Ascorbic Acid reduces the hidden blood loss after Total Knee Arthroplasty: Insights from a Randomized Controlled Trial

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INTRODUCTION:

Blood loss following TKA is one of the complications of TKA, potentially leading to transfusion-related complications and longer hospital stays. Hidden blood loss (HBL) is still a problem during and after TKAs. HBL is the difference between total blood loss (TBL), estimated by hemoglobin drop, and visible blood loss during surgery. It has been demonstrated that instrumentations during TKA may trigger oxidative stress through reactive oxygen species (ROS), which leads to hemolysis, hidden blood loss, and HB drop after surgery. Identifying the aforementioned mechanisms raises the possibility that antioxidants may effectively reduce blood loss following TKA. Ascorbic acid (vitamin C) is a water-soluble and widely used antioxidant that has been proven to protect cells against ROS and blood loss in non-orthopaedic surgeries. Ascorbic acid depletion has also been established in patients who underwent TKA, indicating significant oxidative stress during TKA.

Despite these theoretical benefits, clinical evidence supporting the efficacy of perioperative intravenous ascorbic acid in reducing blood loss during TKA is lacking. Our study aimed to address the gap in the literature through a randomized clinical trial to investigate the effect of intravenous perioperative administration of ascorbic acid on blood loss in patients undergoing outpatient TKA.

METHODS:

In this triple-blinded, randomized, controlled clinical trial, we evaluated patients who underwent primary TKA between June and August 2023 at our institution in an outpatient setting. Patients were randomly allocated into groups. Patients in the ascorbic acid group were administered 3 grams of intravenous ascorbic acid perioperatively. In the control group, patients received an equivalent volume of saline as a placebo at the same frequency. All patients received 1g of intravenous and 1g of intraarticular tranexamic acid. The surgeon, patients, and the analyzer were blind to the grouping.

The primary outcome measure was the amount of HBL estimated by the Gross formula. The blood transfusion rate was recorded. We incorporated the Visual Analogue Scale (VAS) for pain, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score (KOOS), and Forgotten Joint Score (FJS) preoperatively and at six months follow up.

Statistical analysis was executed using SPSS statistical software version 29 (IBM, Armonk, New York). In order to analyze continuous variables that were normally distributed, we utilized the student's t-test and One-way ANOVA. In addition, we used the Mann-Whitney U test and Kruskal–Wallis for analyzing continuous variables that were not normally distributed. The Pearson Chi-Square test was used for categorical variables analysis. Continuous fragility index was calculated to assess the robustness of the continuous variables that were statistically significant. We considered p-values less than 0.05 to be statistically significant.

RESULTS:

After considering the exclusion criteria, 118 patients were included in this study, 59 in each group. The two groups' demographic features, preoperative Hb level, and functional scores showed no statistically significant difference (p-values>0.05). The patients who received ascorbic acid had lower Hb drop (g/dL) (p-value<0.001) and total blood loss on the first postoperative day (p-value<0.001). None of the patients in our study required a blood transfusion (Table 1).

Fewer number of patients who received ascorbic acid reached the minimum clinically important difference (MCID) for Hb drop (2 g/dL) than patients in the control group (15.3% compared to 52.5%, p-value<0.001). Furthermore, the continuous fragility index (CFI) of the Hb drop and TBL were 18 and 19, respectively.

Ascorbic acid reduced the incidence of postoperative anemia, and multivariate logistic regression analysis demonstrated that being male, having lower preoperative Hb, and not using ascorbic acid was associated with an increased likelihood of postoperative anemia.

According to the postoperative functional scores, patients who received ascorbic acid exhibited better functional scores compared to the control group, but the differences were not statistically significant (p>0.05). The detailed findings are demonstrated in Table 2.

No signs of thromboembolic events, infection, failure of the implant, need for reoperation, the incidence of effusion and edema, stiffness, hematoma, and wound complications were detected in the follow-up period.

DISCUSSION AND CONCLUSION: The results of our study demonstrate that patients who received TXA and ascorbic acid had lower amounts of TBL compared to those who received only TXA. The ascorbic acid reduced the total blood loss by around 30% in the first postoperative day. The functional outcomes of the patients who received ascorbic acid were similar to the control group at the 6-month follow-up.

Table 1 Early Postoperative Outcomes of the Study Groups (Mean ± SD)

Variable	Ascorbic Acid n =59	Control n =59	P value
Pre-op Hb level (g/dL)	13.00 ± 1.29	13.13 ± 1.42	0.623
Post-op Hb level (g/dL)	11.69 ± 1.20	11.21 ± 1.20	**0.031***
Hb Drop (g/dL)	1.30 ± 0.72	1.91 ± 0.84	**0.000****
Total Blood Loss (mL)	82.21 ± 44.89	124.57 ± 52.27	**0.000****
Transfusion rate	0 (0 %)	0 (0%)	

Notes: *Hb* hemoglobin, *Post-op:* Postoperative

*: p-value <0.05, **: p-value <0.001

Table 2 Postoperative Functional Scores of the Patients (Mean ± SD)

Variable	Ascorbic Acid Group n = 54	Control Group n = 51	P value
WOMAC	15.25 ± 9.24	21.30 ± 16.63	0.284
OKS	39.26 ± 4.62	36.24 ± 7.74	0.189
FJS	61.11 ± 12.59	51.69 ± 17.58	0.097
KOOS			
Pain	87.22 ± 8.43	84.46 ± 17.26	0.629
Symptoms	89.76 ± 9.17	89.81 ± 9.89	0.936
ADL	84.41 ± 9.54	76.90 ± 17.72	0.224
Sport/Recreation	48.50 ± 28.31	36.11 ± 24.46	0.084
Quality of Life	91.87 ± 10.90	88.88 ± 17.95	0.761

Notes: *WOMAC*: Western Ontario and McMaster Universities Osteoarthritis Index, *OKS:* Oxford Knee Score, *FJS:* Forgotten Joint Score, *KOOS*: Knee Injury and Osteoarthritis Outcome Score, *ADL:* Activities of Daily Living, *: p-value <0.05