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Determination of iron sucrose (Venofer) or iron dextran (DexFerrum) removal by hemodialysis: an *in-vitro* study

Harold J Manley*[1] and Darren W Grabe[2,3]

Address: [1]School of Pharmacy, University of Missouri – Kansas City, Kansas City, Missouri, USA, [2]Albany College of Pharmacy, Albany, New York, USA and [3]Albany Medical College, Albany, New York, USA

Email: Harold J Manley* - manleyh@umkc.edu; Darren W Grabe - grabed@acp.edu

* Corresponding author

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Abstract

Background: Intravenous iron is typically administered during the hemodialysis (HD) procedure. HD patients may be prescribed high-flux (HF) or high-efficiency (HE) dialysis membranes. The extent of iron sucrose and iron dextran removal by HD using HF or HE membranes and by ultrafiltration rate (UFR) is unknown.

Methods: Two *in vitro* HD systems were designed and constructed to determine the dialyzabiltiy of iron from a simulated blood system (SBS) containing 100 mg iron sucrose or iron dextran (system A) or 1000 mg iron sucrose (system B). Both *in vitro* systems utilized a 6-L closed-loop SBS system that was subject to 4 different HD conditions conducted over 4 hours: HE membrane + 0 ml/hr UFR; HE membrane + 500 ml/hr UFR; HF membrane + 0 ml/hr UFR; HF membrane + 500 ml/hr UFR. Blood flow and dialysate flow rates were 500 ml/min and 800 ml/min, respectively. The dialysate compartment was a 192-L open system for system A and a 6-L closed-loop system for system B. Samples from the SBS and dialysate compartments were taken at various time points and iron elimination rate and HD clearance was determined. Iron removal from the SBS > 15% was considered clinically significant.

Results: The greatest percentage removal from the SBS was 13.5% and -0.03% utilizing system A and B, respectively. Iron sucrose and iron dextran dialysate concentration was below the lower limits of assay (< 2 ppm) for system A. Dialysate recovery of iron was negligible: 0 – 5.4 mg system A and 5.47 – 23.59 mg for system B. Dialyzer type or UFR did not affect iron removal.

Conclusion: HF or HE dialysis membranes do not remove clinically significant amounts of iron sucrose or dextran formulations over a 4-hour HD session. This effect remained constant even controlling for UFR up to 500 ml/hour. Therefore, iron sucrose and iron dextran are not dialyzed by HE or HF dialysis membranes irrespective of UFR.

Background

Iron deficiency is a common problem in hemodialysis (HD) patients [1]. Reasons for iron deficiency include increased requirements due to erythropoetin-stimulated red blood cell production, blood loss through the HD procedure, and impaired absorption of oral iron [2]. As

such, many patients require supplementation with intravenous (IV) iron to maintain transferrin saturations > 20% and ferritin concentrations > 100 ng/mL [1].

Iron dextran (InFed®, Watson Pharmaceuticals; DexFerrum®, American Regent, Inc.) was the first IV iron preparation used in HD patients. However, concerns over iron dextran side effects, specifically anaphylactic and anaphylactoid reactions [3], lead to development of other safer IV iron preparations. One such IV iron preparation available for use in HD patients is iron sucrose (Venofer®, American Regent Laboratories, Inc.).

It is recommended that iron sucrose be given by slow injection or infusion during the HD session to patients that require supplemental IV iron [4]. Previous reports have shown that very little iron dextran (InFed®, Watson Pharmaceuticals, molecular weight 90,000 daltons [5]) is removed via HD [6-8]. However it is unknown to what extent the HD procedure removes the other iron dextran product (DexFerrum®, American Regent, Inc., molecular weight 265,000 daltons [5]) or iron sucrose (Venofer®, American Regent, Inc., molecular weight 34,000 – 60,000 daltons [4]).

Iron sucrose, also known as iron saccharate, is a complex of polynuclear iron (III)-hydroxide in sucrose for intravenous use. Iron sucrose has a molecular weight of approximately 34,000 – 60,000 Daltons and a proposed structural formula: [Na2Fe5O8(OH)*3(H2O)]n*m(C12H22O11). The molecular weight of iron sucrose ranges 34,000 – 60,000 daltons as during the manufacturing process, the number of sucrose molecules bound to iron varies [4].

Given the differences between iron dextran products and iron sucrose regarding molecular weight and pharmacokinetic profile [9], one cannot assume that the HD clearances will be the same.

