Clinical Evidence

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Carpediem™

cardio renal pediatric dialysis emergency machine

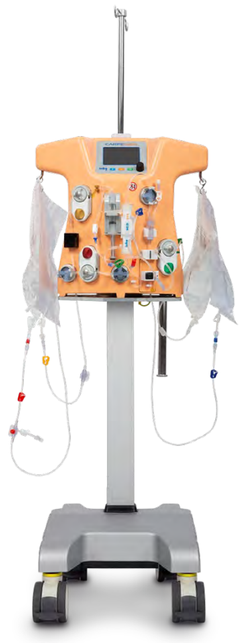
Start

Transforming pediatric care

Neonatal acute kidney injury (AKI) and fluid overload are under-recognized conditions which often lead to morbidity and mortality. The incidence of AKI in critically ill neonates are between 8% and 24%, with mortality rates between 10% and 61%.[1,2]

In today's clinical practice, renal replacement therapies performed on low weight patients, include:

- Acute Peritoneal Dialysis, limited by defects involving the abdominal wall, organs, intraperitoneal surgeries, and complications related to fluid balance.[3]
- Continuous Renal Replacement Therapy (CRRT) performed with adult devices not designed for the needs of neonates or infants.[4,5]
- Hemodialysis mainly to treat hyperammonemia.[2]



Carpediem™ system

The Carpediem™ system is intended for CRRT for pediatric patients weighing 2.5 kg or more.[6]

The system performs as an alternative to peritoneal dialysis (PD) in acute kidney injury, fluid overload, and / or electrolyte disorders, requiring hemodialysis, hemofiltration or ultrafiltration / fluid removal.[6-8]

The Carpediem™ system is designed to offer a dedicated extracorporeal CRRT to low weight patients and responds to the needs of the most fragile patient.[7,8]

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Therapies[6]

- CVVH
- CVVHD
- SCUF

Indications[6]

- Acute kidney injury (AKI)
- Fluid overload
- Electrolyte disorders

Augmented performance[6]

- High-sensitivity air bubble detection alarms (alarm threshold for 10 µL at blood flows <35 mL / min and 15 µL in all other operating conditions).
- High-sensitivity blood leakage detector (alarm threshold for 0.15 mL of blood in 10 mL of ultrafiltrate (hematocrit: 25%) with an effluent flow of 10 mL / min).
- Fluid balance control supervised by high-precision scales with a resolution of 1 g.
- Miniaturized peristaltic pump with three rollers for enhanced accuracy of blood flow starting from 2 mL / min.
- Heparin pump, continuous flow or bolus.

High accuracy[6]

In pump and weight loss control

Treating patients[6]

- Patient weight 2.5 kg or more
- Total Carpediem preassembled device priming volumes of 26, 32 or 41 mL

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Pediatric AKI

Clinical Condition	Key Points	References
Pediatric AKI	After more than 400 hours of extracorporeal treatment in a 2.9 kg neonate, hemofiltration was discontinued and the patient was breathing normally without supplemental oxygen, making adequate amounts of urine and had normal liver function.	Ronco C, et al. *Lancet.* 2014;383(9931):1807-1813.
	AKI and multi-organ failure resolved after 5 days of extracorporeal treatment in a full-term newborn treated with the Carpediem™ system. The child survived with normal renal function and a normal development at 9 months follow-up.	Peruzzi L, et al. *Case Rep Nephrol Urol.* 2014;4(2):113-119.
	Use of daily Kt / V as a measure of CRRT adequacy for critically ill neonates is feasible. The decrease of creatinine concentration was significantly greater during 24 hr treatment sessions with a delivered daily Kt / V > 0.9 than during those with daily Kt / V < 0.9.	Ricci Z, et al. *Pediatr Crit Care Med.* 2017;18(7):623-629.
	The Carpediem™ system successfully delivered diffusive blood purification modality to neonates using small catheters, no blood primes, and excellent concordance between delivered and prescribed treatment duration.	Vidal E, et al. *Blood Purif.* 2019;47(1-3):149-155.
	CRRT may be the right choice for pediatric renal care, but the 'adaptation era' of adult machines was far from providing adequate and safe treatment to infants, newborns, and small children. The Cardio Renal Pediatric Dialysis Emergency Machine (Carpediem™ system) launched the 'fitted era' for pediatric CRRT - a paradigm shift in terms of the provision of adequate and safe CRRT.	Garzotto F, et al. *Nephron Clin Pract.* 2014;127(1-4):172–175.
	CRRT in neonates is easy to initiate and conduct when performed with small central vascular accesses coupled with the Carpediem™ system. A dedicated technology for infant CRRT delivery enables patients to be safely treated — avoiding technical complications.	Garzotto F, et al. *Pediatr Nephrol.* 2020;35(9):1699–1705.
	The ppCRRT subjects had higher rates of vasoactive medication at CKRT initiation. Survival to CKRT termination was higher for Carpediem subjects (33 / 34 vs. 21 / 48). Multivariable logistic regression showed that Carpediem registry cohort was the only variable to retain an association with survival to CKRT discontinuation.	Goldstein SL, et al. *Pediatr Nephrol.* 2022;37(3):667-675.
	Carpediem™ system can be used to successfully manage blood purification, FO, and metabolic conditions such hyperammonemia without experiencing severe complications. The risk / effectiveness balance in low-birth-weight patients should be considered; purification can be obtained successfully using more appropriate blood and dialysate flow rates, small catheters and dedicated dialysis device.	Battista J, et al. *Pediatr Nephrol.* 2023;38(8):2827-2837.
In vitro	Dialysate flow plays an essential role in the blood purification process. The use of CVVHD versus CVVH is justified in cases of high dialysis dose requirement and / or limited blood flow rate.	Lorenzin A, et al. *Pediatr Nephrol.* 2016;31(10):1659-1665.
	First publication on Carpediem™ system: description of the evolution of CRRT in neonates in the last 30 years.	Ronco C, et al. *Pediatr Nephrol.* 2012;27(8):1203-1211.
	With adequate technical equipment (miniaturized roller pump), 4 Fr and 5 Fr catheter could be reliably used in small infants to obtain conceptually adequate flows. The interaction between patient weight and available RRT devices could be considered as the basis of a simple rule for clinicians to follow in the moment of selecting the dialysis catheter.	Garzotto F, et al. *Pediatr Crit Care Med.* 2019;20(3):e170-e179.

