

Unexpected Reduction in Glucose Ultrafiltration Associated to a Continuously “Full Abdomen” Prescription After Introducing a Long Icodextrin Dwell: A Case Series

Case reports

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ABSTRACT

The decline in residual renal function (RRF) and the increasing peritoneal membrane permeability often require a progressive increase in glucose concentrations and the use of icodextrin (ICO) for the long dwell to maintain adequate ultrafiltration (UF). When these strategies are no longer effective and ultrafiltration failure (UFF) develops, patients typically need to be transferred to hemodialysis (HD). We describe four cases in which the introduction of a daytime dwell with ICO was associated with an unexpected and rapid decline in glucose UF with a full abdomen (overnight in Automated Peritoneal Dialysis (APD) and daytime in Continuous Ambulatory Peritoneal Dialysis (CAPD)), which was “resolved” by reintroducing an empty abdomen for part of the day, even while maintaining ICO. The observed phenomenon seems to be less related to the specific solution used during the daytime dwell and more to the continuous 24-hour full abdomen prescription.

KEYWORDS: peritoneal dialysis, icodextrin, ultrafiltration, ultrafiltration failure

Introduction

The peritoneal dialysis (PD) prescription is influenced by residual renal function (RRF) and peritoneal membrane permeability. Over time, RRF tends to decline while peritoneal permeability generally increases. To maintain adequate solute clearance under these conditions, it becomes necessary to increase fill volumes and the number of exchanges. At the same time, to ensure sufficient ultrafiltration (UF), higher glucose concentrations and icodextrin (ICO) solutions for the long dwell are commonly used [1].

We report a case series in which the introduction of ICO for the long dwell was associated with a marked reduction in nocturnal UF, which was reversed by “reducing” the dialysis prescription through the reintroduction of an empty abdomen for part of the day. Although rare, the characteristics and magnitude of the observed phenomenon have relevant practical and theoretical implications, particularly considering that ultrafiltration failure (UFF) remains a leading cause of dropout from PD, accounting for 13.5% of transfers to hemodialysis (HD) in Italy in 2024 [2].

Materials and Methods

We report a series of four cases observed in the peritoneal dialysis units of two Italian centers between 2016 and 2024.

These cases, along with additional ones from two other centers, were discussed during conferences, scientific meetings, and through personal communications. Of the seven cases discussed, three were excluded because, at the time the phenomenon was observed, the dialysis prescription was significantly modified in terms of volumes, dwell times, and glucose concentrations. These changes made it impossible to accurately compare UF achieved with glucose before and after the introduction of ICO for the long dwell.

The UF values reported represent mean values calculated over variable time periods, as indicated in more detail in the text and figures.

All patients except one are on APD, likely due to the availability – starting in 2016 – of new Remote Patient Management (RPM) platforms.

All APD patients performed their final drainage manually in a seated position, while the patient on CAPD carried out all exchanges via Video-dialysis under the supervision of a center-based dialysis nurse [3].

The cases are presented in chronological order.

The clinical decisions taken were guided by individual patient-specific factors, detailed in each case report. As all interventions were part of routine clinical care, the relevant Ethics Committee deemed that no formal review was required beyond ensuring patient anonymity and obtaining informed consent for treatment and publication of anonymized data.

Since these observations derive from routine clinical practice, some otherwise relevant information – such as residual diuresis and its variations, peritoneal permeability assessment, and changes in diuretic therapy – was not recorded. This limitation does not affect the validity of the observations, as they were made prior to any therapeutic changes and under an unchanged dialysis prescription. This condition allowed for a reliable comparison of UF achieved with glucose before and after switching to daytime dwell with ICO. Statistical comparison was limited to Case 3, in which mean UF values recorded over eight consecutive weeks were compared across the five dialysis treatment days (Monday to Friday). Given the small number of data points, the nonparametric Kruskal-Wallis test

for paired data was applied.

Cases Description

Table 1 summarizes the clinical characteristics and dialysis prescriptions of the patients.

All patients started with PD as their first renal replacement therapy, although the observed phenomenon occurred at treatment initiation (incident patient) only in Case 2.