HD patients may be prescribed high-flux (HF) or high-efficiency (HE) dialysis membranes. HF and HE dialysis membranes have very different solute clearance capabilities. These membranes can remove molecular weight substances up to approximately 15,000 daltons[10]. Iron removal by HD may also be dependant upon convection (i.e., solute drag), which is controlled by the ultrafiltration rate (UFR) The extent of iron removal in HD patients using HF or HE membranes or varying UFR needs to be investigated.

Therefore, an in *vitro* HD study was conducted to determine whether HF or HE dialysis membranes, under various UFR, removed clinically important amounts of iron dextran or iron sucrose from a simulated blood system. The null hypothesis was that newer HF or HE dialysis membranes removed iron in clinically significant amounts and that the removal was dependent of UFR.

Methods

In-vitro hemodialysis system A

A closed-loop fixed volume reservoir of 6-L normal saline solution (5750 ml reservoir + 250 ml tubing and dialysis membrane volume) was prepared for a simulated blood system (SBS). A 1000 ml graduated cylinder was used to measure out the normal saline. The normal saline had a pH = 5.0 and an osmolarity of 308 mOsmol/l. The SBS was maintained at 37°C and continuously mixed throughout the *in vitro* HD session. The blood flow rate (BFR) and dialysate flow rate (DFR) was maintained at 500 ml/min and 800 ml/min, respectively. To assess the contribution of convection to drug removal, UFR was set at 0 ml/hr for one-half of the HD sessions and at 500 ml/hr for the other half of the HD sessions. A volumetric HD machine (model 2008H, Fresenius USA, Walnut Creek, CA) controlled all BFR, DFR, and UFR. Two dialysis membranes were tested: CA210 (Baxter) a HE dialyzer and F80A (Fresenius) a HF dialyzer. HD was conducted for 4 hours with UFR a 0 ml/hr and for 4 hours at 500 ml/hr. The dialysate solution ran counter current to SBS within the dialysis membrane. The dialysate temperature was maintained at 37°C. Each HD procedure was conducted in duplicate.

In-vitro hemodialysis system B

Similar to system A, a closed-loop fixed volume reservoir of 6-L normal saline solution (5750 ml reservoir + 250 ml tubing and dialysis membrane volume) was prepared for a SBS. A 1000 ml graduated cylinder was used to measure out the normal saline. The normal saline had a pH = 5.0 and an osmolarity of 308 mOsmol/l. The SBS was maintained at 37°C and continuously mixed throughout the *in vitro* HD session.

The dialysate compartment was also a closed-loop 6-L compartment. A 1000 mL graduated cylinder was used to measure out the dialysate. The dialysate compartment consisted of a holding tank and a pressure chamber. A Shur-Flo® pump (model 4UN54) was used to pump dialysate from the holding tank to the pressure chamber. The pressure chamber was pressurized to at least 20 psi to provide sufficient fluid pressure for the dialysis machine. This dialysate pressure was necessary for the dialysis machine to operate and control the dialysate flow rate at 800 ml/min. Spent dialysate from the hemodialysis machine was collected in the dialysate holding tank. The holding tank dialysate compartment construction allowed for sampling to occur through the top of the holding tank.

The SBS and dialysate compartment was maintained at 37°C and continuously mixed throughout the *in vitro* HD session. The BFR and DFR was maintained at 500 ml/min and 800 ml/min, respectively.

Sample preparation and collection

For the *in vitro* system A study, iron sucrose 100 mg (5 ml of 20 mg/ml solution) or iron dextran 100 mg (2 ml of 50 mg/ml solution) was injected into the SBS. Samples (5 ml) were collected from SBS at 0, 15, 30, 60, 120,180, and 240 min. Collected samples were stored at 25°C until analysis.

Dialysate was sampled (5 ml) at 0, 60, 120, 180, and 240 min. All dialysate during the simulated HD session was collected pooled, volume measured, and then sampled (5 ml) for iron sucrose or iron dextran concentration. The dialysate sample was stored at 25°C until analysis.

For the *in vitro* system B study, iron sucrose 1000 mg (50 cc of 20 mg/ml solution) was injected into the SBS. Samples (15 ml) were collected from SBS and dialysate compartment at 0, 15, 30, 60, 120,180, and 240 min. Collected samples were stored at 25°C until analysis. All dialysate during the simulated HD session was collected pooled, volume measured, and then sampled (15 ml) for iron sucrose. The dialysate samples were stored at 25°C until analysis.

