

Aluminum kinetics using bicarbonate dialysate with the sorbent system

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Aluminum kinetics using bicarbonate dialysate with the sorbent system. In the REDY system a sorbent cartridge is used to regenerate the spent hemodialysate so that only six liters of dialysate are required for a treatment. The manufacturer claims that the cartridge can be used to remove aluminum from the dialysate and that it does not add aluminum to the dialysate. This claim for acetate dialysate is supported by the literature, but there are few data available relative to bicarbonate dialysate. The present study evaluates the use of bicarbonate dialysate and the REDY system in regard to aluminum kinetics both *in vitro* and *in vivo*. *In vitro*, the sorbent cartridge removed aluminum from dialysate prepared from water containing as much as 470 $\mu\text{g/liter}$ of aluminum, giving a dialysate containing less than 10 $\mu\text{g/liter}$. The first 500 ml of effluent contained 13 $\mu\text{g/liter}$ of aluminum but after filtration decreased to below 10 $\mu\text{g/liter}$. Thus, it is unnecessary, as recommended, to discard the first effluent since this unfilterable aluminum will not pass through a dialysis membrane. *In vivo*, in a crossover study comparing the REDY with single pass, there were no significant differences between the pre- and post-plasma aluminum concentrations, and the dialysate aluminum remained below 4 $\mu\text{g/liter}$ during the dialysis. In a second *in vivo* study the effect of dialysate from tap water on plasma aluminum using the predialysis purification procedure was evaluated. There was no differences between the pre- and post-plasma aluminum concentration. The aluminum levels were comparable to those of the crossover study. The dialysate remained below 4 $\mu\text{g/liter}$ during the dialysis.

Sorbent regenerative dialysis (REDY) systems require only six liters of dialysate to perform an entire hemodialysis treatment. This is made possible by passing the effluent dialysate through a chemical sorbent cartridge which converts urea into CO_2 , sodium bicarbonate and water, while adsorbing other uremic and non-uremic toxins. In order to accomplish the urea conversion, the sorbent cartridge utilizes urease which is immobilized by aluminum oxide (alumina). The presence of aluminum oxide in the cartridge has been the source of clinical questioning over the past twenty years. The sorbent system/cartridge manufacturer (Organon Teknika Corporation; Durham, North Carolina, USA) claims that the sorbent cartridge is extremely effective in removing aluminum from dialysate and does not donate aluminum to the dialysate during sorbent hemodialysis treatment. The manufacturer recom-

mends that a dialysate made from water containing an aluminum concentration greater than 30 $\mu\text{g/liter}$ be purified pretreatment by single passing the dialysate through a sorbent cartridge, and that the first 500 ml of effluent be discarded [1]. The manufacturer supports these claims and recommendations on the basis of the following clinical studies.

Odell et al observed, *in vitro*, that the first 2 liters of dialysate coming from the cartridge contained 27 $\mu\text{g/liter}$ of aluminum [2]. Thereafter, the dialysate aluminum concentration fell rapidly to 6.8 $\mu\text{g/liter}$ and decreased even further during the following four hours. The aluminum came off as a spike in the first 100 to 200 ml. In patient studies using tap water, they noted that the initial dialysate aluminum concentration averaged 14 $\mu\text{g/liter}$ due to the water used to prepare the dialysate. After two hours of dialysis the aluminum concentration decreased to 3 $\mu\text{g/liter}$ and then increased to 8 $\mu\text{g/liter}$ at four hours.

Curtis and Sampson [3] passed acetate dialysate through a sorbent cartridge and also noted a spike in the aluminum concentration (average 58 $\mu\text{g/liter}$) in the first effluent. Thereafter, the dialysate aluminum concentration fell rapidly to an average of 8 $\mu\text{g/liter}$, similar to that observed by Odell et al. Using acetate dialysate in patients, they compared the sorbent system with single pass dialysis in a crossover study. There was no significant difference between the pre- and post-plasma aluminum levels. However, the post-dialysis plasma aluminum concentration was significantly higher with single pass hemodialysis.

In contrast to the above favorable results, Drury et al [4] noted a wide variation in dialysate aluminum coming from the sorbent cartridges. Aluminum added to the recirculating dialysate required an average of 50 minutes before the cartridge reduced the aluminum concentration below 30 $\mu\text{g/liter}$.

During the past decade, bicarbonate has replaced acetate as the buffer of choice in the dialysate for both chronic and acute hemodialysis. However, Drukker and Van Doorn [5] discourage the use of bicarbonate dialysate with the REDY system stating that, "With bicarbonate loaded dialysate solubility of aluminum increases and release from the cartridge may be substantially higher, exceeding permissible levels." Likewise, recently, Shapiro has suggested the use of an acetate dialysate whenever sorbent dialysis is performed [6].

