ARC Journal of Pharmaceutical Sciences (AJPS)
Volume 1, Issue 2, July – September 2015, PP 16-20
www.arcjournals.org

Antithrombotic Therapy During Pregnancy

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Abstract: *Antithrombotic therapy is the main therapy for acute deep vein thrombosis. The objectives of anticoagulant therapy in the initial treatment are to prevent thrombus extension and early and late recurrences of deep vein thrombosis and pulmonary embolism. The main objective of our study is to analyze the usage of low molecular weight heparins in women, during the period of pregnancy. Our study, represents a retrospective study, which was undertaken during 01 July – 31 December 2013, in the Department of Gynecology and Obstetrics, at Clinical Hospital in Tetova. Among of 817 pregnant women, 277 of them received anticoagulant therapy, respectively Low Molecular Weight Heparins. 119 of them were patients with risky pregnancy and 68 were with the diagnosis Hypercoagulable State.*

Keywords: *Antithrombotics, Deep Vein Thrombosis, Pregnancy, Low Molecular Weight Heparins.*

Abrevations

LMWH Low molecular weight heparins

VT venous thromboembolism

1. INTRODUCTION

There are two main adverse expriences that are associated with thrombophilia and pregnancy. These are VT and pregnancy complications associated with placental infarction, including miscarriage, intrauterine growth restriction, preeclampsia, abruption, and intrauterine death [1]. Stasis of blood, abnormalities of the vessel wall, and changes in the soluble and formed elements of the blood are the major contributors to thrombosis. Antithrombotic regiments modify one or more of these abnormalities. These regiments include drugs that inhibit blood coagulation, such as the various heparins and heparinoids; warfarin; direct thrombin inhibitors; drugs that inhibit platelet function, such as aspirin and dextran; and techniques that counteract venous stasis, such as compression stockings and pneumatic compression devices. All antithrombotic therapy with either anticoagulants or platelet-active drugs is prophylactic, since these agents interrupt progression of the thrombotic process; but unlike thrombolytic agents, they do not as a rule actively resolve it. Unfractionated heparin, LMWH, thrombolyitic agents and warfarin are used to treat venous thromboembolitic disease [2].

Pharmacological intervention in pregnancy focuses on the use of unfractionated heparin or LMWH due to the fetal teratogenic effects of coumarin. Increasingly, LMWH do not cross the placenta [3-4] and have several clinical advantages over unfractionated heparin. Their bioavailability is better, with a half-life two to four times longer than unfractionated heparin [5].

Over the last 10 years LMWHs have become the preferred anticoagulants for treating and preventing thromboembolism in all patients. They are equivalent or superior to unfractionated heparin in efficacy

and safety in the initial treatment of the acute deep venous thrombosis [6-7] and pulmonary embolism[8-9] outside of pregnancy.

Recent studies provide additional information about the safety of LMWH during pregnancy. As LMWH do not cross the placenta, studies have confirmed that they pose no direct risk to the fetus. The rate of major bleading, heparin induced thrombopenia, and osteoporosis is low when LMWH are used in pregnant women. In addition, the benefits of using LMWH much outweight those potential side effects [10].

The aim of the current paper is to analyze the spectrum of usage of low molecular weight heparins during pregnancy. The study, was conducted in Clinical Hospital of Tetovo, deparment of Gynecology and Obstetrics.

2. MATERIAL AND METHODS

Our study, represents an original research, which was conducted in the Hospital of Tetova, Republic of Macedonia, respectively in the Department of Gynecology and Obstetrics.

The data were collected from the Hospital Archive, for the period of six months, from 1st July to 31 December 2013.

These informations were recordet for each patients:

- Personal information for each patient (name and surname, birthday, living place),
- Information about the pregnancy (week and month of pregnancy, number of pregnancies),
- Time of hospitalization,
- Clinical and laboratory investigations and the diagnosis,
- Drug detail (name of the drug, dosage form, dose frequency, total cost of the drug) and
- The cost for the entire period of hospitalization.

