Original Article

Intra-operative warming blood transfusion contributes little to post-operative recovery quality in patients undergoing joint arthroplasty

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Abstract: Objective: This study aimed to examine effect of warming blood transfusion on post-operative cognitive function and whether warming blood transfusion could substantially improve post-operative recovery quality. Methods: Patients with an American Society of Anesthesiologists (ASA) status I-III for elective knee or hip arthroplasty were randomly divided into warming blood transfusion (W) group and control (C) group. The recovery rates of physiology, nociception, emotion, activities of daily living, cognition and overall patient perspective were evaluated by Post-operative Quality Recovery Scale (PQRS) at pre-operative (T0) and post-operative 15 min (T15), 40 min (T40), day 1 (D1), day 3 (D3) and day 7 (D7). Results: A total of 165 patients completed the trial (82 cases in the W group and 83 in the C group). The nasopharyngeal temperature of W group was significantly higher than C group (P<0.01). By D7, complete recovery rates of each domain between the W and C groups were obtained as follows: 82.7% versus 80% in physiological condition, 85.3% versus 81.3% in nociception, 100% versus 92% in emotion, 82.7% versus 85.3% in activities of daily living and 78.7% versus 66.7% in cognition. The proportion of patients who self-reported being ‘satisfied’ with their anesthetic care was 98% versus 95% between the W and C groups at D7. No significant differences in these domains were observed at T15 to D7. Conclusion: Intra-operative warming blood transfusion did not obviously improve cognitive recovery and only slightly improved post-operative recovery quality of patients undergoing joint arthroplasty.

Keywords: Intra-operative warming blood transfusion, post-operative recovery quality, cognitive recovery

Introduction

Hypothermia, characterized by a core temperature below 36°C, is often experienced by 20% of patients undergoing any type of general anesthesia intra-operatively [1]. Intra-operative hypothermia can increase the occurrence of complications, such as delayed awakening, chills, prolonged drug action, adverse cardiovascular complication, blood coagulation disturbance and infections [2, 3]. To maintain normothermia can prevent surgical infection, avoid shivering, shorten length of hospital stay and improve patient’s comfort [4, 5]. Therefore, active warming measures are applied to prevent intra-operative hypothermia. However, hypothermia is a clinically effective therapy for brain protection. Increasing evidence has shown that mild systemic hypothermia exerts a therapeutic effect on stroke, head trauma and anoxic/ischemic brain injury after cardiac arrest [6]. A recent randomized control trial (RCT) has revealed that active warming increases post-operative cognitive disorder (POCD) from 3.2% to 19.4% at post-operative day 4 [7]. Thus, the present study aimed to investigate whether or not warming blood transfusion substantially improved post-operative recovery quality, including physical function, nociception, feeling, daily activities and cognitive function, in patients scheduled for hip or knee arthroplasty under general anesthesia.
Material and methods

Patients

This study, in accordance with the declaration of Helsinki, was conducted with approval from the Ethics Committee of General Hospital of Ningxia Medical University. Written informed consent was obtained from all participants. The trial protocols were registered at http://clinicaltrials.gov (Registry No. NCT01930305). In brief, adults scheduled for single hip or knee replacement from January 2013 to December 2014 were enrolled into this study. Male or female patients aged 50 to 80 years old with an American Society of Anesthesiologists (ASA) status I-III and needed more than 2 U blood transfusion (perioperative hemoglobin <8 g/dL) were included. Patients with the followings were excluded: a history of central nervous system disorder or use of medications affecting the central nervous system; educational attainment was <7 years; severe visual or hearing impairment; unable to cooperate in the completion of the cognitive function test; needing intensive care after surgery; refusing to sign the informed consent.

