

Type 1 peritoneal membrane failure in a paediatric patient, successfully treated with icodextrin

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Abstract

Introduction: Studies in adults demonstrate type I ultrafiltration failure (UFF) more common type rather than type 2, 3 and type 4 UFF. But in contrast, the incidence of type 1 UFF in children and its management with icodextrin are rarely described.

Case presentation: We describe the type 1 UFF in a case of a 10-year-old boy who was diagnosed with end stage renal failure on Nocturnal intermittent peritoneal dialysis (NIPD) secondary to genetic proved (NPHS1) congenital nephrotic syndrome. His peritoneal equilibrium test (PET) revealed type 1 UFF. Subsequently, he was managed with icodextrin and responded dramatically to our therapy. Although type I membrane failure is well evident in adult populations, acquiring the same in a paediatric child is very limited. Moreover, icodextrin is one of the choices in managing type 1 UFF in adults. But, there have been no case reports in paediatric patients.

Conclusions: Type 1 UFF can occur in a paediatric child, as its cause remains unknown. Early diagnosis and prompt management can be essential to improving the quality of patient care in peritoneal dialysis. Icodextrin may provide an effective modality of treatment.

Introduction

UFF is considered as an important complication in peritoneal dialysis, and it is responsible for 4 to 12% of transfer to haemodialysis [1]. UFF is defined as the inability to maintain adequate fluid balance in patients treated with peritoneal dialysis [2]. Also, Andreoli, *et al.* [3] evidently described UFF as an inability to maintain fluid balance despite hourly cycles of minimum 30 ml/kg dwell of 3.86% (4.25%) dextrose monohydrate. Historically, UFF classified into four types, in which the first type characterized by large effective hyperpermeable peritoneal surface area, second type by low osmotic conductance to glucose, and the third type by low effective peritoneal surface area and fourth type by high effective lymphatic absorption rate [4,5]. Adult populations frequently demonstrate type I UFF as they tend to be on dialysis for many years. Hyperpermeability of the peritoneal membrane is one of the main causes described in adults [6]. In contrast, children tend to have more of type 2 UFF secondary to recurrent peritonitis or cause yet to be elucidated [6]. We need to highlight that classification of peritoneal UFF is mandatory to come to the early conclusion. Also, it may also aid in preventing unnecessary haemodialysis. Moreover, icodextrin is one of the effective modality of treatment especially in the setting of hyperpermeable membrane and aquaporin dysfunction [4].

Herein, we describe a paediatric patient with a type 1 peritoneal UFF and successfully treated with icodextrin.

Case presentation

Our patient was a 10-year-old boy with end-stage renal failure secondary to congenital nephrotic syndrome (homozygous c.3250dupG p. V1084fs NPHS1). He was maintained on NIPD with Fresenius cyclor-sleep safe (V2.2X) since January 2011. His initial NIPD regimen consisted of fill volume 730 ml (1100 ml/m²), 10 cycles 10 hours, with

no day dwell and each using bicarbonate-based physiological solutions (1.5% glucose monohydrate, bicavera, Fresenius medical care (FMC), Bad Homburg, Germany). On follow-up, his peritoneal fill volume was gradually increased to 850 ml (1100 ml/m²), corrected to his body surface area. His average ultrafiltration was 600 to 800 ml/day. He was noted to have some negligible urine at the time of initiating dialysis, however, since May 2011 he remains anuric. He was on diuretic before the onset of dialysis, and it was withheld during the initiation of dialysis as it did not make any impact in his negligible urine output. Moreover, he did not demonstrate any clinical evidence of fluid overload. His growth parameters are very poor and his percentiles are well below 3rd centiles. The patient also complicated with renal osteodystrophy, hypertension and was controlled with calcitriol, multiple antihypertensives namely amlodipine, lisinopril, and minoxidil since 2010. His mean average blood pressure was 115/65 mmHg. His recent echocardiogram does not reveal any signs of left ventricular hypertrophy. His baseline peritoneal transport status (June 2011) revealed high average transport type and his small and middle molecule clearance were optimal (Tables 1 and 2). During his time on peritoneal dialysis, the patient had one episode of peritonitis due to *Streptococcus viridians*, at five years (February 2016) after starting dialysis. He does not have potential living related donor

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Table 1. Clinical and laboratory details of ultrafiltration failure.

Parameters	Baseline 2011	May 2016	June 2016	July 2016	August 2016
Weight (kg)	14.5	19	19.9	20.3	21.5
Height (cm)	107	112	112.2	112.4	112.4
BSA (m ²)	0.65	0.76	0.787	0.796	0.819
Pedal oedema	-	-	++	++	++
Facial puffiness	-	-	++	++	++
BP(mmHg)	98/62	110/70	135/92	134/96	139/98
Peritoneal ultrafiltrate (ml/day)	600-800	500-650	200-300	120-190	< 100
Serum Na(mmol/l)	138	141	145	145	148
Serum albumin (g/l)	29	39	37	37	38

Na: Sodium, BSA: Body surface area, BP: Blood pressure

Table 2. Results of Peritoneal Equilibrium Study (PET).

