# Comparison of the Effects of Anesthesia with Isoflurane and Total Intravenous Anesthesia on the Intensity of Body Temperature Reduction during Anesthesia and Incidence of Postoperative Chills

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***Received: 3 Aug. 2010; Received in revised form: 22 Aug. 2010; Accepted: 15 Sep. 2010***

**Abstract-** This study compared the effects of anesthesia with isoflurane and TIVA (total intravenous anesthesia) on the intensity of body temperature reduction during anesthesia and incidence of chills after lumbar disc surgery. The study was done as a single blinded randomized clinical trial. From 60 patients who underwent lumbar disc surgery, 30 subjects were placed in isoflurane group and 30 in the TIVA group. Maintenance of anesthesia was done with isoflurane (MAC=0.8-1) and $N_2O$ 50% in isoflurane group and in TIVA group with propofol at the dose of 100-150 mg /kg body weight /minute and remifentanil at the dose of 2.0 mg /kg body weight/minute. Chills rate was recorded in recovery room. Changes in body temperature, body surface temperature, systolic blood pressure, diastolic blood pressure and heart rate showed no significant difference between the two groups before and after induction and at different times during the operation ($P$<0.05). Chill rate was not significantly different between the two groups ($P$<0.05). It seems that TIVA (remifentanil at the dose of 2.0 µg/kg body weight/minute in combination with propofol at the dose of 100-150 µg/kg body weight/minute) and 0.81 MAC isoflurane–$N_2O$ 50% can be used as a safe method of anesthesia in patients with good tolerance lumbar back disc surgery without hypothermia, chills and considerable hemodynamic changes.



*Acta Medica Iranica* 2011; 49 (7): 425-432.

**Keywords:** Total intravenous anesthesia; Isoflurane; Chills; Body temperature

## Introduction

Compounds of anesthetic drugs disrupt regulation of body temperature and anesthesiologists are often facing adult patients who suffer from lack of body heat balance during surgery (1). Compounds of anesthetic drugs lead to impaired regulation of body temperature and expose surgical patients to cold environments (2). According to Pickering's statement in 1956 AD, the most effective cooling system in humans is anesthesia (2). Santorio discovered the clinical value of body temperature in 1646 AD, after nearly two centuries body temperature was recognized as a key parameter by Wunderlich. Importance of body temperature remained unknown till the first half of 1960 until a case of malignant hyperthermia was observed (2). Postoperative patients often suffer from cold; even in patients with normal central body temperature, reducing skin temperature significantly leads to pain and discomfort in patients. Hypothermia is associated with unpleasant consequences during the postoperative period. Body temperature often decreases in patients under anesthesia. In long surgeries such as thoracic and abdominal surgery patients are controlled in terms of the incidence of severe hypothermia (3,4) and side effects (4-6). Hypothermia is associated with complications such as wound infection, prolonged hospitalization, intraoperative bleeding, application allogeneic transfusion, cardiac events, ventricular tachycardia after surgery, urinary nitrogen excretion, increased recovery time after surgery, pain, discomfort and chills. Among the complications of hypothermia, chills are known as an important complication. Chills is a complex response of at least three different parts of muscle activity. Chills almost occurs in 40% of patients after general anesthesia recovery with no reason, in 50% with central temperature of 35.5°C and in 90% with central temperature of 34.5°C. Chills is accompanied by high

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adrenergic activity (7), pain and discomfort (8) in patients, and some patients consider the feeling of cold as worse than the pain of surgery (2). With increasing doses, opioids, intravenous propofol, combinations of general anesthesia lead to increase heat response threshold and similarly reduce the vasoconstriction and chills thresholds in a linear manner. Volatile anesthetic compounds such as isoflurane and desflurane reduce threshold the response to cold temperatures in a nonlinear mode. Years ago, injectable drug use for induction of anesthesia was known as the best protocol (9-11). Propofol is the most common drug used alone or in combination with other drugs in TIVA (Total intravenous anesthesia). Like other opioids, remifentanil reduce the need to isoflurane and propofol (12). In most previous studies, isoflurane is compared with other opioids and none of these studies has been conducted about the effect, tolerability to anesthesia techniques and comparison of isoflurane and TIVA with remifentanil and propofol in prolonged surgeries and neurosurgery. Therefore considering the importance of reducing hypothermia in patients under general anesthesia and reducing the complications of hypothermia and chills after surgery, this study was conducted to compare the effects of anesthesia with isoflurane and TIVA on the intensity of body temperature reduction during anesthesia and incidence of postoperative chills.

