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Comparison of restrictive and liberal transfusion strategy on postoperative delirium in aged patients following total hip replacement: A preliminary study

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ABSTRACT

Few studies have examined the association between perioperative blood transfusion and postoperative delirium (POD) in aged patients undergoing total hip replacement surgery. In this prospective study, 186 patients older than 65 years undergoing elective unilateral total hip replacement surgery were enrolled. Of those, 94 patients were randomly assigned to the restrictive strategy transfusion strategy group, in which red blood cells were transfused in order to maintain 10.0 g/dL > hemoglobin ≧ 8.0 g/dL. Ninety-two patients were randomly assigned to the liberal transfusion strategy group, in which red blood cells were transfused in order to maintain hemoglobin ≧ 10.0 g/dL. POD was diagnosed by confusion assessment method. The baseline characteristics of patients, the length of hospital stay, the incidence of POD, myocardial infarction, stroke, wound infection, pulmonary embolism, and the transfusion volume were recorded. No difference was observed in the baseline characteristics, the length of hospital stay, and the incidence of POD, myocardial infarction, stroke, wound infection, and pulmonary embolism between the two groups ($P > 0.05$). The proportion of patients transfused with red blood cell and frozen plasma was decreased in the restrictive transfusion group compared with the liberal transfusion group ($P < 0.05$). In conclusion, restrictive transfusion does not influence the incidence of POD but reduces blood transfusion. Thus, restrictive transfusion may serve as an effective and safe strategy for aged patients following total hip replacement.

1. Introduction

Delirium is a serious neuropsychiatric syndrome, characterized by disturbances in attention and other cognitive functions (Bisschop, de Rooij, Zwinderman, van Oosten, & van Munster, 2011). The prevalence of delirium is observed in 10–62% of all hospitalizations and is more prevalent in the elderly (van Munster et al., 2008), which is associated with a prolonged length of stay, high rate of institutionalization, and increased morbidity and mortality (Saczynski et al., 2012).

Hip replacement surgery is a common procedure in the elderly and is often associated with substantial blood loss, requiring blood transfusion in the perioperative period (Postler, Neidel, Günther, & Kirschner, 2011; Zufferey et al., 2010). Accumulating evidence suggests that a liberal transfusion strategy (hemoglobin concentration >10.0 g/dL) is associated with poorer postoperative outcomes and higher mortality (Wu et al., 2010). On the other hand, a restrictive transfusion strategy (hemoglobin concentration maintained between 7.0 and 9.0 g/dL) reduces organ dysfunction and cost without deteriorating patients' outcomes (Carson et al., 2011). However, few studies have examined the association between perioperative blood transfusion and postoperative delirium (POD) in aged patients undergoing hip replacement surgery. One report suggests that delirium may be the consequence of a low hemoglobin level with poor oxygen delivery, and thus the postoperative level of hematocrit should be kept no less than 30% (hemoglobin = 10.0 g/dL) to prevent POD (Marcantonio, Goldman, Orav, Cook, & Lee, 1998).

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However, another recent published study has reported that individuals receiving an intraoperative blood transfusion are at high risk for development of early POD (Behrends, DePalma, Sands, & Leung, 2013).

Given the conflicting results with regard to the perioperative transfusion strategy on POD development, a randomized controlled trial was undertaken to determine if a restrictive transfusion strategy resulted in any difference in POD in comparison to a liberal transfusion strategy in the aged patients undergoing hip replacement with spinal anesthesia.

2. Methods

2.1. Participants

After obtaining the approval from the Ethics Committee of Jinling Hospital and the written informed consents from all patients, 237 consecutively admitted patients, with the age of more than 65 years, undergoing elective unilateral total hip replacement from October, 2011 to May 2013 were enrolled in the present study. The exclusion criteria were as follows: ASA physical status ≧ IV; preoperative delirium; unwilling to comply with the procedures; inability to understand the language (Mandarin Chinese); hearing loss, or a failure in spinal anesthesia.

Hip replacement was performed by the same surgery team and a cemented double prosthesis was used in all cases through a posterior–lateral approach. No preoperative medication was administered and patients received no sedatives during surgery. Patients were randomly assigned to the restrictive or liberal transfusion strategy group using a random number table and a sealed envelope technique. Patients in the restrictive transfusion group received blood transfusion only if hemoglobin concentration was <8.0 g/dL or when symptoms of anemia developed, while patients in the liberal transfusion group received blood transfusion to keep their hemoglobin concentrations more than 10.0 g/dL. Hemoglobin levels were measured 1 d before surgery, and 1, 2, 3, and 7 days after surgery. To maintain hemodynamic stability, Ringer's lactate and hydroxyethyl starch (HES) 130/0.4 were administered during surgery, whereas the administration of frozen plasma was based on the experiences of the anesthesiologists. Patients who experienced hypotension (systolic blood pressure <90 mmHg or mean blood pressure <60 mmHg) were treated by incremental doses of ephedrine or phenylephrine injection. Tachycardia (HR > 100 beats/min) was treated by esmolol injection, whereas bradycardia (HR < 50 beats/min) was treated with atropine injection.

