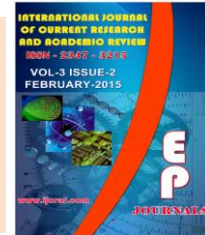




*International Journal of Current Research
and Academic Review*

ISSN: 2347-3215 Volume 3 Number 2 (February-2015) pp. 211-218

www.ijcrar.com



Comparison of low molecular weight heparin (LMWH) and standard unfractionated heparin for hemodialysis anticoagulation

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KEYWORDS

Enoxaparin,
Heparin,
Hemodialysis

A B S T R A C T

Low molecular weight heparin as an effective and safe anticoagulant that has lower side effects and low effect on serum lipids and in hemodialysis recommended for heparin. Long term use of heparin associated with some complications such as platelet dysfunction, thrombocytopenia, lipids abnormality, allergic reaction, osteoporosis and increase risk of bleeding. The aim of this study was comparison of Enoxaparin and standard heparin for hemodialysis anticoagulation. In a cross over study that was performed on hemodialysis patients and anticoagulation effects of standard heparin and LMWH were evaluated. In this study, 30 patients with CRF divided in two groups(A,B) and group A underwent hemodialysis for 12 section with standard heparin and after then for 12 section underwent hemodialysis with Enoxaparin(group C). Group B if first 12 sections underwent hemodialysis with Enoxaparin and after then for 12 sections underwent hemodialysis with standard heparin (group D). At frits of study, at the change anticoagulation time and at the end of study, lipid profile, platelet, prothrombin time, partial thromboplastin time and Kt/v evaluated and bleeding complication and embolus in patients and out of patients in each section of hemodialysis evaluated. Mean of lipoprotein a, triglyceride, high density lipoprotein, prothrombin time, particle thromboplastin time at before dialysis and mean of prothrombin time and particle thromboplastin time at after dialysis in patients underwent heparin and Enoxaparin no significant. Mean of low density lipoprotein at after hemodialysis in patients underwent Enoxaparin was significantly lower than mean of low density lipoprotein in patients underwent heparin (P=0.029). Mean of platelet at after hemodialysis in patients that received Enoxaparin significantly higher than mean of platelet in patients that received heparin (P<0.001). Mean of Kt/v at after hemodialysis in Enoxaparin received patients was significantly higher than heparin received patients (P=0.001). In our study, Enoxaparin without significant complication, prevention decrease of platelet and significant effect on low density lipoprotein and Kt/v, improved quality of hemodialysis.

Introduction

LMWH is recommended as an effective, efficient, and suitable anticoagulant with fewer side effects than and probable advantage over heparin in regard to dyslipidemia in hemodialysis.

The complications of long-term heparin use include platelet function disorders, thrombocytopenia, dyslipidemia, allergic reactions, osteoporosis, and bleeding risk increase. LMWH does not stimulate plasma lipase activity as much as heparin does. LMWH reduces thrombosis in a dialysis machine (1).

It also reduces the risks of osteoporosis, thrombocytopenia, and bleeding after dialysis. Patients are more satisfied with LMWH, and nursing requires less time relative to dialysis with heparin (2).

Anticoagulant therapy during dialysis is a vital, important process in these patients. In earlier years, fractionated heparin or regular heparin itself was used, which caused complications such as thrombocytopenia, obvious hyperkalemia, osteoporosis, and lipid profile disorders in patients. But in recent years, use of LMWH has become prevalent among patients, which has few complications as compared to heparin (3-5). The purpose of this study is to compare the effects and complications of heparin and LMWH.

Materials and Methods

In a study performed on hemodialysis patients in the cross-over form, the anticoagulant effects of heparin and LMWH were examined.

In this study, 30 patients were selected, 16 of whom were men and 14 of whom were women, who were subject to hemodialysis

due to renal failure for an average dialysis period of 3 years. They were divided into two groups: the heparin group received heparin for 12 sessions (group A) and then received LMWH for 12 sessions (group C), and the LMWH group first received LMWH for 12 sessions (group B) and then received heparin for 12 sessions (group D), and the required information was received from the patients and recorded. All the studied patients were dialyzed using fistula.

The exclusion criteria included patients who suffered from cardiovascular, platelet disorders, and potential for bleeding for whatever reason were excluded from the study.

The amount of regular heparin received each session was 5000 units, and the amount of LMWH received was 1 milligram for each kilogram of body weight for each patient in each dialysis session.

