ISSN 2692-5877
DOI: 10.46998/IJCMCR.2021.13.000301

International Journal of
Clinical Studies & Medical Case Reports

Research Article

Retrospective Analysis of Bleeding in Pregnant Patients on Anticoagulation: A Single Center Experience

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Received: August 20, 2021 Published: September 10, 2021

Abstract

Heparin and low molecular weight heparin are considered safe to use during pregnancy because they do not cross the placenta, however these agents do present potential risk, particularly that of bleeding during the peripartum period. We aimed to investigate the safety of anticoagulation therapy in high-risk pregnancies, assessing the blood loss and transfusion requirements at the time of delivery and the immediate postpartum period. We retrospectively analyzed the clinical data and outcomes of 13 patients on anticoagulation ante- and postpartum and compared this to 26 matched controls. All patients delivered at Georgetown University Hospital between January 2016 and December 2017 and were matched by age (± 2 years), delivery date (± 1 month), delivery method (cesarean or vaginal), and gravidity by equal or close approximation. The average age at delivery was 33.0±4.9 years and the majority of patients delivered via cesarean section (85%). Of the 13 patients on anticoagulation therapy during pregnancy, 6 individuals received therapeutic dosing and 7 received prophylactic dosing. We found no significant difference in estimated blood loss between individuals taking anticoagulation during pregnancy as compared to matched controls (P=0.772). There was also no significant difference in antepartum hemoglobin or hematocrit (P=0.735 and P=0.558, respectively), postpartum hemoglobin or hematocrit (P=0.940 and P=0.916, respectively), or a difference in hemoglobin or hematocrit antepartum versus postpartum (P=0.721 and P=0.525, respectively). Additionally, mean transfusion requirements between cohorts were not statistically significant (P=0.298). These data suggest that anticoagulation during high-risk pregnancies is safe with no evidence of increased bleeding or need for transfusion.

Introduction

During pregnancy, women develop a physiologic hypercoagulable state related to hormonal changes and physical factors which can predispose them to the development of Venous Thromboembolism (VTE) [1]. Anticoagulation may be prescribed for women with a history of thrombosis or underlying conditions that add additional risk of developing VTE or predispose to pregnancy loss. Women with a history of VTE or a known thrombophilia may require thromboprophylaxis or therapeutic anticoagulation for VTE prevention. Unfractionated Heparin (UFH) and Low-Molecular-Weight Heparin (LMWH) are preferred in pregnancy because they do not cross the placenta [2, 3], however these agents do present potential risks, particularly that of bleeding for both the mother and fetus [4]. Special consideration must be made to ensure therapeutic concentrations are maintained given the physiologic changes that occur during pregnancy. Increases in maternal blood volume and glomerular filtration rate alter the renal excretion and plasma concentration of heparin, influencing the half-life and peak plasma concentration of these medications [5]. LMWH is favored clinically over UFH due to fewer adverse effects [5] and ease of administration, and the most commonly prescribed LMWH is enoxaparin.

Current guidelines outlined by the American College of Obstetricians and Gynecologists recommend the use of prophylactic or therapeutic anticoagulation for pregnant women with a history of VTE or for women with a high risk of developing a thromboembolism during pregnancy [5-7]. Common conditions conferring increased susceptibility include acquired or inherited thrombophilias [5]. These guidelines are based on limited scientific evidence and expert opinion because no large-scale clinical research trials have been conducted. Concurrent recommendations regarding prevention of VTE in pregnancy outlined by the American Society of Hematology similarly emphasizes the need for additional data due to limited scientific evidence in order to demonstrate a low risk of harm and net health benefit to taking antepartum thromboprophylaxis [6].

To provide further information on the safety of anticoagulation during pregnancy and its implications on delivery, we examined the clinical outcomes, specifically bleeding and transfusion requirements during the peripartum period, in patients taking enoxaparin or UFH in high-risk pregnancies.

Methods

This study was a retrospective, case-control chart review of patients on anticoagulation during pregnancy. Patients admitted

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to Georgetown University Medical Center (GUMC) for labor and delivery between January 1, 2016 and December 31, 2017 were included for review. Patients receiving therapeutic or prophylactic dosing of UFH or LMWH for a thromboembolic disorder for ≥2 weeks prior to delivery were assigned to the study cohort. Patients on anticoagulation were then matched to healthy controls who similarly underwent delivery at GUMC during the aforementioned delivery window. Healthy controls were matched by age ± 2 years, delivery date ± 1 month, and delivery method (cesarean or vaginal). Patients were also matched by gravidity by equal or close approximation. Two patient controls were matched for every one patient on anticoagulation.

Women who underwent additional surgical procedures (e.g., hysterectomy) at or near the time of delivery were excluded, with the exception of tubal ligation. Minimal adverse events have been reported following sterilization at the time of cesarean delivery [8]. Additionally, women receiving anticoagulation for mechanical heart valves were also excluded from this study.