Routine electrocardiogram, pulse oximetry, and invasive blood pressure were continuously monitored after the patients admitted to the operating room. Spinal anesthesia was performed as described previously (Ji et al., 2013). During the surgery period, all the patients received 2 L/min of oxygen inhalation via a nasal catheter. All the patients received postoperative analgesia via a patient-controlled analgesia device for the initial 48 h after surgery (a constant infusion rate of 2 mL/h with a lock time of 15 min) of 3–4 μg/kg of sufentanil plus 600 mg of tramadol and 16 mg of ondansetron. The degree of postoperative pain was assessed 1, 2, and 7 days after surgery with a 10-cm linear visual analog scale (VAS, 0 = no pain, 10 = most severe pain).

2.2. Plasma samples

The blood samples were collected before the induction of anesthesia and 4, 24, 48, and 72 h after the end of surgery. After centrifuging at 3500 g for 5 min, the plasma samples were stored at −80 °C for further use. Plasma levels of tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β, IL-6, and IL-8 were measured by using enzyme-linked immunosorbent assay (All kits were purchased from Jiancheng Biologic Project Company, Nanjing, China) following the manufactures' instructions.

3. Cognition assessment

Mini-mental state examination (MMSE) was used to exam the preoperative cognitive function on a scale of 0 (poor) to 30 (good) in a quiet room 1 d before surgery. Delirium was assessed by the same attending anesthesiologist between 8 a.m. and 9 a.m. preoperatively, and 1, 2, 3 days after surgery. By doing so, the confusion assessment method for the intensive care unit (CAM-ICU) criteria (Chinese version) was used by evaluating the following four clinical features: 1, acute onset of cognitive changes with a fluctuating course; 2, inattention; 3, disorganized thinking; and 4, altered level of consciousness. The diagnosis of delirium is based on the presence of the first two (acute onset or fluctuation course and inattention) plus either the third (disorganized thinking) or the fourth (altered level of consciousness) of the above items (Neufeld et al., 2013).

4. Statistics

Statistical analysis was performed using the SPSS 16.0 software for Windows. Descriptive results of continuous variables are presented as the means ± standard deviations (SD). Categorical data are expressed as counts. Intergroup comparisons were compared by the independent-samples *t*-tests. For comparisons of qualitative parameters, Chi-square or Fisher exact test was used. The repeated-measures analysis of variance was used to examine the within-subjects (time) effect, between-subjects (group) effect, and group by time interaction effect in inflammatory data. For the hemoglobin levels after randomization, data are expressed as medians and interquartile ranges, and the Mann–Whitney *U* test was used to compare the difference. $P < 0.05$ was considered to be statistically significant.

5. Results

Among the eligible 237 patients, 186 were included in the final data analyses (Fig. 1). There was no significant difference in terms of age, sex, weight, ASA classification, years of education, preoperative MMSE scores, comorbidities, length of surgery,

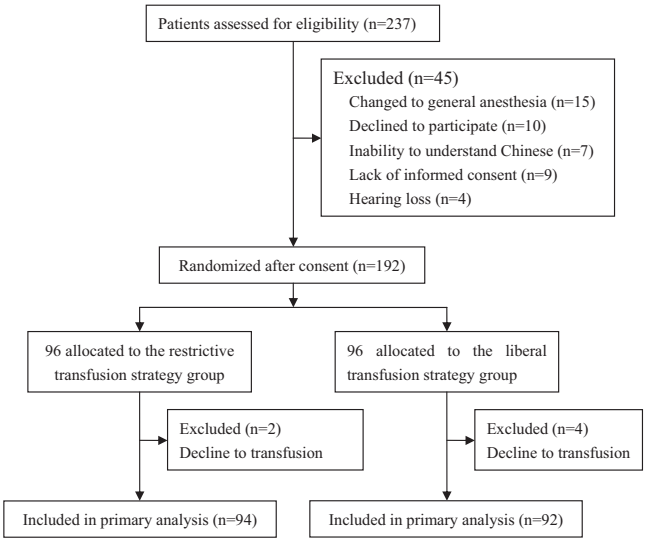

Fig. 1. The CONSORT diagram showing patients'flow through the study.