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Clinical Summary

TITLE Continuous renal replacement therapy in neonates and small infants: development and first-in-human use of a miniaturised machine (CARPEDIEM)
AUTHORS Ronco C, Garzotto F, Brendolan A, Zanella M, Bellettato M, Vedovato S, Chiarenza F, Ricci Z, Goldstein SL.
JOURNAL *Lancet.* 2014;383(9931):1807-1813.

Background

Acute kidney injury (AKI) has been described as a rare disorder in neonates, occurring in 1% to 2% of the hospital-admitted neonatal population. However, more recent single-center systematic investigation into neonatal AKI showed that it occurs in 16% of newborn infants weighing more than 2 kg who are admitted to neonatal intensive care. Previous underappreciation of the prevalence of the disorder has made neonatal AKI an orphan disease and has held back development of technology specifically for renal replacement therapy in infants. Because of the unique nature of AKI in infants and its severe complications, the authors undertook a project to develop a continuous renal replacement therapy (CRRT) machine designed specifically for patients weighing <10 kg body weight (Carpediem™ system), particularly neonates and premature infants.

Patients / Methods

Development

The aim of the project was to create a new miniaturized CRRT machine for neonates and small infants with reduced priming volumes and the capacity to accurately handle very low blood an ultrafiltration flows. A group of qualified technical and medical personnel completed in vitro laboratory assessments of the functioning prototype machine and conducted several sessions of extensive invitro tests to verify functionality, accuracy and reliability. After 30 months in development, the Carpediem™ machine was approved for human use.

First-in-human-use

The authors treated a female neonate with a subgaleal hemorrhage and consequent hemorrhagic shock. At 72 hours after birth, physicians decided to start CRRT. A 5 cm dual lumen 22 Ga (4 Fr) catheter was placed surgically into the femoral vein. The neonate received post-dilution continuous veno-venous hemofiltration (CVVH) with the Carpediem™ system.

Results

- During in vitro testing, circuits were run for 24 hours. No substantial differences in flow accuracy were noted when different sizes of dual lumen catheters (4 and 7 Fr) were used. Tests suggested excellent accuracy of blood-pump flow rate, with a consistent error of <10%. Reinfusion or dialysis flow errors ranged from –8.0% to 7.5%. Importantly, whereas the accuracy of ultrafiltration always remained within the limit of 1 g / h, no substantial variation in relation to different transmembrane pressure and filtration rates was noted.
- The baby developed severe hyperbilirubinemia because of liver dysfunction and massive subgaleal hemorrhage reabsorption; because there was an urgent need to rapidly decrease bilirubin concentration, the hemofiltration treatment was subsequently alternated with three sessions of blood exchange (BE), two sessions of single-pass albumin dialysis (SPAD), and finally four sessions of plasma exchange (PE). CVVH with the additional bilirubin-targeted treatments led to a progressive normalization of fluid overload, creatinine concentration, and bilirubin concentration. In fact, the ability to combine extracorporeal treatments, such as PE, BE, and SPAD, with CRRT extends the range of supportive treatments for critically ill infants.
- After 7 days of CRRT, urine output had partly recovered to 1.2 mL / kg / h and had reached 3.2 mL / kg / h at 26 days. At 25 days after birth and after more than 400 hours of extracorporeal treatment, hemofiltration was discontinued. The patient was then extubated, and she started to advance to complete oral alimentation. After 30 days, the patient was breathing normally without supplemental oxygen, was making adequate amounts of urine, and had normal liver function; at 39 days, she was discharged from the ICU.

Conclusions

The Carpediem™ system is the first CRRT platform designed and developed for small pediatric patients; it could change clinical practice with respect to the management of neonates with AKI.

