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ABSTRACT

BACKGROUND & OBJECTIVES

Control of post operative shivering is essential as shivering is a cause of discomfort and dissatisfaction in patients undergoing operations under anaesthesia.

The aim of the study is to assess the efficacy and safety of intravenous Clonidine, Butorphanol and Tramadol in the treatment of post operative shivering.

✓ Primary objectives

- To assess the effectiveness of tramadol, butorphanol and clonidine in patients with post operative shivering.
- To assess the incidence of Adverse Drug reactions associated with Therapy using NARANJO ADVERSE REACTION PROBABILITY SCALE.
- To compare safety and efficacy of tramadol, butorphanol and clonidine in patients with post operative shivering.

✓ Secondary objectives

- To monitor the patients for recurrence of shivering upon cessation of drugs.

METHODOLOGY

This is a prospective study which was conducted for 6months in the department of anaesthesia. The patients were divided into three groups of 30 each - Group A (n=30) receiving Tramadol 50 mg/kg IV, Group-B (n=30) who received Butorphanol 20mg IV and Group- C (n=30) comprised of the patients who received Clonidine 150mcg intravenously. The efficacy and response rate of the study drugs were evaluated and recorded. Side effects like, nausea, vomiting, hypotension, sedation were recorded. All data were analyzed using One – Way Anova.

RESULTS

A total number of 90 patients were included in the study (N= 90). The study population was categorized into three groups based on drug administration. A marked decrease in the systolic Blood Pressure and Heart Rate with clonidine was observed ($p<0.05$). Tramadol receiving patients reported incidence of nausea and vomiting where as butorphanol is associated with sedation.

CONCLUSION

Complete control of post operative shivering with less or no severe side effects was achieved with Butorphanol in comparisons to clonidine and Tramadol.

KEYWORDS

Shivering, Tramadol, Clonidine, Butorphanol, Post operative shivering.

INTRODUCTION

Regional anaesthesia is widely used as a safe technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70 % of patients undergoing surgery. Shivering is usually defined as readily detectable tremor or fasciculation of face, neck, jaw, head, trunk or extremities lasting longer than 15 seconds. Shivering is very unpleasant, physiologically stressful for the patient undergoing surgery and some patients find the accompanying cold sensation to be worse than surgical pain. Shivering is associated with many hazardous effects like it increases metabolic rate which may lead to increase in oxygen consumption by 100-600% with increased carbon dioxide production. It can cause arterial hypoxemia, raised intracranial and intraocular pressure. It can lead to adverse post operative outcomes like increased wound pain and infection which leads to delayed discharge of the patient. [1]

Anaesthesia impairs the thermo-regulation by inhibiting vasomotor and shivering responses and by redistribution of heat from core to periphery of the body resulting in hypothermia during spinal anaesthesia. Shivering is considered to be a physiological response to core temperature in an attempt to raise the metabolic heat production. It increases oxygen demand, heart rate, cardiac output, lactic acidosis, increased intra ocular pressure, increased intra cranial pressure, increased carbon dioxide production, hemodynamic changes and increased pain perception. Thus it may cause distress to patients especially to those with low cardio pulmonary reserve. To prevent and treat this complication, warming of the patients with warm IV infusion, increasing the operation room temperature is undertaken. Apart from this various therapeutic agents are used, which include Meperidine, Clonidine, Dexmedetomidine, Nefopam, Anticholinergics, Opiate agonist (Tramadol etc). Dexamethasone, however every aforesaid agent has its own adverse effects and the most ideal anti-shivering agent is still not found. [2]

Alpha-2 receptor agonists like Clonidine and Dexmedetomidine are another important class of anti-shivering agents that, unlike meperidine, causes little respiratory depression. Tramadol is an opioid analgesic with opioid action possibly mediated through mu-receptor with minimal effect on kappa and delta binding sites. Tramadol also activates the mononergic receptor of the descending neuraxial inhibiting pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both. Butorphanol, an easily available opioid, is commonly used as an IV analgesic agent but there are very few studies demonstrating its use for control of shivering. Hence it

becomes essential to find an appropriate drug for post operative shivering that is safe, effective and quick in action.

MATERIALS AND METHODS

After obtaining approval from the ethical committee and written informed consent, patients of either sex aged 18 to 60 years scheduled for Patients posted for procedures under anaesthesia were included in study at the department of Anaesthesia of MALLA REDDY HOSPITAL, Suraram, Rang Reddy district, Telangana for a period of six months. Patients who were not willing to participate. Patients with known hypersensitivity to tramadol, butorphanol and clonidine, known history of alcohol or substance abuse. Patients with Fever, Hypo or Hyperthyroidism, Morbid Obesity, Drug Allergy, Severe Diabetes, Urological Diseases were excluded. Categorization of **90** patients in to three groups GroupA : Tramadol -50mg (n = 30);GroupB: Butorphanol-20mg (n =30);GroupC: Clonidine-150mcg (n = 30). Patients were assessed for the improvement in therapy and the time taken from drug administration till the cessation of shivering was accurately noted.Temperature, heart rate, oxygen saturation and blood pressure were monitored at intervals of 10 minutes till the cessation of shivering. Patients were closely monitored for failure of the drug response, recurrence of shivering & adverse effects. Assessment of level of Shivering using Bedside Shivering Assessment Scale.

