

Low Molecular Weight Heparin during Pregnancy

Sihana Ahmeti Lika, Merita Dauti, Ledjan Malaj

Abstract—The objective of this study is to analyze the prophylactic usage of low molecular weight heparin (LMWH) along pregnancy and the correlation between their usage and month/week of pregnancy, in the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetovo. A retrospective study was undertaken during 01 January – 31 December 2012. Over of one year, the total number of patients was 4636. Among the 1447 (32.21%) pregnant women, 298 (20.59%) of them were prescribed LMWH. The majority of patients given LMWH, 119 (39.93%) were diagnosed hypercoagulable. The age group with the highest attendance was 25-35, 141 patients (47.32%). For 195 (65.44%) patients, this was their first pregnancy. Earliest stage of using LMWH was the second month of pregnancy 4 (1.34%) cases. The most common patients were 70 women along the seventh month (23.49%), followed by 68 in the ninth month of pregnancy (22.81%). Women in the 28th gestational week, were found to be the most affected, a total of 55 (78.57%) were in that week. Clexane 2000 and Fraxiparine 0.3 were the most common for which low molecular weight heparin was prescribed. The number of patients which received Clexane 2000 was 84 (28.19%), followed by those with Fraxiparine 0.3 81 (27.18%). The administration of LMWH is associated with long hospitalization (median 14,6 days).

Keywords—Hypercoagulable state, low molecular weight heparin, month of pregnancy, pregnant women.

I. INTRODUCTION

NORMAL pregnancy is accompanied by increased concentrations of factors VII, VIII and von Willebrand factor and by pronounced increases in fibrinogen [1]. Venous thromboembolism is an uncommon but leading cause of illness and death during pregnancy and the puerperium [2]. Essentially, every pregnant patient is at risk for a venous thromboembolic event and the risk is estimated to be five – to 10-fold higher than for the nonpregnant patient [3]. Pulmonary embolism and deep-vein thrombosis are the two components of a single disease called venous thromboembolism. Approximately 30% of apparently isolated episodes of pulmonary embolism are associated with silent deep-vein thrombosis, and in patients presenting with symptoms of deep-vein thrombosis, the frequency of silent pulmonary embolism ranges from 40 to 50% [4].

Anticoagulant treatment for deep-vein thrombosis aims to prevent pulmonary embolism and recurrent thrombosis and also to avoid excessive bleeding [5]. After almost two decades of intensive research, low-molecular-weight heparins have established their niche as an important class of antithrombotic compounds. Unfractionated heparin is a heterogeneous

mixture of polysaccharide chains ranging in molecular weight from about 3000 to 30,000. Low-molecular-weight heparins are fragments of unfractionated heparin produced by controlled enzymatic or chemical depolymerization processes that yield chains with a mean molecular weight of about 5000 [6]. Low-molecular-weight heparins, which are prepared by the depolymerization of standard heparin, have proved to be safe and effective in preventing thromboembolism in patients at high risk and to be at least as safe and effective as standard heparin for the treatment of acute proximal deep-vein thrombosis. In these trials, standard heparin was administered by continuous intravenous infusion, and the dosage was adjusted to keep the activated partial-thromboplastin time within a prescribed range. In contrast, the low-molecular-weight heparins were administered by subcutaneous injection in doses adjusted for the patient's weight, without laboratory monitoring. This more convenient method of administering the treatment is possible because low-molecular-weight heparins have a more predictable anticoagulant response than standard heparin, a longer plasma half-life, and better bioavailability when administered subcutaneously [7]. Therefore, they can be given subcutaneously, without laboratory monitoring, in a dose determined by the patient's body weight alone [5]. Neither heparin or low weight molecular heparin crosses the placenta and both are considered safe in pregnancy [2]. We performed a retrospective study, to assess the incidence of prescribing anticoagulants for prevention of venous deep thrombosis during a period of pregnancy.

II. MATERIALS AND METHODS

A retrospective study was undertaken during 01 January – 31 December of 2012, in the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetovo. The patient demographic data, month and week of pregnancy; diagnosis; drug details; which include name of the drug, dosage form, dose frequency, total cost of the drug, the amount of each given ample application; the cost for the entire period of hospitalization and the duration were recorded. The results were expressed as percentage and proportion, either as pictorial representation in the form of a diagram or in tabular form.

