Joint Diseases and Related Surgery

Jt Dis Relat Surg
2023;34(3):694-699

ORIGINAL ARTICLE

Does epinephrine use reduce perioperative blood loss during pelvic and femoral osteotomy with open reduction of the patients with developmental dysplasia of the hip?

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Combined surgical procedures involving pelvic and femoral osteotomy with open reduction are the major surgeries and needed for concentric reduction of the hip joint in the treatment of developmental dysplasia of the hip (DDH) after walking age.[1,2] These one-stage procedures may cause abundant amounts of blood loss due to extensive vascular plexus of the hip joint and bone osteotomy procedures. This fact increases the probability of blood transfusion and related risks.[1,2] In the literature, the mean blood loss in pediatric proximal femoral osteotomies ranges between 177 and 369 mL, whereas this ranges between 200 and 971 mL in the combined surgeries (i.e., open reduction, proximal femoral, and pelvic osteotomy).[3-6] It has been reported that the blood transfusion rates increase, as the number of osteotomies increases in pediatric hip reconstruction (3.7% *vs.* 58.4%).[7] In pediatric patients, significant amounts of blood loss and blood

Received: June 26, 2023
Accepted: July 31, 2023
Published online: August 22, 2023

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Doi: 10.52312/jdrs.2023.1282

Citation: Türközü T. Does epinephrine use reduce perioperative blood loss during pelvic and femoral osteotomy with open reduction of the patients with developmental dysplasia of the hip?. Jt Dis Relat Surg 2023;34(3):694-699. doi: 10.52312/jdrs.2023.1282.

ABSTRACT

Objectives: In this study, we aimed to investigate whether the use of epinephrine solution-impregnated gauzes and irrigation fluid with epinephrine could reduce perioperative blood loss during the combined surgical treatment of developmental dysplasia of the hip (DDH) patients.

Patients and methods: Between January 2018 and June 2023, a total of 68 pediatric patients (8 males, 60 females; mean age: 32.4±13.2 months; range, 18 to 98 months) who underwent combined surgery for DDH were retrospectively analyzed. The patients were divided into two groups as those who used topical epinephrine in the surgical sites during combined surgical treatment (n=34) and those who did not (n=34). Demographic and clinical characteristics and pre-, intra-, and postoperative data were recorded. To avoid transfusion complications, blood transfusion was performed in only symptomatic patients in the postoperative period.

Results: Age, sex, weight, and surgical duration were similar between the two groups (p>0.05). No statistically significant difference was found between the groups in terms of preoperative hemoglobin and hematocrit levels (p>0.05) There were statistically significantly differences between the groups in terms of postoperative hemoglobin and hematocrit levels, perioperative amount of blood loss, and postoperative length of hospital stay (p<0.001). No significant difference was found between the groups in terms of intraoperative hemodynamic parameters (p>0.05). The differences in perioperative and estimated intraoperative blood loss amounts and length of hospital stay were statistically significant between the groups (p<0.001). There was a significant relationship between the groups in terms of perioperative and estimated intraoperative blood loss, and transfusion of blood products (p<0.01). Blood transfusion was administered to five patients in the no epinephrine group. No local complications were observed in any group; however, one patient had transfusion-related fever and one patient had allergic skin lesions in the no epinephrine group.

Conclusion: The intraoperative topical use of epinephrine irrigation solution and epinephrine solution-impregnated gauze dressings is effective and safe in reducing blood loss in DDH patients.

Keywords: Congenital hip dislocation, Epinephrine, osteotomy, surgical sponges, topical administration.

transfusions are associated with prolonged length of hospital stay (LOS), increased transfusion reactions, and high infection risk.[8,9] The protective precautions required to minimize intra- and postoperative blood loss and to prevent transfusion and complications have been discussed in the literature.[10,11]

Epinephrine shows hemostatic effect as both a vasoconstrictor and a procoagulant. It causes vasoconstriction of the peripheral blood vessels when used topically and it is used to control capillary bleeding. Its procoagulant effect is obtained in two ways. First, it shortens the platelet transport time in the spleen and increases platelet aggregation by alpha (α)-adrenergic activation leading to an instantaneous increase in platelet count at a rate of 20 to 30%. Second, epinephrine provokes the release of multiple coagulation factors such as fibrinogen via beta (β)-adrenergic activation.[12]

Epinephrine is commonly used to reduce blood loss in plastic and reconstructive operations, as well as nasal surgeries.[13,14] Besides this, it is administered together with tranexamic acid in hip and knee arthroplasty, while it is used as an addition to irrigation liquid or via injection to portal entrances in arthroscopic surgery.[15,16]

Although, it is often used in adult orthopedic surgery, the use of epinephrine in pediatric orthopedic surgery has not been examined yet. In the present study, we aimed to investigate whether the use of epinephrine solution-impregnated gauzes and irrigation fluid with epinephrine could reduce perioperative blood loss during the combined surgical treatment of DDH patients.