The results obtained from the study were examined among the four groups studied, and also, the results of the groups receiving heparin (groups A and D) and those of the groups receiving LMWH (groups B and C) were specified, and statistical analyses were also performed between the two groups receiving heparin and LMWH, and the obtained results were presented in the form of a comparison of the results of the two groups under treatment with heparin and LMWH.

Statistical Analysis

The collected data were analyzed by SPSS-17 statistical software. The collected data were expressed as percentage and mean \pm SD. Continuous (quantitative) variables were compared by Independent samples and Paired t test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact

test. P-value ≤ 0.05 was considered statistically significant.

Result and Discussion

In this study, 30 patients under hemodialysis due to renal failure were selected and subject to anticoagulant treatment with heparin and LMWH, where the following results were obtained:

The mean age of the patients under treatment with heparin was 30.84 ± 10.84 and that of the patients under treatment with Enoxaparin was 40.93 ± 14.6 ($P=0.051$).

8 of the patients in the heparin group and 8 of the patients in the Enoxaparin group were men ($P=1$).

The mean length of hemodialysis period was 38.84 ± 9.02 in patients under treatment with heparin and 36.38 ± 8.64 months in patients under treatment with Enoxaparin ($P=0.485$).

Among the patients in the two groups, adverse drug reactions and complications during dialysis due to anticoagulant treatment were not observed during the study.

The amount of pruritus in patients subject to treatment with Enoxaparin was significantly lower than that in patients with heparin ($P=0.022$).

The value of satisfaction with anticoagulant treatment in patients under treatment with Enoxaparin was significantly higher than the value of satisfaction with anticoagulant treatment in patients under treatment with heparin ($P=0.022$).

Analysis of experimental parameters among the patients in the two groups A and C has been displayed in Table 1.

The mean Kt/v in the group A patients was 1.14 ± 0.15 before dialysis, which reached 1.15 ± 0.17 after 12 hemodialysis sessions, and in the group C patients, it was 1.15 ± 0.17 , which reached 1.24 ± 0.04 after 12 hemodialysis sessions ($P=0.870$).

There is not a significant difference in the mean Kt/v after dialysis between the patients in the two groups A and C ($P=0.093$).

The mean local compression time was 3.78 ± 0.7 minutes in the group A patients and 3.9 ± 0.86 minutes in the group C patients ($P=0.699$).

Analysis of experimental parameters among the patients in the two groups B and D has been displayed in Table 2.

The mean Kt/v in the group B patients was 1.42 ± 0.19 before dialysis, which reached 1.43 ± 0.27 after 12 hemodialysis sessions, and in the group D patients, it was 1.43 ± 0.27 , which reached 1.13 ± 0.2 after 12 hemodialysis sessions ($P=0.927$).

The mean Kt/v after dialysis among the group B patients was significantly higher than that in group D ($P=0.002$).

The mean local compression time was 4.41 ± 1.55 minutes in the group B patients and 5.28 ± 1.94 minutes in the group D patients ($P=0.194$).

Analysis of experimental parameters among the two groups of patients receiving heparin and Enoxaparin has been displayed in Table 3.

The mean Kt/v before dialysis in the patients under treatment with heparin was 1.29 ± 0.26 and that in the patients under treatment with Enoxaparin was 1.29 ± 0.22 ($P=0.992$).

The mean Kt/v after dialysis in the patients under treatment with heparin was 1.14 ± 0.19 and that in the patients under treatment with Enoxaparin was 1.35 ± 0.23 . The mean Kt/v after dialysis in the patients under treatment with Enoxaparin was significantly higher than that in the patients under treatment with heparin ($P=0.001$).

The mean dialysis location compression time in the patients under treatment with heparin was 4.56 ± 1.64 minutes and that in the patients under treatment with Enoxaparin was 4.19 ± 1.3 minutes ($P=0.360$).

In a study conducted by Stefoni and colleagues at the department of nephrology and dialysis in Bolojngrb, Italy, by examining patients subject to hemodialysis due to chronic renal failure, they stated that the mean PTT before dialysis in patients under treatment with LMWH was significantly lower than the mean PTT before dialysis in patients under treatment with heparin (5).