The Carpediem™ system can be used to support multiple organ dysfunction, it could reduce the range of indications for peritoneal dialysis and widen the range of indications for CRRT, and it could make the use of CRRT less traumatic and expand its use as supportive therapy even when complete renal replacement therapy is not indicated.

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Clinical Summary

TITLE Neonatal sepsis with multi-organ failure and treated with a new dialysis device specifically designed for newborns.
AUTHORS Peruzzi L, Bonaudo R, Amore A, Chiale F, Donadio ME, Vergano L, Coppo R.
JOURNAL *Case Rep Nephrol Urol.* 2014;4(2):113-119.

Background

Neonatal sepsis due to E.coli is often complicated by multiple organ failure (MOF) and a high mortality risk (50%). In this article, the authors described the case of a male newborn admitted in July 2013 for septic shock due to E.coli on the 11th day of life. He rapidly developed MOF with anuric acute kidney injury (AKI). The child could not be treated with peritoneal dialysis due to severe intestinal bleeding.

Case Report

A male newborn weighing 3,710 g with an Apgar score of 2 / 10 / 10 was discharged in good condition 3 days from birth. After 10 days of breastfeeding, he was transported to the ICU because he developed diffuse cyanosis, hypotonia, and areflexia. His general condition was extremely critical, and he presented with severe metabolic acidosis, hypoglycemia, and a slightly increased C-reactive protein value. The child showed extreme hemodynamic instability, rapidly developing oligoanuria, impaired gas exchange, and a positive hemoculture for E.coli. Nephrological consultation defined a situation of anuric AKI secondary to septic shock and MOF, indicating continuous renal replacement therapy (CRRT).

A double-lumen central venous dialysis catheter (diameter 5 Fr, length 6 cm) was surgically placed in the internal jugular vein; continuous veno-venous hemofiltration (CVVH) was started with the new neonatal device Carpediem™ system (Cardio Renal Pediatric Dialysis Emergency Machine).

The dialysis parameters were blood flow (Qb) of 26 mL / min, net weight loss of 40 mL / h, and reinfusion (QRf) in post-dilution of 255 mL / h. During the first 8 hours, the clinical situation was extremely critical. The patient required high-pressure ventilation because of fluid overload; he also needed high dosage of norepinephrine and epinephrine for persistent hypotension. He showed hemodynamic instability and unsatisfactory control of acidosis and lactic acid, which remained persistently above 8 mmol / L. During the first 2 days of treatment, continuous plasma infusions and repeated platelet transfusions were required because of persistent disseminated intravascular coagulation. In the following 3 days, treatment was intermittent for 12 hours per day. Progressive improvement of bleeding parameters, hepatic function, and general condition allowed the progressive tapering of inotropic drugs as well as plasma and platelet infusions. Diuresis reprisal occurred on day 4, and diuresis normalization, which allowed a treatment interruption, occurred on day 5. During the 5 days of treatment, no anticoagulation was required and no bleeding events occurred.

After 10 days, the patient was released from the ICU. His renal function normalized within 15 days even though his kidneys remained hyperechogenic. At day 60, his neurological condition was almost normal. At 9 months follow-up, the child had normal neurological development without any clinical, ultrasonic, or electroencephalographic abnormalities; he also showed normal growth and development. His blood pressure and renal function were normal without any urinary abnormalities.

Conclusions

The prompt treatment of this patient with CRRT allowed a rapid and uneventful removal of fluid overload, as well as of sepsis-associated cytokines. The ability to promptly reduce fluid overload through an extremely precise control of ultrafiltration contributes to more efficient treatment of critically ill newborns (as in septic shock), allowing proper plasma, calorie, and therapy supply and less stressful ventilatory support with a better outcome and survival rate. The availability of a ready-to-use extracorporeal circuit with an easy-to-use dialysis machine, specifically designed for newborns, can extend the use of this therapeutic option — not only to expert pediatric nephrologists, but also to intensive care neonatology units — to provide prompt treatment of sepsis and fluid overload and therefore better survival rates for patients.

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Clinical Summary

TITLE Dose prescription and delivery in neonates with congenital heart diseases treated with continuous veno-venous hemofiltration.
AUTHORS Ricci Z, Guzzi F, Tuccinardi G, Di Chiara L, Clark W, Goldstein SL, Ronco C
JOURNAL *Pediatr Crit Care Med.* 2017;18(7):623-629.

Background

Acute kidney injury (AKI) in newborns frequently occurs after complex cardiac surgery. Renal Replacement Therapy (RRT) may be needed for a part of these cases (5%) and it has been shown that continuous veno-venous hemofiltration (CVVH) can be used safely in neonates with congenital heart diseases. The aim of the present study was to evaluate the technical and clinical effects of a relatively small dialysis dose on critically ill neonates with severe fluid overload and oligo-anuria requiring CVVH.

Material and methods

- All patients included were treated with equipment specific for pediatric CRRT.
- The primary objective was evaluation of effective dialysis delivery (daily Kt / V).
- The main endpoints were the determination of the correlation between daily Kt / V and serum creatinine deltas, as well as between daily Kt / V and urea deltas.

