Complement and Contact System Activation during Hemodialysis

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Key points

Early complement activation (C3a) occurs within 30 minutes after initiation of hemodialysis.

Late complement activation (sC5b-9) occurs within 60 minutes.

Contact system factor-inhibitor complexes decrease within 60 minutes, likely due to dialyzer adsorption and/or consumption.

Introduction and objectives

Hemodialysis (HD) membranes have the potential to trigger inflammation in a process that has been speculated to be driven by the complement system (1). The complement system interacts with the contact system which has been shown to be triggered by negatively charged surfaces, including dialysis membranes (2). The aim of this study is to quantify complement and contact system activity in a contemporary HD.

Methods

Blood was sampled from 20 consecutive HD-patients before, at 30, 60, 120, 180 and 240 minutes and after the HD-session. HD was carried out with no modifications made for study purposes using either polysulphone or polyarylethersulfone/polyamide/polyvinylpyrrolidone dialyzers. Enzyme-linked immunosorbent assay was used to quantify plasma complement system factors and contact system factor-inhibitor complexes listed in Table 1. Samples taken during and after HD were compared with baseline concentrations using Wilcoxon signed-rank test.

Results

Patient characteristics are presented in Table 2. The plasma concentrations of complement, contact system factors and thrombin-antithrombin are presented in Table 3 and Figure A, B and C respectively. C3a and sC5b-9 levels increased significantly from baseline, peaking at 1 hour and 4 hours respectively. A slight but significant decrease in C3(H_20) was observed at 30 minutes. Plasma concentration of all the contact system factor-inhibitor complexes decreased significantly.

Conclusion

Both complement and contact system factor-inhibitor complexes are significantly altered during hemodialysis. The effect of these alterations in relation to sustaining inflammation remains to be established in future studies.

References

1. Ekdahl KN, Soveri I, Hilborn J, Fellström B, Nilsson B. Cardiovascular disease in haemodialysis: role of the intravascular innate immune system. *Nat Rev Nephrol*. 2017; 13: 285-296.
2. Maas C, Oschatz C, Renné T. The plasma contact system 2.0. *Semin Thromb Hemost.* 2011; 37: 375-81

Table 1. Studied complement and contact system factors

Factor	Abbreviation
Complement system	
C3a	C3a
Soluble C5b-9	sC5b-9
C3(H_2O)	C3(H_2O)
Contact System	
FXIa-Antithrombin	FXIa-AT
FXIa-C1 Inhibitor	FXIa-C1INH
FXIIa-Antithrombin	FXIIa-AT
FXIIa-C1 Inhibitor	FXIIa-C1INH
Kallikrein-Antithrombin	Kallikrein-AT
Kallikrein-C1 Inhibitor	Kallikrein-C1INH
Thrombin-antithrombin	TAT

Table 2. Patient characteristics

Age, years, mean ± SD	73,6 ± 10.1
Male N (%)	15 (75%)
BMI, kg/m^2, median (range)	27.05 (21.0 – 46.7)
Arteriovenous fistula N (%)	6 (30%)
High-flux membrane N (%)	11 (55%)
Hemodiafiltration N (%)	10 (50%)
Dialysis duration, hours, median (range)	4 (4 – 5)
Ultrafiltration, L, mean ± SD	1.89 ± 1.22
Diabetes mellitus N (%)	8 (40%)
Previous CVD events N (%)	14 (70%)
Current smoker N (%)	1 (5%)

CVD = Cardiovascular disease

Table 3. Plasma concentration of complement and contact factors

Factor	Before HD	1 hour into HD	P-value
C3a	89.1 (25.1 – 180)	140 (60.6 – 325)	0.001
sC5b-9	13.5 (0.76 – 35.7)	21.7 (2.77 – 84.6)	<0.001
C3(H_2O)	7170 (3650 – 19500)	5770 (3030 – 19200)	0.083
FXIa–AT	0.0905 (0.017 – 0.892)	0.0635 (0.008 – 0.212)	0.001
FXIa–C1-INH	0.295 (0.054 – 0.541)	0.12 (0.017 – 0.346)	<0.001
FXIIa–AT	1.56 (0.23 – 26.3)	0.918 (0.159 – 2.13)	<0.001
FXIIa–C1-INH	1.76 (0.193 – 6.82)	1.07 (0.115 – 4)	<0.001
Kallikrein-AT	11.6 (1.17 – 159)	7.8 (0.004 – 23)	<0.001
Kallikrein-C1INH	21.4 (0.736 – 139)	8.95 (1.37 – 52.6)	<0.001
TAT	16.3 (3.74 – 882)	12.8 (2.62 – 72.8)	0.002

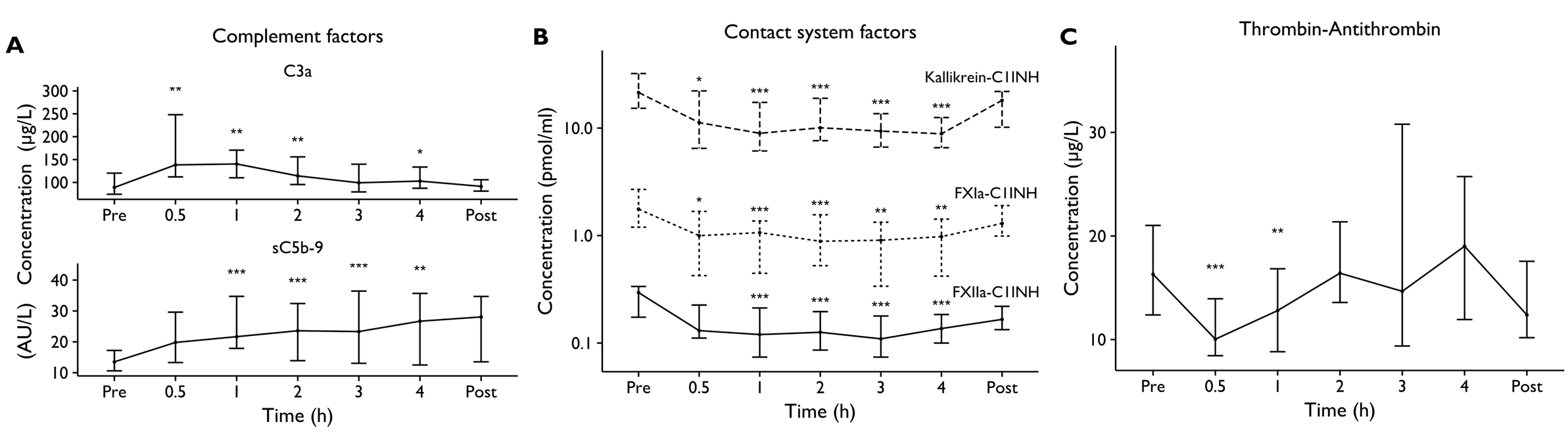

Figure. Plasma concentration of (A) complement system factors (B) contact system factors and (C) thrombin-antithrombin. Data represented as median plasma concentration with bars representing interquartile range. *p < 0.05 **p < 0.01 ***p < 0.001.

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