In our study, the mean PTT before dialysis was 55.93 ± 256.47 seconds in the heparin groups patients and 47.67 ± 23.22 seconds in the Enoxaparin group patients. There was not a significant difference in the mean PTT before dialysis among the patients in the two heparin and Enoxaparin groups ($P=0.219$).

In the above study, it was stated that the serum TG level was significantly lower in patients under treatment with LMWH than the serum TG level in patients under treatment with heparin (5). In our study, the mean TG after dialysis was 204.74 ± 43.53 in the heparin group patients and 197.19 ± 37.89 among the Enoxaparin group patients. Although the TG level in the Enoxaparin group is lower than the TG level in the heparin group, there is not a significant difference in the mean TG between the

patients in the two heparin and Enoxaparin groups ($P=0.499$).

In a study conducted at the department of nephrology in 2002 in China, Liu stated that treatment of dialysis patients with LMWH is healthier and has better anticoagulant effects than that with heparin (6).

In our study, there were fewer complications in the patients under treatment with Enoxaparin than in the patients under treatment with heparin.

In a study performed by Olszowska and colleagues in 2002 at the department of nephrology and dialysis in Bolojngrb, Italy, they stated that LMWH has better hematologic effects, and hematologic complications in these patients are fewer than those with standard heparin (7).

In a study conducted by Farooq and colleagues in 2004, they stated that LMWH has better anticoagulant effects than those with heparin in these patients (8). In our study, the patients in the group under treatment with Enoxaparin were more satisfied with dialysis and its complications than those in the group under treatment with heparin.

During an investigation performed at the department of nephrology of Kangnam-KU hospital in Seoul, South Korea in 2003, Kim and colleagues realized that use of LMWH in hemodialysis patients has better, more acceptable effects than that of heparin (9).

The results of our study are also the same as the findings of the above studies, suggesting the better effects of LMWH than those of heparin. Examining effects of LMWH on patients under hemodialysis in Norway in 2004, Sagedal and colleagues stated that like standard heparin, LMWH is useful in hemodialysis patients, there is less bleeding in patients under treatment with LMWH,

and thrombocytopenia is significantly less prevalent in patients under treatment with LMWH than the results with heparin (10).

In our study, too, there was less thrombocytopenia in the LMWH group patients, and the mean PLT after dialysis was 131.04 ± 21.65 in the heparin group patients and 181.22 ± 37.59 in the LMWH group patients. The mean PLT in the heparin group patients was significantly lower than the mean PLT after dialysis among the LMWH group patients ($P=0.000$).

In a study conducted by Klingel and colleagues in Cologne, Germany in 2004, it was realized that prescription of a single dose of Enoxaparin in hemodialysis patients creates sufficient, proper anticoagulopathy effects in these patients (11).

In a study conducted by Malyszko and colleagues at the department of nephrology and kidney transplant of Biolytostoke University of Medical Sciences in Poland in 2004, the results of anticoagulant therapy of types of heparin in hemodialysis patients was examined, and they stated that hemodialysis patients who were under treatment with LMWH have lower TAFI and more suitable hematologic parameters than those with heparin (12). In a study conducted in Canada in 2006, Lo and colleagues reported that LMWH is an effective medication in hemodialysis patients, which can be used for long periods in these patients and has a low mean number of platelets and thrombocytopenia prevalence as compared to heparin (13).

In our study, too, the number of platelets after dialysis was significantly higher in the patients under treatment with Enoxaparin (LMWH).

In a study performed by Molitor and colleagues, they stated that LMWH has

fewer hematologic complications in hemodialysis patients than heparin does (14). In a study reported by Frank and colleagues in 2006 at the department of nephrology in Aachen, Germany, it was stated that the mean number of platelets in patients under treatment with LMWH was significantly higher than the mean number of platelets in patients under treatment with heparin (15).

In a study reported in Pennsylvania, USA in 2006, by examining effects of anticoagulant treatments in hemodialysis patients, Sinawane stated that the rate of lipid profile disorders is significantly lower in patients under treatment with LMWH than those under heparin treatment (16).

In our study, too, the obtained findings are the same as the results of the above study.

Conclusion

Based on the results of the present study, there is more satisfaction (absence of pruritus, other allergies, bleeding, and thrombosis during dialysis) in patients under treatment with LMWH than in other patients, and the mean LDL after dialysis was significantly higher in the heparin group patients than in the Enoxaparin group patients ($P=0.029$). The mean KT/V after dialysis was significantly lower in the heparin group patients than in the enoxaparin group patients ($P=0.001$).