Results

- A total of 10 neonates (median weight of 2.6 kg and age of 3 days) with congenital heart diseases were received in the pediatric cardiac intensive unit.
- CVVH (7 patients treated with Carpediem™ system, two with Prismaflex, and one with both monitors) was generally delivered as pre-dilution or as combined pre- and post-dilution mode. The anticoagulation method used was heparin.
- The delivered Kt / V of each 24-hour dialytic session correlated with creatinine differences measured between the end and the start of the same session. A correlation between daily Kt / V and delta creatinine was also shown. In addition, daily Kt / V was significantly associated with the difference between starting and ending blood urea nitrogen levels.
- Solute marker concentrations increased during all 24-hour sessions in which daily Kt / V values less than 0.9 were delivered.

Conclusions

There was an association between dialytic efficiency expressed as daily Kt / V and changes in serum creatinine and urea concentration in newborns with congenital heart disease treated with CVVH. The findings suggest that the delivery of a Kt / V of approximately 1 allowed an adequate clearance of these small solutes.

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Clinical Summary

TITLE Continuous veno-venous hemodialysis using the Cardio-Renal Pediatric Dialysis Emergency Machine™: first clinical experiences.
AUTHORS Vidal E, Cocchi E, Paglialonga F, Ricci Z, Garzotto F, Peruzzi L, Murer L, Ronco C.
JOURNAL *Blood Purif.* 2019;47(1-3):149-155.

Background

Carpediem™ system has proven to be the most complete and dedicated CRRT platform for infants and children with particular characteristics. The system has been improved implementing continuos veno-venous hemodialysis (CVVHD). This is an effective technique to remove molecules like creatinine, blood urea nitrogen, potassium and ammonium. Therefore, adding a diffusive-based modality to the Carpediem™ system might expand the number of small children with chronic kidney and metabolic diseases who can use it.

The authors reported the first worldwide experiences with CVVHD in a group of neonates and small babies using the last generation Carpediem™ system.

Methods

Retrospective data collection of 95 consecutive CVVHD treatments administered to 13 patients between November 2016 and May 2018 in 4 Italian centers. Each center had followed local institutional practice with respect to timing and criteria for CRRT initiation, termination, and prescription.

Results

Ninety-five (95) CVVHD sessions were performed in 13 patients (median age at CRRT start of 9 days and median body weight of 3,000 g) with AKI (6 patients), end-stage renal disease (ESRD=4), and metabolic disease (3 patients).

Children received 1,008 hours of CVVHD sessions.

The priming of the extracorporeal circuit was completed using 5% albumin in 12 patients, and with a normal saline solution in the remaining patient, and all patients received heparin as anticoagulation.

In 10 patients, CVVHD was conducted using a 5 Fr double-lumen venous catheter, mainly placed in the right internal jugular vein. In one child, a 6.5 Fr catheter was used, an in the other 2 patients, an 8 Fr was placed.

The median prescribed Qb was 17 mL / min (IQR 10-29.5), with a median Qd of 10 mL / min.

The median delivered / prescribed time ratio was 100% (95–100%). The most common complications that led to downtime of circuits were clotting that however occurred in only 3% of all treatments.

Thirteen (100%) patients survived at CVVHD discontinuation and 9 patients (69%) survived to hospital discharge.

Conclusions

Carpediem™ system allowed to successfully perform treatments for pediatric patients by using small vascular access, no need for blood priming, and excellent concordance between delivered and prescribed treatment duration.

The use of a diffusive or convective modality (respectively CVVHD or CVVH) appeared to be based more on contingent aspects than on specific outcome data.

The CVVHD modality with Carpediem™ system was a safe and effective treatment for both critically ill and non-critically ill newborns and small children.

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Clinical Summary

TITLE The evolution of pediatric continuous renal replacement therapy.
AUTHORS Garzotto F, Zanella M, Ronco C.
JOURNAL *Nephron Clin Pract.* 2014; 127:172–175.

Background

CRRT prescription for younger and smaller children has unique considerations due to problems, including:

- Extracorporeal blood volume
- The need for circuit blood priming
- The adaptation of machines designed for adult-sized patients

Moreover, the provision of renal replacement therapy to neonates presents a unique problem: no more than 10–15 % of their blood volume should be removed by the extracorporeal circuit to prevent hypotension and anemia. In 2012, the Carpediem™ (cardio renal pediatric dialysis emergency machine) system was developed — launching the “fitted era” for pediatric CRRT.

Case review

In 2012 — 24 years after creating the first CAVH — the Department of Nephrology and International Renal Research Institute of San Bortolo Hospital created the Carpediem™ system. Their aim was to develop a CRRT platform specifically for newborns and small infants (2.0–10 kg) with an approximate BSA of 0.15–0.5 m^2. As a result, the Carpediem™ system launched the “fitted era” of pediatric CRRT.

