

RECOVERY OF HEMOGLOBIN LEVEL FOLLOWING TOTAL KNEE ARTHROPLASTY WITH PERIARTICULAR EPINEPHRINE INJECTION

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Abstract

Background: Anemia is one of the common complications occurring after total knee arthroplasty (TKA). A periarticular epinephrine injection could reduce intraoperative blood loss after TKA. However, the duration of hemoglobin recovery to preoperative level remains uncertain. The hypothesis was based on the concept that epinephrine affects vasoconstriction and reduces blood loss. This study was conducted to compare the duration of hemoglobin recovery to preoperative level between periarticular epinephrine injection and periarticular nonepinephrine injection groups and postoperative blood transfusion.

Methods: A total of 141 participants were randomized to receive a periarticular epinephrine and bupivacaine injection (epinephrine group) or periarticular bupivacaine injection (non-epinephrine group) among patients undergoing TKA. The solution consisted of 10 g of epinephrine 1 ml and 20 ml of 0.25% bupivacaine. In another group, the solution consisted of 20 ml of 0.25% bupivacaine alone. All TKAs were managed under spinal anesthesia using a femoral nerve block. Preoperative and postoperative hemoglobin (Hb) and hematocrit (Hct) levels were assessed 1-day, 3-day and monthly until 6 months. Blood loss and the duration of Hb recovery to preoperative level were compared between the two groups.

Results: The percentage of Hb loss was slightly higher in the epinephrine group than that in the nonepinephrine group but without significance ($13.4 \pm 6.6\%$ vs. $13.01 \pm 5.01\%$; $p=0.703$). The duration of Hb recovery to preoperative level was about the same in the epinephrine and nonepinephrine groups (2.52 ± 1.080 months vs. 2.56 ± 1.089 months; $p=0.855$). The calculated total blood loss in the epinephrine group was lower than that in the nonepinephrine group (570 ± 302 mL vs. 573 ± 228 mL; $p=0.955$). In this study, surgery was performed without blood transfusions.

Conclusion: The duration of Hb recovery to preoperative level was 2.5 months which was about the same in both groups. Epinephrine injection did not decrease total blood volume loss after TKA under spinal anesthesia.

Keywords : Total knee arthroplasty, Periarticular epinephrine injection, Hemoglobin recovery, Randomized-controlled trial

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Introduction

Total knee arthroplasty (TKA) is one of the most common procedures in orthopedic surgery performed worldwide⁽¹⁾ with an estimated 10.2% increase in the number of TKA annually. The increasing TKA numbers are related to aging population, technical development of surgical procedures and advanced implants.⁽²⁾ Many comorbidity complications occur during TKA especially perioperative blood loss. This can be reduced by preoperative evaluation and good preparation.

Several strategies have been used to prevent and reduce blood loss in TKA. They can be classified as preoperative, intraoperative and postoperative management. However, anemia is still a common incidence after TKA. Approximately 10% of patients receiving blood transfusion following TKA were at risk of blood-borne infection and transfusion reaction. In addition, prolonged exposure to anemia after TKA may jeopardize these patients and lead to fatigue, late ambulation and extended length of hospital stay.⁽³⁾

Periarticular infiltration of analgesia is a method used for postoperative pain control after TKA. Originally, epinephrine is added for local infiltration analgesia (LIA) to delay systemic absorption of the local anesthetic agents to prevent their systemic toxicity.^(4, 5) Many studies have investigated the use of epinephrine for LIA to minimize blood loss after TKA.⁽⁶⁾ Lombardi et al.⁽⁷⁾ reported reducing both postoperative pain and blood loss following TKA using soft tissue and intraarticular injection of bupivacaine, epinephrine and morphine. Anderson et al.⁽⁸⁾ reported that a 195 mL (32%) decrease in the amount of drain output and no transfusion rate after intraoperative injection of bupivacaine with epinephrine compared with the control group. However, none of these studies reported the duration of recovery from anemia among patients undergoing TKA.

In this study, we aimed to compare the duration of Hb recovery between the periarticular epinephrine and nonepinephrine injection groups undergoing TKA.

