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Novel combination techniques for anaesthetic induction to manage perioperative hypothermia: A prospective, randomized, controlled, single blind trial

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Abstract
Background: Intraoperative hypothermia is common issue with serious consequences occurred during anaesthesia. However, less attention has been directed to preventing redistribution hypothermia there is need of effective techniques to develop.
Objective: In this study, we compared three different anaesthetic induction techniques to standard IV propofol inductions (control) in their effect on reducing redistribution hypothermia.
Methods: Elective, afebrile patients, age 18 to 57 years, were randomly assigned to one of four groups (n = 60 each). Group "PROP" was induced with 2.2 mg/kg propofol, Group "INH/100" with 8% sevoflurane in 100% oxygen, Group "INH/50" with 8% sevoflurane in 50% oxygen and 50% nitrous oxide, and Group "Phnl/PROP" with 2.2 mg/kg propofol immediately preceded by 160 mcg phenylephrine. Patients were maintained with sevoflurane in 50% nitrous oxide and 50% oxygen in addition to opioid narcotic. Forced air warming was used. Core temperatures were recorded every 15 min after induction for 1 h.
Results: Compared to control group PROP, the mean temperatures in groups INH/100, INH/50, and Phnl/PROP were higher 15, 30, 45 and 60 min after induction, averaging between 0.29 °C and 1.0 °C higher ($p< 0.001$ for all comparisons). There were statistically significant differences in the mean temperatures between groups INH/ 100 and INH/50, INH/100 and Phyl/PROP, and INH/50 and Phyl/PROP at any time point (all $p< 0.05$). Few patients in three groups had a core temperature >37.5 °C at T60 time point, except PROP group.
Conclusions: The inhalation inductions with sevoflurane or with prophylactic phenylephrine bolus prior to propofol induction reduced the magnitude of redistribution hypothermia by an average of 0.29 to 1.0 °C in patients aged 18 to 57 years.

Keywords: Hypothermia, redistribution hypothermia, anesthesia induction, induction techniques

Introduction

Mild hypothermia is extremely common event during and post anesthesia (general and regional) and surgery due to redistribution of core body heat to the skin surface due to anesthetic-induced vasodilation and depression of hypothalamic thermoregulatory centers [1]. Hypothermia is defined as a core temperature <35 °C [2]. Perioperative hypothermia may produce a multitude of deleterious effects and it should be avoided [3]. Multiple factors contribute to perioperative hypothermia development. Operating room temperature contributes to intraoperative hypothermia primarily through radiant heat loss [4]. Many general as well as neuraxial anesthesia also impairs autonomic temperature control and resulted hypothermia [5, 6].

Propofol is widely used anesthesia but well known to cause a rapid and clinically important temperature reduction due to redistribution hypothermia, typically by about 1.5 °C [7]. While guidelines for perioperative temperature management have been proposed, there are no specific guidelines regarding the best site or best modality for monitoring temperature intraoperatively. It is reported that an inhalation induction can reduce the hypothermia when used instead of intravenous propofol [7]. However, the use of inhalation inductions has not been widely adapted. The Surgical Care Improvement Project (SCIP) has focused institutional efforts on preventing hypothermic complications during and after surgery and suggested the 'end of case' approach to manage intraoperative hypothermia. However, this method fails due to intraoperative deleterious consequences.

Recent advances in anaesthesia suggested to monitor the area under the core temperature vs time curve. The magnitude of the area under the time vs core temperature curve below a threshold (i.e. 36.0 ℃), is used as an indicator of the degree of hypothermia. The greater the area under 36.0 ℃, the greater the amount of intraoperative hypothermia. To overcome this, it is recommended plausible that if redistribution hypothermia can be reduced, there will be less intraoperative hypothermia (assessed by less area under the curve) and thus fewer intraoperative and postoperative complications associated with hypothermia. Redistribution hypothermia can be achieved via increasing blood flow to the cooler peripheral and dermal thermal compartments with vasodilation. This results in heat transfer away from the warmer core. In the present study, our hypothesis is that anaesthetic inductions causing less vasodilation (than propofol alone inductions) will result in less redistribution hypothermia. The purpose of this effectiveness study is to compare the effect of three such alternative induction techniques to standard propofol inductions on core temperature during the first hour of anaesthesia.

Materials and Methods

Study design

This is a prospective, randomized, controlled, single blind effectiveness study with consent form obtained from patients and approved by Institutional ethics committee.