Results	Baseline 2011	2016
Peritoneal fluid Na concentration (mmol/l)	134	134
Peritoneal Kt/V	2.1	1.9
Peritoneal CCL (l/week/1.73m ²)	52	48
PET	Standard (2.3% dextrose monohydrate)	Modified (4.25% dextrose monohydrate)
Peritoneal Fluid drainage	-	95 ml in one hour, 80 ml in four hours.
Transporter type	High average	High average
D/P Creatinine(umol/l)		
0 minutes	0.07	0.06
2 hour	0.57	0.58
4 hour	0.79	0.88
D/P Urea(mmol/l)		
0 minutes	0.09	0.05
2 hour	0.75	0.73
4 hour	0.91	0.94
D/P Glucose(mmol/l)		
0 minutes	0.97	1.00
2 hour	0.47	0.45
4 hour	0.34	0.31
Dialysate Na(mmol/l)		
0 minutes:	-	0.93
60 minutes:	-	0.82
ΔNa {D Na (0 minutes) – D Na(60minutes) mmol/l}	-	> 5
24hour dialysate Na removal without Icodextrin (mmol/day)	-	32
Icodextrin day dwell Na removal (mmol/day)	-	46

Na: Sodium, PET:Peritoneal equilibrium test, Kt/V: Dialyzer clearance of urea, CCL:Creatinine clearance; D: Dialysate, P: Plasma, Δ: Delta

and he is presently under cadaveric renal transplant list. His antibiotic therapy involved intraperitoneal vancomycin and ceftazidime. His peritonitis was resolved without any complications. Interestingly, his mean peritoneal ultrafiltration remained good (500- 600 ml/day) until May 2016.

On further follow-up, his mean ultrafiltration dropped gradually below 300 ml/day then subsequently to 100 ml/day along with weight gain, increasing blood pressure (139/98 mmHg) and peripheral oedema. His peritoneal dialysis regimen changed to continuous cyclic peritoneal dialysis (CCPD) 850 ml (1100 ml/m²), 10 cycles 10 hours and each using bicarbonate-based physiological solutions (2.3% glucose monohydrate, bicavera,) with 50% of the nocturnal dwell volume as the day dwell, 2.3% glucose monohydrate, bicavera. But despite increasing the percentage of glucose and adding day dwell, his ultrafiltration from nocturnal dialysis remained poor (<100 ml/day). Moreover, he was noted to have accumulation of peritoneal fluid from day dwell (+50 ml to 95 ml/day). As a result, day dwell was withheld after two weeks.

Notably, there was no clinical evidence of a subcutaneous leak. At this juncture, given the persistence of fluid accumulation, we investigated for extrinsic cause for the failure in peritoneal membrane. There was no displacement of the catheter by an abdominal X-ray. His clinical and laboratory details of ultrafiltration failure are well elucidated in (Table 1).

Further, we evaluated peritoneal membrane function (modified PET) using 1100 ml/m² as the volume of exchange, 4.25% glucose monohydrate, bicavera [7]. This test confirmed the presence of UFF (80 ml after 4 hours). Moreover, we were able to classify our patient as type 1 UFF based on high solute transport (Dialysate (D)/Plasma (P) creatinine at 0 minute (0.06), 2 hour (0.58), 4 hour (0.88), D/P urea at 0 minute (0.05), 2 hour (0.73), 4 hour (0.94), D/P glucose at 0 minute (1), 2 hour (0.45), 4 hour (0.31), and low volume drainage [4]. Owing to the above results, our patient was started on 7.5% icodextrin (Extraneal, Baxter, Castlebar Co. Mayo, Ireland) 450 ml (600 ml/m²) as the day dwell and with CCPD consisted of fill volume 850 ml (1100 ml/m²), 10 cycles 10 hours and each using bicarbonate-based physiological solutions (2.3% glucose monohydrate, bicavera. His mean ultrafiltration from day dwell remarkably increased to 550 ml (490 ml to 620 ml/day), but his mean ultrafiltration from nocturnal dialysis remained unproductive (30 to 60 ml/day). Further, there was dialysate sodium dip at 0 and 60 minutes, and delta sodium >5 mmol/l, which eventually confirmed efficient free water transport and preservation of sodium sieving in our patient [7], (Table 2). Also, sodium removal by the dialysis before and after 7.5% icodextrin therapy is well illustrated in (Table 2).

On follow-up, his fluid balance is controlled with improving blood pressure (112/68 mmHg) and clinical oedema. No adverse events noted. We are planning to repeat his PET after 6 months.

