Targeted Versus Fixed Dosing of Nafamostat Mesylate Anticoagulation for Continuous Kidney Replacement Therapy

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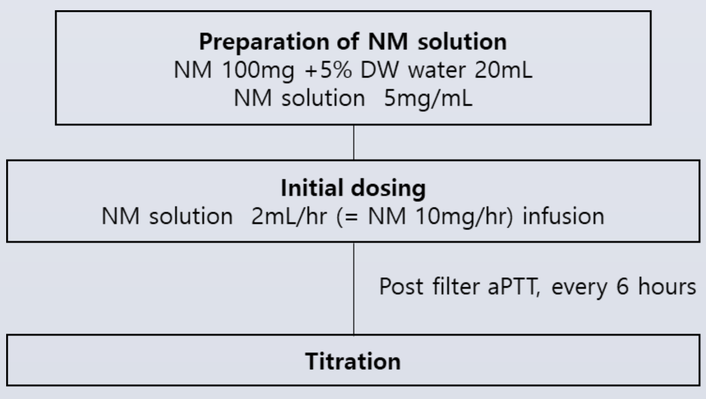
Introduction

Nafamostat mesylate (NM) is a widely used method of anticoagulation for continuous kidney replacement (CKRT) in Japan and South Korea. NM is continuously infused to the CKRT circuit via anticoagulant device mounted on the CKRT machine with a usual dose of 10~20 mL/hr, based on the manufacturer's suggestion. As there has been no study for optimal dosing for NM anticoagulation, we designed NM dosing protocol and tested its performance.

Methods

This is a single center, before-and-after study comparing the performance of NM dosing protocol on CKRT filter life. Before targeted dosing (Oct.2023~April 2024), NM was infused with a fixed dose of 10mg/hr. NM dosing protocol was applied between May 2024 to April 2025; we started NM with the rate of 10 mg/hr then, titrated by 2.5~5mg/hr every 6 hours, targeted to maintain post-filter activated partial thromboplastin time (aPTT) ratio 1.5~2.3, aPTT 46~70 seconds (Figure 1).

All the cases were implemented as continuous veno-venous hemodiafiltration (CVVHDF) mode using an AN69ST membrane. Differences in NM infusion rate (mL/hr), NM consumption (bottle count/day), and filter life were compared before and after program.



	NM dose	Infusion rate
aPTT <35 (<1.2 X control)	+5.0 mg/hr	+1cc/hr
aPTT 35~45 sec (1.2~1.5 X control)	+2.5 mg/hr	+0.5cc/hr
aPTT 46~70 sec (1.5~2.3 X control)	No change	No change
aPTT 71~90 sec (2.3~3 X control)	-2.5 mg/hr	-0.5 cc/hr
aPTT >90 sec (>3 X control)	-5.0 mg/hr	-1cc/hr

Figure 1. PNUH Nafamostat Mesylate dosing protocol for CKRT

Table 1. Baseline characteristics

	Total	Targeted dosing N=60	Fixed doing N=91	P-value
Demographics				
Age, year	68.20±14.23	66.72±14.41	69.18±14.10	0.303
Age>75 years, n(%)	56(37.1)	18(30.0)	38(41.8)	0.413
Male,	104(68.9)	38(63.3)	66(72.5)	0.232
Comorbidities				
Diabetes	78(51.7)	28(46.7)	50(54.9)	0.319
Hypertension	94(62.3)	36(60.0)	58(63.7)	0.643
ESKD	35(23.2)	19(31.7)	16(17.6)	0.045
Cancer	19(12.6)	9(15.0)	10(11.0)	0.467
Disease severity				
Vasopressor	78(51.7)	30(50.0)	48(52.7)	0.741
Ventilator	80(53.0)	27(45.0)	53(58.2)	0.111
Trauma	8(5.3)	3(5.0)	5(5.5)	0.894
Surgery	15(9.9)	5(8.3)	10(11.0)	0.593
Oliguria	105(72.9)	41(68.3)	64(76.2)	0.296
CRRT treatment				
Mode				
CVVHDF,%	100	100	100	NA
Membrane				
AN69ST, %	100	100	100	NA
Prescribe dose	29.72±6.18	28.16±4.55	30.74±6.89	0.012
Delivered dose	26.61±4.68	26.04±3.78	26.99±5.18	0.195

Results

A total of 151 (before 91, after 60) patients received NM-CKRT anticoagulation; 68.9% were male and the mean ages were 68.2±14.2 years. Patients' demographics and disease severity were not different before and after the program (Table 1). We evaluated filter life span of the 344 and 330 filters before and after the NM dosing protocol implementation.

After the program, both NM infusion rate and NM consumption were significantly increased. However, filter life was unchanged before and after the study [before:24.4±14.7, after:24.3±12.8, p=0.968] (Table 2).

Table 2. Changes in Filter life and NM doses before and after the program

	Total	Targeted dosing N=60 Filter=330	Fixed doing N=91 Filter=344	P-value
Filter life, hour	23.7. ±16.86	23.84±16.19	23.63±17.50	0.869
Filter hour>60hr	37(5.5)	16(4.8)	21(6.1)	0.474
Filter hour >30hr	179(26.6)	87(26.4)	92(26.7)	0.911
NM dose, mg/hr	12.75±5.05	15.69±5.95	9.98±0.59	<0.001
# Wasted NM bottles/CKRT day	4.48±2.00	5.74±2.05	3.64±1.45	<0.001

During the implementation of NM dosing protocol, 74.3% of the filters achieved target post filter aPTT level; 18.6% of the filter did not reach the target aPTT level, and the other 7.1% stayed above target aPTT level. The mean NM doses were 16.8±5.8, 16.2±5.6, and 11.5±6.8 mg/hr in in-target, under-target, and over-target group, respectively. Filter life was significantly longer in patients achieved target aPTT level, compared to those with under or over target.

Table 3. Filter life by achievement of target aPTT level

	Targeted dosing N=60, #Filters=330			Fixed dosing N=91# Filters=344	P-value
	Under target (#Filters=61, 18.6%)	In target (#Filters=246, 74.3%)	Above target (#Filters=23, 7.1%)		
aPTT level, sec	35.9±5.9	43.2±9.2	94.7±26.5	NA	<0.001
Filter Hour, hr	14.7±10.5	28.5±16.4	21.0±12.1	23.6±17.5	<0.001
NM dose, mg/hr	16.8±5.8	16.3±5.7	11.5±6.8	9.98±0.59	0.001

Conclusion

1. Post-filter aPTT- based targeted NM dosing program increased filter life in patients with protocol compliant patients.
2. Nearly Around 20% of the patients did not reach the target aPTT level, regardless of the higher dosing of the NM. Further research is required for the NM non- responders.

Reference

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