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Value of accelerated peritoneal examination time in pediatric nocturnal intermittent peritoneal dialysis

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Abstract

Introduction: In clinical practice, most of the pediatric dialysis patients lack optimal dwell time resulting in suboptimal ultrafiltration (UF) and solute clearance. The appropriate dwell time may be possible to delineate from the Accelerated Peritoneal Examination (APEX) time, derived from a standardized peritoneal equilibration test (PET).

Objectives: This primary objective of the study aims to determine the utility of APEX time for optimal UF in pediatric patients on nocturnal intermittent peritoneal dialysis (NIPD). The secondary objective is to analyze the Kt/V and creatinine clearance L/week/1.73m^2 (CrCl) after approximation of optimal dwell time.

Methodology: The study retrospectively analyzed pediatric peritoneal dialysis patients (age range: 1-14 years), from January 2001 to April 2016 followed up at King Abdul Aziz Medical City, Riyadh, Saudi Arabia, Pediatrics Dialysis Unit. This was a retrospective case series based on chart review. Bivariate descriptive analysis was carried out to report the difference in the ultrafiltration before and after the APEX time calculation.

Results: A total of 15 pediatric patients were enrolled in the study. The mean UF significantly improved after determining the dwell time based on the calculated APEX time (189.4 ±44.7 ml vs 140.5±47.1 ml, p<0.001). Additionally, the mean UF remarkably improved in both low/low-average and high/high-average peritoneal transporters (p=0.006). By analyzing small molecule clearance (Kt/V, and CrCl) in relation to peritoneal transporters, CrCl significantly improved in low/low average peritoneal transporters (p<0.001) whereas, it deteriorated (p<0.001) in high average peritoneal transporters. On the other side, Kt/V did not vary (p=0.93) between the peritoneal transporters.

Conclusion: APEX time in NIPD can be helpful in maximizing the ultrafiltration and CrCl especially in patients with low and low-average transporters. The APEX time also provided valuable input in optimizing the UF in high and high average transporters.

Introduction

Pediatric peritoneal dialysis patients depend on optimal dwell time for adequate UF and clearance. In clinical practice, most of the pediatric dialysis patients lack optimal dwell time and resulting in suboptimal UF. It is possible to delineate the appropriate dwell time from the APEX time as derived from a standardized PET [1-3]. The APEX time is represented by the intersecting point between urea and glucose equilibration curves [3]. It is evidenced that optimal APEX time approximates the actual dwell time for good UF, and moreover, twice the APEX time may lead to good clearances [3-6]. The value of APEX time is well recognized and appreciated in adapted peritoneal dialysis (combination sequences of short and long dwells within one peritoneal dialysis session), However, in NIPD it may be a potential parameter in maximizing the UF. Fischbach et al have demonstrated clearly the effectiveness and determination of APEX time in automated adapted peritoneal dialysis. Furthermore, the benefits of varying between short and long dwell times to balance between UF and clearance has been well described in children [3-7]. In NIPD, however, the dwell time cannot be varied. The approximation of the dwell time utilizing the APEX time may aid in optimizing UF and possibly improve the clearance in low peritoneal transporters.

Objectives of the study

The study aimed to analyze the value of APEX time in optimizing UF in NIPD.

Secondary objectives

By approximating the optimal dwell time for ultrafiltration according to the APEX time, the status of clearance namely Kt/V and CrCl were analyzed after three months.

Methodology and materials

This is a retrospective case series based on chart review. Peritoneal dialysis details were derived from the digital memory cards

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incorporated in the dialysis machines (Fresenius cycler-sleep safe (V2.2X). Both paper chart review (for patient data) and electronic chart review (for lab data) were assessed. All the recruited patients not underwent PET previously and had NIPD with short cycles (9-11 cycles) using bicarbonate-based physiological solution (1.3 % bicavera, Fresenius Medical Care, Homburg, Germany) for 10 hours. In addition, all patients routinely underwent three monthly peritoneal Kt/V and peritoneal CrCl as there was no significant residual renal function (<100 ml/m^2/day of urine output) noted in all our patients. Historical dwell time used during the dialysis were taken as controls. No patients had day dwell during the dialysis. Mean UF was analyzed over the last 30 days. Additionally, all patients underwent standardized PET and APEX time calculation using a standard graphical chart. Mean UF was further analyzed over the subsequent 30 days. The difference in the outcome of ultrafiltration were analyzed in patients before and after APEX time and its relationship with peritoneal membrane status was also assessed. After 3 months, peritoneal Kt/V and CrCl were performed for all subjects. Exclusion criteria for the study included missing data, history of peritoneal dialysis of less than three months, history of peritonitis within three months and patients with peritoneal membrane failure or features of encapsulated peritoneal sclerosis

Study area/setting

The study retrospectively analyzed peritoneal dialysis patients aged 1-14 years from January 2001 to April 2016 followed up in King Abdul aziz Medical City, Pediatrics Dialysis Unit, Riyadh, Saudi Arabia.

