Management of Thrombosis during Pregnancy

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The management of thrombosis during pregnancy includes treatment of acute deep vein thrombosis episodes, primary prophylaxis in asymptomatic women, and secondary prophylaxis of recurrences in women with a history of thrombosis. Vilela et al., in their review in this issue of *IMAJ* [1], cover the treatment modalities commonly used for treatment or prophylaxis in pregnant women, as well as dosage and duration of antithrombotic therapy. However, the issue of prophylactic therapy for prevention of thrombosis in women at risk needs to be extended.

In their lifetimes, women face situations associated with an increased risk of thromboembolism. Pregnancy, being a hypercoagulable state, is one of such situations. The hypercoagulability of pregnancy is multifactorial: stasis due to the compression of the venous system by the gravid uterus, increase in coagulation factors VIII and fibrinogen, decrease in fibrinolysis and protein S, and acquired resistance to activated protein C [2]. Pregnancy is associated with a five to sixfold increased risk of venous thromboembolism [3], being 0.71 and 0.15 per 1,000 deliveries for DVT and pulmonary embolism, respectively [4]. Most of the studies suggest that the puerperium is the period of the highest risk for VTE [2,5,6] .

Hereditary thrombophilia and the occurrence of acquired antiphospholipid syndrome underlie many of the thrombotic events seen in pregnancy and became important issues in the management of pregnant women. Hereditary thrombophilia due to

DVT = deep vein thrombosis
VTE = venous thromboembolism

deficiencies of the natural coagulation inhibitors – protein C, protein S and antithrombin – is rare and is associated with VTE in pregnant women [7–9]. The discovery of common inherited thrombophilia such as a mutation in the coagulation factor V (substitution of arginine by glutamine at amino acid residue 506), also named factor V Leiden [10], and a mutation in the prothrombin gene (A to G at position 20210) [11], has increased our understanding of the etiology of VTE.

Thrombophilia appears to further increase the risk of VTE in pregnancy. Gerhardt et al. [3] found a 6.9-fold (95% confidence interval 3.3–15.2) and 9.5-fold (95% CI 2.1–66.7) relative risk of VTE in carriers of the factor V Leiden and the prothrombin mutation, respectively [3]. A recent study by Martinelli et al. [6] estimated the risk of VTE in women heterozygous for factor V Leiden or prothrombin mutation to be 10.6 (95% CI 5.6-20.4) and 2.9 (95% CI 1.0–8.6), respectively.

Since the number of patients affected by antithrombin, protein C and protein S deficiency is small, the studies on treatment of pregnant women with these deficiencies show variable results. Whereas antithrombin deficiency is associated with a highest risk of thrombosis during pregnancy [5], the results are conflicting for protein C and protein S.

Except for antithrombin deficiency, which is associated with a 50% risk of VTE in pregnant women not receiving anticoagulant therapy [8,9], there is no evidence that antithrombotic prophylaxis is warranted in other thrombophilic women when they became pregnant [12]. Since the puerperium is a particularly high risk period, primary prophylaxis after delivery is probably warranted for carriers of all types of thrombophilia.

The two general approaches recommended for pregnant women with previous VTE are prophylactic therapy with unfractionated heparin or low molecular weight heparin and clinical surveillance [12].

The part of the review by Vilela et al. [1] regarding women with antiphospholipid antibodies requires some clarification. The American College of Chest Physicians recommendations are as follows: a) women with aPL antibodies who have had at least two fetal losses should receive prophylactic unfractionated heparin (5,000 IU twice daily) or LMWH and low dose aspirin (0.1 g/day) from the confirmation of pregnancy until 8 weeks after the delivery [12–15]; b) women with aPL and no prior VTE or pregnancy loss should not receive any therapy, including low dose heparin, prophylactic LMWH, and low dose aspirin [12]; c) women with aPL and a history of VTE who are receiving long-term anticoagulation should be treated with adjusted-dose LMWH or unfractionated heparin throughout pregnancy and oral anticoagulants postpartum [12].

In conclusion, the decision to treat or withhold prophylactic anticoagulation during pregnancy or puerperium should take into account the risk of VTE and the presence or absence of underlying thrombophilia.

CI = confidence interval
aPL = antiphospholipid antibodies
LMWH = low molecular weight heparin

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The sage never strives for the great, and thereby the great is achieved

Tao te Ching, 550 BC