PATIENTS AND METHODS

This single-center, retrospective cohort study was conducted at Yüzüncü Yıl University Faculty of Medicine, Department of Orthopedics and Traumatology between January 1st, 2018 and June 1st, 2023. A total of 68 pediatric patients (8 males, 60 females; mean age: 32.4±13.2 months; range, 18 to 98 months) who underwent combined surgery for DDH were included. Only patients aged over 18 months with no health problems except for DDH were included in the study. Those who previously underwent isolated pelvic or femoral osteotomy and who were diagnosed with hemorrhagic or coagulation disorders in the medical past were excluded from the study. Demographic and clinical characteristics of the patients and pre-, intra-, and postoperative data were retrieved from the medical records.

The patients were divided into two groups as those who used topical epinephrine in surgical sites during the combined surgical treatment (n=34) and those who did not (n=34). Irrigation solution containing epinephrine was used during the combined surgery of the patients in the first group. Irrigation solution containing epinephrine was set to contain 1 mg of epinephrine and 250 mL of isotonic solution (dilution 1/250,000). The patients in the second group were administered isotonic solution not containing epinephrine as the irrigation solution during surgery of the patients.

Surgical technique

All patients were operated a single surgeon. A single bikini incision was preferred for open reduction

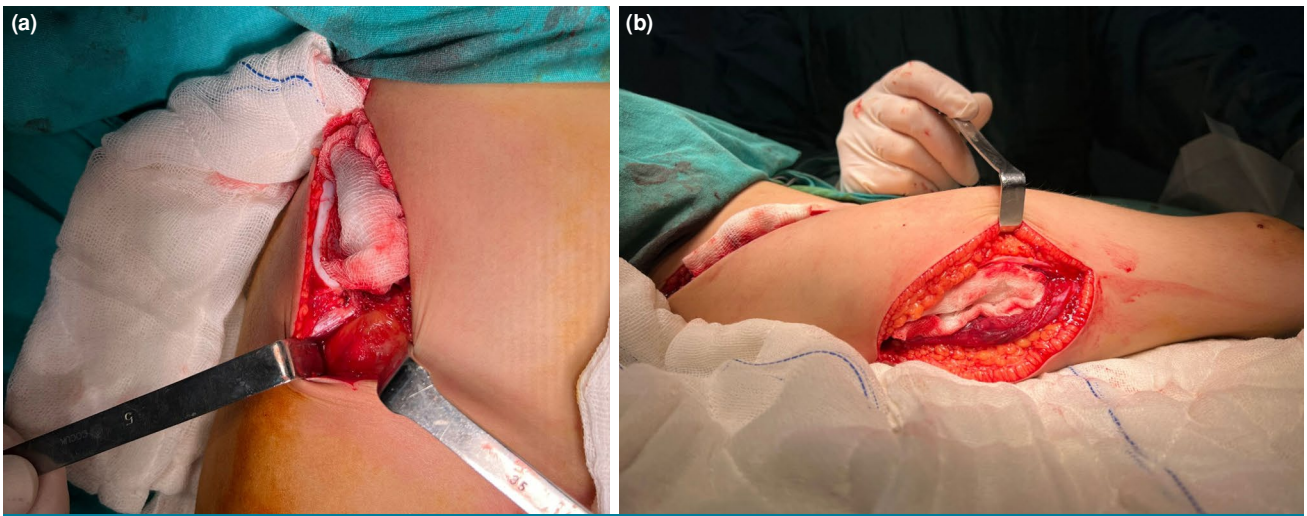

FIGURE 1. Sponges impregnated with epinephrine solution were placed subperiosteally around the iliac bone **(a)** and femur **(b)** before and after osteotomies.

TABLE I
Estimated circulating blood volume according to the age of the patient

Child age	Volemia (mL/kg)
Preterm newborn	90
Term newborn to 3 months	80-90
Over 3 months to 2 years	70-80
Children over 2 years old	70

and Pemberton osteotomy. A second longitudinal incision was used lateral approach to femur for femoral osteotomy. For patients in the first group, sponges impregnated with epinephrine solution (1/250,000) were placed subperiosteally around the iliac bone and femur before and after osteotomies, and surgical sites were frequently washed with this epinephrine irrigation solution (Figure 1). The same procedures were performed using isotonic solution not containing epinephrine (placebo) for the patients in the second group. No drain was placed in any of the patients during the closure of the surgical site.