Data collection methods

Routine PET performed as per standard protocol, in which dialysate urea, glucose, and creatinine values (0, 2, 4 hours), overnight dialysate sample, blood urea, glucose, and creatinine (2 hours) were measured from the lab. All the dialysis details were incorporated into the online system to assess membrane status, CrCl, and Kt/V. APEX time is calculated from the standard graphical chart. Mean ultrafiltration was analyzed over the 30 days from digital memory card incorporated in dialysis machines. All the information's were entered in the peritoneal examination charts.

Data analysis

Bivariate descriptive analysis was carried out to report the difference in the ultrafiltration before and after the APEX time calculation. Results were reported in terms of mean and standard deviation. SPSS version 20 used for analysis. A p value <0.05 was considered to show a statistically significant difference.

Ethical considerations

This study was approved by the Institutional Review Board at King Abdullah International Medical Research Centre. A copy of the ethical approval is available for review by the Editor.

Results

A total of 15 pediatric peritoneal dialysis patients were enrolled in the study. There were 10(67%) girls and 5(33%) boys with a female to male ratio of 2:1 (Table 1). Their ages ranged from 1-12 years (6.3 ± 3.1 years). The dwell time used before the APEX time ranged between 40 -55 minutes with a mean of 46.1 ± 4.6 min (Table 1). The calculated APEX time for these patients ranged between 36- 78 minutes, with a mean of 54.7 ± 16 min. More than half of the patients (n=8, 53%) were low/low-average transporters, and remaining patients (n=7, 46%) were high/high average transporters.

Out of 15 patients enrolled in our study, mean UF significantly improved from 140.5 ± 47.1 to 189.4 ± 44.7 after incorporating the calculated APEX time into the dwell time (Table 2). Moreover, mean UF remarkably improved more in low/low-average as compared to high/high-average peritoneal transporters (Table 3). The mean (SD) were n= 8, 70.4 ±27.7 for low/low-average and n=7, 24.4 ±25.8 for high/high-average peritoneal transporters. In relation to clearance, Kt/V did not change (p=0.16) before and after APEX time (Table 2) whereas in relation to CrCl, significant improvement (p=0.04) was noted in our study (Table 2). The mean (SD) were n=15, 46.8 ± 7. By analyzing small molecule clearance (Kt/V, and CrCl) in relation to peritoneal transporters, CrCl significantly improved (p<0.001) in low/low average peritoneal transporters (Table 3). The mean (SD) were n= 8, 14.8 ± 6.6 whereas, it is deteriorated (p<0.001) in high average peritoneal transporters (n= 7, mean (SD) -3.3 ± 1.9). On the other side, Kt/V did not vary (p=0.93) between the peritoneal transporters (Table 3). The mean (SD) were n=8, -0.13 ± 0.35, for low/low-average peritoneal transporters and n= 7, -0.14 ± 0.38 for high/high-average peritoneal transporters.

Discussion

Most of the studies in pediatric peritoneal dialysis patients are inconclusive on optimal dwell time for better UF and clearance. The dwell time is principally based on individual peritoneal membrane characteristics [7]. Adult peritoneal dialysis patients, who routinely undergo PET, have their peritoneal dialysis prescription based on peritoneal membrane transport status but in contrast, pediatric peritoneal dialysis patients have practical difficulty in performing standardized PET. Hence, most of pediatric peritoneal dialysis patients

Table 1. Clinical and biochemical profile of APEX time.

	Mean ± sd	Min	Max
Age (years)	6.3 ± 3.4	1	12
Kt/V (before APEX time)	2.2 ±0.4	2	3
Kt/V (after APEX time)	2.1±0.3	2	3
Dwell Time (Minutes) Before APEX calculation	46.1 ± 4.6	40	55
Dwell Time (Minutes) after APEX calculation	54.7 ±16.0	36	78
Mean ultrafiltration before APEX time	140.5 ± 47.1	65	230
Mean ultrafiltration after APEX time	189.4 ±44.7	112	274
CrCl L/week/1.73m2 (before APEX time)	40.5±7.7	22	52
CrCl L/week/1.73m2 (after APEX time)	46.8 ±7.0	40	63

APEX: Accelerated Peritoneal Examination time; Kt/v: measures a change in the concentration of urea; CrCl: Creatinine clearance; SD: Standard deviation; Min: Minimum; Max: Maximum.

Table 2. Relationship between mean ultrafiltration, Kt/v and CrCl before and after APEX (N=15).

	Mean ± sd	p-value
Mean ultrafiltration Pre-intervention	140.5 ±47.1	<0.001
Mean ultrafiltration Post intervention	189.4 ± 44.7	
Kt/V Pre-intervention	2.2 ± 0.4	0.16
Kt/V Post intervention	2.1 ± 0.3	
CrCl L/week/1.73m^2 Pre-intervention	40.5 ± 7.7	0.04
CrCl L/week/1.73m^2 Post intervention	46.8 ± 7.0	

Kt/v: measures a change in the concentration of urea; APEX: Accelerated Peritoneal Examination time;CrCl: Creatinine clearance; SD: Standard deviation)

Table 3. Relationship between mean ultrafiltration, Kt/v and CrCl withlow/low average and high/high average transporters.