Methods

A double-blind randomized controlled trial was conducted at Phramongkutklao Hospital, Bangkok from May 2015 to April 2016. Patients with a diagnosis of severe osteoarthritis (OA) knee undergoing TKA were included.

Exclusion criteria comprised patients who had secondary osteoarthritis from rheumatoid arthritis, or posttraumatic OA including revision TKA, bilateral TKA, using postoperative drainage, hypersensitivity to tranexamic acid or epinephrine, history of infection, history of abnormal bleeding or coagulopathy and preoperative anemia (Hb level <10 mg%). In addition to these exclusions, patients who could not take anticoagulant agents or had creatinine clearance <30 mL/min were excluded. Patients were randomly divided in two groups. First, the intervention or epinephrine group with epinephrine and bupivacaine injection received 0.25% bupivacaine 20 mL and epinephrine 10 g. Second, the control or nonepinephrine group received only 0.25% bupivacaine 20 mL. Age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, preoperative Hb level, Hct level and comorbidity were recorded. All operations were performed using a cemented prosthesis (Attune or Sigma, posterior stabilized type, manufactured by DePuy Synthes, USA) by the same orthopedist who was blinded between groups.

The same procedures of operation were performed in all TKAs. The anesthetic technique was spinal block with femoral nerve block. The 350 mm Hg tourniquet pressure was applied during the operation using the medial parapatellar approach. After surgery, patients were provided 10 mg rivaroxaban orally daily and performed ankle pumping exercise for thromboembolism prophylaxis. Complete blood count (CBC) was obtained on the first and third days postoperation. One unit of packed red cell was given in case Hb level was lower than 8.0 mg% or lower than 10 mg% with active or ongoing blood loss. When participants required blood transfusion after TKA, they were not excluded from study. Intention to treat analysis was performed to evaluate all participants.

All patients received the same postoperative rehabilitation protocol such as muscle contraction exercise. The ambulation was immediately encouraged on the second day after operation with a walker. Bleedings from other routes were investigated on a follow-up visit and blood supportive agents were not prescribed in the protocol. Patients had their blood examined for Hb and Hct levels the 3rd postoperative day. Gross's formula was used to calculate total blood loss.⁽¹⁴⁾ The threshold Hb level for blood

transfusion was lower than 8 mg% or 8 to 9 mg% with anemic symptoms.

Estimated blood loss by Gross's formula⁽¹⁴⁾ is described below.

