

Prevention of Postoperative Shivering A Comparative Study between Pethidine & Dexamethasone

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ABSTRACT

Background: The incidence of postoperative shivering-like tremor is reportedly approximate 40%, but it now appears to be less as more patients are kept normothermic and opioids are administered more frequently and in larger doses than in the past. It is a potentially serious complication, with oxygen consumption increased roughly in proportion to intraoperative heat loss.prevention of shivering is important, especially in elderly and ischemic heart disease patients. The aim of this study is the prevention of post-operative shivering using dexamethasone and pethidine in a comparative way. Patients & Methods: 45 patients who were candidates for surgery under general anesthesia and randomly divided into three groups: Group A received normal saline 0.9%, Group B received dexamethasone 0.15 mg/kg and Group C received pethidine 25mg.Induction and maintenance of anesthesia for all patients were similar. Body core Temperature of patients was measured over 5 occasions (basal, post-induction, end of induction, starting recovery, end of recovery), In recovery, patients were monitored for visible shivering.All data were statistically analyzed by analysis of variance (ANOVA) and Chi-square tests. Results: This study had shown that there were no significant differences regarding gender, age, duration of surgery and anesthesia, extubation time, duration of recovery, and basic clinical characteristics in the mentioned three groups.

- Nine cases (60.0%) of placebo group had postoperative shivering.
- One case (6.7%) in dexame has one group had postoperative shivering.

•Four cases (26.7%) in pethidine group had postoperative shivering.

The difference between the last two groups and the first one was significant.**Conclusion:**The prevention of post-operative shivering can be achieved using either:pethidine or dexamethasone, with the preferably use of dexamethasone.

Keywords: Dexamethasone, pethidine, general anesthesia, surgery, shivering

Introduction:

Postoperative shivering occurs in 5-65% of patients recovering from general anesthesia and in about 30% of volunteers undergoing epidural anesthesia.^(1,2,3) The use of Propofol reduces the incidence of postoperative shivering compared with thiopental.

the mainstay of symptomatic treatment of postoperative shivering is radiant heating, forced air rewarming or pharmacological methods as shown on table 1.⁽¹⁾

Table 1: drug treatment of post-anesthetic shivering

Pharmacological Treatment of Post-anesthetic Shivering
Pethidine 0.33 mg/kg (other opioids to a lesser extent)
Doxapram 1.5 mg/kg
Clonidine 2 mg/kg
Methylphenidate 0.1 mg/kg
Physostigmine 0.04 mg/kg
Ondansetron 0.1 mg/kg

Drugs such as dexamethasone reduce the gradient between skin and body core temperature. It could reduce shivering by regulating immune responses⁽⁶⁾ Shivering resembling febrile shakes and chills may be related to the activation of the inflammatory response and release of cytokines. ^(7,8)Cytokines may induce peripheral vasoconstriction, fever, and chills.

^(7,8) Because it can modify the inflammatory response, prevent postoperative fever, and improve peripheral circulation, dexamethasone 0.15 mg/kg has been used in this study for reducing the incidence of postoperative shivering.

The aim of this study is to compare two drugs of pethidine and dexamethasone in terms of reducing the post-operative shivering.

Dexamethasone:

Dexamethasone is a synthetic gluco-corticosteroid which has minimal mineralocorticoid activity. <u>Anti-inflammatory EFFECTS</u> Dexamethasone (0.5mg/kg up to 8mg) has consistently decreased edema compared to placebo and also reduced time to first oral intake over a number of studies.

Adverse Effects

Adverse effects reported in association with dexamethasone include perineal pain associated with intravenous injection⁽²⁴⁾.

The incidence of this complication is unclear, but could range from 25-100%, with females at increased risk compared to men $^{(25)}$.

The speed of injection and the dose may also influence severity.

This discomfort ranges from an 'itching' sensation to 'excruciating', lasting 25-30 seconds.

Dexamethasone administered at the conclusion of anesthesia has effects on late Nausea and vomiting which supports this theory ⁽²⁶⁾.

Avascular necrosis of both the humeral and femoral heads is a known complication of steroid use.

It has been reported after dexamethasone use as part of chemotherapy regimens or to prevent chemotherapy induced nausea and vomiting⁽²⁷⁾. Cumulative dose of dexamethasone was an independent risk factor for this complication.

It has also been reported in neurosurgical patients after 'short' courses (days rather than weeks) of dexamethasone.1

Pethidine:

Pethidine (INN, AAN, BAN) or meperidine (USAN) is a once popular synthetic opioid analgesic of the phenylpiperidine class.^(29,30,31)

Synthesized in 1939 as a potential anticholinergic agent by the German chemist Otto Eislib, its analgesic properties were first recognized by Otto Schaumann while working for IG Farben, Germany.Pethidine is indicated for the treatment of moderate to severe pain, and is delivered as a hydrochloride salt in tablets, as a syrup, or by intramuscular, subcutaneous, or intravenous injection.

