Introduction

The Seraph® 100 Microbind® Affinity blood filter (Seraph® 100) has been in use since 2019 for the treatment of fulminant or difficult to treat blood stream infections as an adjunct to pharmacotherapy. In 2020 the device received emergency use authorization by the US Food and Drug Administration for the treatment of critically ill COVID-19 patients with confirmed or imminent respiratory failure. Results of an international registry showed that the Seraph® 100 was operated under blood flow rates of 100–350 mL/min. As those conditions require a large bore central line, a dialysis catheter is currently considered indispensable to operate the Seraph® 100. The use of smaller catheter lumina has neither been evaluated in vitro nor in vivo.

Methods: In vitro pressure data before and after the Seraph® 100 at various blood pump rates (prepump line 16 G, postpump line 18 G) with saline and human plasma were obtained. Further, anecdotal flow and pressure data of two patients treated with the Seraph® 100 for a COVID-19 infection are reported.

Results: At a pump speed of 50 mL/min pre-Seraph® pressure using saline was −70 [−70 to −60] mm Hg. In comparison, using plasma pre-Seraph® pressure was lower at −120 [−120 to −105] mm Hg; \( p < 0.001 \) (t-test). The post-Seraph® pressure at 50 mL/min using saline of 120 [110–130] mm Hg was not different from plasma at 130 [120–140] mm Hg, \( p = 0.152 \) (t-test). Blood flow rates of 50 mL/min did not lead to preAP levels below −250 mm Hg in the two clinical cases.

Conclusion: Seraph® 100 blood flow rate of 50 mL/min may be achieved using low flow vascular access, allowing to treat a blood volume 72 L in 24 h.

Keywords
Extracorporeal therapy, blood purification, hemoperfusion

Date received: 22 October 2023; accepted: 25 January 2024
extracorporeal therapies, the Seraph® 100 does neither remove anti-infective agents\textsuperscript{15} nor drugs (previously considered) relevant for the treatment COVID-19.\textsuperscript{16,17}

The Seraph® 100 is a single use device that is usually operated under blood flow rates of 200–350mL/min for a time of 4 to <24h.\textsuperscript{6} As those conditions require a large bore central line, a dialysis catheter considered indispensable to operate the Seraph® 100. Based on the paucity of information regarding the use of the Seraph® 100 with central lines with smaller lumina, the aim of our study was to evaluate the in vitro pressure/flow curve using saline as well as human plasma and to evaluate the usability of the Seraph® 100 under low flow conditions in clinical practice.

**Materials and method**

**Patients and study protocol**

Blood plasma was obtained from five voluntary donors during regular therapeutic plasma exchange treatments due to various indications. Written informed consent was given by every patient. The two patients in which the treatment was performed through a non-dialysis catheter also consented to the acquisition of the treatment data.

**Sham hemofiltration with the Seraph® 100**

For all experiments primed a standard hemoperfusion blood tubing system (Fresenius Medical Care, Bad Homburg, Germany) as well as the Seraph® 100 Microbind® Affinity Blood Filter (Exthera Medical, CA, USA) with a total filling volume of about 2200mL with normal saline (n=5) or with human plasma and connected the hemoperfusion circuit with a 20cm tri lumen central venous line (2 × 18 G and 1 × 16 G, Certofix® safety trio s720, B. Braun REF: 4167408S-07; Lot: 19D30A8551) that was inserted into a reservoir. The Multifiltrate (Fresenius Medical Care GmbH, Bad Homburg, Germany) was used to pump the saline through the adsorber. The “arterial”/pre-pump line was connected to the 16 G lumen with a maximum flow rate specified by B.Braun of 46 mL/min and the “venous”/post-pump line to the 18 G lumen of the catheter specified with 22 mL/min. Figure 1 illustrates the experimental setup. Blood flow was raised in steps of 10mL beginning at 20mL up to 100mL. “Arterial” and “venous” pressure was recorded at the different blood pump speeds.

In two patients, who were treated with the Seraph® 100 for severe COVID-19, the hemoperfusion circuit of a Multifiltrate (Fresenius Medical Care GmbH, Bad Homburg, Germany), was connected to a five lumen 20cm catheter (Certofix Safety Quinto S1220, B. Braun, Melsungen, Germany) 1 × 12 G, 1 × 16 G, 3 × 18 G that was inserted into the right internal jugular vein. The maximum flow rates specified by the manufacturer of the central venous catheters are 185 mL/min for the 12 G lumen and 55 mL/min for the 16 G lumen. There is no information on pressure resistance in the data sheet.

