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Clinical and Laboratory Impact of Postpartum Enoxaparin Prophylaxis After Vaginal Delivery: A Retrospective Cohort Study

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What is known on this subject?

Venous thromboembolism is a leading cause of maternal morbidity and mortality postpartum. Low molecular weight heparin is recommended for prophylaxis in moderate- to high-risk women. Limited data exist on the effects of enoxaparin on wound healing and laboratory parameters.

What this study adds?

This study demonstrates that prophylactic enoxaparin after vaginal delivery is not associated with significant bleeding, wound complications, or changes in routine hematological parameters. Risk-based enoxaparin prophylaxis appears feasible and safe, but large-scale prospective studies are needed to confirm these findings and determine the optimal dose and treatment duration.

ABSTRACT

Objective: To assess the clinical and laboratory effects of prophylactic enoxaparin use after vaginal delivery on bleeding, wound complications, and hematological parameters.

Material and Methods: This retrospective cohort study included 36 postpartum women who received enoxaparin prophylaxis for deep vein thrombosis and 95 who did not; all delivered at 37-41 weeks of gestation. Maternal demographic characteristics, delivery-related data, bleeding- and wound-related complications, as well as hemoglobin, hematocrit, and platelet counts before delivery, at 6 hours postpartum, and on the 10th postpartum day were retrieved from the hospital database. Changes in laboratory values between 6 hours and 10 days postpartum were calculated. All variables were compared between the enoxaparin and non-enoxaparin groups.

Results: Women who received enoxaparin were older, had higher body mass index and greater parity, and had significantly lower episiotomy rates ($p<0.001$), compared with those who did not receive enoxaparin. No significant differences were observed between the groups in rates of labor induction or in bleeding- or wound-related complications. The differences in hemoglobin (1.90±0.67 vs. 1.57±0.67 g/dL, $p=0.115$), hematocrit (6.84±2.40 vs. 5.76±2.21%, $p=0.127$), and platelet counts (113.94±62.70 vs. 125.10±70.89×10^3/µL, $p=0.592$) between the 10th day and 6 hours postpartum were also not significantly different between groups.

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ABSTRACT

Conclusion: Prophylactic enoxaparin use after vaginal delivery was not associated with significant adverse effects on bleeding, wound complications, hemoglobin, hematocrit, or platelet counts. Risk-based enoxaparin prophylaxis appears safe and feasible for women after vaginal delivery. Our findings need to be confirmed by large-scale prospective studies.

Keywords: Enoxaparin, hemoglobin, low molecular weight heparin, postpartum prophylaxis, thromboprophylaxis, vaginal delivery, venous thromboembolism

Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis and pulmonary embolism, is a major vascular disorder and a significant cause of morbidity and mortality worldwide (1). Risk factors include surgery, trauma, malignancy, and pregnancy, among others, with events often remaining unprovoked in the absence of clear triggers (2). Pregnancy and the postpartum period are important risk factors for VTE. The incidence of pregnancy-related VTE was approximately 1.2 per 1.000 deliveries (3). Since VTE is one of the leading causes of maternal morbidity and mortality (4), identifying women at high risk is crucial. The incidence of VTE is higher in the postpartum period than at any time during pregnancy, with the risk peaking particularly within the first 6 weeks after delivery (5). The Royal College of Obstetricians and Gynaecologists (RCOG) has proposed a risk assessment scoring system for VTE in the postpartum period (6). According to this protocol, women in the low-risk group are recommended early mobilization and avoidance of dehydration; those in the intermediate-risk group are recommended at least 10 days of low molecular weight heparin (LMWH) therapy; and those in the high-risk group are recommended at least 6 weeks of LMWH therapy (6).