Mechanism of action:

Main article: Opioid

Like morphine, pethidine exerts its analgesic effects by acting as an agonist at the μ -opioid I receptor.

Pethidine is often employed in the treatment of postanesthetic shivering.

The pharmacologic mechanism of this antishivering effect is not fully understood, but it may involve the stimulation of K-opioid receptors.

Pethidine has structural similarities to atropine and other tropane alkaloids and may have some of their effects and side effects.

Adverse Effects:

The adverse effects of pethidine administration are primarily those of the opioids as a class: nausea, vomiting, sedation, dizziness, diaphoresis, urinary retention, and constipation. Unlike other opioids, it does not cause miosis.

Overdose can cause muscle flaccidity, respiratory depression, obtundation, cold and clammy skin, hypotension, and coma.narcotic antagonist such as naloxone is indicated to reverse respiratory depression, serotonin syndrome has occurred in patients receiving concurrent antidepressant therapy with selective serotonin reuptake inhibitors or monoamine oxidase inhibitors.

Convulsive seizures sometimes observed in patients receiving parenteral pethidine on a chronic basis have been attributed to accumulation in plasma of the metabolite norpethidine (normeperidine).

Fatalities have occurred following either oral or intravenous pethidine overdose.

Interactions:

Pethidine has serious interactions that can be dangerous with monoamine oxidase inhibitors (e.g., furazolidone, isocarboxazid, moclobemide, phenelzine, procarbazine, selegiline, tranylcypromine).

Patients & Methods:

Study desian and settinas

The study was conducted in the elective operation theatres in Al-Imamain Al-Kadhumain Medical City, Baghdad, Iraq, from 15th of October 2014 till 15 of January2015.

This study is randomized, double-blinded clinical trial.

The patients were prepared for elective surgery (general, orthopedic, and ENT surgeries), and gynecological surgeries

The patients were in groups of ASA I and II, while none of the patients had taken medication before surgery.

Ethical consideration:

Approval were obtained from Iraqi Scientific Council of Anesthesia & ICU. Written consents had been taken from the patients regarding the study.

Participants

In this study 45 patients were candidate to elective surgery, were randomly divided into three groups of normal saline (10 ml), pethidine (25 mg, the volume of which is brought to 10 ml), and dexamethasone (0.15 mg/kg the volume of which is brought to 10 ml).

All three drugs were prepared in 10 cc syringes of the same type and the anesthetist responsible for the control and registration of the clinical symptoms was blinded to the study drugs.

The inclusion criteria

- Elective operation
- ASA class I and II
- Age 18-55 years.

- Weight between 50 and 100 kilograms.

The exclusion criteria:

Cases with allergy to medications used in the study. Drug abuse.

Long duration surgery.

Neuromuscular disease (because of disturbing of evaluation of shivering grading in these patients) History of taking alpha-2 blocker drugs.

Patient had taken any pre-operative medication. Operations require blood transfusion (intra operative or post-operative), or large amount of i.v. fluids due to hypotension.

Anesthesia protocol

Induction of anesthesia: had been done in the same way for the three groups by injecting fentanyl 2u.g/kg, midazolam 20u.g/kg, Propofol 2-2.5mg/kg (sleeping dose), and vecuronium 0.1 mg/kg.

After intubation:

anesthesia maintained with sevoflurane 2% in oxygen, muscle relaxation maintained, with vecuronium 0.01 mg/kg as intermittent doses and the Patients were mechanically ventilated during surgery, i.v. fluid, and standard Monitoring (including body core temperature).

Reversal:done using neostigmine 2,5mg. with atropine lmg.

Study procedure

Before induction of anesthesia name, age, gender, patient identification number, weight, ASA class, type of operation and initial vital signs (including basal body temperature) all were recorded.

The study drugs were administered after induction of anesthesia, intubation and before surgical incision made.The blinded technique was ensured by preparing the medication by my colleague, so he prepared for us 3 syringes with 10 ml of either normal saline, pethidine or dexamethasone, without our knowledge of the content.

The systolic and diastolic blood pressure and the patients' heart rate were recorded. For all patients, the core temperature was measured and recorded through nasal cavity (thermometer probe put in sterile glove & inserted through the naris to the nasal cavity), and the skin temperature was measured through forehead skin by digital thermometer every 5 min interval in operating room and recovery and values at <u>baseline</u>, post induction, end of operation, <u>starting recovery</u>, and <u>end of recovery</u> were used for analysis.Operation room temperature was maintained during the surgery between 22 and 24°C. Anesthetic time was defined from the start of induction to the time when the anesthetic, including sevoflurane, was discontinued.

