Poster number 30

Nafamostat mesilate as anticoagulant during continuous renal replacement therapy in the patients with high risk of bleeding: a randomized prospective study

Jang- Hee Cho[1,2] , Yun-Jeong Kang [1,2], Ga-Young Park[1,2], Jun-Seop Kim[1,2], Owen Kwon[1,2], Ji-Young Choi[1,2], Sun-Hee Park[1,2], Yong Lim Kim[1,2], and Chan Duck Kim[1,2]

[1]Department of Internal Medicine, Kyungpook National University Hospital, [2]Clinical Research Center for End Stage Renal Disease in Korea

Close

Background

Nafamostat mesilate (NM), a synthetic serine protease inhibitor, has been widely used in Korea as an anticoagulant during continuous renal replacement therapy (CRRT). However, there were limited data from randomized study of nafamostat mesilate in patients with bleeding tendency. This prospective study evaluated the efficacy and safety of nafamostat mesilate in CRRT for patients with acute kidney injury (AKI) who were at high risk of bleeding.

Methods

From July 2008 to June 2012, patients with AKI were randomized to receive NM (NM group) or normal saline (control group) as an anticoagulant during CRRT. Patients who fullfilled one of the following criteria were defined as high risk of bleeding: spontaneous bleeding, aPTT >45 sec, PT >17 sec, thrombocytopenia, recent surgery. Primary outcome was to compare treatment efficacy represented by hemofilter life span. Several parameters of safety and efficacy were analyzed as secondary outcomes.

Results

Table 1-1. Demographic findings of kidney transplant recipients

Characteristics	Nafamostat (N=31)	No-anticoagulation (N=24)	P-value
Demographics			
Age (years)	63.6±11.5	58.6±18.0	0.212
Male sex (%)	21 (67.7%)	15 (62.5%)	0.778
Severity of illness at ICU admission			
APACHE II score	23.5±6.2	25.9±8.4	0.229
Mechanical ventilation	23 (74.2%)	16 (66.7%)	0.565
Cause of AKI			
Sepsis (%)	14 (45.2%)	13 (54.2%)	0.331
Ischemia (%)	6 (19.4%)	4 (16.7%)	
Toxin (%)	6 (19.4%)	2 (8.3%)	
Hypovolemia (%)	1 (3.2%)	3 (12.5%)	
Cardiac failure (%)	3 (9.7%)	0 (0%)	
Other	1 (3.2%)	2 (8.3%)	
Systolic arterial pressure (mmHg)	118.9±22.4	117.4±22.0	0.808
Diastolic arterial pressure (mmHg)	67.4±16.5	67.4±14.6	0.917

Table 1-2. Demographic findings of kidney transplant recipients

Characteristics	Nafamostat (N=31)	No-anticoagulation (N=24)	P-value
Lab data at CRRT start			
White blood cell (x1,000/μL)	13.54±10.16	10.74±6.56	0.246
Hemoglobin (g/dL)	9.36±2.05	8.83±1.84	0.324
Platelet (x1000/ μL)	115.52±75.94	77.70±65.60	0.058
Total cholesterol (mg/dL)	97.8±50.0	80.5±40.7	0.173
Blood urea nitrogen (mg/dL)	77.4±36.9	73.6±37.7	0.705
Plasma creatinine (mg/dL)	4.2±1.9	3.9±1.3	0.408
Prothrombin time (sec)	19.7±6.7	22.8±13.0	0.237
Activated PTT (sec)	52.5±39.3	46.3±28.2	0.523

Table 2. Patient outcome of efficacy and cause of filter failure

Outcome	Nafamostat (N=31)	No anticoagulation (N=24)	p-value
Efficacy			
Filter life span	31.66±24.10	19.52±14.85	0.035
Number of filter per hour	0.06±0.05	0.10±0.092	0.061
Urea reduction ratio of 6hr (%)	16.4±17.7	18.7±16.9	0.691
Creatinine reduction ratio of 6hr	18.72±18.1	16.93±12.9	0.691
Cause of filter failure			
Filter clotting	20 (37.7%)	34 (59.6%)	0.024
High hemofilter pressure	1 (1.9%)	3 (5.3%)	0.619
Vascular asscess malfunction	4 (7.5%)	2 (3.5%)	0.426
Transport to radiology/operation	1 (1.9%)	0 (0.0%)	0.482
Line air bubble	0 (0%)	2 (3.5%)	0.496
Conversion to intermittent dialysis	11 (20.8%)	1(1.8%)	0.002
Expire	12 (22.6%)	13 (22.8%)	1.000
Hopeless discharge	2 (3.8%)	2 (3.5%)	1.000
Dialysis quit	2(3.8%)	0(0.0%)	0.230

