RESEARCH LETTER

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Hemofiltration with the Seraph[®] 100 Microbind[®] Affinity filter decreases SARS-CoV-2 nucleocapsid protein in critically ill COVID-19 patients

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The nucleocapsid protein (N-protein) of SARS-CoV-2 is a structural protein that oligomerizes to form a complex surrounding viral RNA, thus protecting it from the host cell environment. It is abundantly expressed within infected cells, where it facilitates viral RNA transcription, an essential step for viral replication Recently an ultrasensitive Simoa® immunoassay has been described that robustly measures SARS-CoV-2 N-protein in venous blood, dried blood microsamples, and saliva [1]. This study measured N-protein in longitudinal blood samples of COVID-19 patients and demonstrated readily detectable viral antigen two weeks after initial positive PCR testing, with concentrations gradually decreasing, inversely correlated with anti-SARS-CoV2 adaptive immune response. This study supports observations reported elsewhere that viral load in blood correlates with disease severity [2].

The Seraph® 100 Microbind® Affinity adsorber (Exthera Medical, CA, USA) is an extracorporeal treatment currently being explored as an approach to improve the clinical course and outcome of critically ill patients with COVID-19. On April 17, 2020, the FDA granted

of the N-protein prior to treatment with the Seraph®

device, that seemed to be related to the severity of the

disease and the duration of the disease (Table 1). While

hemoperfusion with the Seraph® was executed either

alone or in combination with a wide range of support-

ive treatments, including intermittent hemodialysis and

emergency use authorization for the Seraph® 100 for use

in the context of severe and critical disease, for which

effective treatment options are limited. Bacteria and

viruses bind to the immobilized heparin on the ultrahigh molecular weight polyethylene beads of the Seraph®

device in a manner similar to the interaction with hep-

aran sulfate on the cell surface and are thereby removed from the bloodstream [3]. The spike protein of SARS-

CoV-2 has been shown to bind to cellular heparan sulfate

(and heparin) through its receptor-binding domain, and

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recent studies suggest the heparin binding of the spike protein is much more pronounced in SARS-CoV-2 than in other coronaviruses [4]. In addition to an anecdotal report [5] a recent multicenter study showed that mortality of COVID-19 patients was much lower (37.7%) in the Seraph 100 treated group compared to a control group (67.4%) [6].

Here, we report the effect of the Seraph treatment on the concentration of the N-protein in critically ill COVID-19 patients as part of an ongoing biomarker study, approved by the IRB of the Hannover Medical School (9130_MPG_23b_2020). Six out of seven COVID-19 patients exhibited measurable concentrations

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Kielstein *et al. Crit Care* (2021) 25:190 Page 2 of 4

Table 1 Patient characteristics (laboratory data obtained on the day of Seraph[®] treatment)

# 1	# 2	# 3	# 4	# 5	# 6	# 7
М	F	М	М	F	М	М
77	78	54	41	61	65	72
76.5	75	107	119	122	60.5	71
164	160	188	180	168	166	175
5	19	10	13	9	16	12
60	9	7	Survivor	Survivor	Survivor	18
1021.3	26.6	121,884.2	1070.2	1036.5	19.5	-
769.6	24.1	111,035.2	931.5	376.2	12.1	-
73	443	87	110	156	129	39
2957	830	10,005	838	589	756	1,412
0.7	18.5	4.4	1.1	0.1	0.1	0.1
4.68	35.2	3.26	1.04	0.90	4.00	35.2
IHD (4)	CRRT (24)	IHD (4)	IHD (5)	HP (15)	HP (4)	HP (14)
300	90	250	250	80	200	100
	M 77 76.5 164 5 60 1021.3 769.6 73 2957 0.7 4.68 IHD (4)	M F 77 78 76.5 75 164 160 5 19 60 9 1021.3 26.6 769.6 24.1 73 443 2957 830 0.7 18.5 4.68 35.2 IHD (4) CRRT (24)	M F M 54 77 78 54 76.5 75 107 164 160 188 5 19 10 60 9 7 1021.3 26.6 121,884.2 769.6 24.1 111,035.2 73 443 87 2957 830 10,005 0.7 18.5 4.4 4.68 35.2 3.26 IHD (4) CRRT (24) IHD (4)	M F M M M 77 78 54 41 76.5 75 107 119 164 160 188 180 5 19 10 13 60 9 7 Survivor 1021.3 26.6 121,884.2 1070.2 769.6 24.1 111,035.2 931.5 73 443 87 110 2957 830 10,005 838 0.7 18.5 4.4 1.1 4.68 35.2 3.26 1.04 IHD (4) CRRT (24) IHD (4) IHD (5)	M F M M F 77 78 54 41 61 76.5 75 107 119 122 164 160 188 180 168 5 19 10 13 9 60 9 7 Survivor Survivor 1021.3 26.6 121,884.2 1070.2 1036.5 769.6 24.1 111,035.2 931.5 376.2 73 443 87 110 156 2957 830 10,005 838 589 0.7 18.5 4.4 1.1 0.1 4.68 35.2 3.26 1.04 0.90 IHD (4) CRRT (24) IHD (4) IHD (5) HP (15)	M F M M F M 77 78 54 41 61 65 76.5 75 107 119 122 60.5 164 160 188 180 168 166 5 19 10 13 9 16 60 9 7 Survivor Survivor Survivor 1021.3 26.6 121,884.2 1070.2 1036.5 19.5 769.6 24.1 111,035.2 931.5 376.2 12.1 73 443 87 110 156 129 2957 830 10,005 838 589 756 0.7 18.5 4.4 1.1 0.1 0.1 4.68 35.2 3.26 1.04 0.90 4.00 IHD (4) IHD (5) HP (15) HP (4)

