

MANAGEMENT OF HYPERCOAGULABLE STATE DURING PREGNANCY. PROPHYLACTIC USAGE OF LOW MOLECULAR WEIGHT HEPARIN (LMWH)

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Abstract

The main objective of this study is to analyze the prophylactic usage of low molecular weight heparin, in women during the period of pregnancy. A retrospective study was undertaken during 01 January – 31 December of 2013, in the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetovo. Data were collected for the following: patient demographics, week and month of pregnancy, number of pregnancies for each patient, duration of hospital stay, clinical and laboratory investigations, diagnosis, drug details; which include the name of the drug, dosage form, dose frequency, total cost of the drug, the amount of each given ampoule application and the cost for the entire period of hospitalization.

Among of 643 women whom were prescribed LMWH, 144 of them were found hypercoagulable. The majority of patients given LMWH were aged 25-30 years (56.25 %). For the biggest number of patients, this was their first pregnancy (70.83%). Earliest phase of using LMWH was the second month of pregnancy, respectively sixth week. Patients during the ninth month, appear to be more affected by hypercoagulable state. 56 (38.89 %) women were in the ninth month of pregnancy. Fraxiparine (nadroparin calcium) 3800 IU anti-Factor XA in 0.4 ml was the most prescribed anticoagulant, 64 (44.44 %) patients received this therapy. From the total number of 144 patients, only 4 of them received LMWH twice a day.

Keywords: Hypercoagulable state, management, low molecular weight heparin, pregnancy

Introduction:

Anticoagulant treatment for deep-vein thrombosis aims to prevent pulmonary embolism and recurrent thrombosis and also to avoid excessive bleeding. In addition, both the effect of therapy on the patients' well-being and the cost of therapy are factors to be weighed in determining the optimal treatment. It is current practice to treat acute venous thrombosis with intravenous standard (unfractionated) heparin for at least five days in a dose adjusted to lengthen the activated partial-thromboplastin time into a desired range (Koopman M, *et al*, 1989) Pregnancy is classically thought to be a hypercoagulable state. Fibrin generation is increased, fibrinolytic activity is decreased, levels of coagulation factors II, VII, VIII, and X are all increased, free protein S levels are decreased, and acquired resistance to activated protein C is common. Uncomplicated pregnancy is accompanied by substantial hemostatic activation as indicated by increased markers of coagulation activation, such as prothrombin fragment F1+2 and D-dimer(Paul E. *et al*, 2010)

The main reason for the increased risk of thromboembolism in pregnancy is hypercoagulability, which has likely evolved to protect women from the bleeding challenges of miscarriage and childbirth. Women are at a 4- to 5-fold increased risk of thromboembolism during pregnancy and the postpartum period compared with when they are not pregnant. Eighty percent of the thromboembolic events in pregnancy are venous, with an incidence of 0.49 to 1.72 per 1000 pregnancies. Risk factors include a history of thrombosis, inherited and acquired thrombophilia, maternal age greater than 35, certain medical conditions, and various complications of pregnancy and childbirth (Andra H. James 2009). D-dimer assay testing may be used as a screening test and/or in combination with venous ultrasound to facilitate diagnosis and prediction of a thromboembolic event. D-dimer is a product of the degradation of fibrin by plasmin. Therefore, elevated levels indicate increased thrombin activity and increased fibrinolysis following fibrin formation. The assay employs monoclonal antibodies to detect D-dimer fragments. Commercial assays available include at least three accurate and reliable products: two rapid enzyme lined immunosorbent assays and a rapid whole-blood assay (Rosenberg V *et al*, 2007). On the basis of earlier results, low molecular weight heparin (LMWH) (Forestier, F *et al*, 1984)(Forestier, F *et al*, 1992), like unfractionated heparin (UFH) (Flessa, H *et al*, 1965), does not cross the placenta and is at present considered to be the drug of choice for the prophylaxis of VTEs during pregnancy (Greer, I.*et al* 1993)(Toglia M. *et al* 1996)(Pettila V *et al*, 1999). The use of LMWH has several advantages over unfractionated heparin such as longer half-life (Weitz, J.I. 1997), and more stable and predictable pharmacokinetics (Greer, I.A. 1999), which makes possible subcutaneous once or twice daily self-

administration, with minimal laboratory monitoring. Using the hospital records, we achieved to analyze the prophylactic usage of low molecular weight heparin during pregnancy.