## Materials and Methods

This single blinded randomized clinical trial study was conducted among patients who were candidates for lumbar disc surgery referred to Imam Khomeini Hospital during 2007-2009. 60 cases were selected through simple random method (Sequential). Thus all referring subjects who met the criteria were selected until the completion of the sample size. Patients were noticed to participate in a research project in order to assign the consent form. Patients with the following conditions were excluded: patients who did not consent to participate in the study, addiction, patients with the duration of surgery more than 210 minutes, patients who needed intraoperative blood transfusions during surgery, endocrine disorders, renal disorders, hepatitis, uncontrolled hypertension, and mental disorder, history of allergy to propofol or opioids. Then all individuals were randomly divided into to two TIVA (I) and isoflurane (II) groups through block randomization method as a non-blind foursome blocks including 30 patients in each group. Lumbar disc surgery and anesthesia were performed by one surgeon and one anesthesiology resident. Before induction of anesthesia, patients received 5 ml/kg body weight serum and 100% oxygen for three minutes. In these patients, 2 µg/kg body weight fentanyl, 7.5 mg diazepam and 1 mg/kg body weight lidocaine were administered as premedication. Induction of anesthesia was performed with 5 mg/kg body weight thiopental sodium and 0.1 µg/kg body weight pancuronium. Then anesthesia in half of the patients was maintained with isoflurane (0.8-1 = MAC) and $N_2O$ 50%, 1 µg/kg body weight/30 minutes fentanyl, 0.05 µg/kg body weight/hour pancuronium and in the other half with 100-150 µg/kg body weight/minute propofol and 2 µg/kg body weight/minute remifentanil and 0.05 µg/body weight/hour pancuronium. Room temperature, serum injection and fresh gas flow were measured. The central body temperature for each patient through the tympanic membrane, the surface temperature of the body through the dorsal wrist skin, heart rate and blood pressure were measured as well as arterial oxygen saturation before induction of anesthesia, after that and then every half hour until the end of the surgery and at the time of entering the recovery room and 15 minutes after it. Forced expiratory $CO_2$ level after the induction until the end of anesthesia was recorded every half hour. Chills rate was also recorded in recovery. It should be noted that any catheter insertion or injection was not done on the hand if the temperature was measured through its surface.

Central body temperature was measured by CHY110 lasic thermometer and body surface temperature by Braun-Welch Allyn thermoscan thermometer. All information encrypted and was entered to computer memory using SPSS software. In this study 30 subjects were determined for each group by 50% power, $\alpha$=0.05 and $\beta$=0.2. Then comparison of quantitative variables was performed between two groups by t-test and the changes by using repeated measurement ANOVA. Comparison of qualitative variables was done by chi-square test between groups. Statistically $P$<0.05 was considered significant.

## Results

Table 1 shows the comparison of demographic characteristic between the two groups. In this study, changes in central body temperature before and after induction and at various times during operation in the two studied groups are brought in figure 1 which was not statistically significant.

**Table 1.** Demographic data

| | isoflurane (n=30) | TIVA (n=30) | *P* Value |
|---|---|---|---|
| Age | 42.5±11.2 | 42.6±13.4 | 0.983 |
| Sex; Male: Female | 15:15 | 19:11 | 0.297 |
| Weight ;Kg | 75.73±11.6 | 70.03±9.3 | 0.04 |
| Height; cm | 169.26±11.3 | 168.7±7.3 | 0.818 |

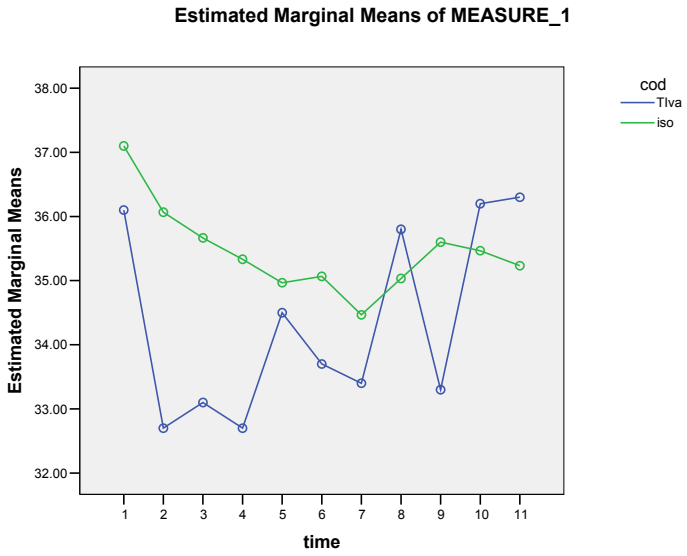


**Figure 1.** Changes in central body temperature before and after induction and at various times during operation in the two groups (*P*=0.490)

Changes in body surface temperature before and after induction and at various times during operation in the two studied groups are brought in figure 2 which was not statistically significant.