The available data provide few direct information on the effect of initially formulated bicarbonate dialysate on the sorbent cartridge. Studies performed by Shapiro, Schilb and

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Porush provide some insight into this question [7]. The data presented by Shapiro et al involves an unconventional use of sorbent cartridges regeneration of hemofiltrate. They noted in an eight patient crossover study which compared single pass hemodialysis with sorbent regeneration of hemofiltrate, that while predialysis serum aluminum levels were similar (58.8 vs. 58.4 $\mu\text{g/liter}$, respectively), post-dialysis plasma aluminum was significantly lower for sorbent hemofiltration (48.3 $\mu\text{g/liter}$) than for single pass hemodialysis (62.5 $\mu\text{g/liter}$).

Therefore, the following questions remain: (1) is the sorbent cartridge effective in removing aluminum from bicarbonate dialysate and (2) does the sorbent cartridge release aluminum to the dialysate during hemodialysis? The present study addresses these questions by assessing, both *in vitro* and *in vivo*, the aluminum kinetics of the sorbent cartridge with bicarbonate dialysate.

Methods

In vitro study

The aim of this study was to evaluate the predialysis procedure recommended by the manufacturer for bicarbonate dialysate prepared from water containing over 30 $\mu\text{g/liter}$ of aluminum [1].

Purified water which assayed at 2.4 $\mu\text{g/liter}$ of aluminum served as the control. An aluminum standard was added to achieve 150 and 500 $\mu\text{g/liter}$ of aluminum. A packet of sodium chloride (21 g) was added to the control and the solutions with two concentrations of aluminum. Each salt solution was then pumped single pass through a Sorb Cartridge (D3160) or HiSorb Cartridge (D3260) using either a Sorbsystem or REDY 2000 dialysis machine. The first 500 ml of effluent from the cartridge was collected separately. Sodium bicarbonate (30 g) was added to the salt solution which had been passed through the sorbent cartridge. To neutralize the pH, either hydrochloric acid from Kit 2 was added or the dialysate was recirculated for 15 minutes through the same cartridge used to purify the salt solution. Then, 11 ml of infusate (prepared from the same aluminum containing water as the dialysate) were added. The dialysate was allowed to recirculate through the cartridge for one minute. After this step, the dialysate would be ready for use with a patient.

Samples for aluminum assay were taken at each step in the above procedure. All samples taken after passage through the sorbent cartridge were assayed prior to and after filtration through a 0.45 μ filter since aluminum, which cannot pass through this porosity filter, cannot pass through a dialyzer membrane.

In vivo study 1

The aim of this crossover study was to compare the aluminum kinetics of sorbent and single pass dialysis. Six patients, free from use of aluminum-containing phosphate binders, were dialyzed with the sorbent dialysis system for four hours using either the SorbSystem or REDY 2000 with a HiSorb cartridge (D3260) and bicarbonate dialysate (kit 2). The same patients were dialyzed with a single pass system using bicarbonate dialysate. All dialysate solutions were prepared with purified water and used without further purification. The patients were treated similarly on both systems. Samples of the patient's

Table 1. Removal of aluminum by REDY sorbent cartridge aluminum, $\mu\text{g/liter}$

	Control	Added aluminum	
Before passage through cartridge			
Water with aluminum	2.4 (5.4)	136 (66)	470 (19)
Addition of NaCl	0.0 (0.0)	149 (66)	464 (20)
After passage through cartridge			
First 500 ml	13 (7.5) ^a	7.5 (6.5) ^b	12.5 (7.6) ^b
First 500 ml filtered	3.3 (5.4)	6.0 (6.3)	8.4 (8.0)
After NaHCO ₃	1.5 (3.0)	2.0 (3.4)	7.0 (13)
After NaHCO ₃ filtered	0.0 (0.0)	3.3 (5.8)	6.0 (6.6)
Final dialysate	0.0 (0.0)	3.3 (3.8)	9.5 (9.4)
Final dialysate filtered	0.0 (0.0)	2.3 (3.7)	4.6 (5.7)

N = 8. Numbers in parentheses are standard deviation

^a *P* < 0.001 between filtered and unfiltered

^b *P* < 0.01 between filtered and unfiltered

plasma pre- and post-dialysis were measured for aluminum, urea, creatinine and electrolytes. The sorbent system dialysate was sampled at the start of dialysis and every hour for aluminum. These samples were assayed prior to and after filtration through a 0.45 μ filter.

In vivo study 2

The aim of this study was to measure the dialysate and patient aluminum levels when using tap water and the predialysis purification procedure to prepare bicarbonate dialysate.

Four patients, free from the use of aluminum-containing phosphate binders, were dialyzed using the REDY Sorbsystem for four hours with HiSorb (D3260) cartridges and bicarbonate dialysate. The dialysate was prepared from tap water and purified as described in the *in vitro* method. The predialysis purification procedure is used routinely in this dialysis unit since the tap water aluminum levels can vary considerably. The patient's plasma was measured for aluminum pre- and post-dialysis. The dialysate was sampled and immediately filtered at the start of dialysis and every hour during hemodialysis for aluminum.