3. RESULTS AND DISCUSSION

During the period of six months, 817 women visited the Department of Gynecology and Obstertrics, 277 of them received antithrombotic therapy (LMWH). The youngest patient, was a 18 years old women (pregnant for the first time) and the oldest patient which received antithrombotic therapy was a 48 old women, pregnant for the eight time, with IV fecundation (she received antithrombotic therapy during all the period of pregnancy, beacuse her diagnosis: hypercoagulable state).

The detailed information about the group age:

- 18 – 20 years 3 (1.08%) patients,
- 21 – 24 years 31 (11.2%) patients,
- 25 – 30 years 142 (51.26%) patients,
- 31 – 35 years 54 (19.49%) patients,
- Older than 35 years – 47 (16.97%) patients.

Information about the number of pregnancies:

- 160 (57.76%) women were pregnant for the firs time,
- 61 (22.02%) women were pregnant for the second time and
- For 56 (20.22%) women this was their third + pregnancy.

The earliest stage of using LMWH was the second month of pregnancy. Number of patients vs month of pregnancy, are ilustrated in the Figure 1.

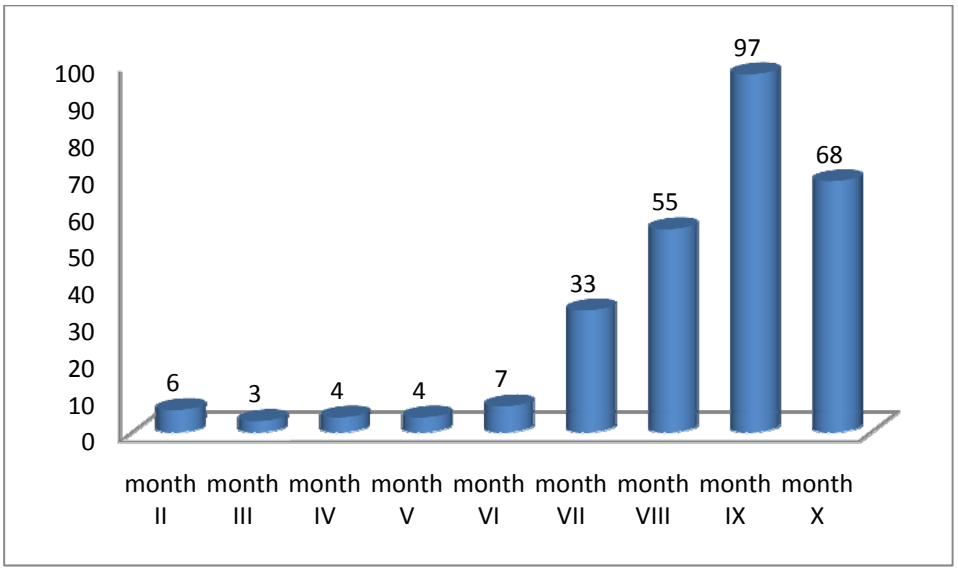

Figure 1. *Number of patients during each month of pregnancy*

The biggest number of patients 97, received antithrombotic therapy during ninth month of pregnancy, followed by them in the last month – 68. Less patiens, just 3 of them, received anticoagulant during third month.

In the Department of Gynecology and Obstetrics, these are 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, Fraxiparine (nadroparin calcium) 3800 IU anti-Xa in 0.4mL [11], Fragmin (dalteparin sodium) 2500 IU anti-Xa in 0.2mL and Fragmin (dalteparin sodium) 5000 IU anti-Xa in 0.2 mL.

Percentage share of usage of different types of LMWH is given in the figure 2.

The most prescribed anticoagulant was Fraxiparine (nadroparin calcium) 3800 IU anti-Xa in 0.4mL , 44.77 % of patients received this therapy. The smallest percent of patients, 0.36% received Fraxiparine (nadroparin calcium) 1900 IU anti-Xa in 0.2mL. Neither of patients received Fragmin (dalteparin sodium) 2500 IU anti-Xa in 0.2mL.

