

**Prophylactic use of intravenous tramadol vs  
intravenous nalbuphine for control of postspinal  
shivering after knee arthroscopy: a randomized double-  
blind placebo controlled trial**

**Thesis**

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## INTRODUCTION

One of the most common complications encountered by an anesthesiologist during the perioperative period is shivering. Shivering occurs during both general anesthesia and regional anesthesia. The incidence of shivering reaches 33% in patients undergoing surgery under regional anesthesia. A number of factors including age, duration of surgery, temperature of the operating room and the infusion solution are risk factors for hypothermia and shivering (*Bhattacharya et al., 2003*).

Shivering causes patient discomfort because of severe muscle movements. It also induces elevated blood pressure and tachycardia, aggravates wound pain by stretching incision, increases intra ocular pressure and increases intracranial pressure. Shivering may also increase tissue oxygen demand by as much as 150% and is accompanied by increase in minute ventilation and cardiac output to maintain aerobic metabolism. This eventually leads to increased oxygen consumption and increased carbon dioxide synthesis that results in an increased pulmonary ventilation capacity and cardiac workload, and an increase in the metabolic rate by up to 400%. Shivering may also interfere with the monitoring of patients by causing artifacts of electrocardiography, blood pressure and pulse oximetry (*Sajedi et al., 2008*).

The proposed mechanism for shivering after spinal anesthesia is the re-distribution of body heat from the center of the body to the periphery. As a result, the afferent temperature signal in the anesthetized area is not transmitted to the thermoregulation center located in the hypothalamus. This causes a disruption of normal temperature regulation, resulting in a decreased core temperature and increased shivering (*Sagir et al., 2007*).

Various drugs have been used to prevent and treat Shivering in patients who receive spinal anesthesia. Among these drugs tramadol and nalbuphine (*Pawer et al., 2011*).

Nalbuphine is a semisynthetic agonist-antagonist opioid,. It acts as an agonist at kappa receptors and has a high affinity for these receptors. While the mechanism of action for nalbuphine is still up for debate, studies have found this drug effective for the treatment of shivering (*Kyokong et al., 2007*).

Tramadol is a  $\mu$ -opioid receptor agonistic drug that has a modulatory effect on central mono-aminergic pathways, and thus inhibits the neuronal uptake of noradrenaline/serotonin and encourages hydroxytryptamine secretion which resets the body temperature regulation center. It has gained a reputation in many clinical trials for the control of shivering (*Zahedi, 2004*).



## **AIM OF THE WORK**

The aim of this work was to compare the efficacy of intravenous tramadol and intravenous nalbuphine for prevention of post spinal shivering in patients undergoing knee arthroscopy.

## POST-ANESTHETIC SHIVERING

**P**ost-anesthetic shivering refers to spontaneous, involuntary, rhythmic, oscillating and tremor-like muscle hyperactivity that increases metabolic heat production up to 600% after general or regional anesthesia (*Ozaki et al., 2009*).

Postoperative shivering is a common complication following regional anesthesia. Even a small decrease of 0.5°C may induce shivering. Patients often identify feeling cold as one of the most unpleasant aspects of their treatment, sometimes worse than any pain associated with the procedure. Shivering is not only subjectively unpleasant but is physiologically stressful because it elevates blood pressure, heart rate, oxygen consumption, and plasma catecholamine concentrations. Moreover, shivering may aggravate pain and hinder wound closure by simply stretching surgical incisions (*Buggy and Crossley, 2008*).

Emergence from even brief general anesthesia is sometimes also associated with shivering. Although the shivering can be part of nonspecific neurological signs (posturing, clonus, or the Babinski's sign) that are sometimes observed during emergence, shivering is most often associated with hypothermia and volatile anesthetics. Regardless of the mechanism, shivering appears to be more common after longer durations of surgery and the use of greater concentrations of a volatile agent (*Morgan et al., 2013*).

Occasionally it is intense enough to cause hyperthermia (38–39°C) and metabolic acidosis, both of which promptly resolve when the shivering stops (*Morgan et al., 2013*).

Postoperative shivering is also a common complication following regional anesthesia both spinal and epidural anesthesia lower the shivering threshold and vasoconstrictive response to hypothermia (*Horn et al., 2003*).

### **Etiology of post-anesthetic shivering**

**Thermogenic:** of all complications of hypothermia, reported shivering is the most frequent and probably the most familiar even a small decrease of 0.5°C may induce shivering (*Horn et al., 2003*).

**Non-Thermogenic:** Other causes of shivering during anesthesia are sepsis, drug allergy, or a transfusion reaction (*Morgan et al., 2013*).

### **Physics of Heat Transfer**

Through several processes, including radiation, conduction and convection, and evaporation Heat loss occurs primarily from the skin of a patient to the environment, of these, radiation is most significant and accounts for 60% of total heat loss. Radiation is emitted in the form of infrared rays, a type of electromagnetic wave. From core body tissues is transported in blood to subcutaneous vessels, where heat is lost

to the environment through radiation. This manner of heat loss is the basis for the familiar technology used to sense and identify the locations of persons in buildings who are out of normal view. Radiation is the major source of heat loss in most surgical patients (*Guyton and Hall, 2006*).