CLINICAL CASE	1	2	3	4
AGE (at start PD -yrs-)	53.9	47.1	72.3	60.5
GENDER	M	M	M	M
ESRD	DM	IgAN	NS	NS
BSA (m ²)	2.25	1.81	1.72	1.68
RESIDUAL GFR (ml/min)	0	6	<3	<3
INITIAL PD PRESCRIPTION WITH FULL ABDOMEN (24 hrs a day)				
PD modality	APD	APD	CAPD	APD **
NIGHT	15 L – 2.27% *	10 L – 1.36%	ICO (1.5 L)	10 L-1.36 / 5L-2.27%
DAY	ICO (1.5 L)	ICO (1.0 L)	(2 L- 2.27%) × 2	ICO (1.0 L)
SUBSEQUENT PD PRESCRIPTION				
TIME OF INTERVENTION (months) ***	53.7	0.72	8.2	11.2 **
NIGHT	15 L – 2.27%	10 L – 1.36%	EMPTY	10 L -1.36 / 5 L-2.27%
DAY	EMPTY	EMPTY	(2 L – 2.27%) × 3	ICO – 6 hrs
FOLLOW-UP				
STOP PD (months)	68.1	4.6	60.4	NO
REASON	HD (social)	Transplant	Death	IN PD

Table 1. Patient's characteristics, dialysis prescription with ICO and, after the occurrence of UFF, without ICO for the entire day (Cases 1–3) or for part of the day (Case 4). *Occasional use of 5 L of 3.86% glucose solution. **The PD prescription illustrated refers to the reintroduction of ICO with manual drainage at midday. DM: diabetes mellitus; IgAN: IgA Nephropathy, NS: Nephroangiosclerosis. * It is the time between the start of the PD and the observed phenomenon.**

Clinical Case 1 – Unexpected Increase in Nocturnal UF Following Discontinuation of Daytime Icodextrin Dwell in an APD Patient

The patient initially started peritoneal dialysis on CAPD in another country. After 33 months, he switched to APD (15 L of 2.27% glucose solution) with an ICO daytime dwell (Continuous Tidal Peritoneal Dialysis, CTPD), drained at the start of the evening cyclor session. Despite initially satisfactory UF, both nocturnal and daytime UF progressively declined during APD. After an additional 5 months, due to poor adherence to fluid and salt intake restrictions (despite excellent compliance with dialysis therapy), an arteriovenous fistula (AVF) was created. However, due to severe peripheral vasculopathy, fistula maturation was difficult. In the following months, a combined treatment was initiated, consisting of daily APD and once-weekly HD. Because of persistent non-compliance with dietary restrictions, presence of anuria, reduced cardiovascular tolerance to HD, and poor AVF maturation, HD frequency had to be increased to twice weekly, and APD continued daily. Additionally, 5 liters of 3.86% glucose solution were intermittently used (at least once per week). Over time, AVF function improved, along with more effective HD clearance. Consequently, 54 months after starting PD, the dialysis prescription was modified by discontinuing the daytime ICO dwell (Nightly Tidal Peritoneal Dialysis, NTPD).

Within a few days, a significant increase in nocturnal UF was observed, rising from 642 ± 158 mL/session to 1.130 ± 222 mL/session (+76.4%), eliminating the need for the 3.86% glucose solution.

Moreover, the improved UF achieved with the NTPD regimen allowed for a reduction in UF during HD, improving HD tolerance, although body weight remained essentially unchanged due to

persistently high fluid intake. The data relating to haemodialysis parameters are shown in Figure 1. The UF increase was sustained until the patient was definitively transferred to HD, due to social reasons, 14 months after reintroducing a daytime empty abdomen. The average UF during the month preceding drop-out from PD was still 1.1342 ± 138 mL/die.