Results

The first in-vivo application of the Carpediem™ system suggested a paradigm shift in the provision of adequate and highly safe CRRT to infants. Catheters (4–7 Fr) tested in vitro have shown excellent results in terms of circuit longevity. For example, a four-french dual-lumen catheter has been used for more than 400 hours in patients with conditions such as:

- Multiple organ failure
- Fluid overload of 63 %
- Acidosis
- Hyponatremia
- Thrombocytopenia
- Oliguria

No hypotension or complications related to CRRT were reported. The treatment led to the control of fluid balance, metabolic waste products, bilirubin, and other humoral disorders. The neonate recovered for multiple organ dysfunction was discharged from the hospital.

Conclusions

In the last decade, the indications for renal replacement in the pediatric patients have changed to include a wide spectrum of diseases. The so-called ‘nonrenal indications’ have contributed to the increase in the number of CRRT applications mainly in critically ill infants and neonates. The renal replacement therapy of choice for this particular population is still PD. However, limitations in terms of efficiency call for the use of a more suitable therapy (i.e. one with higher UF rates and better solute clearance). CRRT may be the right choice for pediatric renal care, but the technology to adequately perform this therapy has never been developed. The Carpediem™ system — specifically designed for neonates and small infants — may be the missing element in pediatric renal replacement.

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Clinical Summary

TITLE Continuous kidney replacement therapy in critically ill neonates and infants: a retrospective analysis of clinical results with a dedicated device.
AUTHORS Garzotto F, Vidal E, Ricci Z, Paglialonga F, Giordano M, Laforgia N, Peruzzi L, Bellettato M, Murer L, Ronco C.
JOURNAL *Pediatr Nephrol.* 2020:35(9):1699–1705.

Background

Acute kidney injury (AKI) affects about 30% of critically ill neonates admitted to neonatal intensive care units (NICU). However, neonates receive renal support infrequently, due to the lack of a specific extracorporeal kidney replacement therapy (KRT) device available for neonates and small children might have contributed to the low number of treatments.

Thanks to the development of new CKRT machines specifically adapted or dedicated for small infants, there was a revolution in the management of AKI in newborns.

Smaller extracorporeal volumes, the ability to prevent blood priming, improved volume management, more graduated flow rate adjustment, and the possibility to use smaller catheter sizes without sacrificing blood flow are some of the benefits of the new devices.

Since June 2013, the Carpediem™ system has been used in several pediatric centers in Italy. This retrospective analysis described a 2.5-year experience with the use of this machine in treating neonates and infants using a convective modality.

Methods

Multicenter experience (6 centers) with the use of Carpediem™ system in treating small infants using a convective modality (CVVH).

The aim of this retrospective registry was to report treated patients' characteristics, therapy data with particular focus on treatment initiation, catheters utilized, technical considerations, and overall outcomes.

Results

Twenty-six neonates and small infants (median age at NICU admission of 1 day and median body weight of 2.9 kg) received 165 CKRT sessions in convective modality with Carpediem™ system. Cardiac disease was the most common primary diagnosis at ICU admission (38%), followed by sepsis (15%), inborn errors of metabolism (IEM) (15%), kidney disease (12%), primary pulmonary disease (12%), and others (8%). Twenty-two (85%) of the patients had AKI with fluid overload as indication for CKRT; the remaining four (15%) had metabolic or electrolyte imbalances.

In 152 out of 165 CKRT sessions (92%), predilution hemofiltration was prescribed, while in 13 sessions (8%), a post-dilution continuous veno-venous hemofiltration (CVVH) was set. Significant differences between settings and filter sizes, in particular with the smallest and biggest ones, being those with the highest blood flows, net UF, and effluent rates.

To prime the extracorporeal circuit, normal saline was used in 58% of cases, in 31% of case colloids (5% albumin) and in 11% packed red blood cells. Heparin was used in 71% of cases, and in the remaining 29% no anticoagulation was prescribed.

The right internal jugular vein (54%) was the most common location for vascular access, followed by femoral (31%), umbilical (11.5%), and subclavian vein (3.5%). In the majority of patients, CKRT was conducted using a 4 Fr (27%) or 5 Fr (35%) venous catheters. Three patients received treatment utilizing a combination of 3.5 and 5 Fr umbilical catheters.

A premature circuit interruption was described in 48 cases: clotting in 22 (13%) sessions, clinical reasons in 12 (7%), vascular access malfunction in 10 (6%), unresolved software alarms, and other unspecified technical problems both in 4 (2.4%) sessions. No serious adverse events directly related to machine application were reported by any center.

Twenty-five (96%) patients survived CKRT discontinuation, and 13 patients (50%) survived both ICU and hospital discharge. Higher mortality (69%) in infants weighing < 3 kg.

Conclusions

This was the largest case series of neonates and infants treated with Carpediem™ system.

CKRT was feasible even with relatively small venous catheters, in particular a 5 Fr catheter represented the best compromise between low vascular impact and adequate extracorporeal treatment.

Carpediem™ system is a dedicated technology for infant CKRT delivery that enabled patients to be safely treated avoiding technical complications.

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Clinical Summary

TITLE Survival of infants treated with CKRT: comparing adapted adult platforms with the Carpediem™.
AUTHORS Goldstein SL, Vidal E, Ricci Z, Paglialonga F, Peruzzi L, Giordano M, Laforgia N, Ronco C.
JOURNAL *Pediatr Nephrol.* 2022;37(3):667-675.