Data collection

Intraoperative hemodynamic parameters and the amount of intraoperative bleeding was obtained from anesthesia records. The estimated intraoperative bleeding amount was determined by the anesthetist and surgeon by considering the sponges and the amount of fluid accumulated in the aspiration bottle. Pre- and postoperative 24th -hour hematocrit (Hct) and hemoglobin (Hb) levels were obtained from laboratory records. Perioperative period blood loss amount was calculated using the Hct values. The formula described by Gross was preferred in calculating the blood loss amount in the perioperative period.[17] The estimated blood volume (EBV) in this formula was calculated using the Moore's formula.[18] The estimated circulating blood volume used in these calculations was determined according to the patient age (Table I).[19]

$$EBV = 70\ mL\ X\ Body\ Weight/kg$$

$$Estimated\ Blood\ Loss = EBV \times \frac{Hct_0\text{-}Hct_f}{Hct_{AV}}$$

EBV; estimated blood volume, Hct_0; initial preoperative hematocrit, Hct_f; final postoperative hematocrit, Hct_{AV}; average of initial and final hematocrit.

The presence of systemic and local complications and requirement of transfusion of blood products were obtained from clinical records.

Statistical analysis

Statistical analysis was performed using the SAS version 9.4 software (SAS Institute, NC, USA). Descriptive data were presented in mean ± standard deviation (SD), median (min-max), or number and frequency, where applicable. The distribution of the variables was assessed using the Kolmogorov-Smirnov test. Unpaired t-test and paired t-tests were respectively used for the continuous variables, while

TABLE II
Demographic and clinical characteristics of the patients

	Epinephrine group (n=34)		No Epinephrine group (n=34)		
Characteristics	n	Mean±SD	n	Mean±SD	*p*
Age (month)		32.5±15.6		32.3±10.5	0.9711
Sex					
Male	4		4		
Female	30		30		
Weight (kg)		15.0±2.9		15.3±2.3	0.5879
Preoperative Hb levels (g/L)		12.5±0.9		12.7±0.9	0.2327
Postoperative Hb levels (g/L)		10.4±1.0		9.3±1.0	<0.0001
Preoperative Hct levels (%)		37.9±2.9		38.8±2.2	0.1619
Postoperative Hct levels (%)		32.0±3.0		27.5±2.9	<0.0001
Surgery time (min)		133.7±18.9		131.6±16.4	0.6341
Intraoperative estimated blood loss		41.1±9.4		87.3±27.0	<0.0001
Peroperative estimated blood loss		169.0±41.6		366.1±75.3	<0.0001
Postoperative LOS (h)		38.1±14.6		50.1±14.9	0.0013

SD: Standard deviation; Hb: Hemoglobin; Hct: Hematocrit; LOS: Length of hospital stay.

TABLE III
Intraoperative hemodynamic values of patients

	Epinephrine group	No Epinephrine group	
	Mean±SD	Mean±SD	*p*
Systolic arterial pressure	88.1±3.8	89.0±3.8	0.3125
Diastolic arterial pressure	50.9±3.3	50.6±3.5	0.7513
Heart rate	111.7±5.4	110.6±5.1	0.3999
Saturation	98.5±0.5	98.5±0.5	1.0000

SD: Standard deviation.

the Pearson correlation test was used to identify the relationship between the variables. The chi-square test was carried out for the analysis of categorical variables. A *p* value of <0.05 was considered statistically significant.

RESULTS

Age, sex, weight, and surgical duration were similar between the two groups (p>0.05) (Table II). No statistically significant difference was found between the groups in terms of preoperative Hb and Hct levels (p>0.05). However, there were statistically significant differences between the groups in terms of postoperative Hb and Hct levels, perioperative amount of blood loss and postoperative LOS (p<0.001) (Table II).

No significant difference was found between the groups in terms of intraoperative hemodynamic parameters (p>0.05) (Table III). The differences between the groups regarding perioperative and estimated intraoperative blood loss amounts, as well as LOS were statistically significant (p<0.001). Besides, there was a significant relationship between the groups in terms of perioperative and estimated intraoperative blood loss, and transfusion of blood products (p<0.01). Blood transfusion was administered to five patients in the no epinephrine group. While no local complications were observed in any of the groups, one patient had transfusion-related fever and one patient had allergic skin lesions in the no epinephrine group.

DISCUSSION

In the present study, we investigated whether the use of epinephrine solution-impregnated gauzes and irrigation fluid with epinephrine could reduce perioperative blood loss during the combined surgical treatment of DDH patients. Our study results showed that intraoperative topical use of epinephrine irrigation solution and gauze dressings impregnated with epinephrine solution were effective in reducing the amount of blood loss and transfusion needs. This reduced transfusion need provides a decrease in the blood-borne infections, serious immunological reactions, and transfusion-related complications.