For anticoagulation intravenous unfractionated heparin was used. An initial bolus of 5000IU was followed by a
continuous infusion of 1000 IU/h (patient #1) and 900 IU/h (patient #2). Blood flow as well as arterial and venous pressure were recorded through the 24 h treatment. Also, parameters of hemolysis were recorded pre- and post treatment.

Results

Five in vitro runs with the Seraph® 100 using saline and five runs using human plasma were performed without any technical difficulties. The relationship between blood pump speed and the arterial as well as venous pressure using saline (left panel) and plasma (right panel) is presented in Figure 2. Differences between the pressure readings using plasma or 0.9% sodium chloride were evaluated using t-test.

Two patients received hemoperfusion with the Seraph® 100® using a Fresenius Multifiltrate (Fresenius Medical Care, Bad Homburg, Germany) in hemofiltration mode. Using heparin in both patients, treatment over 24 h could be performed with a slight change in the “venous” and “arterial” pressure (Table 1). In patient #1 the 16 G line was used as “arterial” line and the 12 G Fr lumen as “venous” line. In patient #2 the 12 G/8.3 lumen was used as “arterial” line and the 16 G/5 Fr lumen as “venous” line. The blood flow pressure readings of the two patients are presented in Table 1.

In patient #1 the pre-/post-Seraph-Treatment levels of LDH and hemoglobin were 578/490 U/L and 13.9/12.7 g/dL respectively. Despite an increase in LDH from 463 to 573 U/L comparing pre- and post-Seraph-Treatment levels in patient #2 the hemoglobin level was not reduced but slightly increased from 13.0 to 13.3 g/dL. Further, the potassium level stayed within the reference range in both patients.

Discussion

Extracorporeal blood purification techniques such as dialysis, continuous kidney replacement therapy (CKRT), or hemoperfusion in the intensive care unit require dialysis catheters. The vascular access diameter and length are the major determinants for the blood flow through these catheters. Based on Poiseuille’s law, the radius is the most important factor determining flow in homogenous fluids.
Whole blood adds another level of complexity to this relationship as viscosity becomes another important deterrent.

While large bore catheters facilitate blood flow, catheters should have diameters as small as possible to decrease blood access complications. These limited diameters can cause high pressure gradients in the blood lines and high blood velocities resulting in an increase of shear forces, leading to hemolysis. Our measured pressure profiles in vitro using saline and human plasma indicate, that negative pressure before the pump and positive pressure after the pump only have a small influence on the blood flow.

As expected, our in vitro experiments showed that the negative “arterial”/pre-pump and positive “venous”/post-pump pressure increased with increasing blood pump speed. Also, due to the higher viscosity, plasma exhibited higher pressure changes than normal saline. Even at a blood pump speed of 100 mL/min “arterial” and “venous” pressure using plasma were within acceptable ranges. The lowest “arterial” pressure did not fall under −300 mm Hg. This is important as it is known that hemodialysis with negative “arterial”/pre-pump pressures lower than −350 mm Hg causes slightly higher hemolysis than dialysis treatments with less negative arterial chamber pressures.19 The National Kidney Foundation K/DOQI clinical practice guidelines for vascular access even recommends that the negative “arterial”/pre-pump pressure should not fall below −250 mm Hg.

The routine clinical chemistry parameters hemoglobin and LDH in the two patients gave no strong indication for hemolysis, with the limitation that high LDH levels are part of the severe COVID-19 disease and the slight increase and decrease of LDH levels may more likely reflect the underlying course of the COVID disease.20

Midline catheters have recently been introduced for the use of extracorporeal therapies like photopheresis.21 Our data suggest that catheters with a diameter smaller than regular dialysis catheters might be used to run the Seraph® 100, especially in situations where concomitant kidney replacement therapy is not necessary.

Conclusion

In summary, our in vitro and anecdotal in vivo data show that at a blood pump speed of 50 mL/min the Seraph® 100 can be safely operated using an “arterial”/pre-pump line 16 G or larger and a “venous”/post-pump line of 18 G or larger.

Author contributions

MTS, JTK, and JJS designed and conducted the in vitro study. JJS collected the plasma. DB and TM treated the two patients. MTS drafted the manuscript. All authors contributed to the refinement of the manuscript.

Data availability statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: MTS, JJS, and JTK received research funding from ExThera Medical. MTS and JTK received travel support from ExThera Medical. All other authors: none to declare.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Written informed consent was obtained from the voluntary plasma donors. The study was performed in accordance with the Declaration of Helsinki and German federal guidelines and the Hanover Medical School IRB approval number is 8634 BO K 2019. The two patients gave written informed consent to the publication of their anonymized treatment data.

ORCID iD

Jan T Kielstein https://orcid.org/0000-0001-8110-9064

References


