Research Article

Effect of Low Molecular Weight Heparin in Patients with Preeclampsia

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Abstract

Introduction: Low molecular weight heparin (LMWH) is a safe and effective drug that has been used to treat various obstetric diseases. In China, LMWH has been used empirically to prevent preeclampsia (PE) in pregnant women at 20 weeks of pregnancy or even earlier. Once PE is established, LMWH treatment can also help to control blood pressure, reduce urinary protein and improve neonatal outcomes. **Patient and methods:** 60 pregnant females divided into three groups (20 patients in each), group A (PE group) received standard treatment of preeclampsia, Group B (PE with LMWH group) received standard treatment of preeclampsia plus Enoxaparin sodium or Clexane, and Group C (Control group) females with normal pregnancy received standard antenatal care. Follow up of systolic and diastolic blood pressure, number of cases with edema, proteinuria, CBC, liver and renal functions. **Results**: as regards systolic and diastolic blood pressure, number of edema cases there was a significant decrease in group C compared with other two groups. Also there was a significant decrease in proteinuria, urea, creatinine in group B & C compared with group A. While there was no significant difference between the three groups regarding CBC and liver function tests. **Conclusion:** LMWH (Enoxaparin sodium or Clexane) has promising application in patients with preeclampsia as determined by significant reduction in systolic and diastolic blood pressure, number of edema cases, proteinuria and serum creatinine level.

Key words: Low molecular weight heparin (LMWH), Preeclampsia (PE), Systolic and diastolic blood pressure, Proteinuria.

Introduction

Preeclampsia complicates 6% to 8% of all pregnancies, and is a major cause of maternal morbidity and mortality. It cannot be accurately predicted or prevented, and the only effective treatment is delivery. Early and accurate diagnosis is critical to optimize pregnancy outcome (Akolekar et al., 2011). Preeclampsia is a syndrome characterized by endothelium dysfunction, systemic inflammation, hypertension and initial kidney injury (Kim et al., 2013).

Low molecular weight heparin is a safe and effective drug that has been used to treat various obstetric diseases. Recent studies have found that the formation of microthrombus caused by the damage of vascular endothelial cells may be related to PE, leading to the hypothesis that LMWH may improve the prognosis in cases of PE (Rousseau et al., 2009).

The kidney is considered the organ to experience greatest damage in cases of PE. LMWH was found to control PE, protect renal function and improve fetal health. So LMWH can potentially be used as a safe and effective anti-PE drug to protect renal function through inhibiting PE induced apoptosis (Yang et al., 2011).

The aim of this study was to evaluate the safety and efficacy of LMWH as a treatment in patients with preeclampsia.

Patients and methods

After approval of the local ethics and scientific committee and obtaining written informed consent from all patients, 60 pregnant females, aged 18 to 42 years old, ASA I & II and patients classified as 40 pregnant female patients with preeclampsia plus 20 pregnant

females with normal pregnancy were enrolled in this prospective randomized controlled study. Patients were excluded from the study if they met the following criteria: patient refusal, uncooperative patients, patients with coexisting chronic diseases, known allergy to LMWH, patients with major organ dysfunction and life threatening conditions.

Patients were allocated into three equal groups of 20 patients each:
Group A (Preeclampsia group): received standard care and medications of preeclampsia.
Group B (Preeclampsia with LMWH group): received Enoxaparin sodium or Clexane in the dose of 4,000 IU once daily by SC injection, in addition to standard care and medications of preeclampsia.
Group C (Control group): pregnant females with normal pregnancy received standard antenatal care of pregnancy.

Once the patients were diagnosed as preeclamptic, they should start oral antihypertensive treatment with follow up of blood pressure. If severe preeclampsia were developed the patients should be admitted into the hospital and start IV antihypertensive treatment (Krishnachetty and Plaat, 2011).

Prevention and prophylaxis against eclamptic seizures was done by magnesium sulfate in the dose of 4g bolus over 10 min followed by 1g/h infusion until 24 hours (Altman et al., 2002).
Age, weight, ASA, parity and past history of previous diseases were recorded for all patients. Systolic and diastolic blood pressure was measured at 20 weeks gestation, 30 weeks gestation, and 38 weeks gestation and postpartum (after delivery by 1 & 15 days).

Proteinuria (≥ 300 mg in 24 hour urine collection) was investigated and edema of the LL was observed at 20 weeks gestation, 30 weeks gestation, and 38 weeks gestation and postpartum (after delivery by 1 & 15 days). Investigations in the form of CBC, liver and renal function tests were done at 20 weeks gestation, 30 weeks gestation, and 38 weeks gestation and postpartum (after delivery by 1 & 15 days).

The collected data were coded, tabulated, and statistically analyzed using SPSS program software version 25. Analyses were done for parametric quantitative data between the three groups using One Way ANOVA test. The level of significance was taken at (P value < 0.05).

Results

There were no statistically significant differences (P > 0.05) between the three groups as regards to age, weight and parity.

Table (1): Changes of SBP (mmHg) in the study groups.