Epinephrine has been successfully used to reduce blood loss in the various operations of orthopedic surgery. Malone et al.[20] proved the efficacy of epinephrine in total knee arthroplasty. Zubairi et al.[21] also demonstrated that epinephrine was effective in reducing the amount of blood loss and transfusion needs in the surgical treatment of knee contracture. Wu et al.[22] reported that epinephrine together with tranexamic acid decreased blood loss in total hip arthroplasty. In the literature, the use of epinephrine in the field of orthopedic surgery involves the studies conducted in the adult patients. To the best of our knowledge, the present study is the first to evaluate the efficacy and safety of epinephrine in reducing the amount of perioperative bleeding in pediatric orthopedic surgery. Of note, there is a very limited number of study in the literature regarding the methods for reducing blood loss in hip reconstruction of pediatric patients.

Furthermore, there is no consensus on the appropriate concentration and administration technique of epinephrine. Different procedures and doses were administered in various specialization fields for reducing blood loss and safe surgery. Topical epinephrine was administered at a concentration of 1/1,000 in endoscopic endonasal sinus surgery.[23] In the pediatric burn patients, the use of subcutaneous epinephrine injection at a concentration of 1/100.000 before debridement and sponge impregnated with epinephrine during debridement were recommended.[24] Epinephrine was applied topically at a concentration of 1/125,000 in the osteotomy site during the total knee arthroplasty surgery.[25] Since the present study included pediatric patient population, we preferred to apply epinephrine topically at a concentration of 1/250,000.

Although epinephrine is used widely as a hemostatic agent via topical application or infiltration, its acute systemic cardiovascular effects have not been exactly clarified. High arterial blood pressure, increased heart rate, cardiac arrhythmia and myocardial infarction are considered as the side effects that may occur in the systemic use of epinephrine. Kinsella et al.[26] encountered no hemodynamic instability in cleft palate surgery in which they applied epinephrine infiltration. Liu et al.[25] applied epinephrine topically on the osteotomy line in the cases of total knee prosthesis and encountered no remarkable hemodynamic change. Also, in this study, intraoperative hemodynamic parameters were within the normal limits and epinephrine significantly reduced the perioperative bleeding volume without leading to any hemodynamic changes.

Hemorrhagic hypovolemia may cause multiple organ failure by leading to tissue hypoperfusion and tissue hypoxia, and consequently ischemic organ damage.[27] Since hepatic and renal functions of the pediatric patients are less-developed, their susceptibility to hypovolemia and ischemia is higher. In terms of postoperative LOS, no epinephrine group exhibited longer LOS than the epinephrine group. The reason is that the patients in the no epinephrine group were followed for a longer period of time for the probability of any ischemic organ damage due to the higher amounts of blood loss.

The general approach of our clinic against postoperative anemia is avoiding to perform blood transfusion, unless it is symptomatic (i.e., tachypnea, tachycardia, hypoxia). Blood transfusion is not an innocent procedure and it should be considered as an organ transplantation. In the present study, transfusion was needed in none of the patients from the epinephrine group; however, erythrocyte transfusion was performed in five patients from the no epinephrine group, since they revealed evidence of symptomatic anemia.

The use of local anesthetics with epinephrine is usually regarded as contraindicated for surgical procedures involving the fingers, toes, penis, outer ear, and the tip of the nose due to ischemic necrosis. Contrarily, many studies have reported that local use of epinephrine is safe.[28,29] Altınyazar et al.[30] found no local complication in the study carried out to observe the vasoconstrictive effect of epinephrine in digital block anesthesia. In another study, finger necrosis was encountered in none of the patients by application of low-dose epinephrine injection during the surgical treatment of polydactyly in the infants.[31] Liu et al.[25] observed no local complications in any of the patients after the topical application of epinephrine in the cases of total knee prosthesis. Also in the present study, no local complication was observed in the epinephrine group.

The main strengths of our study are the fact that the same surgical procedures were applied in the patients of both epinephrine and placebo groups and an identical surgeon performed the surgical operations. The limitations to this study are that it is a single-center, retrospective study, the difference between epinephrine doses was not evaluated, and the number of patients in the study is relatively low. Epinephrine demonstrates high variety regarding clinical application route and application dose. Therefore, further prospective studies with larger patient groups are needed to evaluate the dosage and application route of epinephrine and its complications in the pediatric patient group.

In conclusion, the intraoperative topical use of epinephrine irrigation solution and epinephrine solution-impregnated gauze dressings is effective and safe in reducing blood loss. However, further studies are warranted to draw more reliable conclusions on this subject.

Ethics Committee Approval: The study protocol was approved by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (date: 16.06.2023, no: YYUEC-2023/06-07). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents and/or legal guardians of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The author received no financial support for the research and/or authorship of this article.

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