Materials and Methods:

Surveillance of LMWH usage was done by collecting data for the periode January 1 – Decemember 31, 2013 in the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetovo. Data were collected for the following: patient demographics, week and month of pregnancy, number of pregnancies for each patient, duration of hospital stay, clinical and laboratory investigations, diagnosis, drug details; which include the name of the drug, dosage form, dose frequency, total cost of the drug, the amount of each given ampoule application and the cost for the entire period of hospitalization. The results were computed usig Ms Excel 2008 and the results are expressed as percentage ore proportion either as pictorial representation in the form of diagraeme or tabular form.

Results:

Socio-Demographic data

During the period of one year, 643 women were prescribed LMWH. 144 of them were diagnosed hypercoagulable. Demographic data of the patients are ilustrated in (Table 1).

Table 1: Patients demographic data

Parameters	Number of patients	Percentage
Age		
< 18	0	0
18-20	0	0
21-24	21	14.58
25-30	81	56.25
31-35	29	20.14
>35	13	9.03
Living place		
Urban	45	31.25
Rural	99	68.75

Number and current month/week of pregnancy

For the biggest number of patients, this was their first pregnancy 102 (70.83%), 23 (15.98%) patients declared that this is their second pregnancy and for 19 patients (13.19%) this was third, fourth ore fifth pregnancy.

56 (38.89%) women, were in the ninth month of pregnancy, followed by 32 (22.22%) in the tenth month. The earliest stage of using LMWH, was second month of pregnancy, 2 (1.39%) women received anticoagulant during

that month. The detailed explanation about usage of LMWH during months of pregnancy, respectively number of patients is given in Figure 1.

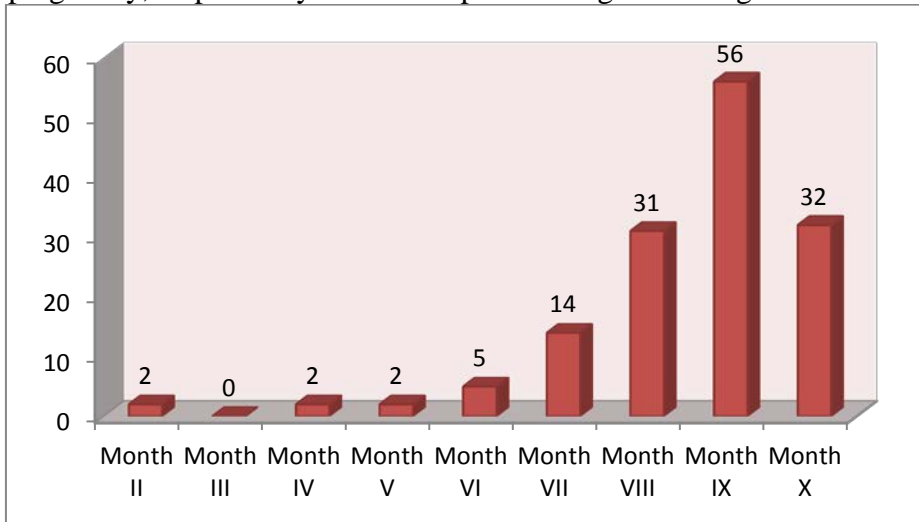


Figure 1: Number of patients/month of pregnancy

Women during ninth month of pregnancy, were most commune patients. From analyzed data, we can notice that 34th and 36th week of pregnancy, are more affected by hypercoagulable state. 17 (30.36%) patients were recorded in each week (Figure 2).

