

Thromboprophylaxis in pregnancy: Do we need new Guidelines?

S Sivasubramaniam, J Paul

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Abstract

Introduction

Venous Thromboembolism is the leading cause of maternal deaths in the UK and most other developed countries. Pregnancy and caesarean section increase the risk of thromboembolism. High Body Mass Index (BMI) further increases the risk and mortality. We sought to evaluate the thromboprophylaxis management in parturient undergoing caesarean section with a BMI of more than 35.

Methods

We studied the thromboprophylaxis management in 50 obese parturient with a Body Mass Index more than 35 who underwent caesarean section. We observed the frequency and dose of thromboprophylaxis they received in the postoperative period.

Results

We observed a significant proportion of women did not receive the appropriate dose of low molecular weight heparin, 32% had a delay in obtaining thromboprophylaxis and 38% did not receive thromboprophylaxis for an adequate length of time.

Conclusion

Management of thromboprophylaxis for obese parturient is still suboptimal and we are in need of more robust guidelines for these patients.

INTRODUCTION

Venous Thromboembolism (VTE) is the leading cause of direct maternal deaths in UK with a mortality rate of 1.56 per 100,000 maternities¹. These figures have not changed much since 1997. Successive reports on Confidential Enquiries into Maternal Deaths have shown failures in recognising risk factors for Venous Thromboembolism and providing adequate prophylaxis. There are several additional risk factors during pregnancy that contribute to venous thromboembolism, the most important of which is a high Body Mass Index. There is an alarming increase in the number of pregnant women who are obese. A body mass index over 35 significantly increases risk of thromboembolism. There were 33 deaths due to pulmonary embolism in the last CEMACH report [2003-2005]. 16 of these patients were overweight. Lower Segment Caesarean Section increases the incidence of thromboembolism. Low molecular weight heparin (LMWH) is the mainstay

medication used for thromboprophylaxis. Given the high mortality due to thromboembolism in obese parturient we sought to evaluate the thromboprophylaxis management in parturient with a BMI of more than 35. Guidelines exist for the management of thromboprophylaxis after vaginal delivery and caesarean section. Current recommendations suggest women should have their first dose of thromboprophylaxis 4 hours after LSCS done under central neuraxial blockade and be continued for 3 to 5 days postoperatively.

METHODS

The audit was registered with the local hospital clinical audit committee. Ethics committee approval was deemed not necessary. We prospectively studied the thromboprophylaxis practice in 50 obese pregnant women with a BMI of more than 35 undergoing caesarean section under central neuraxial block over a 6 month period. We excluded patients who had a general anaesthetic and those who had postoperative

bleeding. Enoxaparin was the thromboprophylaxis medication used in our hospital. All Patients were prescribed enoxaparin electronically in the Hospital electronic records system. Demographic data like age, weight, BMI were collected from the obstetric antenatal records. We recorded whether mothers had completion of risk assessment during antenatal period and whether they had optimal thromboprophylaxis during pregnancy. Data relating to enoxaparin administration was collected from the electronic prescription system. We recorded the hours after surgery the mothers received their first dose of enoxaparin and the dose they received. We recorded delays in delivery of the first dose. We recorded the duration for which they received enoxaparin and their duration of stay in hospital. Finally we also recorded any complications developed by these patients.

RESULTS

Of the 50 women, 3 had a BMI between 35 and 40, 21 had a BMI between 40 and 45, 22 had a BMI between 45 and 50 and 4 had a BMI more than 50. 29 of the 50 women were more than 35 years old.

48 out of the 50 patients had risk assessment during their antenatal period. 46 out of the 50 had been seen by an anaesthetist in the high risk clinic during the antenatal period.

Figure 1
Table 1: BMI distribution

BMI	no. of women
35-40	3
40-45	21
45-50	22
>50	4

Two women were on aspirin during their antenatal period. 43 out of 50 women had a preoperative dose of enoxaparin on the previous day of surgery. We observed 16 out of 50 patients had a delay in administration of their fourth hour dose by more than 2 hours. The subsequent dose was delayed by more than 2 hours in 8 patients. One patient weighing 146 kg had 40 mg twice daily dose of enoxaparin. All other patients had a standard dose of 40 mg once daily dose of enoxaparin.

19 out of 50 patients stayed in hospital for 5 days but received thromboprophylaxis only for three days. None of

the women had clinical evidence of venous thromboembolism.

Hence a significant proportion of the women, around 32% had delay in their thromboprophylaxis dose and 38% of women did not have thromboprophylaxis cover for an adequate length of time.

Figure 2
Table 2: Delay in Enoxaparin dose

Timing	No. of patients
4 th hour dose	16
24 th hour dose	8

DISCUSSION

Several recommendations have been made by the Royal college of Obstetricians and Gynaecologists ² , National Institute of Clinical Excellence and the Confidential Enquiry into Maternal Deaths ³ Reports. The confidential enquiry into maternal deaths report recommends all women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. It recommends women should be reassessed before or during labour for risk factors for VTE. Age over 35 years and BMI greater than 30 or a body weight greater than 90Kg are important independent risk factors for postpartum VTE even after vaginal delivery. The combination of either of these risk factors with other risk factors for VTE, such as pre-eclampsia or immobility should lead the clinician to consider the use of LMWH for three to five days postpartum.

