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Comparison of the Accuracy of the Novel PrisMax Continuous Renal Replacement Therapy System to the Classic Prismaflex System

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Keywords
Acute kidney injury · Citrate · Continuous hemodiafiltration · Critical care · Dialysis efficiency · Dialysis machine · Hemodiafiltration

Abstract
Background/Aims: We assessed how the novel PrisMax continuous renal replacement therapy (CRRT) system performed in an international multicentre setting. The system has multiple novel tools aiming to increase accuracy and dose delivery. ***Methods:*** Data was prospectively collected from 7 intensive care units in 6 countries. The PrisMax device data logs constituted the raw material and last generation Prismaflex data was used as comparison. Clinical parameters like treatment time, filter life span, downtime as well as prescribed and delivered dose were recorded. ***Results:*** PrisMax delivered/prescribed effluent ratios (mean ± SD) 0.92 ± 0.15 vs. Prismaflex ratios 0.85 ± 0.21, $p < 0.001$; delivered effluent dose (mL/kg/h) was 18.16 ± 12.93 vs. 10.95 ± 10.96, $p < 0.0001$; and (Kt/V) 0.76 ± 0.52 vs. 0.44 ± 0.44, $p < 0.0001$. Moreover, downtime was 27 minutes less for the newer device. ***Conclusion:*** The PrisMax CRRT device outperforms its predecessor with regard to dose delivery and accuracy.

Introduction

Since the seminal paper by Ronco et al. [1] showing that survival among AKI patients was improved by increased continuous veno-venous hemofiltration dose, most studies have failed to replicate those findings. Two large randomized controlled trials, the Acute Renal Failure Trail Network (ATN) and RENAL trials from the US and Australia, failed to detect differing mortality between lower- and higher dose regimens [2, 3]. A caveat regarding both ATN and RENAL is the fact that these studies failed to measure antibiotic levels in the higher- and lower dose arms.

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Even if the optimal continuous renal replacement therapy (CRRT) dose is unknown, there must be a lowest threshold; under this theoretical effluent-based dose, outcomes will be affected. Based mostly on ATN and RENAL, the KDIGO AKI Clinical Practice Guideline recommends delivery of an effluent dose of 20–25 mL/kg/h in CRRT [4].

This KDIGO consensus statement regarding delivered CRRT dose [4] suggests that prescribed dose needs to be higher in order to reach that same delivered dose. Indeed, clinical practice seems to differ from how the dose is delivered under research study conditions. In the former, over 80% of the prescribed dose was delivered on average [1–3]. In contrast, Venkataraman evaluated CRRT dose delivery and found mean treatment duration to be 16.1 ± 3.5 (mean ± SD) hours per day, leading to a mean effluent flow rate (averaged over 24 h) of 1.4 ± 0.3 L/h [5]. This equated to a mean prescribed and delivered CRRT doses were 24.5 ± 6.7 and 16.6 ± 5.4 mL/kg/h, respectively ($p < 0.000001$); a delivery of 68% of the prescribed dose. Clotting of the extracorporeal circuit was the most common cause of downtime.

The present study evaluates how the novel PrisMax device performed. In a prospective multinational cohort study, we assessed prescribed versus delivered dose; adding historic Prismaflex data for comparison.

Methods

The local Ethics Committee approved the study and due to the observational design need for informed consent was waived. Prior to commencing the run-in of this novel piece of technology, a decision was made to use the PrisMax data for the purposes of research. A previous study describes these findings in full [6].

Study Population

This prospective observational study was performed in 7 intensive care units (ICUs) (Kings College and West Suffolk [UK] 41 filters, CHU Bordeaux [FR] 49 filters, Skåne University Hospital Lund and Malmö sites [SW] 73 filters, Asklepios [DE] 35 filters, Vicenza St Bortolo [IT] 23 filters and The Alfred [AUS] 84 filters) in 6 countries. In total, 305 filters were run between March and June 2017. Moreover, historical data from 4,247 filters from the same 7 centres was used as comparison for certain data points; these treatment regimens were carried out between October 2013 and April 2017. Only filters with complete data from the treatment were included in each comparison.

CRRT Training

Nursing staff and physicians underwent an educational program, including an online tutorial and hands-on supervision. PrisMax support was available 24/7 during the study.

Device Settings

Most uses of the PrisMax system utilized the ST-150 filter; out of 305 patients, regional citrate anticoagulation was used in 198 (64.9%), heparin in 35 (11.5%) and nothing in 72 (23.6%) filters. Patients were treated with continuous veno-venous haemodiafiltration 236, continuous veno-venous hemofiltration 61, continuous veno-venous haemodialysis 7 and slow continuous ultrafiltration 1 modes. We lack anticoagulation data regarding the Prismaflex control group.