At the end of surgery, neuromuscular blockade was reversed with neostigmine and atropine

The subsequent period until the patient responded to verbal command was recorded as the recovery time.In whole the recovery phase, the patients were monitored by a trained anesthesia nurse responsible for the recovery and he recorded shivering as soon as it happens,This nurse, who was not informed about the kind of prescribed medication, registered shivering occurrence and its severity.The shivering was graded using a five-point scale as shown in table 2:Data analysis

Table 2: shivering grading

Clinical symptoms	Shivering grading
Without shivering	0
Occurrence of one or more of the following criteria: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other specific cause, but without visible muscular contractions	1
Contraction observed limited to a bunch of muscle contraction	2
Contraction observed in more than one group of muscles	3
The whole body clear muscular activity	4

Statistical package for social science version 20 (SPSS 20) was used for both data entry and data analysis.

Continuous variables were presented as mean \pm SD and discrete variables presented as number (%), including demographic data and temperature values over time within groups, were analyzed by using repeated measures analysis of variance.

One-way analysis of variance was used to analyze differences among the groups.

Incidence of shivering was analyzed by using Chisquare test.

Data were expressed considering P-value <0.05 being statistically significant.

Results:

There were no significant difference (P >0.05) between patients regarding age, gender, type of surgery, duration of surgery, and basic clinical characteristics (systolic and diastolic blood pressure, and heart rate, as shown in table 3

<u>Table 3:</u> Comparison of three groups of patients by age, gender, duration of operation, and the type of surgery. Values have been expressed as mean±SD

	Normal saline (n=15)	Dex amethasone $(n=15)$	Pethidine (n=15)	n r
Age(years)	32.66(7.2)	30.93 (13.1)	38.86(11.5)	0.124
Gender(M/F)	3/12	6/9	8/7	0.174
Duration of operation (m)	44.0 (20.9)	37.0(12.3)	42.0 (18.7)	0.543
Type of surgery:				
General (%)	4(25.0)	5 (31.2)	7 (43.8)	
Orthopedics (%)	2 (20.0)	3 (30.0)	5 (50.0)	
Gynecology (%)	8 (66.7)	3 (25.0)	1 (8.3)	
ENT (%)	1(14.3)	4(57.1)	2 (28.6)	

(systolic and diastolic blood pressure, and heart rate, as shown in table 3 We found that there was a reduction in core body temperature as it was recorded in all four stages, as shown in figure 1, this figure also shows that the basic values was higher in control group than the other two groups (P < 0.05).

The incidence of postoperative shivering, in the dexamethasone group, one patient (6.7%) had shivering in the recovery period, this rate compared with the incidence of postoperative shivering in 9 patients (60.0%) of control group and 4 patients (26.7%) of pethidine group shows a significant difference (P=0.006) as shown in table4

Table 4: Comparison of the incidence of shivering in three groups of patients

	Normal saline %	Dexamethasone %	Pethidine %	P-value
shivering	9(60.0)	1(6.7)	4(26.7)	0.006

Discussion:

The post-operative shivering concerned as one of the most important postoperative complication as it may cause sympathetic stimulation, increased production of carbon dioxide, and increased oxygen consumption, i.e. harming the patient.So, it is important to have a preventive measures for such a complication. post-operative shivering, as in 1998 were a dose of 0.6 mg/kg dexamethasone used before induction of anesthesia that can significantly reduce the incidence of shivering (13.1% compared with 33.3% of control group), p), and in 2003, a study was performed on patients undergoing heart valve replacement surgery, where a 100mg dexamethasone were used as a pretreatment that showed a reduction in postoperative shivering incidence ⁽¹⁰⁾.Regarding our study which concerned with the prevention of post-operative shivering using both pethidine and dexamethasone, and shown a significant effect of pethidine on preventing shivering (although mechanism of pethidine is not completely understood, it probably acts directly on the thermoregulatory center or via opioid receptors⁽¹²⁾.

and a significant effect of dexamethasone (through decreasing the temperature gradient between core and skin via its anti-inflammatory action and inhibition of the release of vasoconstrictors and pyrogenic cytokines ⁽¹³⁾. dexamethasone with a dose of 0.1mg/kg that revealed lower results than ours (14).

We used a dose of dexamethasone larger than that used in 1998 study to get a better result, and lower dose than 2003 study to prevent the drug side effects.In similar studies, other drugs have been used to reduce postoperative shivering, most of which cause different problems for patients.

Conclusion:

According to this study, administrating dexamethasone in a dose of 0.15mg/kg post intubation and prior to surgical incision, preventing the post-operative shivering in an incidence from 60,0% to 6.7%, superior to the use of pethidine 25mg, especially in patients with hemodynamic instability.

Recommendation:

Based on this clinical trial, we recommend to use dexamethasone in a dose of 0.15mg/kg post intubation, as a preventive measure for post-operative shivering instead of pethidine as it is being available, cheap and has excellent safety profile.

We also recommend to do another clinical trials regarding variable dexamethasone dosing to get a better (optimal) dose in preventing post-operative shivering.

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