Grade 0: No shivering

Grade 1: Shivering in face and head – MILD

Grade 2: Shivering in face and upper extremities – MODERATE

Grade 3: Shivering in face and lower extremities – SEVERE

Grade 4: Shivering with whole body

RESULTS

A total of 90 patients were included in the study (N=90). Out of which 75 were given spinal 15 were given general anaesthesia.The study population was categorized into three groups based on drug administration.

Table 1: Distribution of study participants based on age group

AGE(yrs)	NO. OF PATIENTS			TOTAL
	Group – A (n=30)	Group – B (n=30)	Group – C (n=30)	
18-25	15(50%)	18 (60%)	16(53.33%)	49
26-30	6(20%)	4(13.33%)	14(46.66%)	24
31-40	6(20%)	3(10%)	0	9
41-50	2(6.66%)	3(10%)	0	5
51-60	0(0%)	1(3.33%)	0	1
>60	1(3.33%)	1(3.33%)	0	2

- Maximum number of patients (49) fell under the category of 18 - 25 class intervals.
- While the minimum number fell under 51 - 60 age group.

Table 2: Distribution of the total population based on surgery performed

TYPE OF SUR-GERY	NO. OF PATIENTS			TOTAL
	Group – A (n=30)	Group – B (n=30)	Group – C (n=30)	
LSCS	16	20	19	55
LSCS WITH TUBEC-	9	6	4	19
DUODENAL ULCER	1	1	0	2
LOWER BRONCHITIS	1	1	0	2
CARCINOMA OF	1	0	0	1
HERNIA	2	2	0	4

- Lower segment c-section surgeries were done more than other surgeries.
- Out of 90 patients 55 (61.11%) were fell under **LSCS.**

HEMODYNAMIC PARAMETERS IN PATIENTS

BLOOD PRESSURE:

Table 3: Comparison of Blood Pressure measurements of the three groups

DRUG	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE
Group – A (Tramadol)	120.20 ± 7.63115	79.6667 ± 8.28931
Group –B (Butorphanol)	119.23 ± 6.55314	79.3667 ± 5.61699
Group – C (Clonidine)	97.6774 ± 7.49839	73.0968 ± 6.08471

- This table shows blood pressure in group-A and group-B remain in the normal range which shows that tramadol and butorphanol do not affect blood pressure.
- The patients in group-C showed below the normal values and therefore it can be inferred that clonidine can lead to low blood pressure and this was found to be Statistically significant using one – way ANOVA ($P<0.05$).

HEART RATE

Table 4: Comparison of Heart Rate of the three groups

DRUG	HEART RATE
Group – A (Tramadol)	83.2333 ± 8.47179
Group – B (Butorphanol)	82.0333 ± 7.95454
Group – C (Clonidine)	62.8667 ± 6.47932

- The Heart Rate in Group – A and Group – B is in the normal range which shows that tramadol and butorphanol does not show any affect heart rate.
- The patients in group – C showed reduced heart rate and this was found to be statistically significant using one – way ANOVA ($P<0.05$).

OXYGEN SATURATION

Table 5: Comparison of Oxygen Saturation of the three groups

DRUG	OXYGEN SATURATION (SpO_2)
Group – A (Tramadol)	97.9000 ± 1.72906
Group – B (Butorphanol)	98.4000 ± 1.45270
Group – C (Clonidine)	98.366 ± 7.35146

- Oxygen Saturation was found to be similar in all the three groups.

AXILLARY TEMPERATURE

Table 6: Comparison of Axillary Temperature of the three groups

DRUG	AXILLARY TEMPERATURE
Group – A (Tramadol)	99.5333 ± 1.23326
Group – B (Butorphanol)	99.7767 ± 1.79879
Group – C (Clonidine)	99.0367 ± 1.92058

- Temperature was found to be in normal range.

TIME TAKEN TO CONTROL SHIVERING AFTER DRUG ADMINISTRATION

Table 7: Comparison of time taken to control shivering in all the three groups

TIME TAKEN TO CONTROL SHIVERING	NO. OF PATIENTS		
	Group – A n=30	Group – B n=30	Group – C n=30
Within 10min	1(3.33%)	18(60%)	1(3.33%)
Between 11 to 20 mins	10(33.3%)	7(23%)	8(26.66%)
Between 21 to 30 mins	9(30%)	3(10%)	9(30%)
Between 31 to 40 mins	2(6.66%)	2(6.66%)	5(16.66%)
Between 41 to 50 mins	6(20%)	0	6(20%)
Between 51 to 60 mins	0	0	0
More than 60mins	2(6.66%)	0	1(3.33%)
Recurrence of shivering	3(10%)	1(3.33%)	0

- Time taken to control shivering was faster with butorphanol i.e., within 10minutes (60%). Out of which few patients showed recovery within 2 – 3 minutes.
- The time taken to control shivering in group – A and group – B was within 11 – 30 minutes (approx. 60%).
- There was no recurrence of shivering in group – C whereas 1 patient in group – B and 3 patients in group – A showed recurrence.