III. RESULTS

A. Socio-Demographic Data, Living Place and the Number of Pregnancies

During the period of one year, 4636 patients were registered. The biggest number of patients delivered: 2324 (50.19%). 1447 (31.21%) were pregnant women and 534 (11.52%) patients with other diagnoses were recorded. The

Sihana A. and Merita D. are with the Faculty of Medical Sciences, Department of Pharmacy, State University of Tetovo, R. of Macedonia (e-mail: sihana.ahmeti@hotmail.com, merita_leka@yahoo.com).

Ledjan. M. is with Medical University of Tirana, Faculty of Pharmacy, R. of Albania (e-mail: ledjan.malaj@gmail.com).

number of patients who had miscarriage was 331 (7.14%). Among the total number of 1447 pregnant women, 298 (20.59%) were prescribed low molecular weight heparin. The age range of pregnant women who visited the Department of Gynecology and Obstetrics was between 18 and 48 and the group with the highest attendance was 25–35: 141 (47.32%) patients. They were followed by 31–35 totaling 75 (25.17%) patients. The youngest age, 18–20, were less involved in the study being only 5 (1.68%) patients. 123 (41.28%) of the patients were from Tetovo and the urban places around and the biggest number, 175 (58,72%) patients, came from rural parts (villages) around Tetovo and Gostivar. For 195 (65.44%) women, this was their first pregnancy, 55 (18.46%) declared that this was their second pregnancy and for 48 (16.10%) of them, this was their third, fourth or fifth pregnancy (3+).

Age, number of patients and their percentage are being shown in Table I.

TABLE I

AGE, LIVING PLACE AND NUMBER OF PREGNANCIES OF THE PATIENTS

Parameters	Number of Patients	Percentage
Age		
< 18	0	0
18-20	5	1,68
21-24	41	13,76
25-30	141	47,32
31-35	75	25,17
>35	36	12,08
Living Place		
Urban	123	41,28
Rural	175	58,72
Number of Pregnancies		
1 st pregnancy	195	65,44
2 nd pregnancy	55	18,46
3 rd + pregnancy	48	16,10

B. Spectrum of Diagnoses for Which LMWH Were Prescribed

The most common diagnosis that was found in the study was Hypercoagulable state, 119 (39.93%) patients. 67 patients (22.48%) had non-pathological pregnancies, but high levels of D- Dimers, 48 (16.11%) of them had risky pregnancies and 12 (4.03%) had risky pregnancies associated with hypercoagulable state. 52 (17.45%) patients had other diagnosis: pregnancy after IVF, pregnancy associated with diabetes mellitus and pregnancy after some miscarriages were among them.

C. Number and Type of LMWH Prescribed

In the Department of Gynecology and Obstetrics, there are fifth anticoagulants which are recommended by the transfusiologist, and prescribed by the gynecologist: Clexane (enoxaparin) 2000 IU anti-Xa in 0.2mL, Clexane (enoxaparin) 4000 IU anti-Xa in 0.4mL, Fraxiparine (nadroparin calcium) 1900 IU anti-Xa in 0.2mL, Fraxiparine (nadroparin calcium) 2850 IU anti-Xa in 0.3mL and Fraxiparine (nadroparin calcium) 3800 IU anti-Xa in 0.4mL. The largest number of patients 84 (28.19%), received Clexane 2000 IU therapy. 81 (27.18%) patients were given Fraxiparine 2850 IU and

Fraxiparine 1900 IU was the least used, only 2 (0.67%) received this.

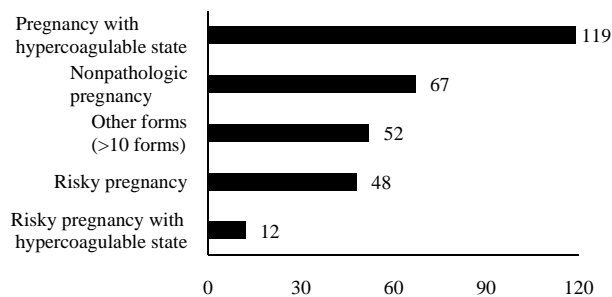


Fig. 1 Spectrum of diagnoses for which LMWH were prescribed

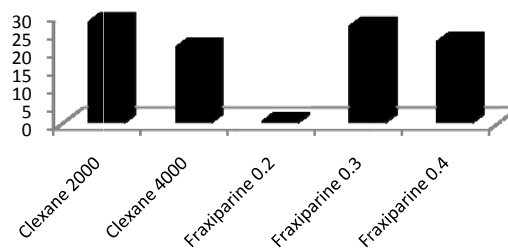


Fig. 2 Percentage and type of LMWH prescribed

D. Correlation of Using LWMH and Month of Pregnancy

The earliest stage of using LMWH was the second month of pregnancy, 4 (1.34%) pregnant women received anticoagulant therapy over that month. The most common patients were women in the seventh month 70 (23.49%), followed by them in the ninth month of pregnancy 68 (22.81%). The usage of LMWH had a significant relationship with patients in their seventh month of pregnancy (r = 0.875).