Anesthesia and temperature management

Anesthesia was induced with 0.05 mg/kg midazolam, 0.2-0.3 μg/kg sufentanil, 0.2 mg/kg etomidate and 0.2 mg/kg cisatracurium besylate. Anesthesia was maintained with propofol continuously infused at 4-6 mg/kg/h and remifentanil continuously infused at 15-20 μg/kg/h by a micropump, followed by intermittent boluses of cisatracurium besylate (0.1 mg/kg per 60 min) for muscle relaxation and then ventilation with a laryngeal mask. Surgical procedures for all patients were performed by an experienced orthopedic surgical team. Patients were randomly divided into warming blood transfusion (W) and control (C) group. The former group received warming blood to 37°C before transfusion using an infusion fluid heating apparatus (Belmont FMS2000, Billerica, MA, USA). The latter group did not receive warming before transfusion (4°C infusion blood was kept at room temperature 22°C for 10-15 min measured 14°C before direct infusion without warming). Surgeons and anesthesiologists were not informed of blood temperature.

Data collection and safety monitoring

All data collection, pre-operative and post-operative management decisions and outcome assessment were made by individuals who were blind to the warming group assignment. Pre-operative data collection included patient general information. Patients were assessed using the Post-operative Quality Recovery Scale (PQRS) [8, 9]. The assessment of PQRS included all domains of physiology (systolic blood pressure (BP), heart rate (HR), temperature, respiratory rate, oxygen saturation, airway control, agitation level, consciousness level and activity on command), nociception (pain and nausea), emotion (anxiety and depression), activities of daily living (ability to stand, walk and dress without assistance and ability to eat and drink) and cognition (orientation, verbal memory, executive functioning, attention and concentration). Cognitive assessment was used by two methods according to original and new PQRS. The latter had more precise score assessment methods [9]. The assessment time points included pre-operative (T0) and post-operative 15 min (T15; approximate time for discharge from the operation room), 40 min (T40; discharge from the post-operative anesthesia care unit, PACU), day 1 (D1), day 3 (D3) and day 7 (D7, almost discharged from the hospital). The recovery rates of physiology, activities of daily living, nociception, emotion and cognition were calculated (the definition of recovery based on PQRS was ‘return to baseline value or better’). The occurrence of post-operative adverse events (including acute accidents, such as myocardial infarction, arrythmia, pulmonary embolism and infection, deep venous thrombosis) were recorded by surgeons.

Statistical methods

The study was designed for the statistical power of 90% based on data of a study in which POCD was detected in 19.4% of the actively warmed group and 3.2% in the standard care group at post-operative day 4 [7]. To detect a between-group difference of 0.162 units as shown above [7] in the mean POCD incidence at a significant level of 5% in two-sided tests would require 79 patients per group. Therefore, necessary trial sample size was estimated to be 186 patients, foreseeing a 15% dropout rate. Statistical analysis was performed using
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SPSS version 16.0. Measurement data were expressed as mean ± standard deviation (SD) and median (interquartile range). Inter-group comparison for normally distributed data was performed using two independent-samples t tests, whereas that for abnormally distributed data was performed using the Wilcoxon test. Count data were expressed in percentage. Chi-square test or Fisher’s exact test was employed for comparison. Statistical significance was considered at $P<0.05$.

Results

A total of 186 patients were initially enrolled in the study, among whom 165 patients completed the trial (82 patients in the W group and 83 patients in the C group). 11 patients in the W group and 10 in the C group were excluded because of insufficient post-operative data (Figure 1).

The clinical characteristics of the 165 patients are summarized in Table 1. The two groups did not significantly differ in age, sex, height, weight, operation style, operation time, anesthesia time, intra-operative blood loss, blood transfusion volume, PACU stay and post-operative hospital stay. The suction drainage in the W group was significantly higher than that in the C group at 24 h after operation ($P<0.05$).

The nasopharyngeal temperature fluctuations in the two groups are shown in Figure 2. The nasopharyngeal temperature in the W group was higher than that in the C group at T2-4 ($P<0.05$).

The recovery rates in post-operative physiology, nociception, emotion, activities of daily living and cognition are shown in Figure 3. No significant differences were found when modified method of PQRS was used in cognitive function measurement (Figure 4).

A comparison of the W and C groups revealed that 65% versus 63% and 98% versus 95% of the patients were ‘satisfied’ with their anesthetic care at D1 and D7; 18% versus 20% and 79% versus 81% of patients stated that their ‘ability to work was not affected’ compared with the pre-operative status; 22% versus 24% and 82% versus 85% of the patients stated that their ‘ability to undertake daily living activities was not affected’ compared with the pre-operative status; 55% versus 57% and 90% versus 88% of the patients felt that their ‘clarity of thought was not affected’ compared with the pre-operative states. There were no significant differences between the two groups (Figure 5).

