Arthroplasty Today xxx (2017) 1–5

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Original research

Continuing versus discontinuing antiplatelet drugs, vasodilators, and/or cerebral ameliorators on perioperative total blood loss in total knee arthroplasty without pneumatic tourniquet

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ARTICLE INFO

Article history:
Received 29 April 2017
Received in revised form
24 June 2017
Accepted 4 July 2017
Available online xxx

Keywords:
Knee
Primary arthroplasty
Bleeding events
Thrombotic events
Noncardiac surgery

ABSTRACT

Background: Although studies have supported the utility of perioperative continuation of antiplatelet drugs, vasodilators, and cerebral ameliorators in most procedures, no study compared total volume of blood loss after total knee arthroplasty (TKA) in patients continuing and discontinuing these drugs.
Methods: We retrospectively reviewed 266 consecutive patients undergoing TKA, and included 67 patients (25.2%) taking antiplatelet drugs, vasodilators, or cerebral ameliorators in this study. All TKAs were performed without a pneumatic tourniquet. The primary outcome was perioperative total blood loss calculated from blood volume and change in hemoglobin. As subgroup analysis, we compared perioperative total blood loss in patients taking antiplatelet drugs.
Results: There was no significant difference between the continuing group ($n = 38$) and discontinuing group ($n = 29$) in terms of the perioperative total blood loss (1025 ± 364 vs 1151 ± 327 mL, respectively; mean difference 126 mL; 95% confidence interval −45 to 298 mL; $P = .15$). No major bleeding or thrombotic events occurred in either group until postoperative 3-month follow-up. In patients taking antiplatelet drugs ($n = 51$), no significant difference was observed in the total blood loss between the continuing group ($n = 30$) and discontinuing group ($n = 21$) (1056 ± 287 vs 1151 ± 305 mL, respectively; mean difference 95 mL; 95% confidence interval −75 to 264 mL; $P = .27$).
Conclusions: No significant differences in terms of perioperative total blood loss were observed between patients continuing and discontinuing study drugs. Continuing these drugs may be preferable in the perioperative period of TKA.

Introduction

Antiplatelet drugs, vasodilators, or cerebral ameliorators are commonly used in elderly patients in clinical settings [1,2]. Although preoperative discontinuation of these drugs has been recommended to reduce perioperative blood loss, concerns have recently been raised because discontinuation would increase perioperative medical complications [3,4]. A recent review including a number of randomized controlled trials recommended that these drugs should be continued for most procedures except in patients at low risk of cardiovascular events undergoing major surgery and those undergoing high-risk procedures, such as intracranial surgery [5]. Orthopedic surgery is recognized as having intermediate cardiac risk [6], and it remains controversial whether these drugs should be continued or discontinued during the perioperative period for such procedures.

As the number of elderly patients undergoing total knee arthroplasty (TKA) has continued to increase [7], the numbers of patients on antiplatelet drugs, vasodilators, or cerebral ameliorators are also increasing. Blood loss in the perioperative period remains an important concern in TKA [8]. Although the rate of major bleeding events after surgery has been investigated [9], we aware of that there are no studies comparing the volume of perioperative total blood loss after TKA between patients continuing and discontinuing these drugs.

No author associated with this paper has disclosed any potential or pertinent conflicts which may be perceived to have impending conflict with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.artd.2017.07.002.

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http://dx.doi.org/10.1016/j.artd.2017.07.002

We investigated whether there were differences in terms of perioperative total blood loss and major bleeding events among patients continuing antiplatelet drugs, vasodilators, or cerebral ameliorators and patients discontinuing these drugs in TKA. The hypothesis of the study was that the volume of perioperative total blood loss would not be different between patients continuing and discontinuing these study drugs.

Materials and methods

This retrospective comparative study was conducted at a single orthopaedic clinic. The study protocol and publication were approved by the ethics committee.

Consecutive patients undergoing TKA between May 2013 and April 2015 were identified based on a review of our institutional database. All medical records of patients undergoing TKA were reviewed and patients taking antiplatelet drugs, vasodilators, or cerebral ameliorators were identified. During the study period, when patients taking antiplatelet drugs, vasodilators, or cerebral ameliorators were scheduled to undergo TKA, we routinely consulted the primary physician of internal medicine who prescribed the drug regarding whether the drug could be discontinued preoperatively. When discontinuation was allowed, the drug was discontinued preoperatively and restarted 1 day after TKA. We instructed the patients in the period of drug discontinuation as summarized in Table 1. The drugs were continued in cases where continuation was recommended by the primary physician of internal medicine.