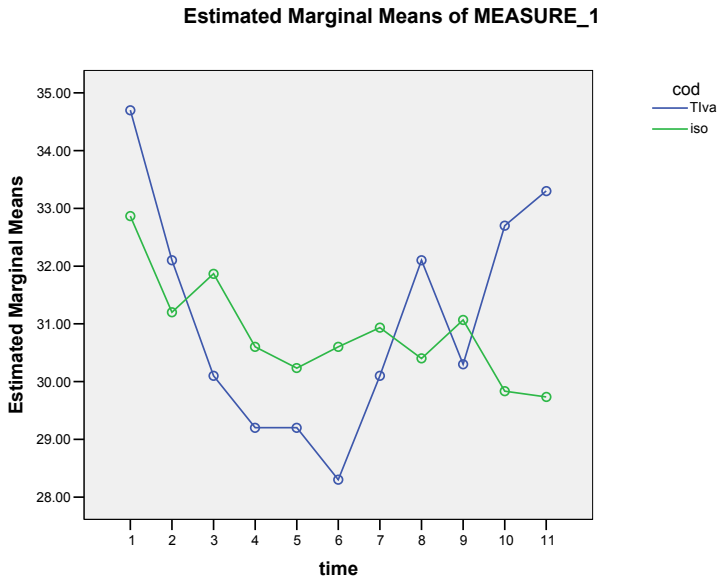


**Figure 2.** Changes in body surface temperature before and after induction and at various times during operation in the two groups (*P*=0.881)

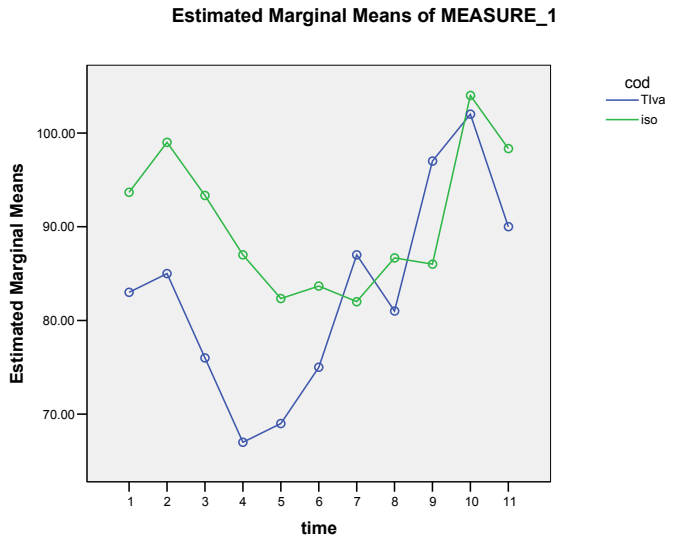


**Figure 3.** Changes in heart rate before and after induction and at various times during operation in the two groups (*P=0.288)*

Changes in heart rate before and after induction and at various times during operation in the two studied groups are brought in figure 3 which was not statistically significant.

Changes in systolic blood pressure before and after induction and at various times during operation in the two studied groups are brought in figure 4 which was not statistically significant.

Changes in diastolic blood pressure before and after induction and at various times during operation in the two studied groups are brought in figure 5 which was not statistically significant.

Comparison of the chills frequency in studied groups is brought in figure 6 which was not statistically significant.

In this study no significant relationship was found between chills and the central body temperature, body surface temperature and surface–central body temperature gradient.