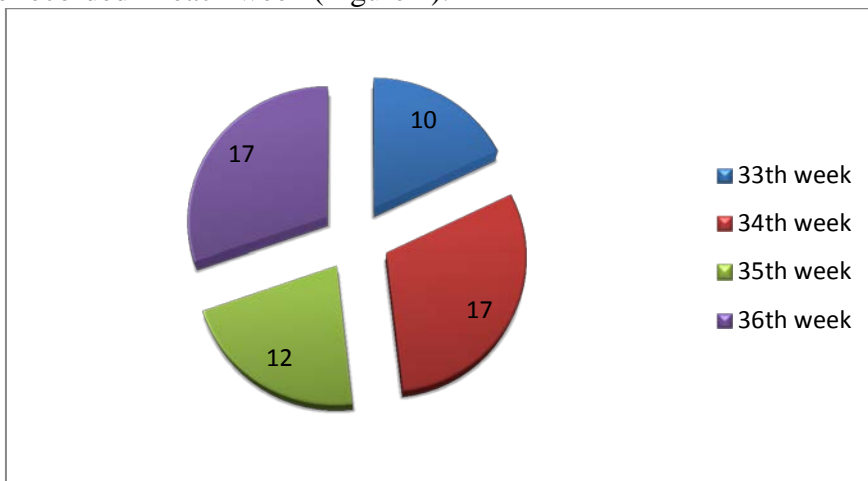


Figure 2: Number of patients in ninth month of pregnancy

Number of prescribed anticoagulants

The biggest number of patients, 64 (44.44%) received Fraxiparine (nadroparin calcium) 3800 IU anti-Factor XA in 0.4 ml, followed by them with Clexane (enoxaparin) 4000 IU anti- Factor XA in 0.4ml 32 (22.22%).

Only one patient received Fraxiparine (nadroparin calcium) 1900 IU anti-Factor XA in 0.2 ml (Figure 3).

140 patients, received a daily dose of anticoagulant, 4 of them, was prescribed to take the anticoagulant twice a day. In the Table 2, are illustrated features of those patients.

Table 2. Features of patients treated with double dose

Nr cases	of Patients week of pregnancy	Patients diagnosis	Received therapy	Number of ampules
Case 1	39 th	Hypercoagulable state	Clexane 4000	26
Case 2	37 th	Hypercoagulable state	Fraxiparine 0.4	50
Case 3	37 th	Hypercoagulable state	Fraxiparine 0.4	28
Case 4	31 th	Hypercoagulable state	Fraxiparine 0.4	20

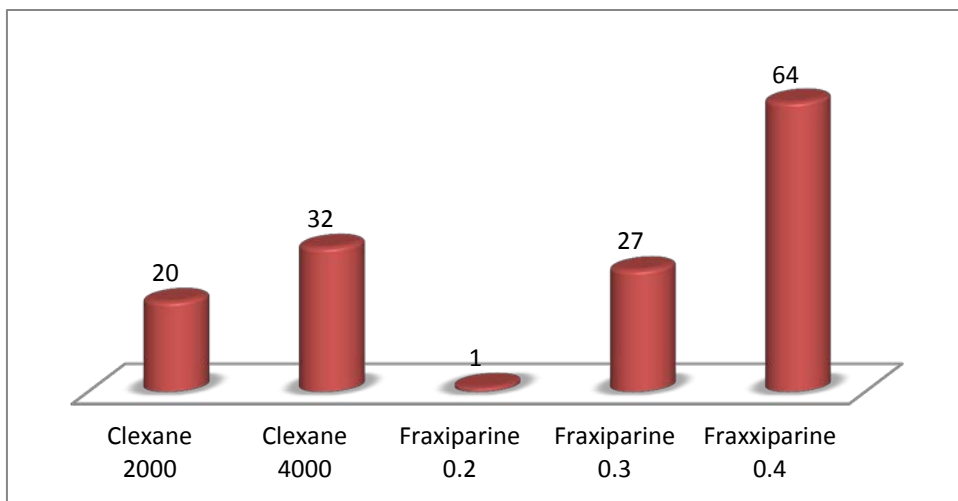


Figure 3. Number of patients / prescribed anticoagulants

Conclusion:

After almost three decades of intensive research, LMWH have established their niche as an important class of antithrombotic compounds and have proved to be both: safe and effective for the prophylaxis and treatment of venous thromboembolism. Unfractionated heparin is the anticoagulant of choice in pregnant women, because unlike warfarin, it does not cross the placenta. Low-molecular-weight heparins also do not cross the placenta and descriptive studies suggest that they are both safe and effective in pregnancy (Weits J.I, 1997).

In the presented study, from 643 pregnant women which received LMWH were included only 144 of them, with the diagnosis Hypercoagulable state.

The age range 25-30 (56.25%) comprised the highest proportion of the patients. Comparatively less cases were found among the age range over 35 years (9.03%). The diagnostic patterns showed that women in their ninth month of pregnancy were most affected by Hypercoagulable state (38.89%), respectively those in 34th and 36th week, represented with 17 patients each other.

The leading anticoagulant prescribed was Fraxiparine 0.4, prescribed in 64 (44.44%) cases.

In conclusion, although current guidelines support use of low dose LMWH in women during pregnancy, this might not be sufficient. For as much as they are safe for the baby, because they do not allow passing placental barrier, this therapy is being used increasingly. It is necessary to improve the habits of prescribing unnecessary usage of low molecular weight heparins, thus enhance their irrational use.

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