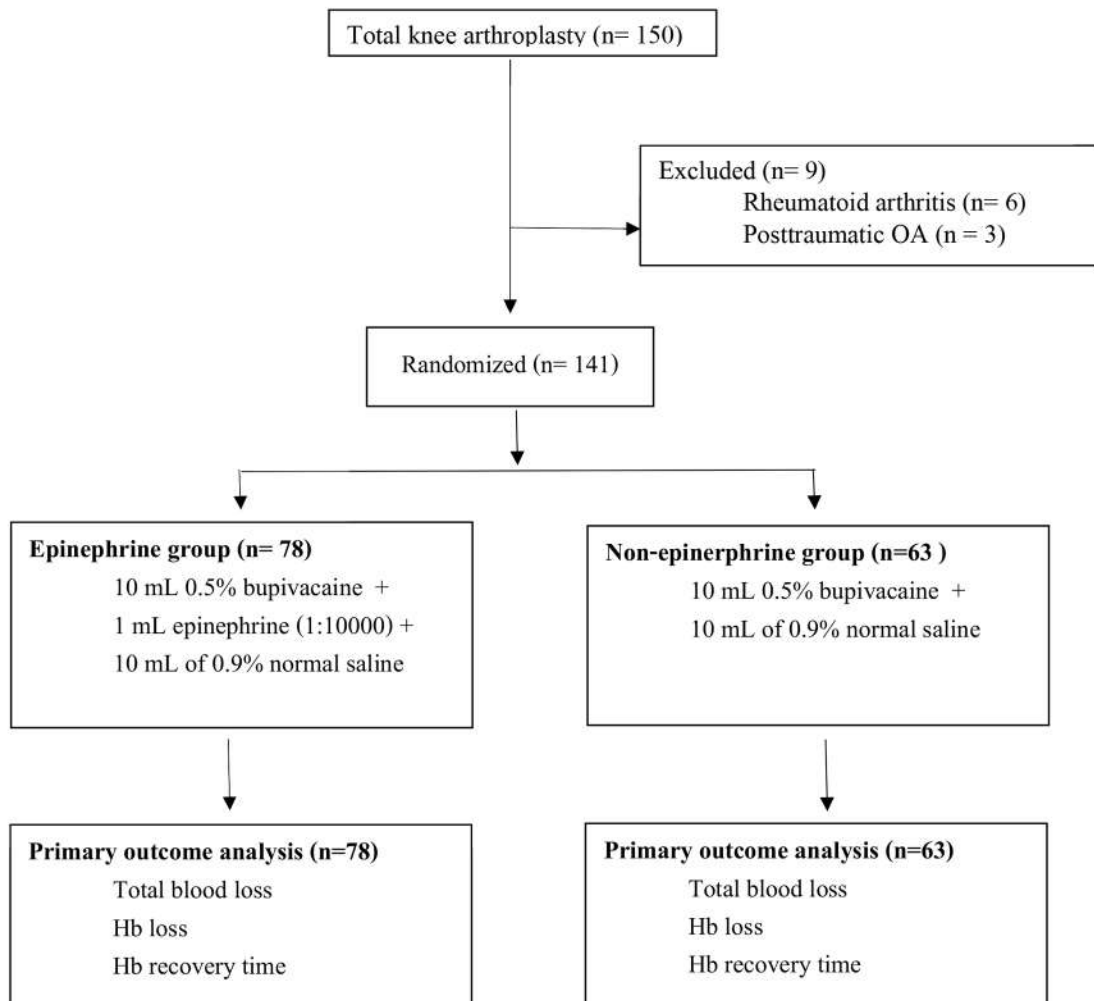
Estimated blood loss = Estimated blood volume x (Hct preoperative - Hct postoperative/ Hct average) + mL of transfused RBC

Estimated blood volume among males: $604 + 0.0003668 \times [\text{height (cm)}]^3 + 32, 2 \times \text{weight (kg)}$

Estimated blood volume among females: $183 + 0.000356 \times [\text{height (cm)}]^3 + 33 \times \text{weight (kg)}$

The duration of Hb recovery to restore preoperative level was calculated from the follow-up data on 1st, 2nd, 3rd, 4th and 5th months postoperatively and until the Hb level returned to normal (the variation of normal Hb level was $\pm 2.46\%$ among males and $\pm 3.15\%$ among females⁽⁸⁾).

Fig. 1 Flow chart of enrollment and randomization of patients undergoing total knee arthroplasty



The enrolled 150 participants were randomized to 78 in the epinephrine group and 63 in the nonepinephrine group. The demographic data between groups were analyzed regarding age, sex, side of TKA, BMI and preoperative Hb and Hct levels using the Chi Squared test for categorical variables and Student's *t* test for continuous variables. The mean differences in Hb recovery duration and 95% confidence intervals (CI) were calculated using Pearson's Chi Square and independent sample *t*-test. A *p* <0.05 was considered statistically significant.

Results

Of 150 patients, 9 were excluded because 6 had rheumatoid arthritis and 3 had posttraumatic OA knee. The enrolled 141 patients were randomized to the epinephrine (n=78) and the nonepinephrine groups (n=63) according to the flow chart of participants shown in **Figure 1**. Demographic data such as age, sex, side of TKA, BMI including preoperative Hb and Hct levels are shown in **Table 1**. Patients were

mostly female and exhibited no significant differences between groups (*p*=0.09 among males, *p*=0.236 among females). Preoperative Hb levels between the two groups did not significantly differ (12.62 ± 1.11 vs. 12.64 ± 1.15 ; *p*=0.891) and demographic data and clinical characteristics did not significantly differ between groups.