Recommendations

Considering the positive effects of LMWH on dialysis adequacy, Kt/v, lipid changes, reduction of thrombocytopenia, and absence of serious complications, it is suggested that LMWH be used instead of regular heparin in hemodialysis patients to obtain better, more proper results in treatment of the disease.

Table.1 Evaluation of laboratory find between Groups A and C

	Group		P
	A	C	
TG before	207.69 ± 47.24	210.31 ± 51.35	0.894
TG after	210.31 ± 51.35	191.33 ± 37.73	0.307
LDL before	145.77 ± 34.27	146.92 ± 34.28	0.934
LDL after	146.92 ± 34.28	119.83 ± 31.94	0.053
HDL before	37.31 ± 6.81	37.85 ± 7.28	0.847
HDL after	37.85 ± 7.28	40.67 ± 8.28	0.374
PLT before	143.08 ± 22.50	126.00 ± 24.34	0.076
PLT after	126.00 ± 24.34	168.75 ± 23.33	<0.001
Hg before	9.59 ± .95	9.74 ± 1.14	0.725
Hg after	9.74 ± 1.14	9.92 ± .80	0.636
Hct before	29.00 ± 2.73	29.24 ± 3.34	0.844
Hct After	29.24 ± 3.34	30.04 ± 2.45	0.493
PT Before	19.00 ± 8.68	14.75 ± 5.14	0.153
PT After	13.15 ± 1.14	14.25 ± 6.27	0.541
PTT Before	77.31 ± 33.60	59.33 ± 25.68	0.149
PTT After	52.00 ± 26.26	43.92 ± 26.27	0.450

Table.2 Evaluation of laboratory finding between Groups B and D

	Group		P
	B	D	
TG before	200.67 ± 33.69	201.87 ± 38.67	0.928
TG after	201.87 ± 38.67	199.57 ± 36.00	0.870
LDL before	116.00 ± 21.65	116.93 ± 19.56	0.902
LDL after	116.93 ± 19.56	124.29 ± 21.57	0.344
HDL before	33.60 ± 3.31	33.33 ± 2.35	0.801
HDL after	33.33 ± 2.35	33.29 ± 3.73	0.967
PLT before	190.27 ± 43.05	191.20 ± 44.25	0.954
PLT after	191.20 ± 44.25	135.71 ± 18.50	<0.001
Hg before	9.69 ± 1.21	9.35 ± 1.10	0.436
Hg after	9.35 ± 1.10	9.31 ± .81	0.910
Hct before	28.79 ± 3.85	28.63 ± 3.66	0.904
Hct After	28.63 ± 3.66	28.27 ± 2.33	0.750
PT Before	13.80 ± 1.21	13.57 ± 1.28	0.625
PT After	20.20 ± 19.94	12.86 ± .66	0.180
PTT Before	48.13 ± 23.55	50.21 ± 24.33	0.817
PTT After	50.67 ± 20.93	59.57 ± 25.13	0.308

Table.3 Evaluation of laboratory finding between Groups LMWH and Regular Heparin

	Group		P
	LMWH	Regular Heparin	
TG before	205.14 ± 42.24	204.57 ± 42.14	0.960
TG after	197.19 ± 37.89	204.74 ± 43.53	0.499
LDL before	130.36 ± 31.81	130.32 ± 30.58	0.997
LDL after	118.22 ± 25.29	135.19 ± 30.13	0.029
HDL before	35.57 ± 5.82	35.18 ± 5.25	0.792
HDL after	36.59 ± 6.77	35.48 ± 6.07	0.528
PLT before	160.43 ± 47.85	168.86 ± 42.87	0.491
PLT after	181.22 ± 37.60	131.04 ± 21.65	<0.001
Hg before	9.71 ± 1.16	9.46 ± 1.02	0.401
Hg after	9.62 ± 1.00	9.51 ± .98	0.687
Hct before	29.00 ± 3.56	28.80 ± 3.21	0.826
Hct After	29.28 ± 3.19	28.72 ± 2.83	0.487
PT Before	14.22 ± 3.49	16.19 ± 6.58	0.187
PT After	17.56 ± 15.49	13.00 ± .92	0.139
PTT Before	53.11 ± 24.70	63.26 ± 31.74	0.196
PTT After	47.67 ± 23.23	55.93 ± 25.48	0.219

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