The iron sucrose sample preparation and data analysis occurred at a Dialysis Clinic, Inc dialysis unit in Kansas City, MO. The iron dextran sample preparation and data analysis occurred at a Renal Research Institute dialysis unit in Albany, NY. Both centers utilized bicarbonate based dialysate solutions.

Control for potential iron contamination

Disposable supplies (e.g., plastics) were utilized whenever possible and the use of glassware was not permitted to minimize iron loss. Additionally, to control for potential iron contamination within the HD procedure, an additional HD session was conducted without iron sucrose or iron dextran injected into the reservoir [SBS]. Dialysate and SBS samples were then collected at same time points as described previously. Any detectable iron found in the SBS or dialysate compartments (native iron) was then subtracted from measured iron concentration from the iron-containing HD sessions.

Samples analysis

The determination of iron concentration in study samples was performed using atomic absorption spectrophotometry. A Perkin-Elmer AAnalyst 300 was set up and operated as per previously described methods.[11] The instrument is equipped with a Perkin-Elmer Lumina™ Fe hollow cathode lamp, with an emission line of 248.3 nm and an air acetylene flame. A stock standard solution of ferrous ammonium sulfate in calcium chloride was used to run a 5-point standard calibration curve, ranging from 2.0 to 10.0 ppm of iron. This method has been validated for ruggedness, method and system precision, giving an overall testing variation of approximately 2%.

In vitro system A

Prior to analysis samples were prepared by pipetting 2.0 mL of sample into a 10.0 mL volumetric flask using a "to contain" pipette. Pipettes were then rinsed with a calcium chloride solution and 0.5 mL of HCl was added to the volumetric flask. Sufficient amount of calcium chloride solution as then added to yield theoretical concentration of 3.33 μg/mL (100 mg/6000 mL × 2.0 mL/10.0 mL × 1000 μg/mg).

In vitro system B

Prior to analysis samples from the SBS compartment were prepared by pipetting 2.0 mL of sample into a 50 mL volumetric flask using a "to contain" pipette. Pipettes were then rinsed with a calcium chloride solution and 2.0 mL of HCl added to the volumetric flask. Sufficient amount of calcium chloride solution (q.s. to 50 mL) was added to yield theoretical concentration of 6.664 μg/mL (1000 mg/6000 mL × 2.0 mL/50 mL × 1000 μg/mL).

Analysis of samples from the dialysate compartment was prepared by pipetting 3.0 mL of sample into a 10 mL volumetric flask using a "to deliver" pipette and adding 0.5 mL of HCl to the volumetric flask. Sufficient amount of calcium chloride solution (q.s. to 10 mL) was added to yield theoretical detection limit of no less than 1.666 μg/mL (i.e. 1% iron transfer)

SBS initial iron concentration (1000 mg/6000 mL = 166.6 μg/mL).

166.6 μg/mL × 1% / 100 = 1.666 μg/mL

1.666 μg/mL × 3 mL/10 mL = 0.5 μg/mL

In the event that a dialysate sample's determined concentration falls outside of the system's calibration curve of 10 ppm (i.e., greater than 20% iron transfer), the sample's preparation was adjusted so that the final determined concentration would fall within the system's calibration range of 0 to 10 ppm elemental iron.

All sample analysis occurred at a central laboratory (American Regent, Inc. Shirley, NY). Each system was visually inspected for color change in either SBS or dialysate compartment.

Data analysis

The mean ± SD iron concentrations were calculated for each sample taken at each time point for iron sucrose or iron dextran. The percent change in iron concentration from beginning to end of HD session and absolute amount of iron eliminated was calculated. A mean loss of greater than 15% from the SBS of the initial concentration was considered as a clinically important loss of iron.

Iron sucrose and iron dextran concentration results were modeled using PK-Analyst® (MicroMath, version 1.0, Salt Lake City, UT) pharmacokinetic data analysis software. A monoexponential model was assumed and pharmacokinetic parameters were calculated using the following formulae:

1. Elimination rate constant for HD period (K_{hd}) was calculated:

$$K_{hd} = \frac{\ln(\text{preHD concentration} / \text{end of HD concentration})}{\text{time}_{hd}}$$

A positive rate constant K_{hd} suggests accumulation of substance in the tank; whereas a negative rate constant K_{hd} suggests removal of substance from the tank.

