

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

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## INTRODUCTION:

Blood loss during total hip arthroplasty (THA) is a concerning challenge, potentially leading to transfusion-related complications and longer hospital stays. Hidden blood loss (HBL) is still a problem during and after THAs. HBL is the difference between total blood loss (TBL), estimated by hemoglobin drop, and visible blood loss during surgery. Studies have reported mean total blood losses ranging from approximately 1,023 mL to 1,785 mL per procedure. Additionally, HBL has been identified as a substantial component, averaging around 429 mL and constituting about 35% of the total perioperative blood loss

It has been demonstrated that instrumentations during THA 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 THA. 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-orthopedic surgeries. Ascorbic acid depletion has also been established in patients who underwent THA, indicating significant oxidative stress during THA.

Despite these theoretical benefits, clinical evidence supporting the efficacy of perioperative intravenous ascorbic acid in reducing blood loss during THA 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 THA.

## METHODS:

In this triple-blind, randomized, controlled clinical trial, we evaluated patients who were scheduled for elective primary THA at our institution. Patients were randomly allocated into groups. Patients in the ascorbic acid group were administered intravenous ascorbic acid before incision and 24 hours postoperatively. 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 total blood loss at 48 hours, estimated from perioperative hemoglobin changes. Secondary outcomes included hidden blood loss estimated by the Gross formula, hemoglobin drop, and transfusion rate. We incorporated the Visual Analogue Scale (VAS) for pain and Harris Hip Score (HHS) at six months follow-up.

Statistical analysis was executed using SPSS statistical software version 29. 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, 95 patients were included in this study. The two groups' demographic features, preoperative Hb level, and functional scores showed no statistically significant difference ( $p$  values > 0.05).

The ascorbic acid group demonstrated significantly lower total blood loss at 48 hours ( $764 \pm 267$  mL vs.  $957 \pm 378$  mL;  $p = 0.005$ ), reduced hidden blood loss ( $308 \pm 287$  mL vs  $497 \pm 405$  mL;  $p = 0.010$ ), and a smaller hemoglobin decline ( $3.26 \pm 1.20$  g/dL vs  $3.87 \pm 1.64$  g/dL;  $p = 0.042$ ). Transfusion was required in 2.1% of the ascorbic acid group compared to 14.9% in the placebo group (OR 6.7;  $p < 0.001$ ).

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. 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 ( $p$ -value < 0.05).

According to the postoperative functional scores, patients who received ascorbic acid exhibited better functional scores compared to the control group at six months; HHS was modestly higher in the ascorbic acid group ( $92 \pm 8$  vs.  $87 \pm 9$ ;  $p = 0.005$ ), while pain scores were similar.

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:

Our findings demonstrated that the intravenous ascorbic acid administered peri-operatively can reduce blood loss and blood transfusion in primary THA with no associated safety concerns. A modest improvement in functional recovery was also noted at 6 months follow-up. These findings support the use of ascorbic acid as an adjunct in blood management protocols

for

THA.

Table 1 Baseline information of the patients of the two groups

Variables	Ascorbic Acid n= 48	Control n= 47	Total n= 95	P-value
Age	43.02 ± 14.52	46.62 ± 10.94	44.80 ± 12.93	0.177
Gender				
Male	27 (56.3)	25 (53.2)	52 (54.7)	0.765
Female	21 (43.7)	22 (46.8)	43 (45.3)	
BMI	25.43 ± 3.30	24.96 ± 3.35	25.20 ± 3.32	0.491
Hospitalization (Days)	4.33 ± 1.60	4.85 ± 2.21	4.59 ± 1.93	0.411
Blood Volume	4.50 ± 0.73	4.45 ± 0.72	4.48 ± 0.72	0.748
Pre-op Hb	13.72 ± 1.88	13.13 ± 1.94	13.43 ± 1.93	0.140
Pre-op VAS	9.46 ± 1.18	9.57 ± 1.33	9.52 ± 1.25	0.258
Pre-op HHS	35.83 ± 10.82	34.87 ± 9.98	35.36 ± 10.37	0.654

Table 2 Postoperative information of the patients of the two groups

Variables	Ascorbic Acid n= 48	Control n= 47	Total n= 95	P-value
Transfusion	1 (2.08)	7 (14.89)	8 (8.42)	<0.001
Post-Op Hb 6h	11.59 ± 1.47	10.96 ± 1.82	11.28 ± 1.68	0.065
Post-Op Hb 24h	11.01 ± 1.38	10.08 ± 1.71	10.55 ± 1.61	0.004
Post-Op Hb 48h	10.45 ± 1.24	9.26 ± 1.21	9.86 ± 1.36	<0.001
Hb Drop 6h	2.13 ± 1.26	2.17 ± 1.43	2.15 ± 1.34	0.858
Hb Drop 24h	2.70 ± 1.18	3.05 ± 1.38	2.88 ± 1.28	0.189
Hb Drop 48h	3.26 ± 1.20	3.87 ± 1.64	3.57 ± 1.46	0.042
TBL 6h	469.29 ± 264.13	526.56 ± 364.44	497.62 ± 317.34	0.384
TBL 24h	614.92 ± 250.90	753.38 ± 362.41	683.42 ± 317.16	0.034
TBL 48h	763.65 ± 266.52	956.76 ± 378.29	859.19 ± 339.07	0.005
HBL (48h)	307.82 ± 286.81	497.39 ± 405.39	401.61 ± 361.43	0.010
Post-op VAS	1.19 ± 0.49	1.55 ± 1.02	1.37 ± 0.81	0.080
Post-op HHS	91.81 ± 8.12	87.36 ± 9.32	89.61 ± 8.97	0.005