Treatment Data

The PrisMax device records ongoing data during treatment, these data logs constituted the raw material. Clinical parameters such as treatment time, filter life span, downtime, delivered treatment dose and number and type of alarms were recorded.

Calculation of Delivered/Prescribed Effluent Ratio

The ratio delivered effluent fluid (mL/kg/h) divided by the prescribed was calculated on the novel Prismax runs ($n = 192$) and compared to the historic Prismaflex runs ($n = 4{,}038$).

Also the absolute difference of this ratio to 1 was compared between Prismax and Prismaflex groups. The difference was calculated either as (1 – the actual ratio), if the actual ratio was lower than 1 or (the actual ratio -1) if higher.

Calculation of the Catch-Up Functionality on the PrisMax System

The catch-up function is limited to the patient fluid removal feature only, and solely accounts for downtime during therapy, when the fluid pumps stop due to alarm conditions or bag changes. The cumulative patient fluid removal catch-up volume is calculated by the system as follows. During the downtime pause the system calculates the net amount of effluent that should have been removed based on the prescription during the pause for up to 10 min of inactivity and the actual effluent pump rate is increased to compensate for the missed fluid removal. After the therapy has started again, the effluent pump runs faster for 10 minutes to make up for the loss of patient fluid removal during the pause.

The rate of the increase is dependent on the 3 equations presented below, from which the system will choose the minimum output value.

Condition	Formula
Normal body weight >20 kg	Makeup rate is 0.2 times PFR
Low body weight 8–20 kg	Makeup rate 2ml/h times weight (kg), will never exceed 0.2 times PFR
Low blood flow rate 0.5 times blood flow rate is < PFR	Makeup rate is always limited by the following (PFR + makeup rate) <0.5 times blood pump rate

During this study period, all patients were of the normal weight range and had thus normal blood flow rates and therefore a modified version of the first equation was used ($n = 273$).

Table 1. The delivered/prescribed ratios for the PrisMax system compared to runs on the Prismaflex, and the absolute difference to the ideal ratio 1

	Prismax runs (n = 192)	Prismaflex historic runs = 4,038	Significance: Prismax compared to Prismaflex, p value
Delivered effluent/prescribed effluent ratio, mL/kg/h, mean ±SD; (Q1, median, Q3)	0.92±0.15; (0.91, 0.96, 0.98)	0.85±0.21; (0.85, 0.92, 0.94)	<0.001
Absolute difference of delivered/prescribed ratio to 1, mean ± SD; (Q1, median, Q3)	0.08±0.15; (0.02, 0.04, 0.08)	0.15±0.21; (0.06, 0.08, 0.15)	<0.001

Calculation of Comparative Data on Crude Treatment Dose, Including Kt/V and Downtime

According to the nomogram from the study by Cerda et al., the formula in order to transform ml/h/kg for continuous technique to Kt/V based on urea clearance and generally used in intermittent technique, assuming that 25 mL/h/kg is 1 Kt/V, is as follows [7]:

$$Kt/V = (1-[(1/24) \times (\text{downtime in hours})]) \times ([\text{effluent dose mL/h/kg}]/25)$$

Downtime can be defined in many ways depending on when the treatment is started and stopped. In this calculation, downtime is strictly defined as the cumulative time during which the blood pump is in the stopped state between the point of time when the START-button is pressed and the point of time when the STOP-button is pressed.

Statistical Analysis

Data was analysed by SAS 9.4; (SAS Institute Inc., Cary, NC, USA) and Excel (Microsoft, Richmond, VA, USA). Descriptive data is expressed in means ± SD for normally distributed data and median and lower, upper quartiles for non-normally distributed data. Wilcoxon Rank Sum test was used for the comparisons between the Prismax and the previous Prismaflex system.

Results

Delivered/Prescribed Effluent Ratio

Table 1 shows significantly higher ratios for the PrisMax compared to the Prismaflex. Moreover, the ratios in the Prismax runs were significantly closer to 1.

Distributions of the delivered/prescribed effluent ratios between 0 and 2 are presented in Figure 1, where we graphically show how delivered/prescribed effluent ratios from the PrisMax are significantly closer to 1, compared to the Prismaflex.

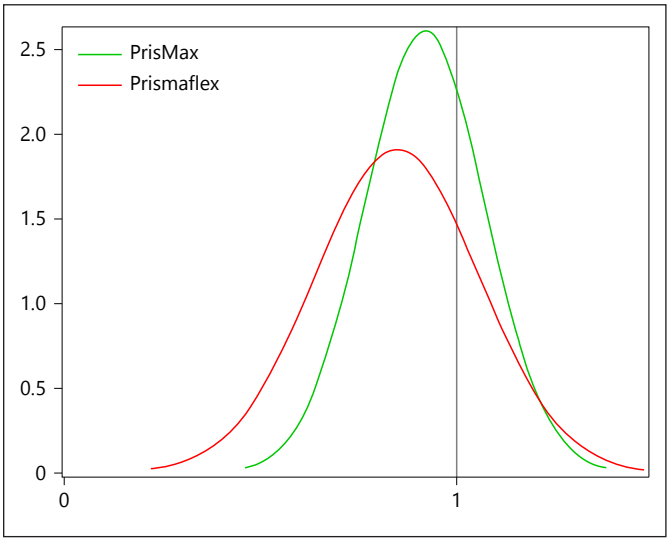

Fig. 1. Distributions of the delivered/prescribed effluent ratios, x-axis ratio and y-axis population density.