 $\textit{IHD} \ intermittent \ he modialysis, \textit{CRRT} \ continuous \ renal \ replacement \ the rapy, \textit{HP} \ he moperfusion, \textit{Q}_b \ blood \ flow$

continuous renal replacement therapy, N-protein concentration was consistently reduced when comparing pre- and post- Seraph treatment blood samples (Table 1). Calculating the Seraph whole blood clearance (CL) by the nucleocapsid concentration upstream ($C_{\rm in}$) and downstream ($C_{\rm out}$) of the Seraph and the blood flow ($Q_{\rm B}$) by the formula: ${\rm CL} = (C_{\rm in} \ / \ C_{\rm out}) \ / \ C_{\rm in} \ \times \ Q_{\rm B}$, resulted in a

measurable device clearance that was not observed with other proteins including total serum protein (Fig. 1).

In conclusion, treating critically ill COVID-19 patients with the Seraph® 100 Microbind® Affinity filter decreased SARS-CoV-2 nucleocapsid protein in blood. The effect of clinically relevant outcome parameters needs to be determined.

Kielstein *et al. Crit Care* (2021) 25:190 Page 3 of 4

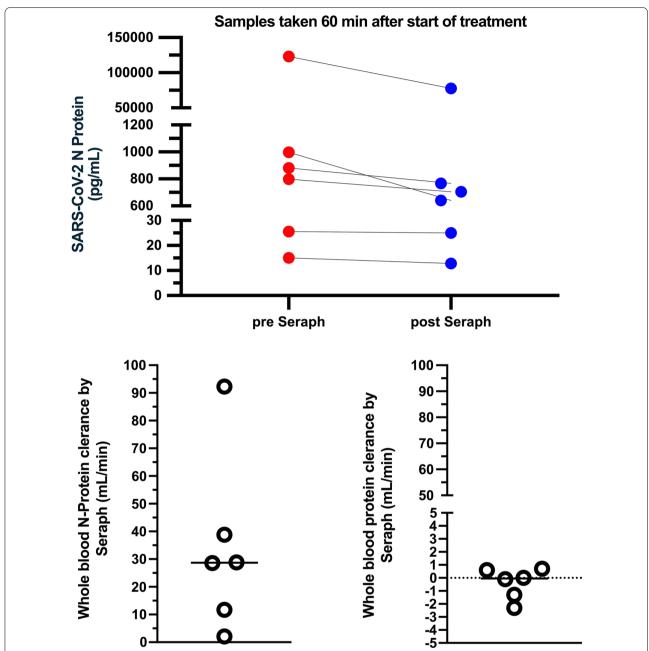


Fig. 1 Concentration of the nucleocapsid protein pre (upstream) and post (downstream) of the Seraph[®] at 60 min of treatment (upper part of the figure) and the resulting device clearance for the N-protein as well as the total plasma protein (lower part of the figure)

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Authors' contributions

JK, DB and TF treated the patients, analyzed and interpreted the data and were major contributor in writing the manuscript. SH, DM, and AB performed measurements and/or analysis of the N-protein. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Kielstein et al. Crit Care (2021) 25:190 Page 4 of 4

Declarations

Ethical approvals

This study was approved by the Ethics Committee of the Medical School Hannover (9130_MPG_23b_2020).

Consent for publication

Not applicable.

Competing interests

SH, DM, and AB are current employees of Quanterix Corporation. JK received research support from ExThera Medical and owns Quanterix stocks.

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