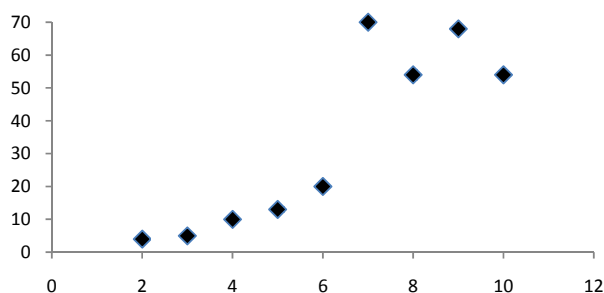


Fig. 3 Correlation of using LMWH and month of pregnancy

E. Incidence of Prescribing LMWH Over Weeks of Seventh Month of Pregnancy

28th gestational week, was found to be the most affected, 55 (78.57%) women were in that week and the less affected were those in 25th (1.43%) week of pregnancy.

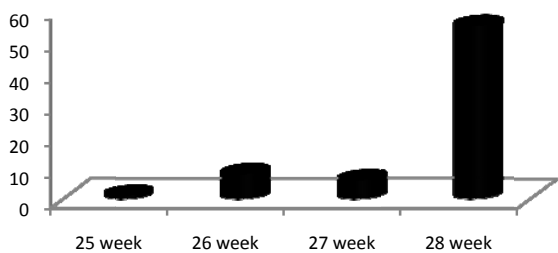


Fig. 4 Incidence of prescribing LMWH over weeks of seventh month of pregnancy

F. Percentage Share of Different Classes of LMWH along Seventh Month of Pregnancy

The biggest number of patients, 31.43% received Clexane 4000 UI. To 25.71% of patients was prescribed Clexane 2000 UI, followed by them with Fraxiparine 0.3 UI 24.29%. Fraxiparine 0.4 received 18.57% of patients.

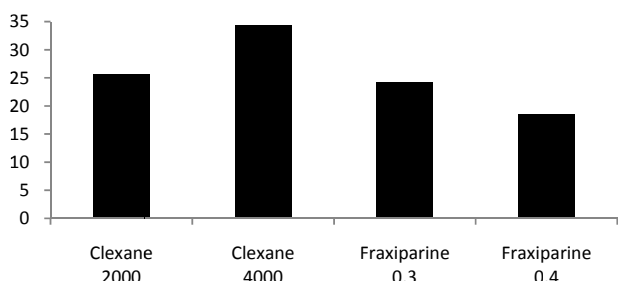


Fig. 5 Percentage share of different classes of LMWH along seventh month of pregnancy

Figs. 6-9 show the percentage of prescriptions of all LMWH over the seventh month of pregnancy, divided week by week. For Clexane 2000 UI the highest prescription rates during the 28th week, also Clexane 4000, Fraxiparine 0.3 UI and Fraxiparine 0.4 UI were the most prescribed during the 28th week of pregnancy.