2. The amount removed (A) by HD was calculated as the mean of:

A = (preHD conc - end of HD conc) * Volume of distribution (Vd) and

A = total iron sucrose or iron dextran collected in dialysate

Vd = SBS volume + tubing volume + dialyzer volume

3. Clearance HD (Cl_{hd}) = Slope of regression line × Vd.

Clearance values that are positive relate to accumulation of substance from the system; negative clearance values represent removal of substance from the system.

Statistics

Iron product pharmacokinetic parameters determined from samples obtained during HF and HE dialysis membranes were compared using two-sample t-test. Pharmacokinetic parameter values at 0 ml/hr and 500 ml/hr UFR were compared using a paired t-test. Finally pharmacokinetic parameters between iron sucrose and iron dextran compounds were compared using two-sample t-test. All t-tests were two-tailed and a p-value < 0.05 was considered significant.

Results

In vitro system A

Instillation of iron sucrose or iron dextran into the SBS resulted in a light brown colored solution. The dialysate compartment consisted of a clear solution. During the entire study there was no visual evidence of color change in the SBS or dialysate compartments.

The mean ± SD dialysate iron recovery values for iron sucrose from each HD session utilizing HF or HE dialyzers and 0 ml/min and 500 ml/min UFR test condition is reported in Table 1. At no time was any iron detected in the dialysate in the iron sucrose experiments, regardless of the dialysis membrane used. The amounts of iron measured in the dialysate compartment were below the limits of detection for the assay (< 2 ppm). The mean ± SD dialysate iron recovery for iron dextran from each HD session utilizing HF or HE dialyzers and 0 ml/min and 500 ml/min UFR test condition is reported in Table 2. In contrast to iron sucrose, some iron (5.44 ± 7.7 mg) from the iron dextran was found in the dialysate when using HE membranes at 0 UFR. However, under other dialysis conditions with HE or HF membranes, no iron was found.

Table 1: Iron sucrose removal by high-flux or high-efficiency hemodialysis membranes over 240 minutes. (System A)

	Iron Sucrose (Venofer®)			
Study condition	**SBS % iron concentration change (mean ± SD)**	**K_{hd} (hr-1) (mean ± SD)**	**Dialysate Iron Recovery (mg) (mean ± SD)**	**Clearance† (ml/min) (mean ± SD)**
F80: 0 ml/hr UFR	13.55 ± 1.56	0.0006 ± 0.0001	0.00 ± 0.00	3.62 ± 0.45
F80: 0 ml/hr UFR Re-run*	6.99 ± 8.55	0.0003 ± 0.0004	0.00 ± 0.00	1.85 ± 2.29
F80: 500 ml/hr UFR	-16.03 ± 8.57	-0.0006 ± 0.0003	0.00 ± 0.00	-2.46 ± 1.23
CA210: 0 ml/hr UFR	-6.20 ± 1.78	-0.0003 ± 0.0001	0.00 ± 0.00	-1.49 ± 0.42
CA210: 500 ml/hr UFR	-14.79 ± 31.51	-0.0003 ± 0.0019	0.00 ± 0.00	-6.87 ± 7.74

SBS = simulated blood solution; UFR = ultrafiltration rate; K_{hd} = hemodialysis elimination rate; % = percent; * = The re-run study condition was an unique experiment that replicated all conditions present in the original F80: 0 ml/hr UFR experiment. † = Clearance values that are positive relate to accumulation of substance from the system; negative clearance values represent removal of substance from the system.

Table 2: Iron dextran removal by high-flux or high-efficiency hemodialysis membranes over 240 minutes. (System A)

Study condition	Iron Dextran (DexFerrum®)			
	SBS % iron concentration change (mean ± SD)	K_{hd} (hr-1) (mean ± SD)	Dialysate Iron Recovery (mg) (mean ± SD)	Clearance† (ml/min) (mean ± SD)
F80: 0 ml/hr UFR	-9.69 ± 3.31	-0.0004 ± 0.0001	0.00 ± 0.00	-2.29 ± 0.75
F80: 500 ml/hr UFR	-7.84 ± 0.73	-0.0003 ± 0.0000	0.00 ± 0.00	-1.26 ± 0.11
CA210: 0 ml/hr UFR	-8.77 ± 6.76	-0.0003 ± 0.0003	5.44 ± 7.70	-2.06 ± 1.54
CA210: 500 ml/hr UFR	-7.48 ± 3.54	-0.0003 ± 0.0001	0.00 ± 0.00	-1.20 ± 0.55

SBS = simulated blood solution; UFR = ultrafiltration rate; K_{hd} = hemodialysis elimination rate; % = percent; † = Clearance values that are positive relate to accumulation of substance from the system; negative clearance values represent removal of substance