The current literature provides insufficient data regarding the efficacy and potential adverse effects of LMWH in the prevention of postpartum VTE. A randomized controlled trial (RCT) evaluated the efficacy of short-term enoxaparin prophylaxis; participation was feasible, but the number of events was very low, highlighting the need for large, multicenter trials (7). A large prospective study compared bemiparin with enoxaparin and reported that both agents reduced the incidence of VTE compared with the control group, with bemiparin showing more favorable outcomes regarding both efficacy and wound complications (8). In contrast, retrospective observational studies indicated that enoxaparin use may increase the risk of wound dehiscence and hematoma following cesarean delivery (9,10). Pilot studies using risk-score models have demonstrated that prophylaxis can effectively prevent VTE in appropriately selected patients while reducing unnecessary drug exposure (11).

Although the use of LMWH is recommended, studies investigating its potential adverse effects in the postpartum period are limited. Moreover, most existing studies focus on cesarean deliveries, whereas studies on vaginal deliveries are considerably fewer. The aim of our study is to systematically evaluate the clinical effects and laboratory parameters of enoxaparin in women undergoing vaginal delivery, focusing on wound complications and laboratory outcomes.

Material and Methods

This retrospective cohort study was conducted at a tertiary care center after approval from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (approval number: KAEK/11.09.2024.222, protocol code: 2024-222, date: 17.09.2024). Data were obtained from the electronic hospital information system, which included clinical, laboratory, and treatment records of eligible patients. Women who delivered vaginally between 37 and 41 weeks of gestation were screened for eligibility. The inclusion criteria were maternal age between 18 and 40 years, singleton pregnancy, and vertex presentation. Women were excluded if they had non-vertex presentation, multiple pregnancy, body mass index (BMI) greater than 40 kg/m², acute chorioamnionitis, known coagulopathies, prior uterine or cervical surgery, cervical or high-grade perineal lacerations, uterine rupture, uterine atony, placental invasion anomalies, placenta previa, vasa previa, placental or cord anomalies, history of postpartum hemorrhage, major or massive intrapartum hemorrhage, thalassemia, sickle cell anemia, sideroblastic anemia, intravenous iron therapy, use of antiplatelet medications, or blood transfusion.

The primary maternal characteristics analyzed were age, BMI, gravidity, parity, gestational age, fetal weight, and ethnicity. Delivery-related data included induction of labor, episiotomy, and the presence of bleeding-related or wound complications. Laboratory values included hemoglobin, hematocrit, and platelet count, which were measured before delivery, at six hours postpartum, and on the tenth postpartum day. Treatment-related data focused on the administration of enoxaparin -including dosage

and duration- and on other prophylactic or therapeutic postpartum interventions. For women with hemogram results available on the 10th postpartum day, changes in hemoglobin, hematocrit, and platelet counts from the 6th postpartum hour to the 10th postpartum day were calculated and compared between groups. In our clinic, postpartum prophylaxis with enoxaparin is administered in accordance with the Turkish Ministry of Health Guideline on the Management of High-Risk Pregnancies and the RCOG recommendations. Under this protocol, early mobilization and prevention of dehydration are advised for women in the low-risk category; a minimum of 10 days (or longer, if indicated) of LMWH therapy is recommended for those in the intermediate-risk category; and at least 6 weeks of LMWH therapy is recommended for those classified as high-risk (6). The first dose of enoxaparin was administered after ensuring hemostasis and the absence of contraindications, particularly active bleeding or complications related to regional anesthesia. Treatment duration and dose adjustments were tailored according to the clinical status, and hematology consultation was requested in complex cases.

Statistical Analysis

All analyses were performed using SPSS version 26.0.1 (SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed variables were presented as mean ± standard deviation and compared using the Student's t-test. Non-normally distributed variables were expressed as median (minimum-maximum) and analyzed with the Mann-Whitney U test. Categorical variables were summarized as frequencies and percentages and compared using the chi-square test. A two-tailed p value less than 0.05 was considered statistically significant.

