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Original Article

The Impact of Intravenous Glucose Administration on Maintenance of Body Temperature during Total Knee Replacement under Spinal Anesthesia in Geriatric Patients: A Randomized Controlled Trial.

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Abstract

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Background: Total knee replacement [TKR], more common in the elderly, can cause inadvertent perioperative hypothermia, which can be prevented. Preoperative intravenous [IV] glucose may minimize heat loss by increasing metabolism and heat generation.

The aim of the work: This study examined how preoperative IV 10% glucose affected body temperature in elderly TKR patients under spinal anesthesia [SA].

Patients and Methods: This randomized controlled trial involved 78 ASA I-II elderly patients scheduled for elective TKR under SA. Eligible patients were randomly allocated into two equal groups: group A received a 10% glucose infusion, while group B received 0.9% normal saline [NS], administered 6 hours before surgery. The occurrence of hypothermia was the primary outcome.

Results: At the end of surgery, group B exhibited a notable significant lower value of core temperature [$p < 0.001$] with a non-significant alteration in surface temperature [$p = 0.087$] than group A. Group B experienced more adverse effects compared to group A with statistically significant differences, particularly hypothermia [$p = 0.040$] and shivering [$p = 0.007$].

Conclusion: Elderly individuals undergoing total knee replacement under spinal anesthesia may benefit from a preoperative intravenous infusion of 10% glucose to help control body temperature and avoiding shivering.

Keywords: Glucose; Temperature; Hypothermia; Total Knee Replacement; Geriatric.



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INTRODUCTION

Osteoarthritis is one of the most prevalent diseases in the elderly people [1]. It affects major joints, such as the knee, resulting in functional limitations and disabilities in numerous elderly individuals, considerably impairing their quality of life [2]. TKR is a widely utilized and very effective orthopedic intervention for end-stage knee osteoarthritis, with respectable long-term results [3]. The procedure is frequently conducted under SA, which causes peripheral vasoconstriction blockade with accompanied vasodilation down to the spinal block level. This may lead to ongoing heat loss as cooler peripheral blood is redistributed to the core circulation, resulting in initial rapid hypothermia. Furthermore, paralysis below the spinal block inhibits shivering. All these elements contribute to hypothermia associated with SA [4]. Elderly has a reduced basal metabolic rate and a delayed sympathetic response, which makes them more vulnerable to intraoperative hypothermia [5]. Perioperative hypothermia may occur unintentionally during major arthroplasty surgery, potentially resulting in avoidable complications such as severe myocardial events, dysrhythmia, coagulopathy, extended recovery, surgical site infections, prolonged hospitalization, and increased mortality risks [6]. Previous investigations indicated that 26.7% of patients experienced hypothermia, characterized by a core temperature below 36 °C immediately post-surgery [7]. Consequently, anesthesiologists consistently take measures to prevent perioperative hypothermia unless specifically indicated [8]. There are various methods for regulating body temperature that have been proposed. Regardless of active warming systems, individuals may still be susceptible to hypothermia [9,10]. One preventive strategy includes the administration of IV nutrients during the perioperative phase. This may decrease heat loss by improving metabolism, in turn increasing heat production [11]. Preoperative and intraoperative amino acid [AA] and fructose solutions increased metabolism and prevented hypothermia [12-14]. Giving carbohydrates [CHO] two hours before surgery has become popular to minimize hunger, thirst, anxiety, and insulin resistance [15]. We hypothesized that administering 10% IV glucose could enhance metabolic heat production, therefore contributing to thermoregulation in sustaining perioperative normothermia. This provided a valid rationale for conducting the present investigation to evaluate the impact of preoperative IV glucose 10% administration on the incidence of hypothermia during TKR under SA in geriatric patients.

PATIENTS AND METHODS

Study design: This randomized, controlled, double-blind trial was performed at Mansoura University Hospitals, Egypt, from October 2022 to January 2025, with approval from the Institutional Review Board [IRB] of Mansoura University Faculty of Medicine [IRB code: R.22.09.1863] and the Pan African Clinical Trial Registry [ID number: PACTR202406634195351]. All participants provided informed written consent after a comprehensive discussion of the benefits and potential drawbacks of the protocol.