From **Table 2**, no significant difference was observed between the epinephrine and nonepinephrine groups concerning total blood loss volume (570.95 ± 302.93 ml vs. 573.56 ± 228 mL; *p*=0.955), postoperative percent Hb loss (13.40 ± 6.66 g/dl vs. 13.01 ± 5.01 g/dl; *p*=0.703) and Hb recovery time (2.52 ± 1.08 months vs. 2.56 ± 1.09 months; *p*=0.855). None of these patients had Hb levels <8.0 g/dl. Thus, no patients received blood transfusion. **Table 2**. Comparison of hemoglobin, hematocrit and hemoglobin recovery time between groups. The Hb level gradually increased to preoperative level at 2.54+1.08 months in both groups as shown in **Figures 2 and 3**. All patients were clinically stable without receiving blood transfusion.

Table1. Demographic and clinical characteristics of the patients in both intervention and control groups

	Epinephrine group (n=78) Mean (SD)	Non-epinephrine group (n=63) Mean (SD)	Total (n=141) Mean (SD)	<i>p</i> -value
AGE, years	70.7 (8.29)	69.11 (7.39)	69.99(7.92)	0.236
SEX, MALE	11 (14.10)	16 (25.40)	27 (19.10)	0.090
SEX, FEMALE	67 (85.90)	47 (74.60)	114 (80.90)	0.236
BMI (kg/m ²)	26.42 (3.52)	25.76 (3.54)	26.13 (3.53)	0.272
Lt	44 (56.40)	26 (41.30)	70 (49.60)	0.074
Rt	34 (43.60)	37 (58.70)	71 (50.40)	0.095
PREOP Hct	38.69 (3.44)	39.00 (3.59)	38.83 (3.50)	0.606
PREOP Hb	12.62 (1.11)	12.64 (1.15)	12.63(1.13)	0.891

Table 2. Comparison of hemoglobin, hematocrit levels and hemoglobin recovery time between groups

	Epinephrine group (n=78) Mean (SD)	Non-epinephrine group (n=63) Mean (SD)	Total (n=141) Mean (SD)	<i>p</i> -value
Hb at Day 3	10.92 (1.24)	10.99 (1.13)	10.95 (1.19)	0.733
Hct at Day 3	33.26 (3.70)	33.53 (3.50)	33.38 (3.60)	0.661
Hb loss	1.69 (0.84)	1.65 (0.67)	1.67 (0.77)	0.743
Hct loss	5.43 (2.68)	5.47 (1.84)	5.45 (2.33)	0.920
% Hb loss	13.40 (6.66)	13.01 (5.01)	13.23 (5.96)	0.703
% Hct loss	13.99 (6.78)	14.02 (4.46)	14.00 (5.84)	0.968
TVB loss	570.95 (302.93)	573.56 (228.00)	572.12(271.10)	0.955
Hb recovery time (month)	2.52 (1.08)	2.56 (1.09)	2.54 (1.08)	0.855

