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ORIGINAL RESEARCH

Intermittent saline flushes or continuous saline infusion: what works better when heparin-free dialysis is recommended?

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Edward Zimbudzi

Department of Nephrology, Monash Health, Monash Medical Centre, Clayton, Melbourne, VIC, Australia

Introduction: Coagulation-free dialysis, also commonly known as "heparin-free" dialysis, can be a challenging procedure as it increases the risk of clotting the dialysis circuit. Utilizing a better saline flushing technique can lead to improved patient outcomes as well as huge financial benefits to the health institution. The purpose of this study was to compare the effectiveness of continuous saline infusion (CSI) and intermittent saline flushing (ISF) in preventing clotting of the dialysis extracorporeal circuit (ECC).

Methods: Fifty heparin-free treatments were randomized into two treatment arms, namely CSI and ISF. Predialysis full blood count and coagulation studies were performed for all patients. During ISF, 100 mL saline was infused via the arterial line every 30 minutes while occluding the blood inlet line. Normal saline was infused into the ECC at a rate of 200 mL/hour throughout the duration of dialysis under CSI. The ECC was inspected for clotting and graded accordingly post-dialysis.

Results: Seventy-six percent of the CSI treatments were completed without losing the ECC while 52% of the ISF treatments were also successful. Patients who were treated with CSI were less likely to have clotted ECCs (odds ratio 3.4, 95% CI, 1.04 to 11.2; $P = 0.04$). No significant differences existed between the two groups' hematological factors that could influence clotting, such as hemoglobin and platelets.

Conclusion: This study demonstrates that, when heparin-free dialysis is indicated, CSI might be a better method of preventing the ECC from clotting. There is a greater chance of realizing long-term benefits to patients and the health service with the CSI method since there is a likelihood of a reduction in the use of erythropoietin-stimulating agents and blood transfusions with the CSI method.

Keywords: continuous saline infusion, hemodialysis, heparin-free dialysis, intermittent saline flushing

Video abstract

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Correspondence: Edward Zimbudzi
Department of Nephrology,
Monash Medical Centre, Clayton,
VIC 3168, Australia
Tel +61 3 9594 3618
Fax +61 3 9594 6907
Email edward.zimbudzi@southernhealth.org.au

Background

Dialysis membranes and lines are inherently procoagulant and, therefore, for hemodialysis (HD) to be successful, the use of anticoagulant treatment is mandatory to prevent clotting in the extracorporeal circuit (ECC). However, coagulation-free dialysis, also known as "heparin-free" dialysis, may be indicated in patients with a high risk of bleeding, for instance, patients with acute bleeding disorders, recent and planned surgery, acute heparin-induced thrombocytopenia syndrome, and systemic anticoagulation for other reasons.[1] Heparin-free dialysis presents a lot of challenges both to the clinicians and the patients undergoing dialysis, with the main problem being an increased risk of clotting the ECC. To counteract this, saline flushing has been commonly used because it is relatively safe.[2] However, mechanisms by which

saline flushes exert an antithrombotic effect are still to be scientifically proven. It is possible that high blood flow rates[3] (>250 mL/minute) combined with saline flushes may prevent the buildup of serum proteins, platelets, and leukocytes, which play a pivotal role in the initiation of the clotting cascade.[4] The saline flushing procedure can be done as intermittent saline flushes (ISF) or continuous saline infusion (CSI).[5]

ISF involves flushing of the ECC with saline (100–300 mL) every 30 minutes.[6] A major disadvantage of this method is increased nursing time. Apart from that, it is not quite clear whether ISF offers a substantial benefit in reducing clotting of the ECC. One study that aimed to find out if ISF during HD reduces clotting in the bubble trap and the dialyzer concluded that ISF does not alleviate coagulation, but rather promotes clot formation.[7] This study suggested that saline flushes may lead to momentary ECC dilution of the anti-coagulation Factor Xa activity, which may contribute to increased coagulation.

On the other hand, ISF is associated with an acceptable filter life, less risk of bleeding, and fewer blood transfusion requirements compared to heparin anticoagulation.[8] ISF effectively maintains the ECC, especially in patients with elevated activated partial thromboplastin time (APTT). Low levels of clotting may still occur in some patients and this is associated with fouling or obstruction of dialyzer capillaries with a loss of effective dialyzer surface area and reduced solute clearances.[9]

CSI can also be used as an alternative to coagulation during dialysis. Utilizing this technique, saline is administered to the ECC continuously throughout the dialysis session at a given rate, for instance, 200 mL/hour. This method alleviates fluctuations of cardiac anterior load in patients, especially those with cardiac insufficiency, since saline is delivered at a constant rate.[10] From a nursing point of view, CSI is easier to perform and it also substantially lessens the workload of dialysis personnel.

In our dialysis unit, ISF had been the standard treatment procedure when heparin-free dialysis was recommended. In recent years, our unit has had a huge influx of patients requiring heparin-free dialysis and we noticed that there were several episodes when these patients lost their ECC due to clotting. The purpose of this study was to compare the effectiveness of CSI and ISF in preventing clotting of the dialysis ECC.