In general, no iron or insignificant levels in the case of iron dextran was lost from the SBS reservoir for either iron product. However in the experiment in which iron sucrose and HF membranes were run at 0 UFR, significant amount of iron (13.55% ± 1.56) were lost from the SBS reservoir at 240 minutes (Table 1.). This finding contributed to greater elimination rate (p = 0.003), clearance (p = 0.003), and greater amount of iron removed (p = 0.005) between the HF and the HE dialysis membranes. Since these results were very disparate to other HD conditions tested and since no other iron was recovered from the dialysate under these conditions, the entire experiment was re-run under the identical condition (HF membrane; 0 UFR; 500 mL/min BFR; 800 mL/min DFR; 4 hours). Results from the re-run test condition are provided in table 1. During the re-run experiment, some iron (6.99% ± 8.55) was again lost from the SBS reservoir, but again no comparable increase in iron was found in the dialysate. Statistical analysis of the data including data from the re-run yielded non-significant comparisons between elimination rate (p = 0.24), clearance (p = 0.24), and greater amount of iron removed (p = 0.22) between the HF and the HE dialysis membranes. In conclusion, no significant amount of iron was found in the dialysate regardless of dialysis membrane used or UFR. Furthermore, no significant loss of iron was observed in the SBS reservoir irrespective of iron product used or the test conditions.

In vitro system B

Instillation of 1000 mg iron sucrose into the SBS resulted in a dark brown (nearly black) colored solution. The dialysate compartment consisted of a clear solution. During the entire study there was no visual evidence of color change in the SBS compartment. The dialysate compartment became lightly yellowish in color by the end of 240 minutes.

The mean ± SD percentage recovery from each HD session utilizing HF or HE dialyzers and 0 ml/min and 500 ml/min UFR test condition are reported in Table 3. Iron sucrose SBS percent removal ranged from – 3.13 ± 0.06% to -0.30 ± 1.15%. Iron sucrose elimination rate from the SBS was less than 0.0001 hr^{-1} for all conditions. The dialysate recovery of iron sucrose ranged from 2.79 ± 1.89 mg to 23.59 ± 3.96 mg when 1000 mg was instilled in the SBS reservoir (i.e., 0.3 – 2.4% injected iron from SBS compartment). Within dialyzer type and between dialyzer types statistical analysis revealed non-significant comparisons between elimination rate, clearance, and percent removed by dialysis. These non-significant results remained while controlling for UFR.

Discussion

Intravenous iron is frequently given to HD patients to treat or prevent iron deficiency anemia[1]. Clinicians may have concern over the dialyzability of iron sucrose or iron dextran administered at anytime point during the HD session. This is the first study to investigate the *in-vitro* dialyzability of iron sucrose (Venofer, American Regent, Inc.) or iron dextran (DexFerrum, American Regent, Inc.).

The appearance of iron sucrose or iron dextran in the dialysate compartment is the best determinate of the respected agent's dialyzability. The results of our study demonstrate that no iron sucrose was ever detected in the dialysate and a negligible amount of iron from the iron dextran (maximum 5.44% of administered dose) was recovered from the dialysate compartment only with the HE membranes at 0 ml/hr UFR. In all other conditions, no iron was detected in the dialysate for iron dextran. These effects remained constant even controlling for UFR up to 500 ml/hr. The HF and HE dialysis membranes do not remove clinically significant amounts of these iron formulations from the SBS compartment over a 240-minute HD session.

Our results are consistent to previous *in-vitro* and *in-vivo* reports [6-8]. In a 30-minute HD *in-vitro* study iron

Table 3: Iron sucrose removal in a closed-loop system by high-flux or high-efficiency hemodialysis membranes over 240 minutes. (System B)

Study condition	Iron Sucrose (Venofer®)			
	SBS % iron concentration change (mean ± SD)	K_{hd} (hr-1) (mean ± SD)	Dialysate Iron Recovery (mg) (mean ± SD)	Clearance† (ml/min) (mean ± SD)
F80: 0 ml/hr UFR	-3.13 ± 0.06	-0.0001 ± 0.0000	13.82 ± 13.34	-0.76 ± 0.01
F80: 500 ml/hr UFR	-0.03 ± 1.15	0.0000 ± 0.0000	23.59 ± 3.96	0.05 ± 0.19
CA210: 0 ml/hr UFR	-1.41 ± 3.77	-0.0001 ± 0.0002	5.47 ± 1.52	-0.34 ± 0.92
CA210: 500 ml/hr UFR	-1.58 ± 3.08	-0.0003 ± 0.0002	2.79 ± 1.89	-1.08 ± 0.93