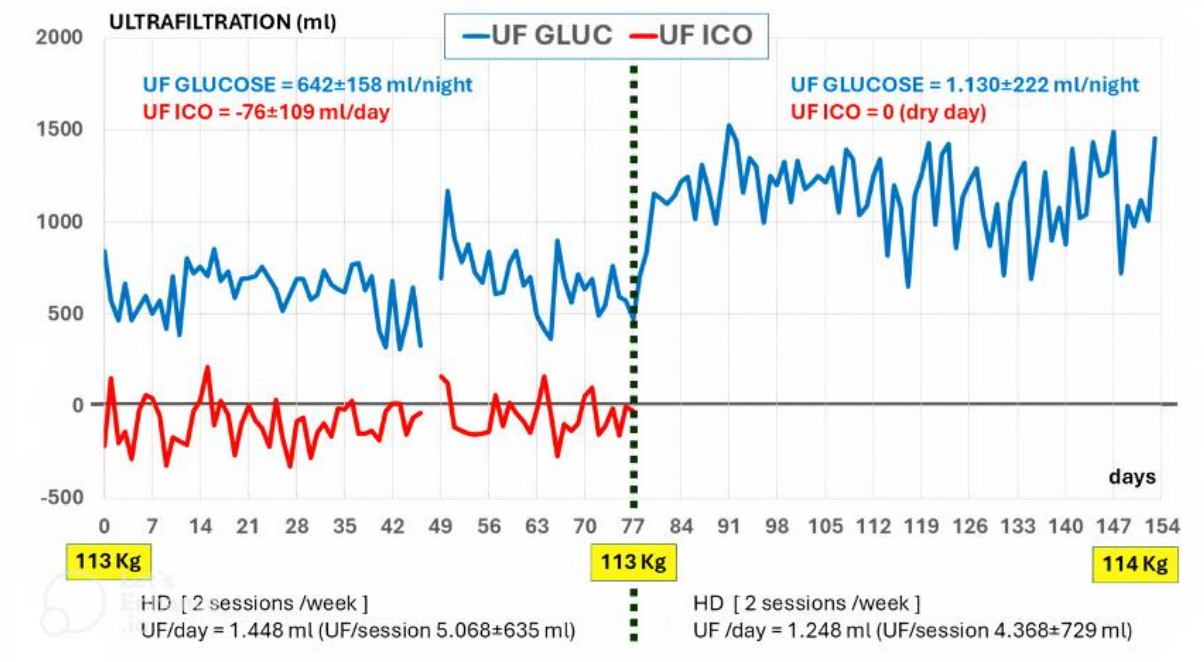


Figure 1. Clinical Case 1. Daily nocturnal (glucose) and daytime (ICO) UF derived from Sharesource data, comparing mean UF during the 10 weeks prior (nocturnal UF 642 ± 158 ml; daytime UF -76 ± 109 ml) and the 10 weeks following icodextrin discontinuation (nocturnal UF increased to 1.130 ± 222 ml). In both periods, two HD sessions per week (mainly UF) were performed. The greater glucose UF after switching to an empty abdomen translated into a reduced UF during HD sessions, but did not result in a reduction of body weight, which remained essentially unchanged.

Clinical Case 2 – Unexpected Reduction of Nocturnal UF at the Start of Dialysis Treatment (Training Phase) Associated with the Use of Icodextrin for Daytime Dwell and Resolved by Restoring an Empty Abdomen During the Day

The patient initiated renal replacement therapy with an incremental Continuous Cycling Peritoneal Dialysis (CCPD) prescription (5 L of 1.36% and 5 L of 2.27% glucose solution, and 2.5 L of ICO for the daytime dwell). In the days immediately following the start of PD, during home training, a gradual reduction of UF was observed not only during the icodextrin daytime dwell but also during the nocturnal glucose exchanges (Figure 2). UF became negative, requiring – without benefit – an increase in glucose concentrations. UF returned to baseline values after the usual 1-2 day interruptions of training (training was suspended during the weekend), but decreased again upon resumption in the following days. Definitive discontinuation of ICO daytime dwell, after 16 days, allowed restoration of adequate nocturnal UF with a reduced glucose concentration (10 L of 1.36%) until kidney transplantation, which was performed 5 months after initiation of dialysis (Figure 2).