Therapy Duration

The therapy duration was 32.12 hours as compared to 25.76 h for the classic Prismaflex system (p = 0.0007) [6].

The Catch-Up Functionality

The catch-up function fraction of the delivered/prescribed patient fluid removal ratio was (mean ± SD) 0.04 ± 0.04, (O1, median, O3) 0.02, 0.03, 0.05.

Comparison of Crude Treatment Dose between Prismax and Prismaflex

Table 2 highlights the actual delivered effluent dose and corresponding Kt/V as well as the downtime in the Prismax and Prismaflex groups. The newer CRRT device delivers significantly higher absolute doses and has more than 27 min less downtime.

Table 2. Comparison of crude treatment dose between the Prismax runs and the Prismaflex runs

	PrisMax (n = 136), mean ± SD	Prismaflex (n = 2,715), mean ± SD	Significance: Prismax compared to Prismaflex, p value
Delivered effluent dose, mL/kg/h	18.16±12.93	10.95±10.96	<0.0001
Delivered Kt/V	0.76±0.52	0.44±0.44	<0.0001
Downtime min	6.56±9.54	34.12±254.37	<0.0001

Discussion

This study demonstrates that the novel PrisMax device is more accurate, providing significantly improved ratios with respect to delivered/prescribed dose as compared to its predecessor Prismaflex. Thus, the higher absolute doses as measured by mL/kg/h or Kt/V and the lower downtime are unsurprising.

As mentioned in the introduction, multiple studies report that high dose CRRT removes antibiotics [8–10]. This casts a shadow over all dose studies as not one has measured antibiotic levels or tried to compensate for antibiotic removal in the different high dose arms. Should we have expected *a higher mortality in the high dose arms* of ATN and RENAL [8–10]?

The present study might be considered a tiny glimpse into the future of medical devices. We are likely to see more tools to help clinicians achieve best practice. These tools will probably range from automatic algorithms to full on artificial intelligence. In this case, we have a novel CRRT system with better user interface, faster priming time and fewer serious alarms [6] – thus less likelihood of the blood pump stopping as compared to the predecessor, Prismaflex. The catch-up mechanism "only" serves to achieve adequate fluid removal, for instance, when the critically ill patient must undergo surgery, radiological examinations or advanced physiotherapy. As all active ICU clinicians know, these events are common and contribute to the mismatch between prescribed and delivered CRRT dose. We believe that this catch-up tool is benign and quite helpful. However, the introduction of built in tools in the advanced organ support devices for the intensive care setting, should be examined critically. Will future physicians and nurses be pacified to an extent where changes in patient physiology risk being missed? Can we trust the afferent limb of the detection systems, feeding information to the artificial intelligence tools?

Study strengths include its prospective, multicentre, multinational design. This increases generalizability. Our ability to examine the current generation (PrisMax) datalogs and to compare them to last-generation (Prismaflex) data is important; we do not have to rely on paper-based reporting. We provide data on how the catch-up mechanism works and have high resolution data on prescribed/delivered dose as well as on downtime. Study weaknesses exist. We do not have information about anticoagulation strategy in the Prismaflex data and a bias is possible if more regional citrate anticoagulation is use with Prismax than with Prismaflex. Could the prescribed versus delivered dose ratio be affected by the fact that this was a brand-new machine, tested in environments where CRRT is well understood? Did this contribute to research-like conditions, where we already know that delivered dose is better than in ordinary clinical situations? The comparison data, with last-generation technology, indicates that this is not the case. However, we acknowledge that all these centres have an expertise in CRRT use, which may not be generalizable in all ICUs.

In conclusion, the novel PrisMax device provides improved delivered to prescribed ratio as compared to last generation CRRT technology. This clearly helps clinicians achieve an adequate CRRT dose in the present-day ICU setting, where downtime is common. Future studies in the field of AKI, and especially septic AKI, are urgently needed to shed light on what minimal CRRT dose regimens we should aim for.

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Disclosure Statement

All authors declare that they have had multiple exchanges with the manufacturer of the PrisMax device, Baxter Healthcare. No financial support pertaining to this study has been awarded, nor has the manufacturer had any influence over the study design or the drafting of the manuscript.

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