Clinical outcomes during delivery were assessed using documented delivery report accounts of estimated blood loss (EBL) and blood transfusion requirements. Additionally, hemoglobin (Hgb) and hematocrit (Hct) values were documented antepartum, defined as ≤48 hours prior to delivery, and postpartum, defined as ≤48 hours after delivery. Patients who were discharged postpartum without Hgb and Hct results were not included for review.

Analysis

Data were analyzed using the statistical software Minitab version 18. Descriptive data were presented as mean, standard deviation, and percentages. Comparison of quantitative variables between women on anticoagulation and matched controls was done using Independent Samples T-Tests. Results with $P < 0.05$ were deemed significant.

Results

A total of 39 patients were included in this study, 13 taking anticoagulation and 26 matched controls. The average age at delivery was 33.0±4.9 years. The majority of patients delivered via cesarean section (85%), 11 taking anticoagulation and 22 matched controls. Of the 13 women on anticoagulation therapy during pregnancy, 6 individuals received therapeutic dosing and 7 received prophylactic dosing.

During the immediate antepartum period, the mean Hgb and Hct in patients taking anticoagulation was 11.76 gm/dL and 34.99%, respectively, compared to 11.92 gm/dL and 35.70%, respectively, in matched controls. There was no significant difference in antepartum Hgb or antepartum Hct between the two groups (P=0.735 and P=0.558, respectively). Postpartum, the mean Hgb and Hct in patients taking anticoagulation was 10.13 gm/dL and 30.46%, respectively, compared to 10.16 gm/dL and 30.67%, respectively, in matched controls. These results were also not statistically significant (P=0.940 and P=0.916, respectively). Furthermore, the difference in Hgb or Hct antepartum versus postpartum between the two groups was not statistically significant (P=0.721 and P=0.525, respectively).

Intrapartum, the mean estimated blood loss (EBL) in patients taking anticoagulation was 615 mL compared to 594 mL in matched controls, which was not statistically significant (P=0.772). One patient taking anticoagulation required blood transfusions during the postpartum period, receiving 10 units (packs) of red blood cells (RBCs) due to intraperitoneal hemorrhage. Despite the one patient receiving numerous units of RBCs, the mean transfusion requirements comparing patients taking anticoagulation to matched controls was not statistically significant (P=0.298).

Discussion

Patients on anticoagulation during pregnancy exhibited similar hematologic outcomes during delivery compared to matched controls. There were no significant differences in total estimated blood loss between the two groups, suggesting that anticoagulation during high-risk pregnancies does not increase the risks of bleeding. Women taking anticoagulation also displayed similar laboratory results for antepartum and postpartum Hgb and Hct, further supporting this statement and indicating that no adverse hematologic changes are seen in this maternal fetal medicine population.

One woman who received therapeutic anticoagulation during pregnancy experienced intraperitoneal hemorrhage due to bladder flap and incisional site hemorrhage two days following cesarean section. She underwent embolization of the affected arteries and required multiple blood transfusions as well as fresh frozen plasma and platelets during her treatment course. This patient was reportedly not taking anticoagulation for an estimated two weeks leading up to delivery, restarting therapy approximately four days prior to delivery. A review of 64 studies examining LMWH use in pregnancy found that the rate of postpartum hemorrhage is 0.94% (95% CI, 0.61%-1.37%), and an overall rate of significant bleeding of 1.98% (95% CI, 1.50%-2.57%) [9]. Our data fall above these percentages at 7.6% for postpartum hemorrhage and overall bleeding, however this is likely a consequence of having a small patient population. Future studies should evaluate the significance of transfusion requirements for patients on anticoagulation for high-risk pregnancies in a larger study cohort.

Most of the patients in this study delivered via cesarean section, which is not representative of the typical delivery method of women in this patient population. When selecting patients for our analysis, vaginal deliveries accounted for approximately 50% of all deliveries, however most women who delivered vaginally did not have postpartum CBCs drawn and were ultimately removed from our analyses.

This study was also limited by the overall low proportion of women who are candidates for anticoagulation therapy during pregnancy. GUMC maternity services are relatively small and while they specialize in the management of high-risk pregnancies, including women on anticoagulation, low patient volume constrained the scope of our review. Confining this study to a single center and analyzing patients within a two-year window further restricted the number of patients available for analysis, however this helped limit the number of care providers and controlled for inter-rater variability when conducting delivery procedures and estimating total blood loss during delivery.

Conclusion

In summary, anticoagulation during high-risk pregnancies is not associated with an increased estimated blood loss during delivery or increased transfusion requirements. Additionally, anticoagulation did not result in a significant reduction in postpartum Hgb or Hct, suggesting minimal risks associated with anticoagulation in this maternal fetal medicine population.

DOI: *10.46998/IJCMCR.2021.13.000301*

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