The Use of Exchange-Free Periods Alternating with Daily Exchanges of Icodextrin in the Initial Treatment of Peritoneal Dialysis-Associated Peritonitis: a Safety Study

Editor,

Repeated infusion of large volumes of low pH, hypertonic dialysis fluid rich in glucose and its degradation products impairs neutrophil and macrophage function (1,2), interfering with normal host responses to microbial contamination.

We propose that daily 12-hour exchange-free periods during the critical first few days of a peritonitis episode result in improved intra-peritoneal host defence mechanisms and better resolution of peritonitis and could reduce the risk of long-term damage to the peritoneum. We rationalized that a daily 12-hour exchange of icodextrin (for 3 days at the beginning of a peritonitis episode) would provide sufficient solute clearance and fluid removal to offset the lack of dialysis in the exchange-free periods.

METHODS

This trial was conducted from January 2010 to June 2011 at Auckland City Hospital, New Zealand, to test the safety of this approach.

After obtaining ethics approval, 8 continuous ambulatory peritoneal dialysis (CAPD) patients provided consent and were randomized into one of two groups, 5 patients (the I group) received icodextrin peritoneal dialysis (PD) solution as initial treatment. This was loaded with antibiotics as per the unit's peritonitis standing order for an initial dwell of 12–20 hours depending on the timing of patient presentation (Figure 1). The dialysis effluent was then drained out and the patient did not infuse a new solution for at least 12 hours, i.e. remain "dry" for at least 12 hours. This procedure was repeated twice in the first 60 hours after presentation with peritonitis, ending with a third icodextrin exchange. Afterwards, patients reverted to their usual CAPD prescription and continued on antibiotics as determined by the unit protocol. Three control patients (C group) received intraperitoneal antibiotics and dialysis as per usual practice.

Eight outpatient visits/patient occurred over 2 weeks of follow-up for clinical assessment, blood and dialysate sampling. Serum samples were analyzed for sodium, potassium, bicarbonate, glucose, amylase, total peripheral white cell count (WCC), hemoglobin, urea, creatinine, liver function tests and C-reactive protein (CRP). Plasma and dialysate samples were assayed for interleukin (IL)-1 β , IL-8, IL-6 and transforming growth factor (TGF)- β .

Figure 1 — Study design and procedures. (A) Study procedure for the Interventional group. (B) Procedure for the Control group. abs = antibiotics; D = dextrose.

RESULTS

Baseline characteristics were similar in both groups of patients, but causative organisms tended to be more virulent in the interventional group (Table 1). Patients tolerated the procedure well. None were hospitalized or required removal of their PD catheter due to the study. The time to resolution of peritonitis (as defined by number of days to a dialysate WCC <100) was significantly shorter in the control group than in the intervention group (mean 3.7 ± 1.2 days vs 6.6 ± 0.9 days, $p = 0.007$). However by day 5 and thereafter, both groups had equivalent peritoneal WCC.

Group I patients developed significant asymptomatic hyponatremia on days 3 and 5 compared to the controls. This was associated with a rise in the plasma osmolality.

There were no other safety features identified (Table 2, Figure 2).

The mean serum CRP (Table 2, Figure 2), plasma and effluent IL-1 β , IL-8, IL-6 and TGF- β tended to be higher during the interventional phase of the study in the I group patients (data not shown).

DISCUSSION

This novel approach to peritonitis treatment in a small carefully selected group of patients was well tolerated. Patient symptoms were similar in both groups. None were hospitalized due to the peritonitis episode. No catheters were removed during the study. Those in the intervention group had no clinical features of fluid overload or underdialysis. This satisfactory outcome occurred despite the

TABLE 1
Causative Organisms on Presentation with Peritonitis

	Interventional group (I)	Control group (C)
Causative organisms	<i>Stenophomonas maltophilia</i> (1) <i>Staph aureus</i> (2) <i>Streptococcus</i> (mitis and salivarius) (1) Sterile (1)	Coagulase-negative staph (2) (lugunensis and epidermidis) Sterile (1)

TABLE 2
Summary of the Biochemical Results in Both Groups During the Interventional Phase of the Study