Inclusion criteria: The major inclusion criteria were age 18 to 57 years inclusive; supine or lithotomy positioning; scheduled for general anesthesia.

Experimental design and assignment of groups

After enrolment, patients were randomly assigned in four different groups. A baseline blood pressure was taken prior to induction and formal preoxygenation regimen was not performed.

Group I: PROP – intravenous induction with 2.2 mg/kg intravenous propofol

In this group, anaesthesia was induced by 2 mL of 2% lidocaine (40 mg) added to 20 mL of 1% propofol. Subjects in this group were preoxygenated with 100% O2 (minimum of 2 min) and then mL of 2% lidocaine (60 mg) was administered followed immediately by 2.2 mg/kg propofol (approximately 5 mg) at T0. Muscle relaxant was administered immediately after propofol administration.

Group II: INH/100 – inhalation induction with sevoflurane in 100% oxygen (O2) At time T0, with an unprimed circuit, the O2 flow meter was set at 6 LPM and the sevoflurane vaporizer was turned on at 8%.

Group III: INH/50 - inhalation induction with sevoflurane in 50% nitrous oxide (N2O) / 50% O2

The protocol was identical to group INH/100 except that induction was performed with 3 LPM N2O and 3 LPM O2 (instead of 6 LPM O2) with 8% sevoflurane.

Group IV: Phnl/PROP – intravenous induction with 2.2 mg/kg intravenous propofol preceded by 160 mcg phenylephrine

The protocol differed from group PROP only in that 2 mL of 80 mcg/mL phenylephrine (160 mcg) was administered immediately after the administration of 3 mL 2% lidocaine but before the 2.2 mg/kg propofol.

In patients from all the groups, blood pressures were recorded every minute starting 1 min after T0 (T1) until airway intervention commenced. Laryngeal mask airway (LMA), endotracheal intubation was provided as a support if required. To avoid hypotension, if necessary, the Sevoflurane concentration was decreased while waiting for adequate muscle relaxation. Systolic blood pressure (if dropped below 85 mmHg) is managed either with phenylephrine or airway intervention. After securing either the LMA or endotracheal tube, anaesthesia was maintained with sevoflurane in 50% nitrous oxide (1 LPM) and 50% O2 (1 LPM). Opioid narcotics (fentanyl, hydromorphone, methadone), neuromuscular reversal agents (glycopyrrolate, neostigmine), dexamethasone, and ketamine were administered as per the discretion of the attending anaesthesiologist.

Statistical methods

We compared differences in mean core temperature between the propofol only induction control group (PROP) and each of 3 groups administered alternative induction techniques (INH/100, INH/50, and Phnl/PROP) at each of 15, 30, 45, and 60 min (T15, T30, T45, and T60) after induction using unpaired t-tests and corresponding 95% confidence intervals (95% CIs).

Results

After randomization and withdrawals, 60 patients in each group were analyzed. Demographic and forced air warming data are presented in Table 1.

Table 1: Demographics and forced air warming data of the 240 patients analyzed

Group	PROP	INH/100	INH/50	Phnl/PROP
n	60	60	60	60
Age (years)				
Mean (SD)	45.3 (4.7)	45.5 (4.9)	45.1 (4.6)	45.2 (4.5)
Range	25-57	26-55	23-56	23-55
Sex				
Male n (%)	25 (42)	30 (50)	34 (57)	28 (47)
ASA classification				
1 n(%)	2 (3)	4 (7)	6 (10)	5 (8)
2 n(%)	25 (42)	30 (50)	23 (38)	35 (58)
3 n(%)	23 (38)	26 (43)	31 (52)	20 (33)
BMI (kg/m^2)				
Mean (SD)	28.7 (3.3)	29.1 (3.1)	31.2 (3.3)	30.5 (2.9)
Range	23.7-42.1	21.7-40.5	22.3-41.8	23.1-39.8

Preoperative Screening Temperature (°C)				
Mean (SD)	36.8 (0.2)	36.7 (0.2)	36.8 (0.2)	36.8 (0.3)

We have compared three alternative techniques of anaesthesia with the PROP induction. In all the three alternative induction groups (INH/100, INH/50 and Phnl/PROP) the mean core temperatures was higher than PROP group at all the time points tested (Table 2).

In the successive time intervals (T15 to T30, T30 to T45, and T45 to T60), the percentage of patients (all groups combined) whose temperature decreased were (35.9, 18.2, and 12.8% respectively). The percentage of patients whose temperature increased were (41.2, 53.2, and 60.1% respectively). The remaining patients had no temperature changes within these time intervals.