Inclusion criteria: Patients aged 60 years or older, of both sexes, classified as American Society of Anesthesiologists [ASA] class I or II, and undergoing elective TKR under SA were enrolled.

Exclusion criteria: Patients under 60 with extreme BMI [>30 kg/m² or <20 kg/m²], a history of thyroid, renal, hepatic, cardiac, diabetic, or muscular illnesses were excluded. Patients having a body temperature of over 37.5 °C or below 36 °C on operation day or who have thermoregulation-affecting medicines such as calcium channel blockers, B-blockers, or NSAIDs, and patient refusal were not included. Individuals with a dextrose allergy, ear infection, contraindications to

SA, and hemodynamic instability requiring inotrope infusion were also excluded.

Randomization and Blindness: Computer-generated random numbers were hidden within opaque, sealed envelopes. During the study, outcome assessors and patients were both blinded to related information. The preparation and administration of the infused drug were performed by an anesthesiologist not associated with the investigation. Participants were equally divided into two random groups. Group-A [39 patients] received 500mL [10%] of glucose, initiated six hours before surgery at a rate of 84 mL/h [corresponding to 8.4 g/h for a 70 kg patient; at a dosage of 2 mg/kg/min]. Group B [control group] involved 39 individuals who received 500 ml of 0.9% NS, commencing six hours before surgery, at a uniform infusion rate. Upon the patient's arrival in the operating theatre, regular monitoring was conducted during the procedure, including non-invasive arterial blood pressure, pulse oximetry and heart rate [HR]. Two wide bore IV catheters [18-G] were placed into the forearm and IV premedication was provided [midazolam 0.01 mg/kg].

Technique of spinal anesthesia: Spinal anesthesia was administered to all patients in a seated position using a Quincke 25-gauge needle inserted via the L4 and L5 interspaces under conventional aseptic conditions. Following the verification of CSF flow, 2.5ml of hyperbaric bupivacaine [0.5%] combined with 15 micrograms of fentanyl was administered. Thereafter, the sensory block was confirmed using the pinprick test, whereas the motor block was tested using the modified Bromage scale [16]. The surgical procedure commenced with the attainment of the T10 sensory block level.

Methods of temperature control: To avoid hypothermia, both groups were subjected to identical warming protocols. Patients were permitted thirty minutes to acclimatize to the operating theatre environment; during this interval, two double-folded cotton blankets were utilized to cover them before the procedure. The room temperature was kept at 22 °C. Regardless of the patient's core temperature, no heating techniques were used; including heated IV fluids, blankets, or forced air warming. Standard surgical drapes were employed to cover the patients. During the procedure, the irrigation of IV fluids was administered at room temperature. If the core temperature was less than 35°C, the forced-air warming device [Bair Hugger, 3M Company, USA] should be utilized to envelop the patient's chest and arms until it exceeds 35°C. That patients were subsequently excluded from the trial. Once the internal body temperature exceeded 38°C, the system was deactivated until the temperature dropped beneath 38°C.

Assessment of body temperature: Core and surface body temperatures were assessed utilizing a tympanic thermometer [Beurer, Beurer GmbH, Germany] at the tympanic membrane and a mercury-in-glass thermometer at the axillary region, respectively. Temperature was documented in the preoperative preparation unit as baseline values and at the end of the surgery for both studied groups. Blood glucose levels were assessed bi-hourly from the commencement of the infusion to the end of the procedure using a portable glucometer. Patients who achieved the discharge criteria were permitted to exit the recovery unit. Blood glucose management was initiated when levels fell below 70 mg/dL or exceeded 200 mg/dL, with the administration of glucose or insulin in accordance with our protocol.

Primary outcome: The primary outcome measured intraoperative hypothermia incidence, classified as per core temperature as mild [35-35.9°C], moderate [34-34.9°C], or severe [$<34^{\circ}\text{C}$].

Secondary outcomes: Intraoperative hemodynamics changes, incidence of shivering, blood glucose level, and cardiovascular complications.