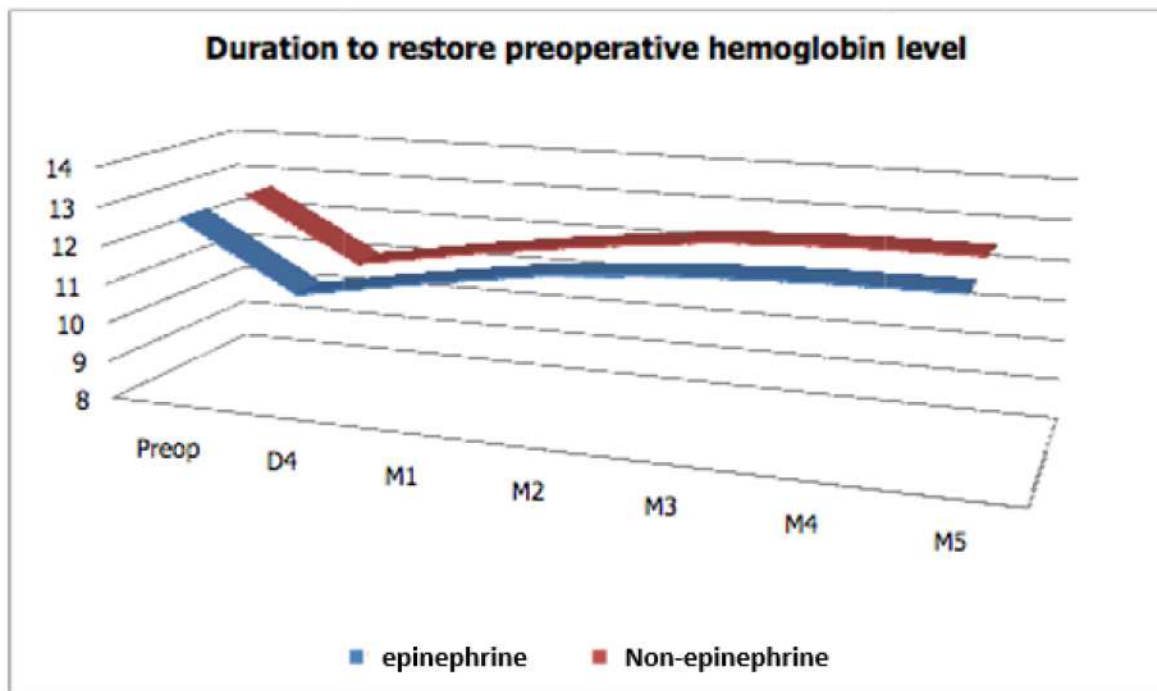


Fig 2. The duration to restore preoperative haemoglobin levels

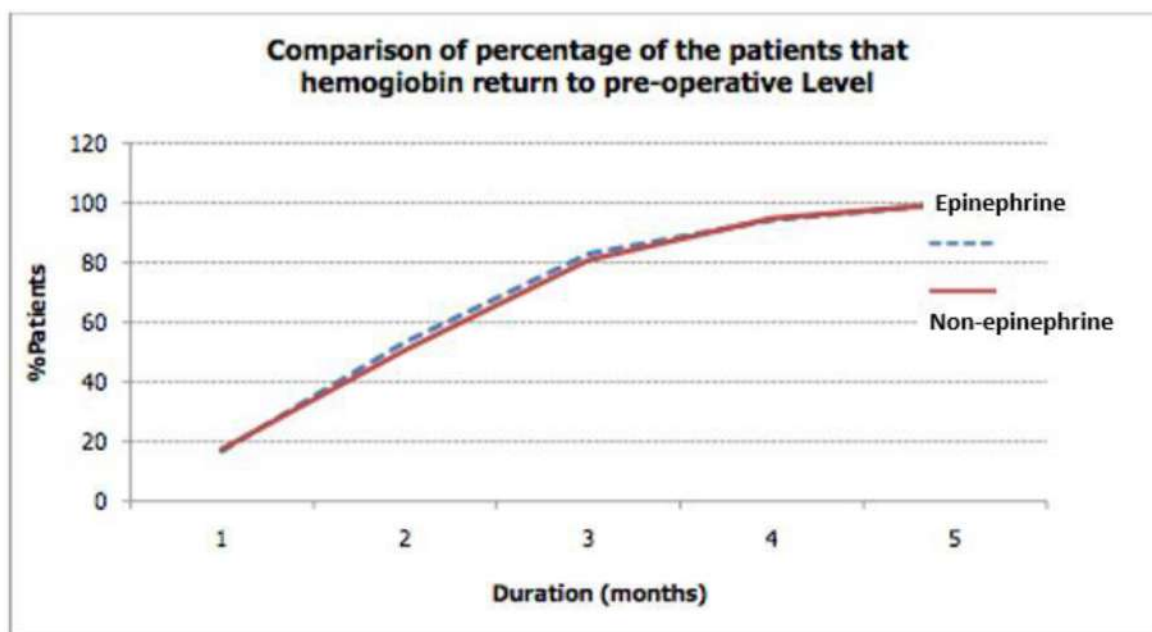


Fig 3. Comparison of percentage of Hb preoperative recovery between groups

Discussion

Recently, technology and surgical techniques involving TKA have been improved using computer navigation, minimal invasive surgery and patient specific implants. Minimal pain, early knee motion, early ambulation, shorter length of hospital stays are beneficial results of surgery and one of the important outcomes is minimal blood loss. Blood loss in TKA usually totals about 500 to 1900 mL. Concealed hemorrhage constitutes one important reason, mainly caused by blood remaining in the intraarticular space up to 500 mL.^(9, 10) With hidden blood loss in the tissue, total blood loss amount could be 765 mL.⁽¹¹⁾ Several techniques have been employed to reduce blood loss in TKA such as drain clamping, intravenous or intraarticular tranexamic acid injection and periarticular epinephrine injection. However, anemia is one of the common postoperative sequelae in TKA.

The 1992 to 1995 baseline data of tourniquet and drain clamping after surgery showed blood in the bottle of the first 24 hours totaled 600 mL with blood transfusion at about 18%. In 2006, we started to use a clamp drain from 1 to 4 hours and eventually 4 hours for primary TKA and 5 hours for revision TKA.⁽¹²⁾ Using a tourniquet, drainage with 4-hour clamp including less operative time could

reduce blood transfusion to less than 5%.

To compare computer navigation with minimal invasive surgeries, TKA showed the amount of drainage within 24 hours was 338 mL and 361 mL, respectively.⁽¹³⁾ Regarding patient specific instrument (PSI) compared with the conventional TKA, postoperative blood loss within 24 hours was 294.3 mL and 311.8 mL as well as Hb loss was 1.7 g/dl and 2.7 g/dl, respectively.⁽¹⁴⁾ In 2014, our related study showed that the use of a tourniquet, drainage and 2 gm tranexamic acid by intravascular injection yielded blood transfusion less than 1% and postoperative Hb levels before blood transfusion were reduced from 10 to 9 g/dl. Patients receiving blood transfusion mostly had preoperative Hct levels less than 33%. These patients showed a Hb loss of 1.7 g/dl.