The inclusion criteria were patients undergoing TKA and taking antiplatelet drugs, vasodilators, and/or cerebral ameliorators. Patients taking anticoagulating drugs were excluded because they received heparin bridging therapy. Patients taking antiplatelet drugs, vasodilators, and/or cerebral ameliorators who were recommended by the primary physician of internal medicine to receive heparin bridging therapy were also excluded. In addition, patients with severe deformity of the knee joint, for example, due to a history of osteomyelitis or severe trauma, were excluded. Patients who could not be followed up for 3 months were excluded because a follow-up period of more than 1 month would be required to assess major bleeding or thrombotic events [6,10,11].

Outcomes

Primary outcome

The primary outcome of this study is the perioperative total blood loss in TKA. We calculated the total volume of blood using the calculated blood volume and change in hemoglobin from preoperative to postoperative day 4 [12].

Table 1
Days of study drug discontinuation prior to total knee arthroplasty.

Agent	Days of discontinuation
Antiplatelet drug	
Aspirin	7
Clopidogrel	10
Ticlopidine	7
Cilostazol	3
Ethyl icosapentate	7
Beraprost	1
Sarpogrelate	1
Vasodilator	
Limaprost alfadex	1
Kallidinogenase	2
Dipyridamole	2
Cerebral ameliorator	
Nicergoline	2
Ifenprodil	2
Ibudilast	2

First, the blood volume of the patient in liters was calculated using the formula of Nadler et al [13] as follows:

$$\text{Blood volume} = \left(\text{k1} \times \text{height [m]}^3\right) + (\text{k2} \times \text{body weight [kg]}) + \text{k3}$$

where k1 = 0.3669 for male patients and 0.3561 for female patients; k2 = 0.03219 for male patients and 0.03308 for female patients; and k3 = 0.6041 for male patients and 0.1833 for female patients.

Second, the loss of hemoglobin was estimated according to the following formula:

$$\text{Hb}_{\text{loss}} = \text{blood volume} \times (\text{Hb}_{\text{i}} - \text{Hb}_{\text{e}}) \times 0.001 + \text{Hb}_{\text{t}}$$

Hb_{loss} (g) is the amount of hemoglobin lost up to day 4 after surgery; Hb_i (g/L) is the hemoglobin concentration before surgery; Hb_e (g/L) is the hemoglobin concentration on day 4 after surgery; and Hb_t (g/L) is the amount of hemoglobin transfused.

Finally, the total blood loss was calculated as follows [12]:

$$\text{Total blood loss(mL)} = 1000 \times \text{Hb}_{\text{loss}}/\text{Hb}_{\text{i}}$$

Secondary outcomes

Secondary outcomes of the study were intraoperative blood loss, rate of blood transfusion, major bleeding events, and major thrombotic events.

Intraoperative blood loss was calculated as the sum of the blood aspirated into the suction canisters and weighing gauzes.

Major bleeding events were defined as (1) cerebral hemorrhage, (2) intra- or retroperitoneal hemorrhage documented by computed tomography scan, (3) bleeding requiring an intervention (ie, surgical reoperation, endovascular embolization, or endoscopic intervention), and (4) bleeding requiring 3 U of red blood cells [11]. Major thrombotic events were defined as (1) stroke, (2) transient ischemic attack, (3) acute coronary syndrome, (4) peripheral arterial ischemia, (5) mesenteric arterial ischemia, (6) deep proximal and distal venous thrombosis based on clinical symptoms, and (7) pulmonary embolism [11].

Subgroup analyses

We planned subgroup analyses for patients taking antiplatelet drugs. In patients taking antiplatelet drugs, we compared the volumes of perioperative total blood loss and intraoperative blood loss, the rate of blood transfusion, major bleeding events, and major thrombotic events.

Surgery and postoperative treatment

All surgeries were performed by one of the 2 surgeons (S.T. and M.W.). Neither a pneumatic tourniquet nor drain was used in any of the patients undergoing TKA during the study period. A subvastus approach was used in all surgeries except in patients with valgus knees, for whom a lateral approach was used. All patients received a cemented, posterior stabilized prosthesis (Scorpio NRG; Stryker Orthopaedics, Mahwah, NJ).

We administered 1 g of tranexamic acid intravenously (Transamin; Daiichi Sankyo, Tokyo, Japan) just prior to skin incision and again at 6 hours after the first administration.

We subcutaneously administered 1.5 or 2.5 mg of fondaparinux (Arixtra; GlaxoSmithKline, Tokyo, Japan) for thromboprophylaxis once every evening for 10 days, starting from postoperative day 1. The dosage was determined based on the renal function and body weight.

For postoperative pain control, intraoperative periarticular injection including ropivacaine, morphine, epinephrine, ketoprofen, and/