Table 3. Patient outcome of safety

Variable	Nafamostat (N=31)	No anti-coagulation (N=24)	p-value
Recovery of renal function	9 (29.0%)	3 (12.5%)	0.194
RBC transfusion	13 (41.9%)	8 (33.3%)	0.584
GI bleeding	2(6.5%)	0 (0%)	0.499

The mean hemofilter life span was 29.8±23.0 hrs in the NM Group which was significantly longer than 19.5±14.9 hrs in the control group (p=0.001). The most common cause of filter failure was filter clotting which was significantly higher in control group than NM group (59.6% vs 37.7%, p=0.024). There were no significant differences in transfusion and major bleeding between groups. The patient survival rate of NM group at 30 days and 90 days after initiation of CRRT were comparable to that of control group.

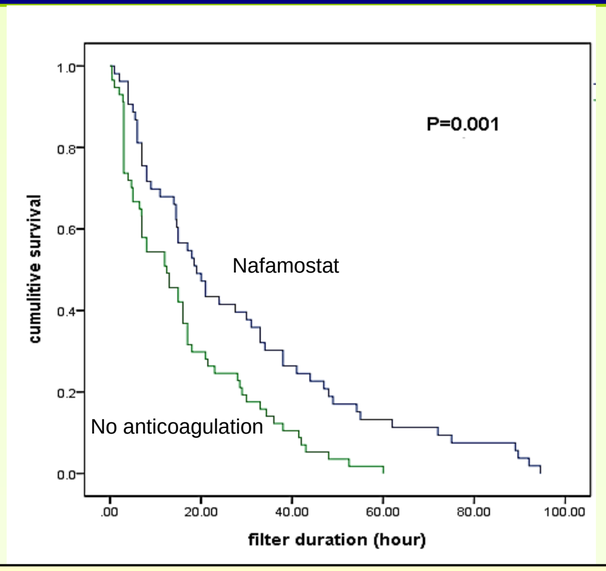

Figure 1. Kaplan–Meier survival function indicating hemofilter survival times between Nafamostat and no anticoagulation treatment group. The median he mofilter life span was 29.8±23.0 hrs in NM Group which was significantly lon ger than 19.5±14.9 hrs in normal saline group

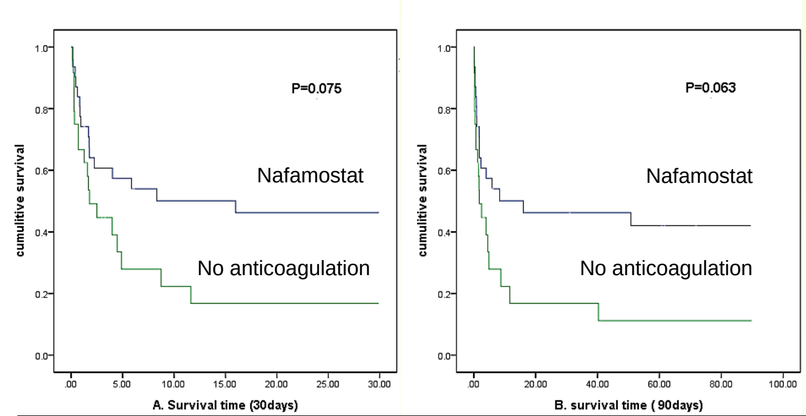

Figure2. Kaplan-Meier patient survival curve between Nafamostat and no anti coagulation treatment group (A. 30 days B.90 days). A Kaplan–Meier survival analysis showed no statistically significant difference in survival up to day 30 and 90 between two treatment groups.

Conclusions

Nafamostat mesilate could be used as anticoagulant during CRRT providing sufficient filter survival without additional risk of bleeding in critically ill AKI patients with bleeding tendency.

This study was supported by a grant from the Korea Healthcare Technology R & D Project, Ministry for Health, Welfare & Family Affair, Republic of Korea (A102065).