There were statistically significant differences in the mean temperatures between groups INH/ 100 and INH/50, INH/100 and Phyl/PROP, and INH/50 and Phyl/PROP at any time point (all $p< 0.05$). Few patients in three groups had a core temperature >37.5 ℃ at T60 time point, except PROP group.

At all four time points (T15, T30, T45, T60), the mean temperatures in group PROP were between 0.29 and 1.0 ℃ lower than in groups INH/100, INH/50 and Phnl/PROP (Table 3). All 12 comparisons achieved statistical significance as $p\leq 0.001$ for each of the above comparisons.

Table 2: Mean Temperature ± SD and Number (n) in Each Group at Each Time Point (°C)

	T15	T30	T45	T60
PROP	35.83±0.3	35.94±0.35	36.15±0.33	36.21±0.34
INH/100	36.45±0.4	36.49±0.36	36.62±0.31	36.65±0.32
INH/50	36.49±0.38	36.53±0.32	36.60±0.32	36.71±0.33
Phnl/PROP	36.83±0.29	36.36±0.31	36.44±0.36	36.53±0.37

Table 3: Differences between the mean core temperature (°C) of each of three alternative induction groups and the standard propofol alone group at each time point

Comparison Groups	T15	T30	T45	T60
INH/100 minus PROP	0.62	0.55	0.47	0.44
INH/50 minus PROP	0.66	0.59	0.45	0.5
Phnl/PROP minus PROP	1	0.42	0.29	0.5

Apnea did not occur in either group INH/100 or INH/50. In the first 2 min, treatment of hypotension (systolic BP < 85 mmHg) was required in 3 patients in Group PROP (5%) and 2 patients in group Phnl/PROP (2%). Treatment for hypotension was not needed for INH/100 or INH/50 groups.

Discussion

In the present study we have found that inhalation inductions with sevoflurane or the administration of 160 mcg phenylephrine immediately prior to 2.2 mg/kg propofol is effective in causing less redistribution of hypothermia than intravenous inductions with propofol alone in patients between age 18 to 57 years. Our results are consistent with previous work [7-9] and thus provide support for this study's conclusion. These studied have reported a 0.5-0.7 ℃ average thermal advantage of sevoflurane inhalation inductions over intravenous propofol. We found a slightly higher (0.3 ℃ to 1.0°) difference in our new induction techniques than the PROP alone group. Smaller mean age in these studies may support the small differences in results in these studies as a higher mean age than study group PROP and/or random variation.

Within each group, the differences in mean core temperature between T15 and T30, T30 and T45, and T45 and T60 were small and clinically insignificant. We found a bolus dose of phenylephrine reduced redistribution hypothermia. The bolus phenylephrine induced inhibition of propofol induced vasodilation may contribute to the reduction in the amount of redistribution hypothermia [7].

Several techniques are in use to reduce redistribution hypothermia. These includes prewarming, inhalation inductions use of pharmacological agents such as ketamine, etomidate, phenylephrine infusions, amino acid infusions, fructose, and bolus phenylephrine prior to propofol [7, 10-14]. However, alone these techniques failed to solve the hypothermia problem fully. Combinations of these techniques may result in additional thermal benefit. Our study employed the combination of these tetchiness and observed the benefits.

In this study, we have gradual inhalation was employed to reduce apnea, which is unlikely to occur with rapid inhalation. Interestingly apnea was not noticed only on PROP and Phnl/PROP group but not in the sevoflurane inhalation groups. This suggests that inhalation inductions were more hemodynamically stable than IV propofol inductions similar to previous study [15]. Retrospective studies found that adverse outcomes were associated with even short periods of hypotension, but not hypertension. Hypotension can occur rapidly with intravenous propofol inductions, however, in any inhalation induction patients we did not observe hypotension (systolic BP < 85 mmHg). Neither BMI nor sex was associated with the degree of redistribution hypothermia as observed in the multivariable analysis indicating that differences in BMI and sex between treatment groups were not responsible for the differences in mean core temperatures (redistribution hypothermia) between groups.

Conclusions

We conclude that inhalation inductions and prophylactic bolus phenylephrine administration with propofol to induce anaesthesia is effective to provide thermal benefits over standard intravenous propofol alone inductions in adults age 18 to 57 inclusive. This offers quick, simple, and easy to use partial solutions to the on-going problem of intraoperative hypothermia.

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