Background

Critically ill neonates and small children had high rates of AKI associated with poor outcomes. In the past three decades, continuous kidney replacement therapy (CKRT) technology has been adapted for use to support neonates and infants. Although these adaptations have been associated with 30–40% survival rates in children < 10 kg, the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) registry data showed a lower survival rate in children < 10 kg compared to those > 10 kg (44% vs. 64%, p < 0.001).

A CKRT device designed specifically to address the unique challenges in providing support for critically ill neonates and infants (e.g., low blood volumes, accurate low blood pump and replacement / dialysis pump rates, extremely accurate scales) could improve outcomes.

The Carpediem™ system is specifically dedicated CKRT platform for newborns and small infants. The machine can perform continuous veno-venous hemofiltration (CVVH) in pre or post-dilution configuration and continuous veno-venous hemodialysis (CVVHD).

Methods

This was a retrospective cohort analysis from Carpediem registry, involving 6 Italian centers, using either CVVH or CVVHD.

Thirty-eight subjects from the Carpediem registry and 84 subjects from the ppCRRT registry < 10 kg were screened for comparison.

A weight-matched cohort (< 5 kg) consisting of 34 patients from the Carpediem registry and 48 patients from the ppCRRT registry was used to compare patient outcomes.

Results

The ppCRRT subjects had higher rates of vasoactive medication at CKRT initiation. There was higher survival to CKRT discontinuation in the patients treated with the Carpediem™ system (33 / 34 vs. 21 / 48, p < 0.0001). Likewise, the survival rate to CKRT termination for subjects with AKI as an indication for CKRT initiation was higher in the Carpediem group (25 / 26 vs. 15 / 24, p < 0.0001).

The survival rates to ICU discharge did not differ for the Carpediem vs. the ppCRRT registries (17 / 34 vs. 21 / 48, p = 0.58), nor for subjects with AKI as an indication for CKRT initiation (13 / 26 vs. 14 / 34, p = 0.60).

Multivariable logistic regression showed that Carpediem registry cohort was the only variable to retain an association with survival to CKRT discontinuation.

Conclusions

The authors suggested that small children undergoing CKRT with Carpediem™ system have excellent survival.

Considering the retrospective comparison between two eras that are more than a decade apart, this data should be interpreted with caution.

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Clinical Summary

TITLE CARPEDIEM® for continuous kidney replacement therapy in neonates and small infants: a French multicenter retrospective study.

AUTHORS Battista J, De Luca D, Eleni Dit Trolli S, Allard L, Bacchetta J, Bouhamri N, Enoch C, Faudeux C, Guichoux J, Javouhey E, Kolev K, Regiroli G, Ranchin B, Bernardor J.

JOURNAL *Pediatr Nephrol.* 2023;38(8):2827-2837.

Background

In neonatal intensive care, acute kidney injury (AKI) is a frequent consequence that is associated to increased mortality, especially in newborns (31.3%) and children who need dialysis (27.1%). Continuous kidney replacement treatment (CKRT) is necessary for AKI management in cases where conservative methods (such as peritoneal dialysis) are ineffective in controlling fluid overload (FO) and metabolic abnormalities.

Since 2012, the Carpediem™ system was used to treat newborns and small infants requiring CKRT.

The aim of the study was to retrospectively assess the effectiveness, feasibility, outcomes, and technical considerations relating to the use of Carpediem™ system.

Methods

Retrospective multicenter study including a case series of 19 newborns and 6 infants treated with the Carpediem™ system between December 2018 and January 2022 in five French pediatric and neonatal intensive care units.

Laboratory parameters were collected at the initiation and end of the first treatment session.

Results

Twenty-five patients (birth weight 2.7 kg), including nine preterm neonates (36%), and two very preterm (25 and 28 weeks of gestational age) initiated a treatment with the Carpediem™ system at a median age of 4 days and with a body weight of 3.3 kg with a FO % of 18%.

Fifteen patients (60%) had AKI with FO, 5 patients (20%) had chronic kidney disease (CKD) stage 5, three patients (12%) had inborn error of metabolism (IEM) with hyperammonemia, and two patients (8%) had electrolyte disorders.

Overall, 131 CKRT sessions for a total of 2125 h of treatment were performed. The duration of CKRT per patient was 42 h, whereas the duration for one CKRT session was 19 h.

CVVH modality was performed in 20 patients (Qb 8 mL / kg / min, effluent flow 74 mL / kg / h, net UF flow 6 mL / kg / h), in the remaining five patients, CVVHD was prescribed (Qb 6 mL / kg / min, Qd 600 mL / h, net UF flow 9 mL / kg / h).

Anticoagulation with heparin was used 22 patients, one did not have any anticoagulation, and two benefitted from a loading dose of heparin at treatment initiation.

To prime the circuit, normal saline was used in 54 sessions (41%), 4% albumin or isofundine in 69 sessions (52%) and packed red blood cells in 8 sessions (used in one patient).