Conclusion

Peritoneal UFF in pediatrics remains challenging over the years. However, dialysis modalities in children are considered as temporary measures until renal transplantation [5]. Moreover, renal transplantation is principally considered as the ideal treatment in pediatric patients with chronic dialysis and it provides a major impact on survival advantage over dialysis [8-10]. As a result, most of the paediatric patients needing shorter duration of dialysis and renders the type 1 UFF as unnoticed. Neiberger, *et al.* [6] conducted a retrospective study to determine the cause of UFF in children. He further reported that type 2 membrane failure were common in children as compared to adults. Andreoli, *et al.* [3] reported the same incidence but could not identify the type of UFF. In contrast, Heimbürger, *et al.* [9] found that prevalence of UFF steadily increased with increasing duration of dialysis, and it is principally due to the hyperperitoneal membrane. Moreover, it is implicated that classification of types 1, 2 and 3 UFF

in children may not be useful in children as they tend to have type 2 failure as the common entity [6]. But in contrast, classification of the UFF stays essential in our case, as it aids in early diagnosis and prompt intervention.

Criteria for diagnosing true loss of peritoneal ultrafiltration capacity is based on low drain volumes in PET. However, it may be due to catheter malposition, internal dialysate leak, and recent peritonitis, but it can be safely excluded by history, examination, and performing abdominal X-ray. In addition, type 1 and 2 UFF are differentiated based on peritoneal transporter status. Type 1 UFF is characterized as high peritoneal solute transport and low peritoneal drain volume, whereas patients with low peritoneal solute transport and low peritoneal drain volume point towards type 2 UFF [4].

In our case, clinical and laboratory details of fluid overload (Table 1) along with high peritoneal solute transport and low drain volume in PET (Table 2) illuminating the diagnosis as type 1 UFF. Peritonitis is considered as an important contributing factor for peritoneal membrane changes, but Ates, *et al.* [11] demonstrated that a single episode of peritonitis did not permanently affect membrane transport. Interestingly, our patient had peritonitis before the onset of UFF but notably had good preservation of ultrafiltration until three months after peritonitis. However, we speculate peritonitis may have played the role in reducing the total ultrafiltration capacity. Other common causes of type 1 UFF are due to uremic states, sustained contact with glucose and its degradation products (GDPs). It may result in the rapid dissipation of the osmotic gradient and eventually lead to very low ultrafiltration [12]. But particularly, our patient underwent dialysis with solutions labeled as low GDPs. Further, for some of the patients neither of these causative factors has been linked to membrane failure.

It is very prudent that importance of classifying ultrafiltration failure prompting to analyze the peritoneal capacity in detail and explore the further treatment options. Moreover, it prevents unnecessary haemodialysis and its complications. Also, social, school, psychological and parental issues related to haemodialysis treatment are well confined and preserved. Moreover, many studies have acquired and highlighted the use of icodextrin-based exchanges to yield higher or equivalent ultrafiltration than compared to hypertonic dextrose exchanges [13,14]. Wilkie, *et al.* [15] demonstrated that patients using icodextrin might extend the peritoneal technique survival, especially with ultrafiltration problems. Further, he also demonstrated that transfer rate to haemodialysis was considerably low on patients using icodextrin. It is also evident that icodextrin induces colloid osmosis through small pores of the membrane and not through aquaporin 1 channels [16]. Importantly, our case demonstrates good preservation of sodium sieving (Table 2) as evident by significant sodium dip at 0 and 60 minutes in an initial hour of peritoneal dialysis, which eventually confirmed preservation of aquaporin function and illustrates that aquaporin dysfunction may not be the major contributor in UFF in children [7]. In addition, our patient did not have any significant hypoalbuminemia nor hyponatremia and as well clinical ascites (Table 1). Also, test for osmotic conductance to glucose (OCG) was not done in our case as it may delineate the efficiency of icodextrin in UFF. Milia, *et al.* [7] demonstrate absent OCG in PET needs prompt transfer to haemodialysis therapy, on another side, reduced OCG ($<1.5 \mu\text{l}/\text{min per mm Hg}$) may benefit from icodextrin treatment.

Icodextrin also effectively remove the sodium removal and thereby prevent salt and water retention as compared to short dextrose exchanges [17]. This highlights that patient with hyperperitoneal membrane needing short dwell exchanges, icodextrin may serve as an

effective rescue treatment for both improving ultrafiltration and net sodium removal. Furthermore, the dosage of icodextrin in children is still debatable, however with $600 \text{ ml}/\text{m}^2$ of 14-hour long dwell could result in prompt clearance, good ultrafiltration and without impact on oligosaccharide load [18]. We also highlight up to our knowledge that none of the case reports has been so far published in a paediatric child with type I UFF and its management with icodextrin. It also directs the way of the alternate modality of management in a young paediatric patient with ultrafiltration problems. To conclude, optimal fluid balance and preventing the complications of fluid overload is utmost essential in paediatric patients, especially in preventing cardiovascular morbidity and mortality. Managing peritoneal UFF in paediatric patients is challenging and needs a prompt classification and intervention at the earliest.

Consent

Written informed consent for the publication of this case report and any accompanying images has been obtained from his father.

Competing interest

The authors declare that they have no competing interests.

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Authors' contributions

- Mohammed Azar: Data analysis, writing and review of the manuscript
- Malek Oeid Otaibi: Data collection.
- Flor: Data collection
- Khalid Alfakeeh: Review of the manuscript.

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