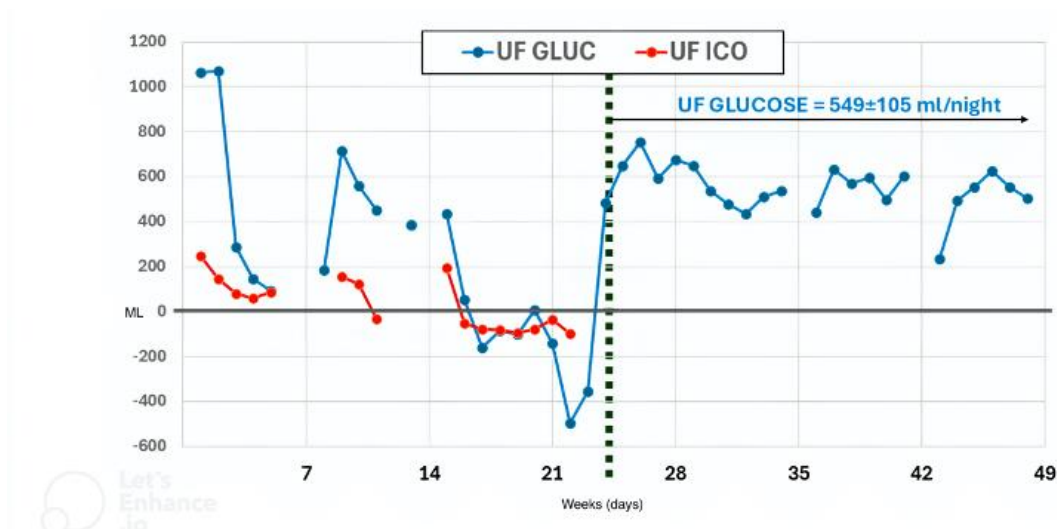


Figure 2. Clinical Case 2. Incident patient at the start of APD training. During the first two days, PD prescription was 5 L of 1.36% and 5 L of 2.27% of glucose, then reduced to 10 L of 1.36% from day 3 onwards, until transplantation. The interruptions shown in the graphic correspond to treatments skipped during training and subsequently due to the incremental PD prescription (6 days per week). A continuously full abdomen resulted in a progressive worsening of nocturnal UF (in this case also affecting icodextrin), which was resolved by switching to an empty abdomen. However, as shown, the first day after skipping a session was associated with lower UF, likely due to “reconstitution” of the residual volume.

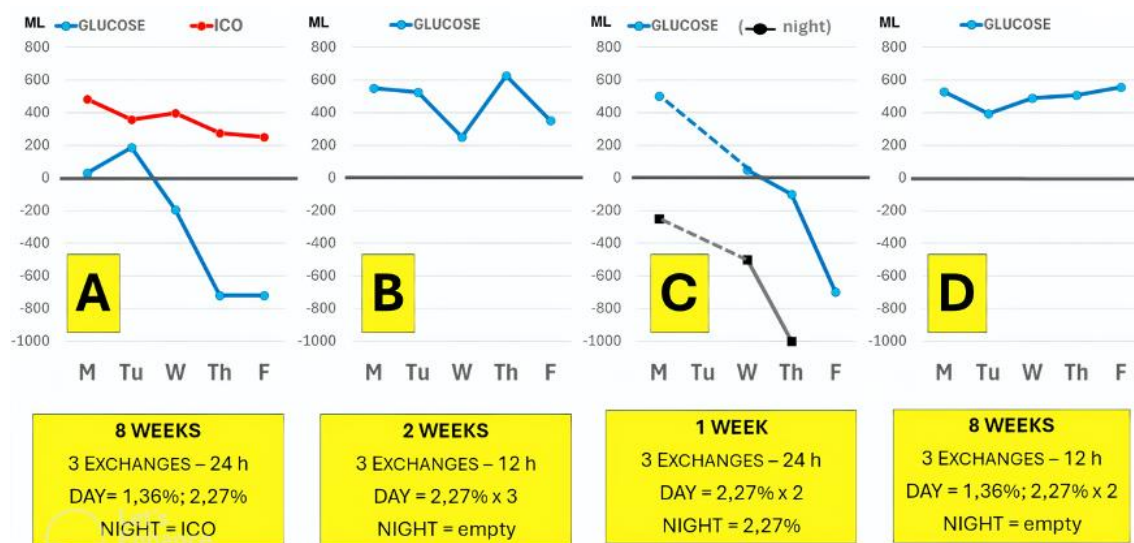
Clinical Case 3 – Is the Issue the Icodextrin Solution or a Continuously Full Abdomen?