No significant differences in the occurrence rates of adverse post-operative events (arrhythmia, pulmonary infection, pulmonary embolism or deep venous thrombosis) were found between the W and C groups (Figure 5).

Discussion

In this study, joint arthroplasty patients were selected as subjects and used the PQRS as the scale to assess post-operative recovery. Most of the joint arthroplasty patients are elderly with a high risk of POCD, and the PQRS is a new tool that was developed over a period of time by a consensus of experts. The PQRS scale and its constituent parts can track recovery from immediate to long-term time periods in patients of varying ages, languages and cultures, and in multiple domains between individuals over time after surgery and anesthesia. The cognitive test of PQRS is an integrated approach based on many extensively used and validated neurocognitive tests. There are two kinds of methods evaluated cognitive function [8, 9]. The new method had a more precise result in evaluating cognitive function. In our study, we used both kinds of methods which could fully
show the cognitive recovery perioperatively. Our results showed that the physiology, nociception, emotion, activities of daily living and cognition of the patients recovered with time. However, patients with intra-operative warming blood transfusion showed no influences in all above domains of post-operative recovery.

Generally, people may feel warm and comfortable when the body temperature is maintained at approximately 37°C. Surgical patients with general anesthesia experience low core temperature (<36°C) because of anesthetic inhibition, operation field exposure and low environmental temperature. Almost all drugs including intravenous, inhalation and intraspinal anesthetic that work on the hypothalamus and influence the temperature-regulating mechanism are followed by an induced hypothermia [10]. Most patients with arthroplasty are elderly [11], and the surgical wound is large with a considerable amount of blood loss [12]. Studies showed that blood loss from single-knee arthroplasty is 100-180 mL and that post-operative suction drainage is 280-950 mL. The average blood requirement is 600 mL (including plasma, red cell suspension and whole blood) [13]. Blood transfusion volume positively correlates with poor post-operative recovery quality [14]. In the present study, the average intra-operative blood loss was approximately 620 mL and the average blood transfusion was approximately 530 mL between the two groups. In either group, more than 80% of the patients completely recovered in their physiology, nociception, emotion and activities of daily living functions. However, more than a quarter of the patients had incomplete recovery in their cognitive performance at D7.

Transfusion of refrigerated blood products could lead to hypothermia, chills, coagulation disorders and arrhythmia [15, 16]. Thus, intra-operative hypothermia is regarded as a severe
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complication, especially in surgery for elderly patients and children. However, considerable experimental and clinical studies have confirmed that mild hypothermia confers neuronal protection on ischemic brain [17]. A previous work showed that patients >65 years of age receiving active warming would have an increased incidence of early POCD [7]. Fresh evidence confirmed that haemodynamic parameters, including arterial pressure and HR, would not be influenced by peri-operative hypothermia (33°C) in patients undergoing cerebral aneurysm surgery. Furthermore, this hypothermia cannot increase the occurrence of peri-operative cardiovascular events, including hypothermia-related arrhythmias [18].

In consideration of the consequences in prior studies, the absence of changes in cardiovascular events and post-operative function with peri-operative warming blood transfusion needs a thorough comparison of these apparently contradictory results. Frank et al [19], reported that patients with peri-operative hypothermia (recovery room temperature <35°C) were more prone to myocardial ischemia (36% vs. 13%) and angina (18% vs. 2%) than patients with temperature ≥35°C, but these patients showed no differences in the incidence of myocardial infarction. Then, the same research group reported that hypothermic patients (35.4°C in recovery) have a higher incidence of cardiac morbidity (6% vs. 1%) and ventricular tachycar-

Figure 3. Percentage of Patients Recovered on Items of the Post-operative Quality Recovery Scale. Data are shown as a percentage of recovery (return to pre-operative values or better) in all domains. Evaluation points were pre-operative, T15, T40, D1, D3 and D7 after anesthesia cessation. No significant difference between W and C Group. The cognitive function was evaluated by original methods.
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Figure 4. Data are shown as the percentage (%) of patients in the W and C group recovered in the cognitive domain at 15 min (T15), 40 min (T40), day 1 (D1), day 3 (D3) and day 7 (D7) after anesthesia cessation for the modified scoring methods. No significant difference between W and C Group. The cognitive function was evaluated by the modified method.

