

Use of Protamine to Reverse Therapeutic Heparin Infusion in a Patient with Postoperative Hemorrhage After Cesarean Delivery

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Introduction

Venous thromboembolism (VTE) is an important cause of maternal morbidity and mortality during the antepartum, intrapartum, and postpartum periods. Subsequently, the use of anticoagulation (AC) has increased significantly in the obstetric population. However, guidelines for starting and stopping AC can be vague and disparate; confusion over when to restart previously held AC can result in adverse outcomes for obstetric patients. Although the dangers of certain anticoagulants are mitigated due to the availability of emergency reversal agents (protamine for heparin, andexanet alfa for factor Xa inhibitors, etc.), there is a paucity of research demonstrating their safety in the obstetric patient population.

Case Description

A 36 year old G3P0020 at 39 0/7 weeks gestation presented for induction of labor after premature rupture of membranes. Her antepartum course was complicated by a DVT involving the left common femoral, superficial femoral, and external iliac veins diagnosed at 32 2/7 weeks gestation, for which she was started on therapeutic enoxaparin.

On admission, enoxaparin was held and an epidural catheter was placed uneventfully. Her labor was complicated by chorioamnionitis. Due to Category II tracing (fetal tachycardia, moderate variability, significant decelerations), she underwent an uncomplicated low transverse cesarean delivery. The epidural catheter was removed after surgical wound closure, and therapeutic AC via heparin infusion was restarted 3 hours later.

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Over the next 12 hours she developed worsening hypotension, tachycardia, abdominal distension/pain, and pallor concerning for intraabdominal bleeding. A second IV and a radial arterial line were placed. Labs showed a decline in postoperative Hgb from 10.5 to 7.6. Bedside FAST scan was positive for ~4cm fluid in Morrison’s pouch. 2 units pRBCs were administered and a phenylephrine infusion initiated. In addition, the patient’s heparin infusion (therapeutic, aPTT 84.2) was stopped and reversed with 50mg protamine given in 10mg increments over 10 minutes. Repeat aPTT after reversal was 28.8. Her condition improved significantly after heparin reversal and transfusion, with subjectively improved abdominal pain and serial FAST scans showing unchanged fluid. AC with enoxaparin was restarted on POD day 3 and gradually up-titrated to therapeutic doses by post-operative day 6 without incident. Figure shows worsening clinical status during the 10-hour period up to the time of protamine administration, along with rapid improvement following administration of protamine, pRBCs, and phenylephrine.



Worsening hypotension and tachycardia, then improvement following reversal of heparin using protamine. Protamine was administered at the time indicated by the red arrow.

Discussion

This case illustrates the quandary regarding the optimal time to restart AC after cesarean section for a patient with a history of antenatal DVT. There are few published guidelines regarding the safest period to resume therapeutic AC in a post-cesarean patient; SOAP guidelines recommend waiting >1 hr after a neuraxial block or pulling a catheter before resuming heparin infusion. Other published guidelines have recommended waiting 24 hours after delivery before resuming heparin infusion. In our patient's case, therapeutic AC may have been resumed too early, contributing to postoperative intra-abdominal hemorrhage. Although it is well known that reversal of heparin is accomplished through protamine, there are few case reports demonstrating its use in the obstetric population. As such, we opted to give 50mg, which is the maximum dose of protamine recommended for reversal outside of cardiac surgery, and pharmacologically logical given the dose of heparin administered. We think this dose would be sufficient for reversal in most cases due to the short half-life of heparin and current recommendations to give 0.5mg-0.75mg per 100 units of heparin.

References

1. Bates, S.M., Middeldorp, S., Rodger, M. et al. Guidance for the treatment and prevention of obstetric-associated venous thromboembolism. *J Thromb Thrombolysis* 41, 92–128 (2016). <https://doi.org/10.1007/s11239-015-1309-0>
2. Leffert L, Butwick A, Carvalho B, Arendt K, Bates SM, Friedman A, Horlocker T, Houle T, Landau R, Dubois H, Fernando R, Houle T, Kopp S, Montgomery D, Pellegrini J, Smiley R, Toledo P; members of the SOAP VTE Taskforce. The Society for Obstetric Anesthesia and Perinatology Consensus Statement on the Anesthetic Management of Pregnant and Postpartum Women Receiving Thromboprophylaxis or Higher Dose Anticoagulants. *Anesth Analg*. 2018 Mar;126(3):928-944. doi: 10.1213/ANE.0000000000002530. PMID: 29099429.
3. McLintock C, Brighton T, Chunilal S, Dekker G, McDonnell N, McRae S, Muller P, Tran H, Walters BN, Young L; Councils of the Society of Obstetric Medicine of Australia and New Zealand; Australasian Society of Thrombosis and Haemostasis. Recommendations for the diagnosis and treatment of deep venous thrombosis and pulmonary embolism in pregnancy and the postpartum period. *Aust N Z J Obstet Gynaecol*. 2012 Feb;52(1):14-22. doi: 10.1111/j.1479-828X.2011.01361.x. Epub 2011 Oct 6. PMID: 21972999.
4. Yee J, Kaide CG. Emergency Reversal of Anticoagulation. *West J Emerg Med*. 2019;20(5):770-783. Published 2019 Aug 6. doi:10.5811/westjem.2018.5.38235

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