The internal jugular vein (18 patients; 72%) was the most common location for vascular access, followed by left subclavian vein (5 patients; 20%), umbilical vein (1 patient; 4%), and femoral vein (1 patient; 4%). The vascular access sizes used were 4.5 Fr (32%), 5.5 Fr (24%), 6 Fr (16%), 6.5 Fr (24%), and 8 Fr (4%).

The dialysis downtime was 79%. Hemodynamic instability with a need for volume replacement occurred in 31 sessions (23%). Clotting was observed in 25 sessions (19%), catheter dysfunction in 3 sessions (2%), pressure dysfunction due to machine issues in 7 sessions (5%), restitution failure in 4 sessions (3%). Thrombocytopenia was observed in 29 sessions (22%), and in 15 of 20 patients this was present before CKRT initiation.

All patients survived at the end of sessions with the Carpediem™ system, 17 patients (68%) died from their primary severe disease. Higher survival in chronic kidney disease (CKD) group (50%), only 13% of AKI patients survived.

Creatinine, urea and serum potassium decreased significantly after the first CKRT session. With the use of the Carpediem™ system, hyperkaliemia could be controlled, and kaliemia remained stable within the normal range.

For the patients treated for hyperammonemia (two with CVVH and one with CVVHD), a minimum of tenfold decrease in ammonia was found in each patient after 24 h of treatment. Two of them were still alive at hospital discharge.

Conclusions

These data confirm that the Carpediem™ system can be used to successfully manage blood purification, FO, and metabolic conditions such hyperammonemia without experiencing severe complications.

The risk / effectiveness balance in these such low-birth-weight patients should be considered; purification can be obtained successfully using more appropriate blood and dialysate flow rates, small catheters and dedicated dialysis device.

The use of the Carpediem™ system is safe and effective in critically ill neonates and infants. More studies to compare the efficacy of the Carpediem™ system with that of PD and adult devices are needed, as well as long-term kidney assessment remains to be evaluated.

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Clinical Summary

TITLE CVVHD treatment with CARPEDIEM: small solute clearance at different blood and dialysate flows with three different surface area filter configurations.

AUTHORS Lorenzin A, Garzotto F, Alghisi A, Neri M, Galeano D, Aresu S, Pani A, Vidal E, Ricci Z, Murer L, Goldstein SL, Ronco C.

JOURNAL *Pediatr Nephrol.* 2016;31(10):1659-1665.

Background

The Carpediem™ system (cardio renal pediatric dialysis emergency machine) was originally designed to perform only continuous veno-venous hemofiltration (CVVH). However, in cases when increased dialysis efficiency is needed or adequate convective clearance may not be reached due to limited blood flow rate, the convective clearance achievable in neonatal patients may be insufficient to control uremic solutes. In many conditions, such as hypercatabolic diseases, the application of diffusive clearance (continuous veno-venous hemodialysis [CVVHD]) would help optimize blood purification via increased urea and creatinine removal. In this study, the authors modified the Carpediem™ system to enable the circulation of dialysis through the filter to test the performance of the Carpediem™ system in CVVHD.

Methods

- Three different polyethersulfone hemodialyzer prototypes (surface area of 0.1 m^2, 0.2 m^2, and 0.35 m^2, respectively) equipped with two ports in the ultrafiltrate / dialysate compartment were developed to allow the CVVHD modality.
- CVVHD treatments were performed in vitro with a scheduled combination of plasma flow rates (Qp = 10-20-30 mL / min) and dialysis fluid flow rate (Qd = 5-10-15 mL / min).
- Three sessions were performed in co-current configuration and one in counter-current configuration (as control) for each filter size. Clearance was measured from the blood and dialysate sides, and results with mass balance error >5% were discarded.
- Urea and creatinine clearances for each plasma / dialysate configuration were collected.

Results

The authors observed an incremental increase in clearances for every filter as plasma flow increased. Similarly, clearances increased progressively with dialysate flow rates at a given plasma flow. The clearance curve presented a steep increase for small increases in plasma flow below 10 mL / min, while the curve tended to plateau for values averaging 30 mL / min. As expected, the plateau was reached earlier with the smaller filter, showing the effect of membrane surface-area limitation. They showed that complete saturation of effluent dialysate was not achieved in any of the experimental conditions tested. The authors also performed an analysis using whole blood instead of plasma or using co-current versus counter-current dialysate flow configuration, and they observed no differences.

Conclusions

The results obtained in this in vitro study indicate that dialysate flow plays an essential role in the blood purification process, justifying the use of CVVHD versus CVVH in cases of high dialysis dose requirement and / or limited blood flow rate. The data provide a framework that allows the clinician to select the best dialysate flow and hemodialyzer prescription for specific patients according to size and clinical requirements.

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Clinical Summary

TITLE CA.R.PE.DI.E.M. (Cardio-Renal Pediatric Dialysis Emergency Machine): evolution of continuous renal replacement therapies in infants. A personal journey.
AUTHORS Ronco C, Garzotto F, Ricci Z.
JOURNAL *Pediatr Nephrol.* 2012; 27(8):1203-1211.