SBS = simulated blood solution; UFR = ultrafiltration rate; K_{hd} = hemodialysis elimination rate; % = percent; † = Clearance values that are positive relate to accumulation of substance from the system; negative clearance values represent removal of substance

dextran removal was determined for HF and HE dialyzers [7]. The greatest amount of iron removed (8%) was observed with a F8 (Fresenius) HF dialyzer [7]. Other investigators utilizing a cuprophane coil dialyzer *in-vitro* system determined a 0.5% iron dextran removal over 240 minutes [6]. The only *in-vivo* dialyzability study utilized iron dextran and HE membranes (Terumo 165 cuprammonium dialyzer) [8]. The investigators determined a maximal 2% iron dextran removal over 160 minutes.

At no time point over the sample collection period additional iron was injected into the SBS or dialysate compartments. However, negative regression analyses (Khd) and clearance results reported in the tables suggest that there are increasing amounts of iron in the system (i.e., appearance of additional iron). These findings may be the result of error amplification through multiplication of measured iron concentration and volume of dialysate or SBS reservoir at various time points. Sources of potential error include human (sample preparation), device (1000 mL graduated cylinder) and the atomic absorption spectrophotometry assay. Nonetheless, these negative value results suggest that no iron sucrose or iron dextran was removed from the SBS.

The positive iron sucrose regression analyses (K_{hd}) and clearance results (Table 1) obtained from the HF membrane 0 UFR HD session, support the decreasing amounts of iron in the SBS system (6.99%). However, no iron sucrose was found in the dialysate compartment. A potential reason for the drop in iron sucrose in the SBS compartment is iron sucrose adsorption to the dialysis membrane or tubing. This effect was not seen with the HE membrane nor was it observed under dialysis conditions with a positive UFR.

In order to determine whether the decreasing amounts of iron were due to either adsorption to the dialysis membrane or actual loss of iron to the dialysate compartment, the closed-loop studies were conducted (*in vitro* system B). In those studies between 0.3 and 2.4% (23.59 mg of 1000 mg dose) of iron sucrose was recovered in the dialysate compartment when using 1000 mg of iron sucrose (10 times the current recommended dose) in the SBS reservoir. Therefore, the majority of loss seen in the earlier experiments with HF membranes is not due to transfer of iron to the dialysate compartment; rather the loss is probably due to adsorption to the dialysis membranes.

A potential limitation to our *in-vitro* model is that we utilized normal saline instead of blood in our SBS. Use of an *in-vitro* model raises concerns over the ability to extrapolate the data to humans. In regards to the various intravenous iron formulations, iron appears to dissociate from sucrose rapidly allowing for more immediate systemic iron utilization. This is illustrated in a study which compared iron sucrose, iron dextran and iron gluconate [12]. In that study, serum iron, ferritin and transferrin saturation increased more rapidly and were significantly higher in those patients who received iron sucrose compared to the other iron products. The pharmacokinetic profile of iron sucrose in normal healthy adults suggests that the dissociation of iron from the iron sucrose complex allow for immediate and substantial iron availability. However, it is unknown whether HD would remove the iron more rapidly than it is utilized. Even if the iron in our *in-vitro* study was 100% dissociated from the iron sucrose complex, we recovered virtually no iron in the dialysate and the percent change in iron concentration from baseline was minimally lower with HE dialyzers under 0 ml/hr UFR. No loss of iron was detected under other test conditions with HE or HF membranes. Therefore, HD would not remove significant amounts or iron sucrose prior to it being utilized in the body.

Conclusion

It is therefore concluded that iron sucrose (Venofer®, American Regent, Inc.) and iron dextran (DexFerrum®, American Regent, Inc.) are not significantly removed by either HF or HE dialysis membranes. Furthermore, under laboratory conditions in a closed-loop system, a maximum of 2.4% of iron sucrose is found in the dialysate, well below the clinically relevant level of 15%. These data show that neither iron dextran or iron sucrose are significantly dialyzed under conditions that mimic the clinical situation.

Competing interests

The authors received funding for this study by American Regent, Inc. The authors have no other competing interests.

Authors contributions

HJM and DWG mutually conceived the study, participated in its design, collected samples (HJM – iron sucrose; DWG – iron dextran), and prepared the manuscript.

HJM performed the statistical analysis.

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