The patient, with severe ischemic dilated cardiomyopathy and limited autonomy, initiated renal replacement therapy with CAPD via telemedicine (two daytime 4-hour exchanges with 2 L of 2.27% glucose solution each, and 1.5 L of icodextrin for a 16-hour nocturnal dwell). Exchange duration was defined according to a pre-established telecare schedule. To preserve residual renal function and due to the unavailability of the telecare caregiver on weekend, the Saturday dialysis scheme was limited to two exchanges (2 L of 1.36% from 8:00 to 12:00 and 1.5 L of ICO from 12:00 to 20:00), while from Saturday evening to Monday morning the patient remained with an empty abdomen. After several weeks, a pattern of insufficient ultrafiltration (UF) emerged, showing a weekly trend. Specifically, UF gradually declined from Monday to Friday, particularly during daytime glucose dwells (Table 2, Figure 3A).

Based on previous experience, the icodextrin exchange was therefore discontinued, maintaining an empty abdomen overnight and increasing the number of daytime exchanges from two to three 4-hour exchanges using 2.27% glucose solution. Over the following two weeks, mean daily total UF improved significantly, increasing from -42 ± 299 ml/die to $+425 \pm 347$ ml/die after 1 week and $+567 \pm 149$ ml/die after 2 weeks following the restoration of an empty abdomen. Importantly, the progressive reduction of UF from Monday to Friday disappeared (Figure 3-B). To optimize depuration by minimizing telemedicine contacts, an attempt was made to reintroduce a nocturnal dwell with 2.27% glucose. Although reduced UF was expected during the nocturnal glucose dwell, the phenomenon observed with icodextrin – progressive reduction of daytime glucose UF from Monday to Friday – recurred (Figure 3-C). The patient therefore returned to the Daytime Ambulatory Peritoneal Dialysis (DAPD) scheme with three daytime exchanges of 1.36%, 2.27%, and 2.27%, maintaining an empty abdomen overnight. Mean UF values over the following 8 weeks are reported in Table 2 and Figure 3-D.

SOLUTION (type)	PRE (NIGHT FULL) – 8 weeks			POST (NIGHT EMPTY) – 8 weeks		
	1,36%	2,27%	ICO	1,36%	2,27%	2,27%
DWELL TIME (hrs)	4	4	16	4	4	4
Monday	-294 ±126	325 ±75	481 ±79	-121 ±59	269 ±134	381 ±66
Tuesday	38 ±127	150 ±168	356 ±138	-181 ±97	225 ±175	350 ±139
Wednesday	-156 ±95	-38 ±48	397 ±77	–	125 ±122	363 ±86
Thursday	-363 ±54	-356 ±77	275 ±158	-163 ±82	325 ±103	344 ±88
Friday	-425 ±130	-294 ±95	250 ±125	-144 ±95	356 ±126	344 ±81
	p<0,001	p<0,001	p<0,01	N.S.	p<0,05	N.S.
DWELL TIME (hrs)	4	NO	6	NO	4	4
Saturday	-263 ±162	–	406 ±88	–	181 ±75	319 ±86

Table 2. Mean of UF values over 8 consecutive weeks for each exchange, before and after icodextrin discontinuation. Differences between weekdays were all significant in the PRE period, whereas in the POST period, only the difference in UF recorded during the second exchange remained significant (Kruskal-Wallis test).



Clinical Case 4 – Nocturnal UF With Glucose and Daytime UF With Icodextrin in APD Are Preserved by Restoring an Empty Abdomen for Part of the Day (“Midday Icodextrin Drainage”)

The patient, on NTPD for 7 months, introduced a daytime icodextrin dwell for depurative needs (CCPD). Nocturnal UF decreased rapidly (from 682 ± 85 ml/night in the two preceding weeks to progressively -12 ml after 4 days of the daytime dwell), without compensation from daytime UF achieved with icodextrin (ranging from 146 to 361 ml), resulting in a reduction of total UF (Figure 4-A). After 4 days, the patient returned to the NTPD regimen, with restoration of previous UF values (667 ± 105 ml/night in the following two weeks). Three months later, icodextrin was reintroduced but drained manually after 5-6 hours of dwell time (duration determined by the patient’s work

needs). Nocturnal UF decreased slightly, but total UF increased significantly due to the considerable UF obtained with ICO (from 146 to 361 ml/die with a full abdomen daily to 279 ± 103 ml/die with a midday icodextrin drainage) (Figure 4-B).