In this study, TKA was performed without drainage. The most accurate way to determine the total or true blood loss from the operation was the use of calculation. Gibon et al. reviewed using a formula and found that Gross' formula proved reliable and easy to use.⁽¹⁵⁾ We used a safety dose of epinephrine injection to reduce blood loss from TKA operation. Our results showed no significant difference concerning the aspect of reducing blood loss regarding Gross' formula.

Similar results have been reported from other studies. Anderson et al. and Lombardi et al. studied the use of bupivacaine injection along with epinephrine and reported no significant difference in reducing Hb or the bleeding index.^(3,6) However, one advantage of epinephrine injection was demonstrated. Gao et al. reported the use of local tranexamic acid combined with epinephrine injection and observed significantly reduced blood loss and transfusion rate.⁽¹⁶⁾ Epinephrine combined directly with tranexamic acid could increase the tranexamic acid reaction.

In this study, we found no significant differences between the epinephrine and nonepinephrine groups regarding total blood volume loss (518.89 ± 174.19 vs. 521.7 ± 209.12 ; $p=0.953$), % Hb loss (13.69 ± 4.61 vs. 13.67 ± 4.39 mL; $p=0.986$). About 77.8% of TKA patients had anemia but remained asymptomatic. The duration to restore preoperative hemoglobin levels were about the same (2.52 vs. 2.54 months; $p=0.855$). Periarticular epinephrine injection neither decreased blood loss after TKA nor decreased the duration of anemia.

We used the same threshold for blood transfusion similar to other studies;⁽¹⁶⁻¹⁸⁾ however, surgery was performed without blood transfusion in this study. The limitations of our study involved using an indirect method to calculate blood loss and the safety dose of epinephrine injection was inadequate to have an effect on blood loss control. All techniques previously used included LIA with epinephrine injection and could not reduce further blood loss. All patients who had anemia postoperatively could recover to preoperative Hb levels within 2.54 months without anemic symptoms. Surgical techniques and patient conditions were the main causes of reducing blood loss in TKA.

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