Aluminum measurement method and statistical analysis

Blood samples were collected in heparinized tubes and immediately centrifuged. The plasma was separated and stored in the refrigerator until assayed. Dialysate samples were placed in the refrigerator until assayed. The measurements were performed with atomic absorption spectrophotometry using a Perkin-Elmer 3030 spectrometer, a graphite furnace and AS 60 autosampler. The sensitivity of this method in our laboratory over the last decade has been within 1 to 2 $\mu\text{g/liter}$, and the coefficient of variation is < 7%.

All results are expressed as the mean \pm SD. Statistical analysis was performed by Student's *t*-test and analysis of variance when needed.

Results

In vitro study

The results are given in Table 1. Whether the water supply aluminum concentration was 2.4, 136 or 470 $\mu\text{g/liter}$, the

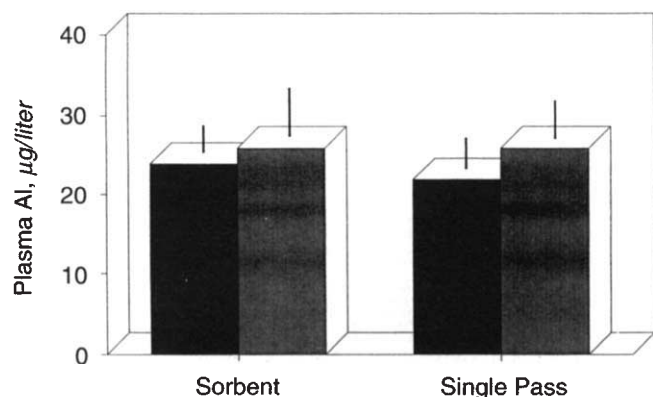


Fig. 1. Comparison of plasma aluminum levels, in six patients, (■) pre- and (□) post-dialysis between sorbent and single pass system (Crossover study). There were no significant differences, $P > 0.05$.

purified dialysate contained less than 10 $\mu\text{g/liter}$ prior to filtration and less than 5 $\mu\text{g/liter}$ after filtration. Filtration of the first 500 ml gave a significantly lower assay for the control than the unfiltered sample ($P < 0.001$). However, these differences were less for the test samples to which aluminum had been added but still significant. When all the filtered samples were compared with the unfiltered, the filtered values were significantly lower than the unfiltered ($P < 0.01$). There were no significant differences between the Sorb and HiSorb cartridge, nor between using a SorbSystem or REDY 2000 dialysis machine, nor between using hydrochloric acid from bicarb Kit 2 or recirculating for 15 minutes.

In vivo study 1

The pre- and post-plasma aluminum values for the sorbent and single pass dialysis are shown in Figure 1. There were no significant differences between the pre- and post-aluminum values nor between the sorbent and single pass dialysis. Urea, creatinine and electrolyte values were as expected. The dialysate aluminum results during the four hours of sorbent dialysis are shown in Figure 2. The dialysate aluminum concentration remained below 4 $\mu\text{g/liter}$ in all samples.

In vivo study 2

The filtered tap water contained 10.2 $\mu\text{g/liter}$ of aluminum. The pre- and post-plasma aluminum concentration for the sorbent dialysis are displayed in Figure 3. There was no significant difference between the pre and post dialysis values. The hourly dialysate aluminum concentrations during sorbent dialysis are shown in Figure 2. The dialysate remained below 4 $\mu\text{g/liter}$ in all samples.

Discussion

This study confirms the sorbent cartridge's ability to remove aluminum from dialysate containing as much as 470 $\mu\text{g/liter}$ of aluminum. Secondly, during a four hour treatment utilizing bicarbonate dialysate, the sorbent cartridge does not release aluminum to either the dialysate or patient. Our results are in agreement with those reported by Odell et al [2] and Curtis et al using acetate containing dialysate [3].

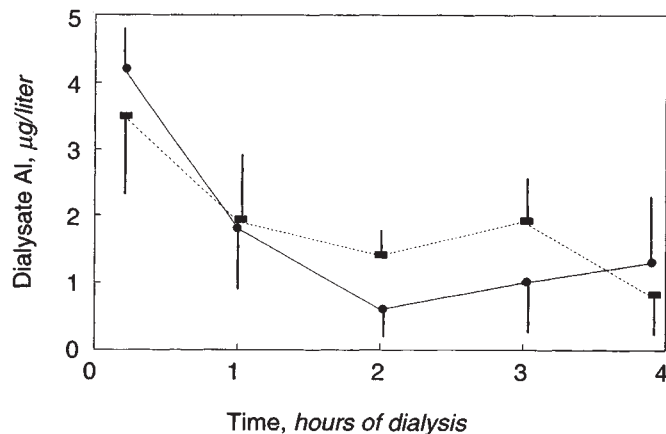


Fig. 2. Dialysate aluminum concentration during sorbent system in four hemodialysis using purified water (—●—, study 1) and tap water (---■---, study 2).