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 7
Mean serum Na (mmol/L)						
I	139 $\pm$ 3	136 $\pm$ 3	131 $\pm$ 4 ^a	134 $\pm$ 2	134 $\pm$ 4 ^b	138 $\pm$ 2
C	140 $\pm$ 2	139 $\pm$ 3	140 $\pm$ 2	142 $\pm$ 7	140 $\pm$ 1	140 $\pm$ 0.6
Mean serum Osmolality (mOsm/kg)						
I	321 $\pm$ 12	331 $\pm$ 12	328	324 $\pm$ 1	335 $\pm$ 15	327 $\pm$ 17
C	317 $\pm$ 9	322 $\pm$ 1	320 $\pm$ 10	323 $\pm$ 5	319 $\pm$ 2	323 $\pm$ 7
Mean serum K (mmol/L)						
I	3.7 $\pm$ 0.6	3.9 $\pm$ 0.3	4.2 $\pm$ 0.3	4.0 $\pm$ 0.6	3.9 $\pm$ 0.6	4.0 $\pm$ 0.5
C	4.7 $\pm$ 1.2	4.4 $\pm$ 0.8	4.4 $\pm$ 1.0	4.2 $\pm$ 0.6	4.1 $\pm$ 0.6	4.1 $\pm$ 0.4
Mean serum creatinine (umol/L)						
I	676 $\pm$ 406	754 $\pm$ 437	916 $\pm$ 551	855 $\pm$ 576	923 $\pm$ 555	777 $\pm$ 587
C	621 $\pm$ 330	602 $\pm$ 290	598 $\pm$ 293	623 $\pm$ 308	625 $\pm$ 277	649 $\pm$ 293
Mean serum CRP (mg/L)						
I	86.0 $\pm$ 98	189 $\pm$ 109	218 $\pm$ 57 ^c	109 $\pm$ 32 ^d	59 $\pm$ 38	33 $\pm$ 23
C	46 $\pm$ 7.6	43 $\pm$ 19.8	30 $\pm$ 12	21 $\pm$ 8.5	15 $\pm$ 5.6	7.8 $\pm$ 3.1

I = interventional group; C = control group; CRP = C-reactive protein.

^a $p = 0.03$.

^b $p = 0.04$.

^c $p = 0.005$.

^d $p = 0.01$.

Figure 2 — Trends over the interventional phase of the study. (A) Mean serum sodium both groups over the intervention phase. (B) Mean serum CRP both groups over the intervention phase. (C) Mean log dialysate WCC both groups over the intervention phase. CRP = C-reactive protein; WCC = white cell count.

fact that the intervention group suffered more virulent organism peritonitis (*Staph aureus*, *streptococci* and *sternophomonas*) (3,4).

There was a non-significant trend toward better fluid management in the intervention group. There were however non-significant increases in serum urea and creatinine levels in the I group in the first 5 days after the onset of peritonitis (Table 2).

Patients in the I group had significantly lower serum sodium in the interventional days which correlated with an increased serum osmolality indicating pseudohyponatremia thought to be secondary to circulating icodextrin metabolites. In addition to the more virulent nature of the organisms noted in the I group, the persisting high effluent WCC is likely to be partly related to the fact that the samples collected on days 1–4 represent 24 hours of white cell production in this group versus about 10 hours in the control group. Given the small numbers studied and the increased organism virulence in the I group, no conclusions can be reached about a possible independent inflammatory impact of icodextrin as previously documented by others (5,6).

In conclusion, we have shown that the use of exchange-free periods alternating with icodextrin (and appropriate antibiotics) in the first 60 hours of the treatment of a new episode of PD peritonitis can be associated with subsequent satisfactory resolution of infections without significant side effects. The procedure was well tolerated apart from the development of pseudohyponatremia. Additional trials would need to be undertaken to further establish the safety of this approach and to explore the hypothesis that enhanced host defences with exchange-free periods can improve peritonitis outcomes.

DISCLOSURES

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Maha Yehia^{1*}
Grace Muyoma¹
Nicholas Topley²
John F. Collins¹

Department of Renal Medicine¹
Auckland City Hospital
Auckland, New Zealand
Institute for Translation, Innovation, Methodologies
and Engagement (TIME)²
Cardiff University School of Medicine
Cardiff, UK

*email: mahay@adhb.govt.nz

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