About 22% of heat loss occurs by evaporation, as energy in the form of heat is consumed during the vaporization of water. Water evaporates from the body even when not sweating, but mechanisms that enhance sweating increase evaporation. As long as skin temperature is greater than its surroundings, radiation and conduction provide heat loss. At very high environmental temperatures, these processes cannot work, and evaporation is the only manner in which heat can be dissipated. This generally is not the case in the clinical setting (*Hanania and Zimmerman, 2005*).

Conduction refers to loss of kinetic energy from molecular motion in skin tissues to surrounding air. Water absorbs far more conducted heat than air, and this accounts for more rapid hypothermia during accidental drowning, as well as the efficacy of water baths to cool hyperthermic patients. For this to be effective, warmed air or water must be moved away from the skin surface by currents, a process called convection. This accounts for the cooling effect of wind and laminar air flow in many surgical suites. Conduction and convection account for 15% of body heat loss (*Morgan et al., 2013*).

## **Thermoregulation**

The processing of thermoregulatory response has three components: Afferent thermal sensing, Central regulation and Efferent responses. Together they work to maintain normal core body temperature (*Bhattacharya et al., 2003*).

### ▪ **Afferent**

Thermal sensing Signals from cold receptors (excited by temperatures below a set threshold) travel along a delta fibers and Signals from warmth receptors (excited by temperatures above threshold) are traveled along c fibers Thermal inputs get integrated at the level of spinal cord eventually it arrives at the hypothalamus, the primary thermoregulatory control center in mammals (*Pehl et al., 2000*).

### ▪ **Central regulation**

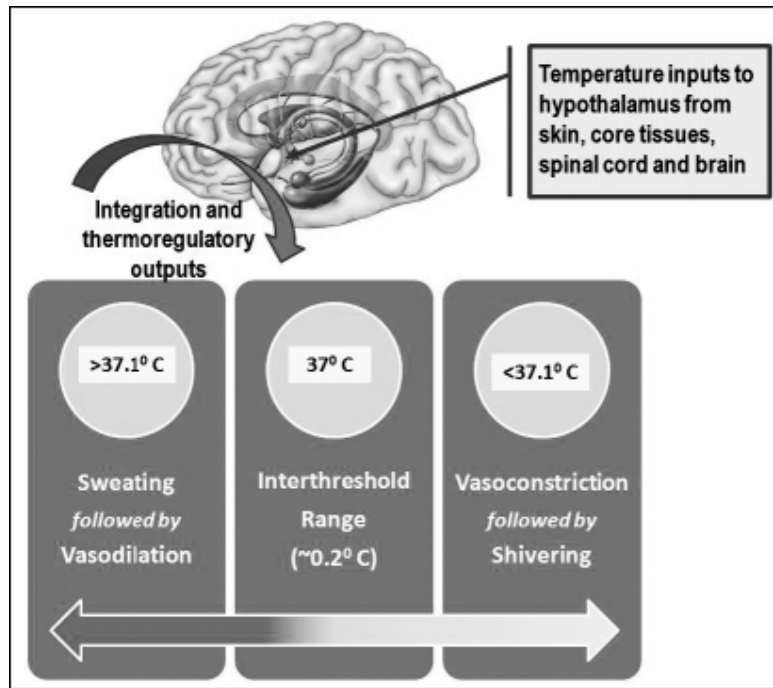
Preoptic region of the anterior hypothalamus is the dominant autonomic thermoregulatory controller in mammals (*Bhattacharya et al., 2003*).

It is unclear how the body establishes the temperature threshold, but its appear to involve several neuro transmitters including dopamine, norepinphrine, acetylcholine, factors such as food intake thyroid dysfunction menstrual cycle infection, circadian rhythm and other drugs are known to alter temperature thresholds (*Guyton and Hall, 2009*).

▪ **Efferent responses**

Behavior is the most effective response for thermoregulation. This includes dressing appropriately, modifying environmental temperature, assuming bodily positions that diminish or enhance heat loss, and increasing voluntary movement to generate heat production (*Buggy and Crossley, 2000*).

As temperature receptors transmit information to the hypothalamus, it is integrated and compared with threshold settings. Values above or below these thresholds determine the efferent response that is generated. Efferent outputs from the hypothalamus regulate body temperature by altering subcutaneous blood flow, sweating, skeletal muscle tone, and overall metabolic activity (*Sessler, 2008*).



**Figure (1):** Hypothalamic thermoregulation. Temperature inputs to the hypothalamus are integrated and compared with threshold temperatures that trigger appropriate thermoregulatory responses. Normally these responses are initiated at as little as 0.1°C above and below normal body temperature of 37°C (98.6°F). Therefore the difference between temperatures that initiate sweating versus those initiating vasoconstriction is only 0.2°C. This is defined as the interthreshold range and represents the narrow range at which the body does not initiate thermoregulatory efforts (*Sessler, 2008*).