Results

A total of 131 women who met the eligibility criteria were included in the analysis. Of these, 36 women received enoxaparin prophylaxis for 10 days following vaginal delivery, while 95 did not receive prophylaxis. A total of 28 women received 40 mg/day, seven received 60 mg/day, and one received 80 mg/day of enoxaparin prophylaxis for ten days. Baseline demographic and clinical characteristics are summarized in Table 1. Women who received enoxaparin were significantly older (30.14±6.69 vs. 25.21±4.15 years, $p<0.001$) and had a higher BMI (31.54±4.75 vs. 27.81±3.92 kg/m², $p<0.001$). Gravidity and parity were higher in the enoxaparin group ($p<0.001$ for both). Gestational age at delivery and fetal birth weight were comparable between groups. Ethnic distribution did not differ significantly. The frequency of episiotomy was lower among enoxaparin users (22% vs. 66%, $p<0.001$). Rates of labor induction and bleeding-related or wound-related complications did not differ significantly between groups.

The hematological changes between the 6th postpartum hour and the 10th postpartum day are presented in Table 2. No statistically significant differences were observed between the groups. The mean reductions in hemoglobin (1.90±0.67 vs. 1.57±0.67 g/dL; $p=0.115$) and hematocrit (6.84±2.40% vs. 5.76±2.21%; $p=0.127$) were greater in the enoxaparin group, although these differences were not statistically significant. Changes in platelet count were also similar (113.94±62.70 vs. 125.10±70.89)×10³/µL ($p=0.592$).

Table 1. Demographic and obstetric characteristics of the study groups

Parameter	Enoxaparin non-users (n=95)	Enoxaparin users (n=36)	p value
Age[a] (years)	25.21±4.15	30.14±6.69	<0.001
BMI[a] (kg/m²)	27.81±3.92	31.54±4.75	<0.001
Gestational age[b] (days)	275 (259-287)	276 (259-287)	0.816
Gravidity[b]	1 (1-5)	3 (1-6)	<0.001
Parity[b]	1 (1-5)	3 (1-5)	<0.001
Fetal weight[a] (g)	3210.45±389.28	3322.92±416.91	0.150
Turkish ethnicity[c] (n)	73 (77%)	29 (81%)	0.814
Episiotomy[c] (n)	63 (66%)	8 (22%)	<0.001
Labor induction[c] (n)	20 (21%)	11 (31%)	0.253
Bleeding-related and wound complications[c] (n)	14 (15%)	1 (3%)	0.067

[a]: Normally distributed data; presented as mean ± standard deviation, compared using t-test, [b]: Non-normally distributed data; presented as median (min-max), compared using Mann–Whitney U test, [c]: Categorical data; presented as n (%), compared using chi-square test. BMI: Body mass index.

Table 2. Comparison of the difference between 10th postpartum day and 6th postpartum hour laboratory values in the study groups

Difference	Enoxaparin non-users (n=30)	Enoxaparin users (n=17)	p value
HB[a] (g/dL)	1.57±0.67	1.90±0.67	p=0.115
HCT[a] (%)	5.76±2.21	6.84±2.40	p=0.127
PLT[a] (10^3/μL)	125.10±70.89	113.94±62.70	p=0.592

[a]: Normally distributed data; presented as mean ± standard deviation, compared using t-test. HB: Hemoglobin; HCT: Hematocrit; PLT: Platelet count.

Discussion

Rates of bleeding and wound complications were similar in women who received enoxaparin prophylaxis and in those who did not. Changes in hemoglobin, hematocrit, and platelet counts between the 6th postpartum hour and the 10th postpartum day did not differ significantly between groups. Compared with non-users, enoxaparin users were older, had higher BMI and parity, underwent episiotomy less frequently, and had similar rates of labor induction.