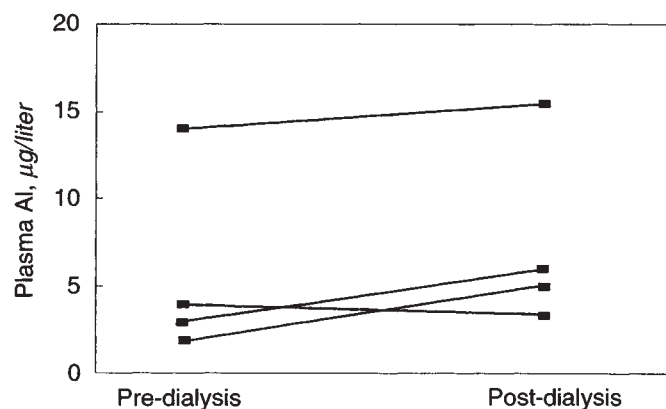


Fig. 3. Pre- and post-dialysis plasma aluminum concentrations in four patients after sorbent system dialysis (Study 2). There were no significant differences ($P > 0.05$).

We also noted a relatively high aluminum concentration in the initial effluent from the cartridge. However, the initial increment was primarily aluminum which could not pass through a 0.45 μ filter since the filtered values were significantly lower. Therefore, it seems unnecessary to collect the first 500 ml for retreatment as recommended by the manufacturer. This will eliminate the need to monitor the dialysate flow during the purification procedure in order to collect this 500 ml.

In comparing the sorbent system with single pass, Curtis et al [3] reported a significantly higher post-plasma aluminum levels with single pass dialysis than with the sorbent system. We observed no differences, perhaps because our single pass dialysate contained no aluminum whereas Curtis et al [3] reported a range of 1.1 to 8.1 $\mu\text{g/liter}$.

The average post-dialysis plasma aluminum is usually higher than the pre-dialysis values. Since plasma aluminum concentration is a good indicator of an acute aluminum load, the small nonsignificant increment observed in post-dialysis plasma aluminum may be due to dialysate aluminum passing across the membrane into the blood of the patient. Another possibility is that the higher post-dialysis aluminum may be a reflection of the

extracellular volume reduction due to ultrafiltrate loss during dialysis. Recent studies have shown that most of plasma aluminum (85 to 95%) is bound to transferrin [8]. Significant fluid removal after hemodialysis usually leads to an increment of plasma transferrin which should result in a variable increment in the aluminum-transferrin bound fraction. Similar observations were made more than a decade ago in regard to the hypercalcemia observed during dialysis; it was observed that an increment in serum albumin and consequently in the albumin-bound fraction of serum calcium (40 to 50%) was an important factor in the post-dialysis hypercalcemia [9].

Shapiro, Schilb and Porush observed a significant decrease in plasma aluminum after sorbent hemofiltration [10]. They attributed the decrement to the relatively high aluminum clearance (43 ml/min).

Sorbent cartridges used to purify bicarbonate dialysate and subsequently used during the dialysis of a patient did not release aluminum to either the dialysate or patient. On the day the clinical study was performed the tap water aluminum concentration happened to be 10 $\mu\text{g/liter}$ which was not known until the tests were completed. Thus, the cartridge was not challenged with a high aluminum concentration. It was considered inappropriate to repeat the study with aluminum added to the water.

As reported by Drury et al [4], we also noted a relatively wide variation in dialysate aluminum concentration with sorbent dialysis when only the unfiltered samples are evaluated. This variation disappears when the samples are filtered, again strongly suggesting that the variations are due to filterable aluminum. In the assay procedure used by Drury et al [4], they shook each vial immediately prior to assay and added nitric acid to an aliquot for analysis. This would dissolve any unfilterable aluminum in the aliquot resulting in high and variable results depending upon whether or not filterable particles happened to be in the aliquot.

Conclusion

In summary, (1.) passing a dialysate containing aluminum through a sorbent cartridge in accordance with the manufactur-

er's recommendation effectively removes aluminum. In addition, there is no need to retreat or discard the first 500 ml exiting from the cartridge since this contains primarily unfilterable aluminum. (2.) Pre- and post-plasma aluminum levels from patients dialyzed with the sorbent dialysis system are comparable to patients dialyzed with single pass system. (3.) The use of the sorbent system to remove dialysate aluminum and then for patient dialysis produces a dialysate with an aluminum level below 4 $\mu\text{g/liter}$.

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