dia (8% vs. 2%) but no significant difference in the incidence of electrocardiographic myocardial ischemia during the first 24 h after surgery [20]. The significant differences between our study and previous consequences are due to differences in study design and operation characteristics. In addition, these studies used different surgical styles, including thoracic, abdominal and vascular, which lead to longer operative times, more blood loss and more transfusion requirements. In our study, intra-operative blood loss was almost 620 mL and blood transfusion was almost 530 mL in arthroplasty operation without a large volume of peritoneal irrigation taking away heat generation, which resulted in slight core temperature fluctuation. Core temperature in recovery between two groups were not lower than 35.4°C, which could explain why the two groups in our study showed no different incidences of cardiovascular diseases.

Patients with active warming had a much higher incidence of POCD (19.4% vs. 3.2%) on day 4, but this difference diminished at 3 months [7]. In this study, 88% of standard-care patients
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suffered from a tympanic temperature decline to less than 35°C, whereas 25.3% of warmed patients had a temperature of more than 36°C. A temperature higher than 36°C is an independent risk factor for POCD (odds ratio, 8.48) [7]. These results are consistent with our study. In the present study, the W group did not show a higher incidence of early POCD than the C group. No significant differences between the two groups were detected when both the original and new PQRS were used. This result can be attributed to the low volume of blood transfusion and the short duration of <36°C in the present study.

Clinical methods include invasive methods, such as cavity irrigation and extracorporeal circulation, which are always used in cardiac surgery and treating severe hypothermia patients [21]. In general surgeries, use of thermal insulation blankets, improvement of external environmental temperature, circulating water blanket or mattress, and warming blood and liquid transfusion are effective methods [22].

The degree of temperature reduction increases haemoglobin affinity by 5.7%, making tissues hypoxic [23]. In the present study, intra-operative low temperature did not affect ventilation with ventilator support. Intra-operative core temperature did not obviously change because of the small blood transfusion volume. Thus, post-operative recovery was not considerably increased.

The recovery rates of post-operative nociception and emotion were not considerably lower in the W group than in the C group. It is indicated that post-operative discomfort was gradually serious when the patients were completely awake, with a high incidence at T40. The patient conditions gradually improved with prolonged hospitalization. No differences in the recovery of daily activities were detected between the two groups. Post-operative nociception and emotion exert different degrees of influence on post-operative recovery quality [24]. In the present study, differences in all these observed items were not obvious between the two groups.

These results indicate that blood transfusion temperature does not significantly affect the incidence of post-operative venous thromboembolism when the amount of blood transfusion is not large. No significant differences in post-operative suction drainage were detected between the two groups. However, the suction...
drainage of the W group was higher than that of the C group at D1. This phenomenon can be attributed to temperature changes caused by body temperature regulation [1]. Enzyme activities normalize as the body temperature regulation function gradually normalizes. This phenomenon could explain the lack of difference in subsequent blood loss between the two groups.

Previous research showed that hypothermia affected the function of PLT membrane receptor, which could decrease PLT deformation ability, blood PLT amount in the circulation, aggregation and release. Hypothermia may also inhibit the release of the thrombus alkane B2, thereby decreasing PLT aggregation and thrombogenesis [25].

Limitations

This study has some limitations. First, cases of massive transfusion were not observed. Thus, we were unable to determine the real effect of massive warming blood transfusion on postoperative recovery quality, particularly on the brain function of elder surgical patients.

Second, long-term observation should be conducted. Patients were only assessed when they were in the hospital. Follow-ups after discharge from the hospital are necessary to clarify and define the long-term prognosis.

Conclusion

Intra-operative warming blood transfusion did not obviously improve the cognitive recovery, and only slightly improved the post-operative recovery quality of patients undergoing joint arthroplasty.

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Disclosure of conflict of interest

None.

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References

[11] Maldonado M and Nam J. The role of changes in extracellular matrix of cartilage in the pres-
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