Methods

Stable HD patients aged 18 years or more who had been on dialysis for at least 1 month with an order for heparin-free dialysis from their treating nephrologist met the inclusion criteria. The participants had dialysis access that could sustain blood flow rates of ≥250 mL/minute and they all used the Fresenius FX 80 dialyzer (Fresenius Medical Care AG & Co, KGaA, Bad Homburg, Germany). Patients taking drugs with potential interference with clotting, such as warfarin, clopidogrel, and those who required transfusion of blood products such as fresh frozen plasma and packed red blood cells were excluded from the study.

This study was a controlled, randomized, non-blinded trial. Due to the nature of the treatment arms, which were difficult to provide in an identical form, a blinded design was not considered. The researcher clearly explained the purpose of the study to participants before they signed the Participant Information and Consent Form (PICF). Prospective participants were conveniently sampled until 50 heparin-free treatments were achieved. This sample size ensured that there was an 80% chance of detecting at the 5% level a statistically significant decrease in clotting the ECC in the experimental group (CSI). Randomization was done by preparing 50 opaque envelopes that contained instructions to allocate participants to either of the treatment arms. Envelopes were prepared and mixed by a staff member who was not involved in the research. These envelopes were later opened as patients were accepted into the project and the allocated treatment arm was followed. By the end of randomization, the CSI treatment arm had 15 patients, nine males and six females. The ISF group had eleven males and nine females. There was only one current smoker in the ISF group and none in the CSI treatment arm. The age of the participants ranged from 26 to 82 years for both groups. Predialysis full blood count and coagulation studies were done for all participating patients.

During ISF, 100 mL saline was infused via the arterial line every 30 minutes of HD while occluding the blood inlet line. The ECC was observed for signs of clotting after every flushing session. On the other hand, CSI involved infusing saline into the ECC at a rate of 200 mL/hour throughout the duration of dialysis. The infusion set was connected to the arterial line, just before the dialysis machine blood pump. After every dialysis session, the ECC was examined and graded accordingly (Table 1). Patients were dialyzed at varying blood flow rates (QB), with the minimum being 250 mL/minute. QB was mainly dependent on patients' access and, at times, the nephrologists' orders. Dialysis time also ranged from 4 to 5 hours and this was prescribed by the patients' nephrologists.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) (v 7.5; IBM Corporation,

Table 1 Grading of the extra corporeal circuit (ECC) post-heparin-free dialysis

Grade	Outcome
1	No clotting of ECC
2	Slightly streaky dialyser, presence of fibrin in arterial (ABT) and/or venous bubble trap (VBT)
3	Streaky dialyser, clots present in ABT and/or VBT, but can still continue with dialysis
4	ECC clotted. Dialysis ceased

Armonk, NY, USA). Descriptive data were presented as the mean plus or minus standard deviation (SD). Differences between the two groups were tested using the Student's *t*-test (two-tailed, paired) for equality of means. The results were considered to be significant if $P < 0.05$. This study received ethical approval from the Southern Health Human Research Ethics Committee.

Results

A total of 50 heparin-free treatments were included in the study, which occurred from May to November 2012. After randomization, each of the treatment arms (CSI and ISF) had 25 heparin-free treatments. Seventy-six percent of the CSI treatments were completed without losing the ECC and half of these treatments were rated grade 2 or better (Figure 1). On the other hand, 52% of the ISF treatments were successful and 12% of them achieved grade 2 or better. Patients who were treated with CSI were less likely to have clotted ECCs (odds ratio [OR] 3.4, 95% CI, 1.04 to 11.2; $P = 0.04$).

Some hematological factors that affect clotting were also considered. The mean hemoglobin level was 96.6 ± 16.2 g/L in the CSI group and 101.9 ± 17.8 g/L in the ISF group and, by conventional criteria, there was no statistically significant difference between the two groups ($P = 0.31$). The mean platelet level for the CSI group was 194 ± 60 × 10^9/L and 220.4 ± 106.9 × 10^9/L for the ISF group and no statistically significant difference between the two groups was shown ($P = 0.32$). Other factors influencing the coagulation cascade, such as APTT, fibrinogen, and the international normalized ratio (INR), were also evaluated, with no significant difference found between the two treatment arms (Table 2). Blood flow rates and prescribed dialysis time between the two groups were also not significantly different (Table 3).

Discussion

This study demonstrates that both saline flushing methods did not entirely prevent clotting of the ECC, as highlighted by previous studies,[7,11] but the CSI method proved to be a better treatment option (OR 3.4, 95% CI, 1.04 to 11.2; $P = 0.04$). One study noted that the ISF method can be effective only when dialysis is initiated for patients whose APTT levels are on the higher side.[8] There are, however, several instances when heparin-free dialysis would have to be initiated regardless of the level of APTT. In stable HD patients, one study revealed that ISF does not alleviate clotting or intravascular coagulation.[7] Unfortunately, not much work has been done to demonstrate the benefits of the CSI method in preventing circuit clotting among patients who require dialysis without anticoagulant due to increased bleeding risk.