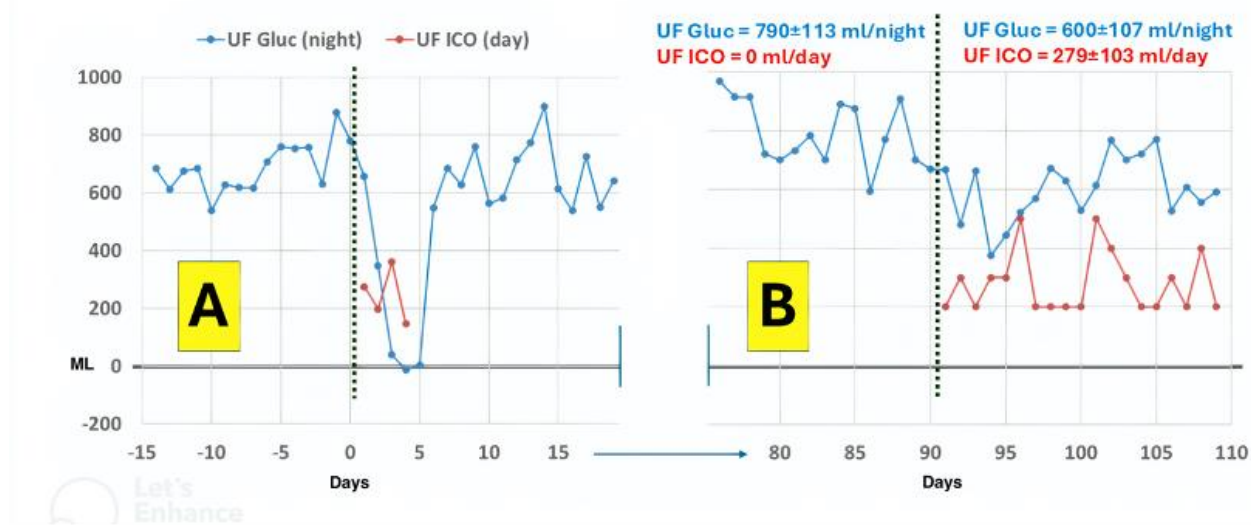


Figure 4. Clinical Case 4. Patient on APD. Box A: initial introduction of icodextrin, then discontinued after only 4 days due to marked reduction of nocturnal UF. The pattern is consistent with that described in the other cases. Box B: Ninety days after the first attempt, a final icodextrin fill was again prescribed which the patient manually drained at midday (according to professional activity), generally after a 5-6 hour of dwell. Manual drainage was recorded by the patient on a dedicated chart after collection in a graduated container. Values are therefore approximated to 100 ml, but there is no overestimation due to overflow as the filled volume is recorded by the Cyclor.

Discussion

Ultrafiltration failure represents an important cause of dropout from peritoneal dialysis, with its incidence increasing over time due both to the progressive decline in RRF and to structural and functional alterations of the peritoneal membrane [4]. In general, UFF is managed by increasing glucose concentrations and fill volumes, as well as by using ICO for the long dwell [1, 5].

In all reported cases, a continuously full abdomen achieved through a daytime (in APD) or nighttime (in CAPD) icodextrin dwell was associated with a significant and unexpected reduction in UF obtained during the remaining part of the day with glucose (nocturnal cycles in APD and daytime dwells in CAPD). Another feature is the gradual yet rapid onset and disappearance (within 2-3 days) of this phenomenon (Figure 5). This finding is unexpected both because the condition of a constantly full abdomen should prevent the repeated formation of residual volume (RV) – which is inevitably reabsorbed during daytime hours with an empty abdomen – and because, in all these cases, a final manual drainage (performed in the sitting position) was prescribed to avoid icodextrin drainage occurring while the patient was still supine. In all cases, the glucose concentrations used after discontinuation of ICO dwell remained unchanged (in Case 1 and Case 2, they were even reduced). At last, regarding the magnitude of the observed phenomenon: the variation in UF generated by glucose after introducing the continuously full abdomen with icodextrin ranged from -43% to over -100% (in three of the four cases, glucose UF became negative), corresponding to an absolute daily value reduction of 488 ml to 1200 ml.