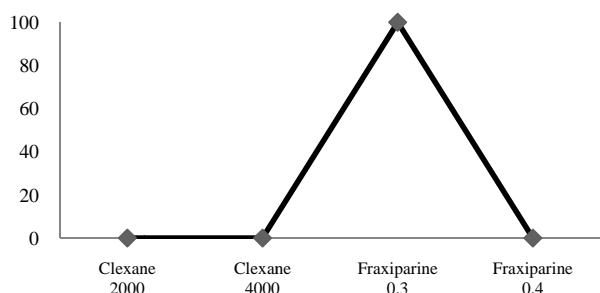


Fig. 6 Percentage of using LMWH over 25th week of pregnancy

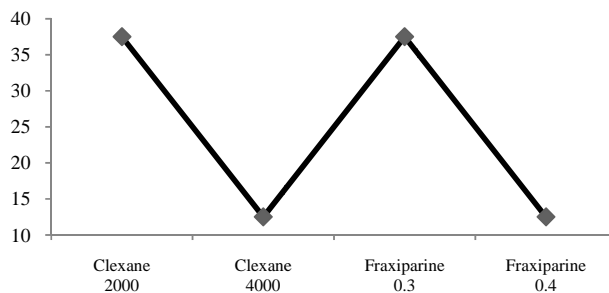


Fig. 7 Percentage of using LMWH over 26th week of pregnancy

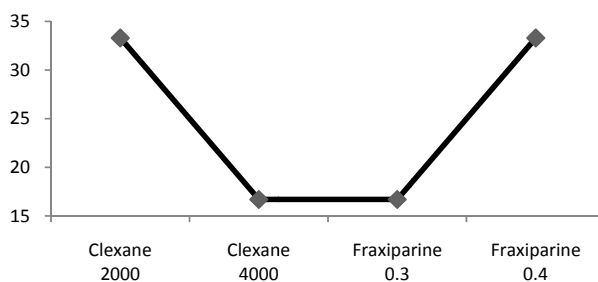


Fig. 8 Percentage of using LMWH over 27th week of pregnancy

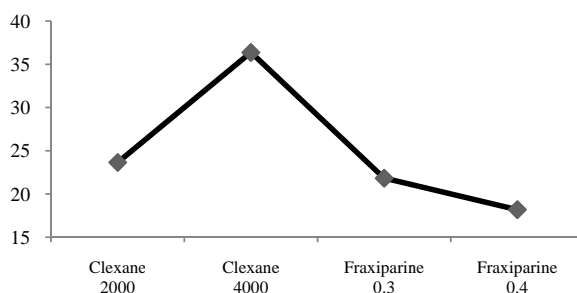


Fig. 9 Percentage of using LMWH over 28th week of pregnancy

G. Frequency of Diagnosis

To 52.86 percent of patients was found the diagnosis hypercoagulable state, 25.71 percent were patients with risky pregnancies associated with hypercoagulable state and patient with diabetes, pregnancy with twins and pregnancy after fecundation in utero were represented with percentage 1.4. Fig. 10 represents the detailed explanation.

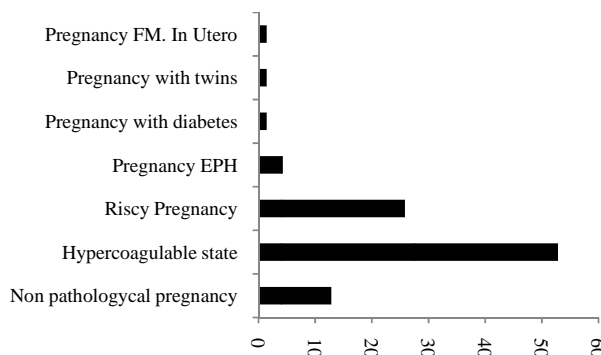


Fig. 10 Frequency of clinical diagnosis

IV. CONCLUSION

Pregnant women should visit the cardiologist in every trimester of pregnancy. LWMH have been shown to improve pregnancy in women with obstetric complications and to prevent recurrent fatal loss. Nevertheless, a further detailed investigation is required in order to suggest the usage of a low molecular weight heparin as prevention for reducing the risk of deep-vein thrombosis, such as venous insufficiency.

ACKNOWLEDGMENT

The authors express their gratitude to the Chief of the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetovo, Dr. Nagip Rufati, for his support and advices on this research.

REFERENCES

- [1] A. H.James, "Thrombotic Challenges Beyond Hematology (Book style)," Durham, North Carolina, 2009, pp. 277-285
- [2] M. R. Togli, J. G. Weg, "Venous thromboembolism during pregnancy" The New England Journal of Medicine, vol. 335, no. 2, pp. 108-114, July 1996
- [3] V .A. Rosenberg, C. J. Lockwood, "Thromboembolism in Pregnancy," Obstetrics and Gynecology Clinics, vol. 34, no. 3, pp. 481-500, Sep. 2007
- [4] P. E. Marik, L. A. Plante, "Venous Thromboembolic Disease and Pregnancy," New England Journal of Medicine, vol. 359, pp. 2025-2033, Nov 2008
- [5] M. M.W. Koopman, *et al.* "Treatment of Venous Thrombosis with Intravenous Unfractionated Heparin Administered in the Hospital as Compared with Subcutaneous Low-Molecular-Weight-Heparin Administered at Home," New England Journal of Medicine, vol. 334, pp. 682-687, March 1996
- [6] J. I. Weitz, "Low-Molecular-Weight-Heparins," The New England Journal of Medicine, vol. 337, pp. 688-699, Sep.1997
- [7] M. Levine, "A Comparison of Low-Molecular-Weight Heparin Administered Primarily at Home with Unfractionated Heparin Administered in the Hospital for Proximal Deep-Vein Thrombosis," The New England Journal of Medicine, vol. 334, pp. 677-681,Nov 2008