The impact of other hematological factors on clotting of the ECC was also considered in this study. Previous studies have shown that high hemoglobin levels increase the risk of clotting into the dialysis circuit.[12] It is worth noting that, in our treatment groups, the mean hemoglobin levels were much lower than the recommendations of the CARI (Caring for Australasians with Renal Impairment), KDIGO (Kidney Disease: Improving Global Outcomes) and KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines.[13] Our study demonstrated that there was no significant difference in the hemoglobin levels of both treatment arms ($P = 0.31$).

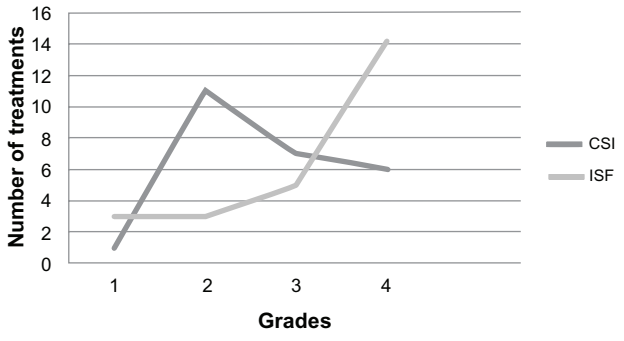

Figure 1 Grading of the extracorporeal circuit on completion of dialysis.
Abbreviations: CSI, continuous saline infusion; ISF, intermittent saline flushes.

Table 2 Mean levels of some hematological factors influencing the coagulation state

Variable	Intermittent saline flush	Continuous saline infusion
Hemoglobin	101.9 ± 17.8	96.6 ± 16.2
Platelets	220.4 ± 106.9 × 10^9/L	194 ± 60 × 10^9/L
APTT	29.5 ± 4.4	32.4 ± 14.4
INR	1.15 ± 0.6	1.03 ± 0.1
Fibrinogen	4.21 ± 0.8	4.30 ± 1.0

Note: Data were given as the mean ± SD and differences between the two groups were not significant for the five categories ($P > 0.05$).
Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio; SD, standard deviation.

Table 3 Clinical characteristics of study participants

variable	Intermittent saline flush	Continuous saline infusion
Prescribed QB (mL/minute)[a]	276 ± 25.5	278 ± 25.3
Prescribed dialysis time (minutes)[a]	270 ± 30.0	262 ± 23.4
Actual time completed (minutes)[a]	222.2 ± 74.4	245.4 ± 44.8
Number of AVFs	16	19
Number of double lumen CVCs[b]	9	6

Notes: [a]Data were given as the mean ± SD. Differences between the two groups were not significant for any categories ($P > 0.05$); [b]double lumen CVCs, also known as permacaths, were used.
Abbreviations: AVFs, arteriovenous fistulas; CVCs, central venous catheters; SD, standard deviation; QB, blood flow rate/minute.

A similar result was also obtained when platelet levels, APTT, INR, and fibrinogen levels between the two groups were analyzed. The elimination of some these hematological confounding factors strengthened our main research finding that patients treated with CSI have a lesser risk of clotting their ECC compared to those treated with ISF.

Treatment for patients recruited in this study followed an almost homogenous prescription plan. A previous study highlighted a linear relationship between low blood flow rates and the risk of clotting the dialysis circuit.[14] To alleviate this problem, participants who had dialysis access that could sustain blood flow rates of ≥250 mL/minute were recruited for this study. Several studies have also shown that the dialysis membrane may have an impact on clotting of the dialysis circuit.[15,16] In relation to this, our study utilized the same dialyzer (Fresenius FX 80) for all study participants. In addition, the impact of the type of vascular access on clotting cannot be underestimated. In this study, the native arteriovenous fistula accounted for 64% of ISF treatments and 76% of the CSI treatments and the twin-needle technique was utilized. The rest of the treatments were delivered via double lumen catheters (permcaths).

One of the primary limitations of this study is that the sample size was very small. Furthermore, not all variables that could influence the findings of this project were controlled. For instance, some plasma factors, such as antithrombin and plasminogen deficiency, may contribute to a clinical hypercoagulable state leading to clotting of the ECC. In line with this, the hypercoagulable state may also be initiated by some acquired factors, such as obesity and smoking, which this study did not cater for. The dialysis treatment time was also not consistent. Some patients were dialyzed for 4 hours while others received 5 hours according to their dialysis prescription.

Conclusion

This study demonstrates that, when heparin-free dialysis is indicated, CSI might be a better method of preventing the ECC from clotting compared to ISF. Utilizing this procedure may result in long-term benefits to the patients as well as health institutions, since there is a likelihood of a reduction in expenses related to blood transfusions and erythropoiesis-stimulating agents.

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Disclosure

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