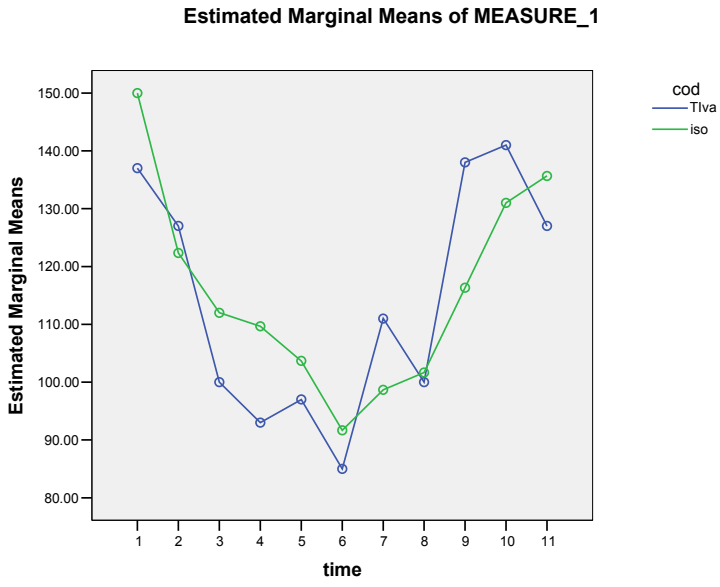


**Figure 4.** Changes in systolic blood pressure before and after induction and at various times during operation in the two groups (*P*=0.931)

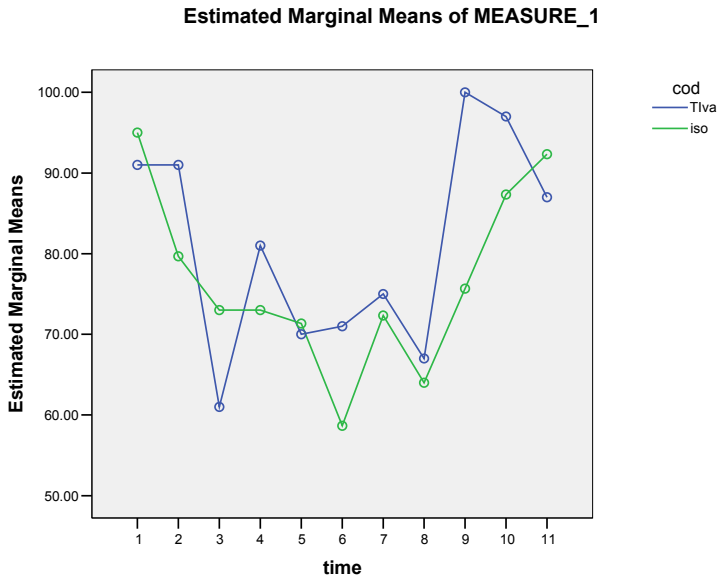


**Figure 5.** Changes in diastolic blood pressure before and after induction and at various times during operation in the two groups (*P*=0.583)

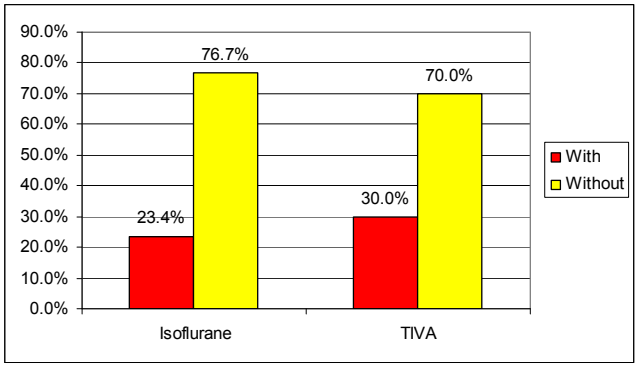


**Figure 6.** Comparison of the chills frequency in the two groups (*P*>0.05)

## Discussion

In the present study, body temperature at various times during the surgery and recovery in the TIVA group was less than that of isoflurane but the difference was not statistically significant between the two groups. Some studies reported that the redistribution of heat from the center to the body surface, reduce body temperature by 1-1.5°C during the first hour of general anesthesia (13). Some studies reported that after the first hour of general anesthesia the central body temperature decreases more slowly. The reduction is linear because the loss of body heat leads to increased metabolic heat production (14). Probably the more slow decrease in central temperature after the first hour of general anesthesia is through vasoconstriction that can clinically be dangerous for patients, because the average temperature and total body heat continues to decrease despite the maintenance of central body temperature. Vasoconstriction alone is effective in keeping the temperature and central temperature rarely decreases more than one degree centigrade during operation. In a study it is reported that vasoconstriction threshold has a negative relationship with isoflurane concentration (15). This finding has been confirmed by the studies as well and in the present study the central body temperature was better in isoflurane-$N_2O$ group. Body surface temperature in the TIVA group was higher than isoflurane at various times during the surgery and recovery, but showed no significant difference. Considering the fact that remifentanil-propofol has synergism effects together, it seems that medications used in TIVA cause more inhibition and

vasoconstriction and due to more vasoconstriction caused by propofol it leads to redistribution of heat from the center to the surface which causes to increase the body surface temperature in TIVA group. In this study, the central- surface body temperature gradient was lower in TIVA group at various times during surgery and recovery that showed no significant difference between the two groups. Considering the pharmacokinetics and pharmaco-dynamic of anesthetic drugs during induction, the maintenance and recovery of anesthesia vary depending on the dose. Also the pharmacokinetics and pharmacodynamic of anesthetic drugs at different surgeries are not the same, it seems that lumbar disc surgery with isoflurane at the dose of 0.8-1MAC-50% $N_2O$ reduces central body temperature less than TIVA.