Pregnancy and the postpartum period represent physiologic states in which all three components of Virchow's triad (venous stasis, endothelial injury, and hypercoagulability) are present and collectively contribute to an elevated risk of VTE (12). Venous stasis occurs primarily due to pregnancy-related alterations in the venous system. Although total blood volume and venous return increase during gestation, linear flow velocity in the lower extremity veins decreases because of hormonally mediated dilation of capacitance veins, promoting venous pooling and valvular incompetence (13). This effect is further amplified by compression of the inferior vena cava and the iliac veins by the gravid uterus, particularly in late pregnancy, and may be accentuated in the supine position (13,14). Additionally, compression of the left iliac vein by the right iliac artery contributes to the observed predominance of left-sided deep vein thrombosis in pregnancy (15,16). Endothelial injury is another important factor, as delivery involves vascular disruption at the uteroplacental interface. Instrumental deliveries (forceps or vacuum extraction) and cesarean section can exacerbate vascular intimal damage, thereby increasing immediate postpartum VTE risk (16). Hypercoagulability during pregnancy is characterized by progressive increases in several coagulation factors (I, II, VII, VIII, IX, X) alongside decreased protein S activity (16,17,18). Resistance to activated protein C increases during the second and third trimesters and correlates with increased thrombotic risk (19). Fibrinolytic inhibitors, such as plasminogen activator inhibitor-1 and -2, also increase, although total fibrinolytic capacity may remain unchanged (20). The postpartum period carries the highest VTE risk, particularly within the first six weeks following delivery, after which the risk gradually declines to approximate baseline levels by 13-18 weeks (5). Pregnancy itself is a recognized VTE risk factor, and this risk is further magnified in the presence of inherited thrombophilias, such as factor V Leiden, the prothrombin G20210A mutation, antithrombin III deficiency, protein C or protein S deficiency, and antiphospholipid syndrome (17,21,22,23). Patients with these conditions, particularly those with a personal or family history of VTE, may experience a several-fold increase in thrombotic risk during the antepartum and postpartum periods (23,24). In our study, enoxaparin users were older and had higher BMI and parity than non-users. These findings are consistent with the risk factors outlined in the RCOG protocol (6). The episiotomy rate was significantly lower among patients who received enoxaparin. We attribute this finding to episiotomy being more commonly performed during first deliveries and to parity being scored as a risk factor according to the RCOG protocol.

Only a limited number of studies have investigated the association between enoxaparin and bleeding and surgical-site complications in the postpartum period, and their results are inconsistent. In a prospective pilot study, Cavazza et al. (11) reported that postpartum LMWH prophylaxis after cesarean delivery was not associated with hemorrhagic events. Similarly, in a pilot RCT, Blondon et al. (7) evaluated enoxaparin in women undergoing cesarean or vaginal delivery and demonstrated that it had no significant effect on surgical wound complications. In the study by Ferres et al. (9), wound complications were reported more frequently among women receiving enoxaparin after cesarean delivery, with the risk particularly pronounced among morbidly obese women (BMI >35). In contrast, rates of deep vein thrombosis and pulmonary embolism remained low and did not differ significantly between groups. In our study, however, enoxaparin use among women who delivered vaginally was not associated with any significant effect on bleeding, wound complications, or hematological parameters. This discrepancy may largely stem from differences in the characteristics of the studied populations. The cohort in the study by Ferres et al. (9) consisted of women with a higher maternal risk profile who

underwent a surgical procedure (cesarean delivery), whereas our study focused on women who delivered vaginally, a population at lower surgical risk. Therefore, postoperative recovery and additional comorbidities among cesarean patients may have contributed to the increased wound complication rates, whereas the lower surgical risk associated with vaginal delivery could explain the absence of such complications in our study. To our knowledge, this is the first study in Türkiye to specifically investigate the prophylactic use of enoxaparin after vaginal delivery at a tertiary-care center. Previous research in Türkiye has largely focused on prophylaxis following cesarean section (25). Şahin and Şahin (25) evaluated 41 women who received enoxaparin after cesarean delivery, comparing doses of 40 mg/day and 60 mg/day. Although there were no significant differences between the two dosing groups in age, gravidity, gestational age, or hematological parameters, higher-dose enoxaparin was associated with a marked increase in surgical site complications, including wound infections and hematomas. Reductions in platelet counts were also more pronounced in the 60-mg/day group. These findings highlight a potential dose-dependent increase in the risk of surgical-site complications without conferring additional hematological benefit. In contrast, our study focused on women delivering vaginally, a population in which surgical-site complications are less frequent. Accordingly, we observed no significant increase in bleeding-related or wound-related complications among enoxaparin users; the hematological parameters remained stable. Taken together, these data suggest that prophylactic enoxaparin may be safely administered after vaginal delivery and may support risk-stratified prophylaxis based on maternal characteristics.