Sample size: The Power Analysis and Sample Size software tool [PASS] version 2021 for Windows was utilized to calculate the sample size based on data from pilot research involving 14 patients with an assessment of hypothermia as the primary outcome. The null hypothesis claimed that both treatment regimens exhibited identical hypothermia rates. The pilot study identified a 14% incidence of hypothermia in Group-A and a 43% incidence in Group B. The suggested study necessitated a sample size of 35 patients per group to get 80% power [1- β] utilizing a two-sided Z-Test with unpoled variance and a 5% significance threshold [α]. Each group consisted of 39 participants after expected 4 drop-out patients per group.

Statistical analysis: Data were analyzed using IBM's SPSS Statistics [version 25]. The normality of data distribution was assessed using the Kolmogorov-Smirnov tests. Continuous normally distributed data were presented as mean $\pm$ SD, whereas categorical variables were represented as counts and percentages. The student's t-test analyzed two independent normally distributed data. The Chi-square test was employed for categorical data with crosstabs. All tests will utilize a 95% confidence interval. A P-value <0.05 signifies statistical significance.

RESULTS

This research evaluated 78 patients for eligibility were randomly assigned into two equal groups. All assigned patient was followed up and statistically analyzed [Figure 1]. There were no significant differences between the groups comparing patient characteristics,

intraoperative blood loss, blood transfusions, infusion volume, length of hospital stay, and surgical duration [Table 1]. Comparing the surface temperature between groups A and B indicates a non-significant alteration regarding the baseline [$p=0.266$] and the end of surgery [$p=0.087$] values. However, a notable significant change in surface temperature [$p=0.001$] was observed [Table 2]. Group A's mean baseline core temperature was 37.36 °C [± 0.283 SD], while by the end of surgery, it was 37.09 °C [± 0.341 SD]. On the other hand, the mean baseline core temperature of group B was 37.4 °C [± 0.313], and at the end of surgery, it was 36.57 °C [± 0.417]. The development of a highly significant difference between groups was noticed by finishing the surgery [$p<0.001$]. The change in core temperature between the two groups was significantly higher, with $p<0.001$ [Table 2].

Among the cases receiving IV glucose in group A, no case had hypothermia; only 1 [2.6%] experienced shivering, and 9 [23.1%] presented hypotension. Conversely, in group B, 4 patients [10.3%] experienced mild hypothermia, 9 [23.1%] exhibited shivering, and 10 [25.6%] had hypotension with no instances of bradycardia or arrhythmia in either group. A statistically significant difference was noticed across groups, with group B experiencing a greater incidence of adverse effects, specifically hypothermia and shivering [p -values =0.040 and 0.007, respectively] [Table 3]. The comparisons of mean arterial pressure and HR showed no statistically significant differences throughout the studied periods [Figure 2&3]. There were significant variations in blood glucose levels between group A and group B were seen at 4h, 2h, and 0h before surgery [$p<0.0001$], with no significant differences noted from baseline measurements until the 6th preoperative hour and during the intraoperative period [Figure 4].