The four cases reported here illustrate how adequate UF could be restored simply by maintaining an empty abdomen for part of the day, and how this effect occurred within a relatively short timeframe. The key question is why the introduction of a long dwell with icodextrin (and, in Case 3,

even with glucose) was occasionally associated with reduced glucose ultrafiltration during the remaining dwells/cycles. Although the underlying pathophysiology could not be thoroughly investigated in routine clinical practice, the available data suggest the following considerations.

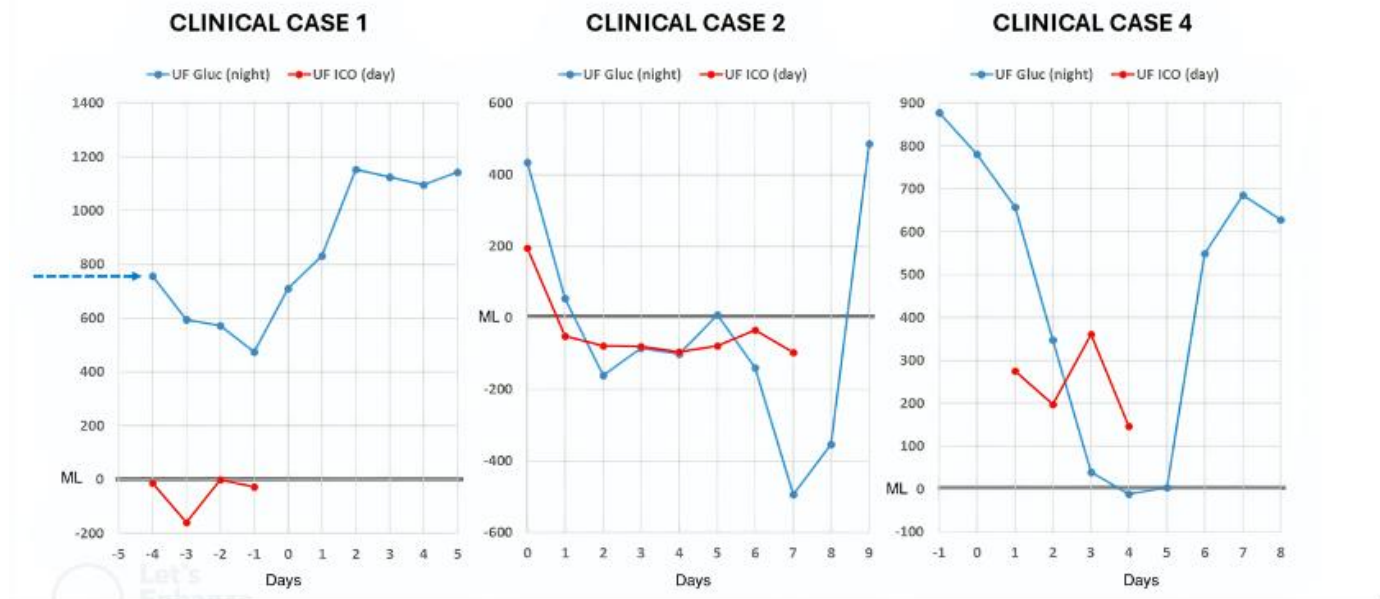


Figure 5. Daily UF generated by glucose and icodextrin at the times of their introduction and discontinuation. As shown, changes occur within 2-3 days and are considerable. For each day, UF values are derived from the initial drainage and the subsequent nocturnal session.