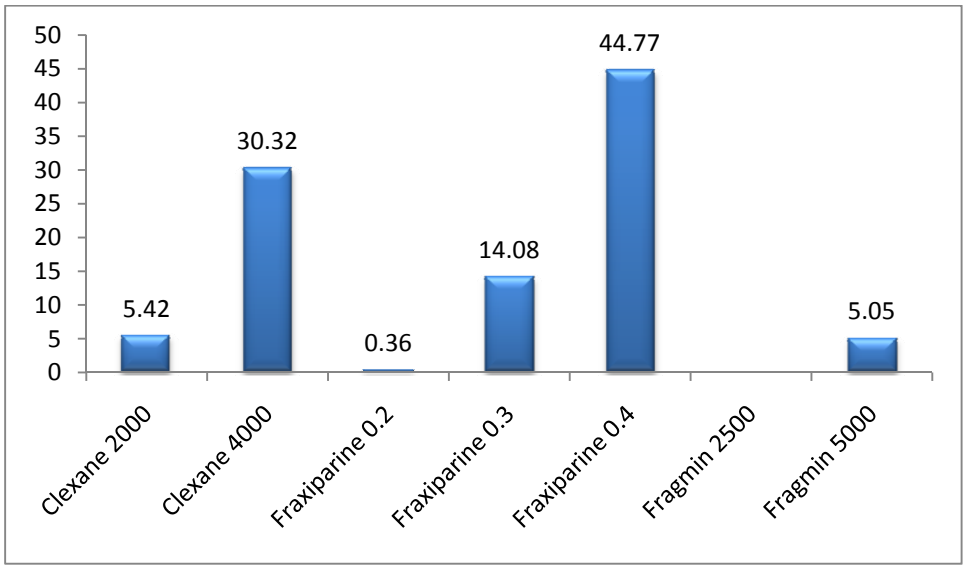

Figure 2. *Percentage share of LMWH-s used during pregnancy*

The most common diagnosis that was foud in the study was Risky pregnancy, 119 (42.96 %) patients. 68 (24.56 %) patients had hypercoagulable state and 42 (15.16 %) had nonpathologycal pregnancies, but high levels of D-Dimers. 48 (17.32 %) patients had other diagnosis: pregnancy after IVF, pregnancy associated with diabetes mellitus and pregnancy after some miscarriages were among them.

Table 1. *Frequency of Diagnosis*

Diagnosis ID	Type of diagnosis	Total frequency (N)	Percent (%)
D1	Risky pregnancies	119	42.96
D2	Hyperthrombotical pregnancy	68	24.56
D3	Nonpathologycal pregnancy	42	15.16
D4	Pregnancy afer some miscarriages	7	2.53
D5	Hypothrombotical pregnancy + hypoalbuminemia	5	1.82
D6	EPH gestosis pregnancy	4	1.45
D7	Gestosis pregnancy	3	1.08
D8	Pregnancy associated with hypoalbuminemia	3	1.08
D9	Pregnancy after IVF	3	1.08
D10	Pregnancy with thrombophlebitis cruris	3	1.08
D11	Hypothrombotical pregnancy + risky pregnancy	3	1.08
D12	Pregnancy with twins	2	0.72
D13	Varices cruris pregnancy (Pregnant women with varicose veins)	2	0.72
D14	Risky pregnancy E gestosis	2	0.72
D15	Risky pregnancy + Diabetes Mellitus	2	0.72
D16	H gestosis pregnancy	2	0.72
D17	AB IMMINENS pregnancy	2	0.72
D18	Risky pregnancy Nodulus Myomatus	1	0.36
D19	Pregnancy after FM In utero Varices	1	0.36
D20	Risky pregnancy + Olygohydromnion	1	0.36
D21	Hyperthrombotical pregnancy+E gestosis	1	0.36
D22	Risky pregnancy + Polyhidramnion	1	0.36

4. CONCLUSION

So long as they don't cross the placenta, studies have confirmed that they are safe to use during pregnancy. Their usage is much easier than the unfractionated heparin because the biological monitoring is reduced and they are very easy to use – with one or two daily subcutaneous injections administered.

Just because benefits of using LMWH outweight the side effects, the number of patients treated with low molecular weight heparins is growing.

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