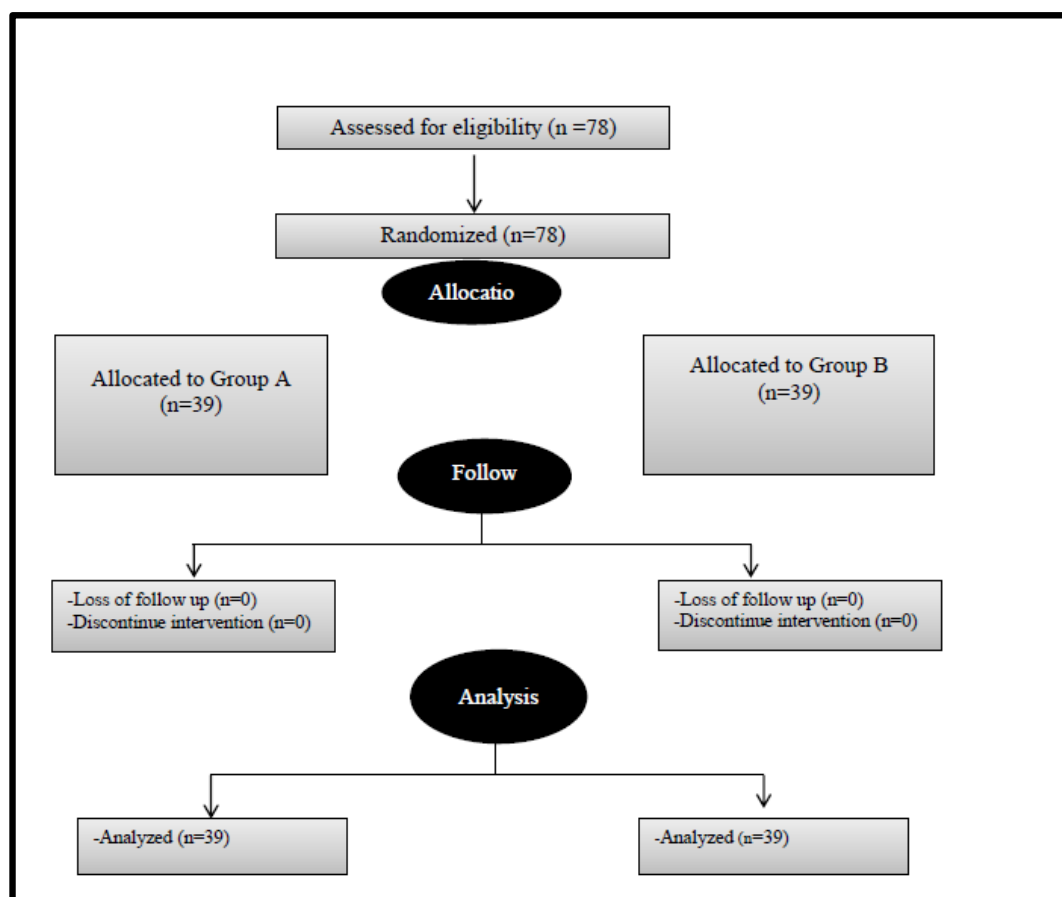


Figure [1]: CONSORT [Consolidated Standards of Reporting Trials] 2010 flow diagram of the consecutive steps of the study

Table [1]: Demographic characteristics, ASA classification, operative details, and duration of hospitalization in the studied groups:

		Group A [n= 39]	Group B [n= 39]	95% CI	P
Age [years]		72.56 ± 3.782	72.46 ± 3.926	-1.64, 1.84	0.907
Gender	Male	13 [33.3%]	14 [35.9%]	-	0.812
	Female	26 [66.7%]	25 [64.1%]		
Weight [kg]		67.04 ± 10.779	70.58 ± 13.153	-8.96, 1.89	0.198
Height [meter]		1.67 ± 0.067	1.70 ± 0.083	-0.06, 0.01	0.196
BMI [kg/m ²]		23.92 ± 3.272	24.51 ± 3.739	-2.17, 1.00	0.465
ASA	I	7 [17.9%]	4 [10.3%]	-	0.329
	II	32 [82.1%]	35 [89.7%]		
Duration of surgery [minutes]		118.08 ± 19.215	125.77 ± 20.246	-16.59, 1.21	0.089
Infusion volume [ml]		1450.0 ± 158.11	1534.6 ± 266.34	- 183.4, 14.17	0.092
Intraoperative blood loss [ml]		301.28 ± 89.947	325.64 ± 84.193	-63.65, 14.93	0.221
Need for blood transfusion		0 [0.0%]	0 [0.0%]	-	1
Duration of hospitalization [days]		2.92 ± 0.900	2.77 ± 0.902	-0.25, 0.56	0.453

Data are reported as mean and standard deviation [Mean±SD] or percentage and frequency-95% CI:95% confidence interval of the mean difference between both groups. P:is significant if <0.05.
ASA: American Society of Anesthesiologists. ml: milliliter, Kg/m²: Kilograms/square meter. Group A:10% glucose, Group B: 0.9% normal saline.

Table [2]: Surface and core temperature changes.