Type of solution and role of icodextrin

The use of icodextrin is recommended for long dwells, particularly in patients with high peritoneal transport status [6]. Several reports have demonstrated greater efficacy when icodextrin is employed in more than one exchange per day. The first two cases appear to suggest a causal role of icodextrin in triggering, through unknown mechanisms, the observed phenomenon. However, in the third case, the progressive reduction of glucose UF recurred even when glucose – not icodextrin – was used for the long nighttime dwell. Most notably, in clinical Case 4, the negative effect disappeared when icodextrin was manually drained after 5-6 hours of dwell, suggesting that the underlying determinant of the phenomenon was the continuously full abdomen, regardless of the type of solution employed. Finally, although it is well established that UF with icodextrin can vary considerably between individuals [7] and is influenced by peritoneal transport status [6], intraperitoneal pressure, dwell duration, and PD modality [8–10], effects such as those described here on glucose UF, have not previously been reported.

Residual Volume

Intermittent treatments entail the continuous reformation of RV, which may reduce UF, while an excessively elevated RV can impair UF during continuous treatments [11]. In the reported cases, the opposite was observed. After a short period with an empty abdomen – even if only occasional, such as during holidays (Clinical Case 3) or during training (Clinical Case 2) – nocturnal UF returned to “high” levels, only to decrease again in the following days. This does not imply that RV reformation did not occur, but rather that the increase in UF was sufficient to outweigh its effect.

Furthermore, catheter displacement, even if only temporary, has always been ruled out as the most frequent cause of increased VR. Finally, it should be emphasized that all APD patients described had been trained to perform both the initial drainage and, most importantly, the final drainage in the sitting position.

Alterations in peritoneal permeability

Peritoneal permeability alterations are generally considered an important cause of UFF, typically associated with “irreversible” structural changes of the membrane. In contrast, the rapid recovery of UF and the “normalization” of permeability indices in our cases would suggest the predominance of functional rather than structural mechanisms.

Peritoneal membrane rest

It has long been known that temporary discontinuation of PD (for 4 weeks or longer) with transfer to HD allows recovery of UF and improvement of peritoneal permeability [12]. In our cases, PD was never discontinued.

Increased lymphatic absorption or leakage

An important cause of UFF – although difficult to assess and usually diagnosed by exclusion – is increased lymphatic absorption, for which APD with a daytime empty abdomen is often recommended, a strategy that also proved effective in our experience. However, in the cases reported here, the main issue was not the UF of the daytime dwell, but rather that of nocturnal APD, or, in clinical Case 3 (CAPD), of the daytime glucose dwells. This observation suggests a “time-dependent” leakage or increased lymphatic absorption. In all patients, conventional leakages (pleuroperitoneal communication, subcutaneous leakage, hydrocele/hernia) were excluded, whereas lymphatic absorption was not evaluated. Only one outdated study [13] compared UF in seven unselected patients transferred from CAPD to DAPD (nighttime empty abdomen), hypothesizing lymphatic absorption as a possible cause of reduced UF. However, UF did not vary significantly (728 ± 377 ml with 4 exchanges vs 761 ± 288 ml with 3 exchanges and an empty nighttime abdomen), although there was a significant but modest reduction in daily glucose load (from 146 ± 37 to 131 ± 37 g, $p < 0.01$). By contrast, our cases were all selected based on the marked UF variation occurring when a continuously full abdomen with icodextrin was adopted.

Estimation of the phenomenon and open issues

Overall, considering the number of patients initiated on PD in the two Centers, the incidence of this phenomenon can be estimated at <5% of PD patients, although it is possible that the same mechanism may act, to a lesser degree, in a larger number of individuals. In the past, when icodextrin was not available, a common solution to UFF was the midday drainage of the last fill. At that time, it was, in a sense, natural to attribute reduced UF to glucose reabsorption. However, the observations made with icodextrin suggest that, in rare cases, other time-dependent factors may also play a role in influencing dialysate reabsorption.

Conclusions

In conclusion, in rare cases of UFF, restoring an empty abdomen for several hours may rapidly restore adequate UF. The aim of our work is not to propose a solution to the problem of UFF but, given its practical relevance, to suggest reconsidering – when UF represents the most critical issue – the use of an empty abdomen for part of the day, according to dialysis prescriptions used in the past. It is possible that different factors, with variable impact from patient to patient, may have contributed to the genesis of such cases. In our opinion, this phenomenon warrants further investigation through larger observational studies or, ideally, randomized controlled trials.

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