In this study heart rate, systolic and diastolic blood pressure were higher in TIVA group during induction and recovery, but no significant difference was reported between the two groups. This finding has been confirmed in previous studies as well. Özköse *et al.* (16) and Philip *et al.* (17) reported cardiovascular stability in patients receiving TIVA. Grudmann *et al.* compared anesthesia with desflurane and propofol-remifentanil in lumbar disc surgery and reported that cardiovascular stability was better in TIVA (18). In previous studies no significant difference in patients' hemodynamic status was found between groups. Probably this increase is due the activity of peripheral sympathetic nervous system which leads to increase arterial blood pressure by increasing norepinephrine and vasoconstriction. It seems that remifentanil at the dose of 2.0 µg/kg body weight/minute in combination with propofol at the dose of 100-150 µg/kg body weight/minute causes hemodynamic stability of patients.

In this study arterial oxygen saturation at various times during induction and recovery was lower in the isoflurane -50% $N_2O$ group. Some inhaled drugs appear to lead to changes in oxygen in respiratory system. Probably in the TIVA group due to further reduction of body temperature and metabolism, oxygen consumption by cells is reduced and arterial oxygen saturation has been increased.

In the current study ET $CO_2$ was reduced at various times during induction and recovery in the TIVA group. It is probably due to more decrease in central body temperature in TIVA group, decreased metabolism and more decrease in production of $CO_2$ in the TIVA group.

In the present study patients' hemodynamic status, $O_2$ saturation, and ET $CO_2$ showed no significant difference between the two groups. However due to the rapid metabolism of remifentanil and propofol TIVA group had a better hemodynamic status. Larsen et al in a study reported that in the recovery, return of patients to their normal function in remifentanil-propofol group was faster than those of Suflurane-$N_2O$and Desflurane-$N_2O$ (19,20).

In this study, 26.7% of the patients suffered from chills. Most of them (30%) were in the TIVA group, but between two groups no significant differences were reported. Postoperative chills affect patient's general status so that chills in patients with heart failure leads to increased risk and the need for oxygen (21). Probably in the first stage of patient recovery from anesthesia, with loss of narcotics, the regulation of body temperature is returned quickly and with loss of body heat to less thermal threshold, chills occurs. In this study it seems that rapid metabolization of remifentanil in TIVA group caused to increase chills. Atarashi K et al reported that 1 MAC concentration of sevoflurane and isoflurane reduce the vasoconstriction threshold (22). Ozaki M *et al's* study demonstrated that $N_2O$ impairs thermoregulation less than isoflurane and isoflurane (23). Smith D *et al.* reported that isoflurane without $N_2O$ causes more decrease in body temperature in comparison with enflurane (24). In other studies chills has been reported in a large numbers of patients in the TIVA group after recovery from anesthesia (25,26).

Probably 0.8-1 MAC isoflurane in combination with 50% $N_2O$ reduces vasoconstriction and chills threshold. Probably due to rapid metabolism of TIVA, the inhibitory effect of chills has been removed faster and chills in the TIVA group has been reported more. So after the elimination of inhibitory effect of TIVA and chills, the need for therapeutic interventions in this group is increased.

In this study, ET $CO_2$ levels and room temperature did not show significant correlation with the central body temperature. In contrast Uchida K et al's study showed that environmental hypothermia decrease body temperature followed by redistribution of heat (27). It seems that in the present study room temperature of 25°C was suitable.

In this study, drug regimes in the early hours of anesthesia were associated with fluctuation in central and surface body temperature, heart rate and blood pressure, but gradually remained stable during anesthesia and recovery. Considering the results of this study it seems that in the lumbar disc surgery TIVA (remifentanil at the dose of 2 µg/kg body weight/minute in combination with propofol at the dose of 100-150 µg/kg body weight/min) and 0.8-1 MAC isoflurane -50% $N_2O$ can be used as a safe method of anesthesia with

good tolerance without hypothermia, chills and considerable hemodynamic changes. It is also recommended to the anesthesiologists to monitor patients' vital signs and body temperature carefully for more than 30 minutes in order to improve patients' surgical outcome.

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