Temperature [°C]		Group A [n=39]	Group B [n=39]	95% CI	P
Surface	Baseline	36.85 ± 0.240	36.92 ± 0.283	-0.19, 0.05	0.266
	End of surgery	36.50 ± 0.334	36.34 ± 0.441	-0.02, 0.33	0.087
	Change	0.35 ± 0.188	0.57 ± 0.332	-0.34, -0.10	0.001
Core	Baseline	37.36 ± 0.283	37.40 ± 0.313	-0.17, 0.10	0.571
	End of surgery	37.09 ± 0.341	36.57 ± 0.417	0.35, 0.69	< 0.001
	Change	0.27 ± 0.190	0.83 ± 0.293	-0.67, -0.45	< 0.001

Data are expressed in mean and standard deviation. 95% CI:95% confidence interval of the mean difference between both groups. P-value of <0.05 is measured significant. °C: Celsius. Group A:10% glucose, Group B: 0.9% normal saline.

Table [3]: Incidence and grade of hypothermia and relevant intraoperative complications:

		Group A [n=39]	Group B [n=39]	Odds ratio	P
Hypothermia		0 [0.0%]	4 [10.3%]	undefined	0.040
Grade of hypothermia	Mild	-	4 [100%]	-	-
Complications	Shivering	1 [2.6%]	9 [23.1%]	7.10[.852-59.24]	0.007
	Bradycardia	0 [0.0%]	0 [0.0%]	undefined	1
	Hypotension	9 [23.1%]	10 [25.6%]	1.14[0.408-3.24]	0.792
	Arrhythmia	0 [0.0%]	0 [0.0%]	undefined	1

Data is expressed as percentage and frequency. Odds ratio was calculated for group B compared to group A [as reference]. P is significant when <0.05. Group A:10% glucose, Group B: 0.9% normal saline.

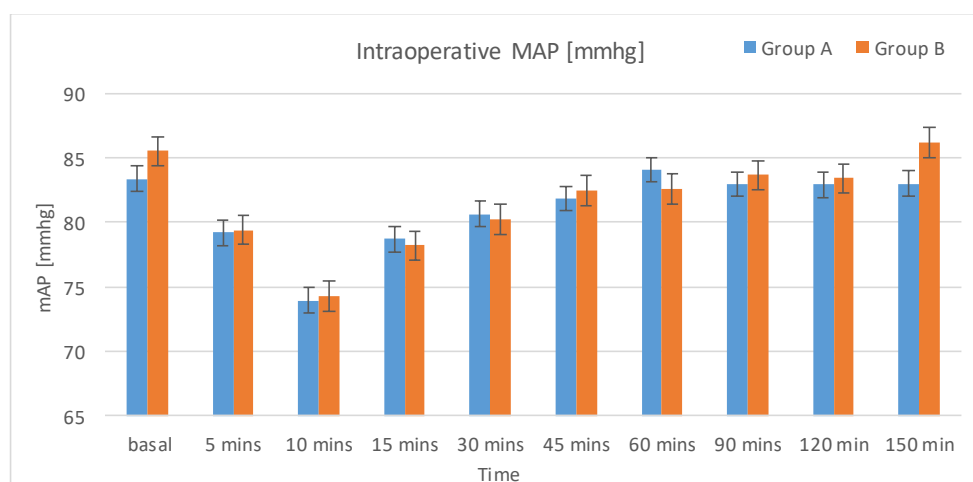
**Figure [2]:** Mean Arterial Pressure [MAP] between Group A [10% glucose] and Group B [0.9% normal saline] at each time point.



Figure [3]: Heart Rate [HR] between Group A [10% glucose] and Group B [0.9% normal saline] at each time point. Bpm: beat per minute.