Variable	Group A	Group B	Group C	P value		
At 20 weeks:				**< 0.001***		
-Range	(145-150)	(145-155)	(110-120)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	148±2.5	148.3±3.4	117±4.1	0.970	**<0.001***	**<0.001***
At 30 weeks:	#	#		**< 0.001***		
-Range	(130-145)	(130-150)	(110-120)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	141±4.5	142±5.2	117±4.7	0.789	**<0.001***	**<0.001***
At 38 weeks:	#	#		**< 0.001***		
-Range	(130-150)	(130-150)	(110-120)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	137±7.7	139.5±5.4	116±4.5	0.390	**<0.001***	**<0.001***
1 day PP:	#	#	#	**< 0.001***		
-Range	(130-140)	(125-140)	(100-120)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	134±4.5	132±4.7	112±7.7	0.524	**<0.001***	**<0.001***
15 days PP:	#	#	#	**< 0.001***		
-Range	(120-130)	(110-130)	(110-120)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	124±4.5	122.5±7.7	112±3.4	0.666	**<0.001***	**<0.001***

Table (2): Changes of DBP (mmHg) in the study groups.

Variable	Group A	Group B	Group C	P value		
At 20 weeks:				**< 0.001***		
-Range	(90-100)	(95-100)	(75-80)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	97.5±3.4	98±2.5	78±2.5	0.845	**<0.001***	**<0.001***
At 30 weeks:	#	#		**< 0.001***		
-Range	(80-95)	(80-95)	(70-85)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	88±4.7	90.5±4.3	76±6.4	0.290	**<0.001***	**<0.001***
At 38 weeks:	#	#	#	**< 0.001***		
-Range	(80-95)	(80-95)	(70-80)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	88.5±4.6	88±4.1	75±4	0.926	**<0.001***	**<0.001***
1 day PP:	#	#	#	**< 0.001***		
-Range	(80-95)	(80-90)	(70-80)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	86.5±4.6	86±4.5	72±4.1	0.931	**<0.001***	**<0.001***
15 days PP:	#	#	#	**< 0.001***		
-Range	(70-90)	(70-80)	(65-75)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	80±5.6	76.5±4.6	69±3.8	0.060	**<0.001***	**<0.001***

There were no statistically significant differences between the three groups regarding to CBC parameters and liver function tests.

Table (3): Serum creatinine level (mg/dl) in the study groups.

Variable	Group A	Group B	Group C	P value		
At 20 weeks:				0.426		
-Range	(0.3-0.9)	(0.5-0.9)	(0.5-0.9)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	0.7±0.2	0.7±0.1	0.7±0.1	0.627	0.936	0.416
At 30 weeks:	#			**<0.001***		
-Range	(0.4-1.1)	(0.6-0.9)	(0.5-0.8)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	0.9±0.2	0.8±0.1	0.7±0.1	**<0.001***	**<0.001***	**0.029***
At 38 weeks:	#			**<0.001***		
-Range	(0.7-1.2)	(0.5-1.2)	(0.5-0.9)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	0.1±0.1	0.8±0.2	0.6±0.1	**0.001***	**<0.001***	**0.004***
1 day PP:	#			**0.003***		
-Range	(0.6-1)	(0.5-1)	(0.5-1)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	0.9±0.1	0.8±0.2	0.7±0.1	0.079	**0.002***	0.390
15 days PP:		#		0.144		
-Range	(0.5-0.9)	(0.4-0.9)	(0.5-0.9)	***A vs B***	***A vs C***	***B vs C***
-Mean ± SD	0.7±0.1	0.6±0.1	0.6±0.1	0.163	0.260	0.962

- ***: Significant difference at p value < 0.05**

Discussion

Preeclampsia is a serious disorder that typically occurs after 20 weeks of pregnancy. It is usually associated with high blood pressure and proteinuria. Without treatment, PE can develop into life-threatening eclampsia (Zhang et al., 2015).

Low molecular weight heparin is a safe and effective drug that has been used to treat various obstetric diseases. For example, LMWH has been suggested to treat recurrent miscarriage caused by obstetric thrombophilia, and to control and treat pregnancy thrombo-embolism (Gandara et al., 2014).

In China, LMWH has been used empirically to prevent PE in pregnant women at 20 weeks of pregnancy or even earlier. LMWH treatment can also help to control blood pressure, reduce urinary protein and improve neonatal outcomes. Recent studies have found that the formation of microthrombus caused by the damage of vascular endothelial cells may be related to PE, leading to the hypothesis that LMWH may improve the prognosis of PE (Rousseau et al., 2009).

LMWH was found to control PE, protect renal function and improve fetal health. The mechanism of renal protection is likely to be related to the inhibitory effect of LMWH on apoptosis in kidney tissue (Yang et al., 2011).

The study was performed by Zhang et al., 2015 to investigate the effect of LMWH for the treatment of PE and the AKI associated with it in rats. Three groups of ten pregnant rats for each group were enrolled as the following rats with normal pregnancy (control group), rats with preeclampsia (PE group) and rats with preeclampsia injected with 40 µl /kg fraxiparine (LMWH group). They concluded that blood pressure, urinary protein, urea and creatinine were higher in PE group compared with control group and LMWH group. Apoptosis was found in kidney tissue in PE group which was inhibited in LMWH group.

The results of Zhang et al., 2015 are similar to the presented results of the current study according to blood pressure, proteinuria, blood urea level and serum creatinine level.

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