse effects.($p=0.0195$).

Therefore, treatment with pethidine was not associated with any side effects whereas treatment with ketamine did show some adverse effects. These included recurrence of shivering in two patients. The other 3 patients had nausea. However, vomiting, hemodynamic instability, nystagmus, "walking in space", hallucinations were not observed in either groups.

Though ketamine is known to be associated with drowsiness, sedation and hallucinations, the absence of these adverse effects may be correlated with lower dosage(0.3mg/kg) used in this study.

Conclusion
Based on the findings in this study, it has been observed that ketamine at a dose of 0.3mg/kg given i.v had a definite anti-shivering effect. It had a more rapid onset(47.8 seconds) compared to pethidine (102.5seconds) in treating shivering occurring postoperatively after general anesthesia. However, out of the 30 patients in Group K, two patients had a recurrence of shivering requiring treatment with pethidine to stop shivering. Also 3 out of 30 had nausea which was treated with Ondansetron(4mg) given intravenously. Pethidine had a slower onset of around 102.50 seconds. This difference in resolution of shivering was statistically significant. But it was noted that the treatment of shivering with pethidine was more definite with no incidence of adverse effects.

To conclude, ketamine is an effective anti-shivering agent highlighting the role of NMDA antagonism in thermoregulation. However, the occurrence of adverse effects and recurrence of shivering may limit its usefulness compared to pethidine. However, larger studies may be required to further establish these findings.

Conflicts of interest
The authors have none to declare

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