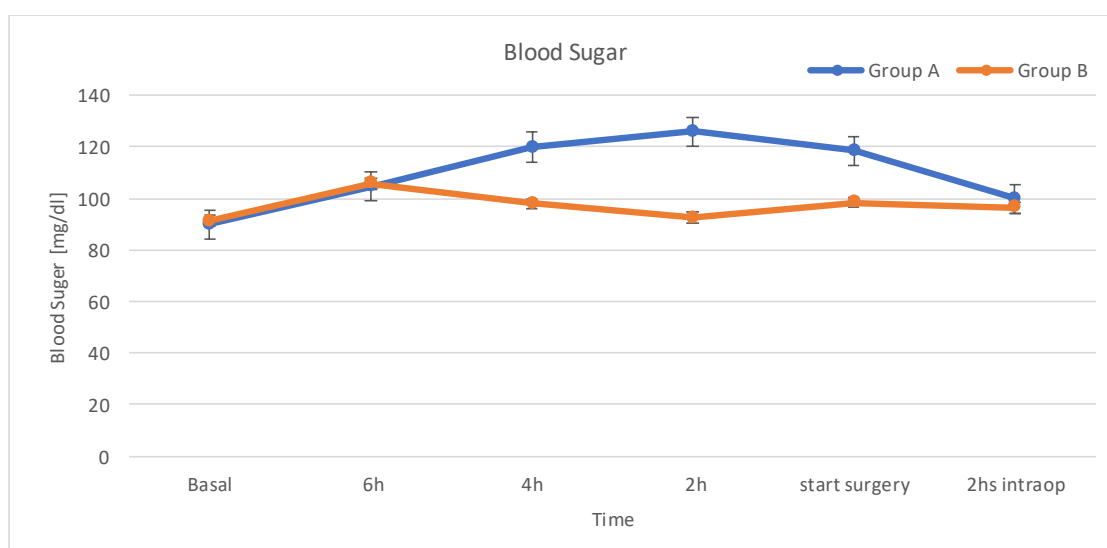


Figure [4]: Trend curve showing the blood sugar levels over time for Group A [10% glucose] and Group B [0.9% normal saline]. The x-axis represents the time points, and the y-axis shows the mean blood sugar levels [mg/dl].

DISCUSSION

Perioperative hypothermia induces detrimental effects, including shivering, impaired consciousness, hemorrhage, and infection, hence exacerbating morbidity and mortality^[17].

Elderly individuals are susceptible to hypothermia due to the diminished capacity to control their body temperature. Moreover, their lowered physiological reserves heighten the consequences of hypothermia-related complications. Consequently, it is vital for older patients undergoing elective surgery to receive extra care with prevention and early detection of unintentional hypothermia^[18].

Effective temperature management should begin preoperatively while the patient is still in the ward, as those presenting with pre-existing hypothermia before surgery are at increased risk of persistent hypothermia during and after the procedure^[17].

In this study, we assessed the effects of preoperative IV glucose delivery in preserving body temperature in elderly individuals

undergoing TKR under SA. The study's findings indicated that individuals administered preoperative IV glucose 10% [Group A] had a markedly reduced incidence of shivering and hypothermia compared to those received 0.9% NS [Group B]. The lack of significant differences in demographic features between the compared groups strengthens the validity of our findings and the association between glucose administration and temperature maintenance.

Our study revealed no significant changes in baseline surface and core temperatures between both groups. However, by the end of the procedure, group B exhibited a significantly lower core temperature [$p < 0.001$] with a non-significant alteration in surface temperature [$p = 0.087$] in comparison to group A. Temperature changes in surface and core temperatures pointed to significant differences, with group B experiencing a marked change. This indicated that, without glucose infusion, group B exhibited a more pronounced temperature drop by the end of the surgery.

Our result agreed with **Mizobe et al.** administered a fructose infusion three hours before anesthesia induction and continued it for one-

hour post-induction. The core temperature with fructose was markedly elevated between the 20th and 180th minutes of anesthesia induction [13].

Research by **Green and Macdonald** investigated the impact of IV glucose infusion [20%] on thermogenesis [TMG] and factors affecting heat loss in six healthy adults. Following IV glucose delivery, there was a 20% increase in TMG and cutaneous temperature that accompanied the improvement in peripheral blood circulation. They noted a slight decrease in core temperature following the administered glucose. The increased heat generation may be partially attributed to the direct glucose metabolism, rather than hyperosmolality or catechol-amine response [19].

It is comparable to the rise we previously saw with fructose and AA infusion in SA and in volunteers who were not anesthetized, indicating that perioperative nutrition may be responsible for the temperature increase [13]. Similarly, in experimental anesthetized rats with IV glucose administration, there was a significant rise in energy expenditure [EE], which would account for 2–7% of the energy content of the administered dextrose [20]. This outcome is in good agreement with earlier human researches [19,21,22,23].