INCIDENCE OF ADVERSE DRUG REACTIONS

Adverse drug reactions were assessed through Naranjo Causality assessment scale.

Table 8: Comparison of incidence of adverse drug reactions in all the three groups

ADVERSE DRUG REACTIONS	GROUP - A N = 30	GROUP -B N= 30	GROUP – C N=30
Sedation	0	9(30%)	0
Itching	0	2(6.66%)	0
Nausea	13 (43.3%)	0	4(13.33%)
Vomiting	6(20%)	0	0
Hypotension	0	0	20(66.6%)

- Incidence of Adverse drug reactions was higher in group-A with nausea (43%) and vomiting (20%) being the commonly reported ADR's.
- Patients of clonidine reported hypotension with significant affect on systolic blood pressure.
- Sedation was the most common ADR in group – B patients.

DISCUSSION

Anaesthesia carries two dreaded side effects, one is hypotension and another is shivering. Ironically every anaesthesiologist and allied persons are well prepared to deal with the hypotension and every pre and Para operative arrangement and precautions are taken to counter it because it may become life threatening, whereas shivering is least taken care off unless it appears, though it happens in 40-70% of cases, and is very agonizing to the patient. Various pharmaceutical agents are being used to treat it though the most effective with least ADR's is not yet determined. The patients were divided into three groups based on the drug administration. The drugs administered here are Group-A (n=30) receiving tramadol 50 mg IV, Group -B (n=30) who received butorphanol 20mg IV and Group-C (n=30) comprised of the patients who received Clonidine 150mcg intravenously.

Clonidine is a centrally acting selective α2 agonist and apart from being well known for its sedative effects, it is an established anti shivering agent. Tramadol is an opioid analgesic with opioid action preferably mediated through 'μ' receptors with minimal effect on kappa and delta binding sites. Tramadol also activates the mononergic receptors of the descending neuraxial pain inhibiting pathway. The mechanism of

anti-shivering actions of Tramadol is not fully understood as yet though it is probably mediated through its opioid or serotonergic and noradrenergic activity or both. Butorphanol, an easily available opioid, acts through k and μ receptor agonistic modulation.

The study population showed more number of patients in the age group of 18 – 25 years with female predominance and this is because lower segment C- section was the highest performed surgery in this study site.

Tramadol was given at a dose of 50mg in this study which was in accordance with the study conducted by **Mohta *et al*** [28] which showed three doses of Tramadol, i.e., 1mg, 2mg and 3mg per kg were effective for prophylaxis of shivering. Time taken to control shivering is fast in Group – B when compared with tramadol and clonidine which is similar to the study conducted by **Dr. Niranjan Kumar Verma *et al.*** [23] Recurrence of shivering was seen in Group – A and Group – B which is in accordance with the study conducted by **Dr. Niranjan Kumar Verma *et al.*** [23] The patients in Group – C did not show any recurrence which is in contrast to the study conducted by **Sheikh Mustak Ali *et al.*** [21] Axillary Temperature and Oxygen Saturation did not show much variance on administration of the drugs which is in contrast to the study conducted by **Astha Palan *et al.*** [19] A marked decrease in the systolic blood pressure and heart rate with clonidine was observed which is similar to **Dr. Niranjan Kumar Verma *et al.*** [23] Both tramadol and butorphanol did not have much affect on hemodynamic parameters of the patients which is similar to the study conducted by **Maheshwari *et al.*** [26]

Patients on tramadol reported very severe nausea and vomiting that require further management and this was in accordance with the study conducted by **Mohta *et al.*** [28] Butorphanol is associated with sedation which is similar to the study conducted by **Joshi *et al.*** [20]

CONCLUSION

The study drugs tramadol, butorphanol and clonidine are effective to control shivering. Tramadol is better when compared to clonidine due to lesser sedation and no hypotensive effect, but nausea and vomiting are more common and severe with tramadol. Though clonidine is effective in controlling shivering, it causes a prominent reduction in blood pressure and heart rate which makes its use difficult in all the age groups and also for the patients with cardiovascular co-morbidities. Butorphanol is better when compared to tramadol and clonidine in treating shivering because of its higher success rate and fewer side effects. Butorphanol was found to be safe and effective in prevention and treatment of post operative shivering with no hemodynamic, cardio respiratory side effect in comparison to Clonidine and Tramadol.

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