	Low / Low Average (n=8)			High / High Average (n=7)			
Pre- Post intervention difference	Mean	±	sd	Mean	±	sd	p-value
Mean Ultrafiltration	70.4	±	27.7	24.4	±	25.8	0.006
Kt/V	-0.13	±	0.35	-0.14	±	0.38	0.93
CrCl L/week/1.73m^2	14.8	±	6.6	-3.3	±	1.9	<0.001

Kt/v: measures a change in the concentration of urea; CrCl: Creatinine clearance; SD: Standard deviation.

have their prescription based on an assumption of high transport status [8-12]. Younger children have been described to have high peritoneal membrane transport status as compared to older pediatric populations [8]. But a significant number (8 out of 15) of our patient populations were low/low-average peritoneal transporters, and remaining seven were high/high-average peritoneal transporters. Further, pediatric populations are expected to grow and peritoneal membrane status tends to change over the years. Hence, it is important to do the PET test in children and delineate the appropriate dwell time in order to optimize the peritoneal UF and clearance.

Shortening of dwell time has more pronounced effects on CrCl than on Kt/V because creatinine equilibrium across the peritoneal membrane is slower than that of urea. This is more evident and clinically relevant in low peritoneal membrane transporters. Further, peritoneal membrane slow transporters have sustained osmotic gradient and tend to have better UF and poor small molecule clearance. In contrast, high peritoneal membrane transporters have a rapid osmotic gradient and tend to have better small molecule clearance and poor UF [13-17]. Importantly, osmotic gradient tends to shift only after maximizing the dwell point, hence with optimization of dwell time using APEX time, low/and high peritoneal transporters tend to work efficiently well in relation to UF as compared to CrCl. The above hypothesis, as clearly demonstrated by Fischbach, *et al.* [3,4] explained the effectiveness and determination of APEX time in automated adapted peritoneal dialysis. But so far up to our knowledge none of the studies have been published in describing the value of APEX time in NIPD. It is prudent to identify the appropriate APEX time and explore the significance of its utilization in terms of clearance and UF in NIPD. In addition, by approximating the optimal dwell time, sodium removal can also be enhanced and potentially improves hypertension and fluid overload [18,19].

This study highlights the change in mean dwell time (based on APEX time) from 45 minutes to 62 minutes, led to significant improvement in the mean UF in patients with low/low-average peritoneal membrane transporters (Table 3). Some other studies have also described that low average peritoneal membrane transporters tend to have efficient UF as compared to other peritoneal membrane transporters [13-15]. In addition, our patients with low/low average peritoneal membrane transporters demonstrated statistical significance in CrCl. Other published studies suggesting that CrCl may deteriorate in low peritoneal membrane transporters and Kt/V may not vary significantly between the peritoneal membrane transporters [13,20-23]. In this study, Kt/V did not vary statistically (p=0.93) both in low/low average and high/high average peritoneal membrane transporters and it is possibly due to the subtle difference between the approximate and calculated dwell time especially in high peritoneal membrane transporters. The approximation of APEX time may have played a vital role in improving the UF and CrCl in low peritoneal membrane transporters noted in our study. On the other side, slow osmotic dissipation in low transporters may have reduced the urea clearance (Kt/V) but it is not evident in this study as well as other published studies [20,22-25]. Mean UF also improved significantly in the patients with high to high average transporters but it is not so with CrCl which is significantly deteriorated. But on the contrary, Rocco, *et al.* describes good small molecule clearance in high peritoneal membrane transporters [20]. Hence from this study, it is possible that by shortening the dwell time, CrCl is significantly affected and thus the patient with high/high average transporters may need a day dwell with icodextrin or shift to adapted peritoneal dialysis to balance between UF and clearance [3,21-28].

Fischbach, *et al.* [3-5] identified the importance of the APEX in adapted automated peritoneal dialysis and concluded both short and long cycles are needed to maintain the balance between UF and the clearance. However, in our study incorporation of calculated APEX time into dwell time significantly improved the mean UF in NIPD but did not affect both Kt/V and CrCl in patients with low/low average peritoneal membrane transporters. Larger randomized trials are needed to examine the effectiveness of APEX time and its role in improving the UF in children on NIPD.

Conclusion

APEX time in NIPD can be useful in maximizing the UF and CrCl especially in patients with low and low-average transporters. Also, APEX time gives a valuable support to high and high average transporters in optimizing the UF. Limitations of our study are that it is a single center study with a relatively small number of patients.

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Consent

Ethical approval for the publication of this article is obtained. A copy of the ethical approval is available for review for the Editor.

Conflict of interest

The authors declare that they have no competing interests.

Authors' contributions

- Mohammed Azar: Data analysis, writing and review of the manuscript
- Wee-Song Yeo: Review of the manuscript
- Aamir Omair: Statistical Review.

Khalid Alfakeeh: Review of the manuscript.

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