Our study demonstrated that prophylactic use of enoxaparin after vaginal delivery did not have a significant adverse effect on bleeding, surgical site complications, or routine hematological parameters (hemoglobin, hematocrit, and platelet count). These preliminary findings suggest that applying risk-based prophylaxis in low-surgical-risk vaginal deliveries may be feasible without undue concern regarding the hematological side effects of enoxaparin. However, due to the limited sample size and the retrospective design of our study, further confirmation in larger cohorts and prospective RCTs is required before more definitive and reliable recommendations can be made for clinical practice. We propose several directions for future research. Dose-response studies comparing different doses and durations (e.g., 10 days vs. 6 weeks; 20/40/60 mg regimens) may address an important gap in clinical practice. In addition, studies that incorporate measures of treatment adherence, treatment burden, patient satisfaction, and cost-effectiveness may provide valuable insights into the feasibility of prophylactic use of enoxaparin. Furthermore, large-scale prospective studies to capture rare VTE events and investigations evaluating the short-term effects of enoxaparin on hemostasis through biomarkers such as thrombin generation, D-dimer, and fibrinogen may be conducted.

The strengths of our study include that it is the first dataset obtained from a tertiary care center that specifically focuses on the vaginal-delivery population. This provides insight into a distinct clinical group, in contrast to previous studies that largely focused on prophylaxis following cesarean delivery. In addition, the careful application of well-defined exclusion criteria (such as coagulopathies, severe anemia, and major intrapartum hemorrhage) ensured that the analyzed patient group was more homogeneous and targeted.

Study Limitations

The limitations of our study include its retrospective design, small sample size, and the limited number of patients with 10th-day laboratory data. This limited sample size substantially reduces the study's power to detect small effect sizes and rare events, such as VTE. Additionally, patients in the enoxaparin group had a higher baseline risk for VTE, characterized by older age, higher BMI, and greater parity. This may have influenced both event rates and bleeding profiles, potentially masking or exaggerating the true effect of the drug. Limitations in follow-up duration and methodology may have led to under-detection of late or asymptomatic VTE events. The study did not systematically assess dose-response relationships or the impact of treatment duration, which limits the ability to draw definitive conclusions regarding optimal dosing and therapy length.

Conclusion

In this retrospective cohort study, prophylactic enoxaparin use after vaginal delivery was not associated with significant adverse effects on bleeding, wound complications, or routine hematological parameters. These findings suggest that risk-based enoxaparin prophylaxis may be feasible and safe in women following vaginal birth. However, due to the retrospective design and limited sample size, definitive conclusions cannot be drawn. Large-scale prospective RCTs are needed to validate these preliminary findings and to investigate dose–response relationships and optimal treatment durations.

Ethics

Ethics Committee Approval: Approval for the study was received from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (approval number: KAEK/11.09.2024.222, protocol code: 2024-222, date: 17.09.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.D., A.S.Y., C.T., Ş.B., N.S., E.A., Y.K., Concept: E.D., C.T., Y.K., Design: E.D., A.S.Y., Ş.B., N.S., E.A., Data Collection or Processing: Ş.B., N.S., E.A., G.G., Analysis or Interpretation: E.D., Literature Search: E.D., A.S.Y., C.T., Y.K., G.G., Writing: E.D., A.S.Y., C.T., Y.K., G.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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