In contrast to our investigation, **Ozer et al.** [15] found that preoperative CHO administration prior to surgery did not produce the expected rise in tympanic temperature; instead, it resulted in a decrease. The authors elucidated this discrepancy for multiple reasons, including the lack of control group to assess the differences. Furthermore, a modest dose of nutrients was employed, potentially affecting the outcomes. Ultimately, oral glucose was administered, though it is less effective than IV CHO [15].

Hamamoto et al. evaluated the impact of preoperative CHO administration on the operative body temperature in those undergoing laparoscopic colon surgery. They asserted that CHO had no detrimental impacts on perioperative outcomes and no influence on increasing the intraoperative core temperature. These findings can be attributed to the lack of heat loss accompanied laparoscopic operations as seen in open surgeries, and the insufflated CO₂ maintained body temperature [24].

Numerous theories have attempted to elucidate the CHO effect on thermoregulation, indicating that the sympathetic nervous system [SNS] activation induced by glucose intake or IV administration may account for 30% of the thermic response following glucose and insulin infusions, while norepinephrine and epinephrine enhance EE and oxygen consumption [22,23].

Other investigations indicated that heat generation occurs independently of SNS activation. Plasma levels of norepinephrine remained unaffected by glucose or NS infusion. This aligns with human studies indicating that sympathetic activity does not trigger glucose-mediated TMG [20,25,26,27].

According to **Kobayashi et al.** giving anesthetic rats 20% glucose [1.3 osmol/kg] for 5 minutes raised their osmolality by 4.50±0.88 mosmol/kg and oxygen consumption, while physiological saline had no impact. High plasma osmolality increases blood flow via vasodilating skin, kidneys, gut, and skeletal muscles, vascular smooth muscle. Higher regional blood flow and circulatory redistribution of stored body heat may have generated organ temperature fluctuations [20].

Energy expenditure is directly associated with glucose disposal rate and inversely correlated with the inhibition of hepatic glucose synthesis and insulin resistance [28]. Kobayashi et al. investigated the thermogenic effects of glucose infusion during anti-insulin serum administration

since glucose triggers pancreatic β -cell insulin secretion, which in turn promotes heat production [20].

Surgical trauma causes catabolism characterized mainly by insulin resistance, which occurs even with minor surgeries. Insulin sensitivity drops dramatically the day after surgery and may last three weeks. Preoperative CHO intake aims to stimulate breakfast-related metabolic changes. Infusion of glucose overnight or two hours before surgery reduced postoperative insulin resistance, enhancing metabolism and endogenous insulin secretion [29].

The adverse effects showed that group B experienced a statistically significant higher occurrence compared to group A, including hypothermia [10.3% vs 0%] and shivering [23.1% vs 2.6%]. Our results supported by **Ozer et al.** who reported decreased hypothermia and shivering in patients received CHO [15].

All groups exhibited hypotension, even non-significant, primarily attributable to SA. Neither group experienced bradycardia nor arrhythmia, which aligned with **Kausar et al.** discovered that preoperative CHO delivery enhanced intraoperative intravascular volume and hemodynamic stability, with no significant cardiovascular complications, evidenced by a reduced incidence of hypotension and dysrhythmias [30].

Shokri and Ali noted significantly diminished arrhythmias, inotropic or vasopressor support, cardiac muscle dysfunction, ventilatory, and ICU stays with preoperative IV glucose infusion [31].

The use of IV 10% glucose/CHO to maintain body temperature is a cost-efficient and easily applicable technique that can be easily integrated into clinical life. However, our study limitations include insufficient sample size, necessitating a larger sample size to augment the statistical power of the findings, and an absence of long-term follow-up to evaluate the extended effects of glucose infusion on recovery and complications.

In conclusion, the preoperative administration of 10% intravenous glucose is an effective measure to maintain body temperature, alleviate the risk of perioperative hypothermia, and prevent shivering in elderly patients undergoing total knee replacement under spinal anesthesia.

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