Patients assessed as high risk should receive heparin prophylaxis and, in addition, leg stockings. They should receive a twice daily dose of enoxaparin and prophylaxis until the fifth postoperative day or until full mobilisation is advised.

Women with a BMI of 40 or above are at a high risk of VTE but current RCOG guidelines recommend the same prophylactic doses of low molecular weight heparin (LMWH) for all women with a BMI over 30 or a weight exceeding 90Kg.

During pregnancy the volume of distribution and clearance of LMWH is different. The volume of distribution of

LMWH is high throughout pregnancy, and clearance may be higher in early pregnancy and then decline as pregnancy progresses to delivery. Hence, anti-Xa levels should be assessed during the first week of pregnancy and then at least once per month in each trimester. Antifactor-Xa activity in blood is used to monitor anticoagulation efficacy with LMWH therapy. The desired anti-Xa range for prophylaxis is 0.1 to 0.3 IU/mL⁴. Frederiksen et al⁵ demonstrated a strong negative correlation between total body weight and heparin activity (as measured by anti-Xa assay) with fixed doses of the LMWH enoxaparin.

A study in critically ill patients also shows similar findings⁶.

In a nonrandomized retrospective study by Scholten et al⁷ in 481 obese patients undergoing gastric bypass surgery, they observed enoxaparin 40 mg every 12 hours was superior to enoxaparin 30 mg every 12 hours with respect to the incidence of postoperative deep vein thrombosis, without an increase in bleeding complications.

In an open-label trial⁸ evaluating two doses (75 and 175 IU/kg) of the LMWH tinzaparin given to otherwise healthy obese volunteers (100 to 165 kg) concluded that prophylactic tinzaparin dosing should be based on actual body weight, independent of the presence of obesity. These studies support the notion that prophylactic LMWH doses (like therapeutic doses) should be weight-adjusted in all patients, with or without obesity.

An analysis of cardiovascular patients using full weight-adjusted doses of LMWH found no differences in haemorrhage rates between obese and normal weight groups⁹. Similarly, anti-Xa activity is not significantly increased when LMWH is administered to obese patients based on total body weight^{10,11}.

These data suggest that weight-adjusted doses may be more appropriate than fixed doses for VTE prophylaxis in morbidly obese patients. Majority of the women in our study did not receive an appropriate dose of enoxaparin.

CONCLUSION

Obesity is an epidemic that has become a significant public

health issue with profound health and economic consequences. It is also a significant risk factor for the development of venous thromboembolism. The current guidance from the Royal college of Obstetricians and Gynaecologists recommend the same dose of enoxaparin for all obese women with a BMI more than 30. We are surely in need of new guidelines for thromboprophylaxis doses for obese pregnant women.

CORRESPONDENCE TO

Dr Subash Sivasubramaniam M. D., FRCA Department of Anaesthetics Queen's Hospital Burton on Trent U. K.
Telephone 0044 (0) 1785 257389 Fax 0044 (0) 1785 257389
E mail. subashken@yahoo.com

References

1. Eldor A. Unexplored territories in the non surgical patient: a look at pregnancy. *Semin Hematology* 2001; 38(2 Suppl 5):39-48.
2. RCOG guideline Jan 2004 guideline no. 37 section 5.2.
3. Saving Mothers' Lives 2003-2005 Confidential Enquiry into maternal Deaths Reports.
4. Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of antithrombotic agents during pregnancy: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126(3 Suppl):627S-644S.
5. Frederiksen SG, Hedenbro JL, Norgren L. Enoxaparin effect depends on body-weight and current doses may be inadequate in obese patients. *Br J Surg* 2003; 90:547-548.
6. Priglinger U, Delle Karth G, Geppert A, et al. Prophylactic anticoagulation with enoxaparin: is the subcutaneous route appropriate in the critically ill? *Crit Care Med* 2003; 31:1405-1409.
7. Scholten DJ, Hoedema RM, Scholten SE. A comparison of two different prophylactic dose regimens of low molecular weight heparin in bariatric surgery. *Obes Surg* 2002; 12:19-24.
8. Hainer JW, Barrett JS, Assaid CA, et al. Dosing in heavyweight/obese patients with the LMWH tinzaparin: a pharmacodynamic study. *Thromb Haemost* 2002; 87:817-823.
9. Spinler SA, Inverso SM, Cohen M, et al. Safety and efficacy of unfractionated heparin versus enoxaparin in patients who are obese and patients with severe renal impairment: analysis from the ESSENCE and TIMI 11B studies. *Am Heart J* 2003; 146:33-41.
10. Wilson SJ, Wilbur K, Burton E, Anderson DR. Effect of patient weight on the anticoagulant response to adjusted therapeutic dosage of low-molecular-weight heparin for the treatment of venous thromboembolism. *Haemostasis* 2001; 31:42-48.
11. Smith J, Canton EM. Weight-based administration of dalteparin in obese patients. *Am J Health Syst Pharm* 2003; 60:683-687.

Author Information

Subash Sivasubramaniam, M.D., FRCA

Department of Anaesthetics, Queen's Hospital

Jaison Paul, M.D.

Department of Anaesthetics, Queen's Hospital