Background

Pediatric acute kidney injury (AKI) is a well-described clinical syndrome that is dominated by an abrupt decrease in renal function with a reduction of urine output, hypertension, vomiting, edema, and lethargy. Moreover, AKI in critically ill babies is frequently associated with multiple organ dysfunction (MODS). In the last years, a dramatic increase in the incidence of AKI in the pediatric population has been observed. Unfortunately, the absence of sufficiently effective preventive and therapeutic measures has limited significant improvements in AKI care. Mortality in patients with severe AKI remains unacceptably high (>50%), with renal replacement therapy (RRT) remaining the most effective form of support for critically ill infants. Some recent epidemiological studies have confirmed that the presence of AKI in these patients represents an independent risk factor associated with mechanical ventilation, increased length of stay in the ICU and hospital, and mortality. In this article, the authors the authors report on AKI management in infants and children, based on their 30-year experience of research in the field. They describe the evolution of pediatric RRT and the development of the Carpediem™ system (cardio renal pediatric dialysis emergency machine) project, which has recently been established to finally provide neonates and infants with a reliable dialysis machine specifically designed for this age group.

Review

The modern practice of continuous RRT in infants

The indications for RRT in pediatric patients with AKI have changed over the years, and the current trend is toward a wider spectrum of applications, including the prevention of fluid accumulation and MODS. In fact, critically ill infants with AKI are at the highest risk of water accumulation and inflammation, especially in the post-heart surgery phase. Until recently, peritoneal dialysis (PD) has been the RRT treatment of choice in neonates, except when specific contraindications are present (i.e., peritonitis, abdominal masses, or bleeding). Extracorporeal dialysis in children can be managed with a variety of modalities, including intermittent hemodialysis and continuous hemofiltration or hemodiafiltration. The choice of dialysis modality is influenced by several factors, including the goals of the dialysis, the unique advantages and disadvantages of each modality, and institutional resources. Critically ill children generally are treated with CRRT, which allows for slow fluid removal, solute re-equilibration, and the likely removal of pro-inflammatory mediators.

AKI in neonates and infants is an “orphan disease”

Pediatric AKI is a dramatic syndrome requiring careful clinical management, but to date a truly pediatric CRRT system has never been developed. Consequently, dialysis / hemofiltration in critically ill children is currently performed by adapting adult systems to much smaller pediatric patients. In these cases, most machines are used off-label when patients with a body weight of <15 kg are being treated. The small number of cases — together with the limited interest of industry to develop a fully integrated device specifically designed for the pediatric population — have made AKI in infants and neonates an “orphan disease.”

The Carpediem™ system project

Because of the need to create RRT equipment specifically dedicated to newborns and small infants in the weight range of 2.0 to 9.9 kg, the Carpediem™ system project was developed by the Department of Nephrology and International Renal Research Institute of the San Bortolo Hospital in Vicenza.

The goal of the project was to design the first neonatal CRRT monitor with the help of modern miniaturization engineering skills. In particular, they aimed to reduce priming volumes of the circuits to a minimum level and allow roller pumps to run at a slow speed, thereby guaranteeing the integrity of the lines and maintaining an excellent level of flow and balance accuracy.

Conclusions

AKI is a severe clinical condition that is further complicated in small children by the different problems of these patients. Outcomes may vary significantly depending on the underlying disease, the severity of illness, and the time of intervention. To date, outcomes of critically ill children with AKI are poor, and a strategy for improvement is needed urgently. In this scenario, new technological advances — such as miniaturized circuits and membranes and accurate CRRT machines, as well as effective prescription schedules — promise to improve the quality of clinical treatment.

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Clinical Summary

TITLE Choice of Catheter Size for Infants in Continuous Renal Replacement Therapy: Bigger Is Not Always Better.
AUTHORS Garzotto F, Zaccaria M, Vidal E, Ricci Z, Lorenzin A, Neri M, Murer L, Nalesso F, Ruggeri A, Ronco C.
JOURNAL *Pediatr Crit Care Med.* 2019;20(3):e170-e179.

Background

Thanks to recent advancements in technology, extracorporeal renal replacement therapies (RRT) are frequently utilized in critical care settings for the treatment of severe diseases like sepsis, multiple organ failure, and inborn metabolic abnormalities in children.

Improved RRT devices specifically designed for the needs of neonates may improve outcomes and raise survival rates. Adequate vascular access is one of the crucial factors to achieve an effective RRT in small infants.

The aim of the study was to characterize both the operating conditions and performance of three (4 Fr, 5 Fr, and 7 Fr) central vascular catheters sizes connected to two different extracorporeal blood circulation models (adult and pediatric).

Methods

Series of in vitro tests to simulate extracorporeal circuit models of continuous pediatric and neonatal RRT were conducted with different setups: a two-roller pump was used to simulate a standard adult dialysis machine, whereas a small three-roller pump served as pediatric renal replacement therapy device.

The first experimental setting was a pressure-flow set-up aimed to collect pressure and flow values under different test conditions. The second one was focused on hemolysis estimation induced by the extracorporeal system. The last one was conducted to evaluate the hemolysis induced to the blood by the 4 Fr catheter only.

Results

Using 4 Fr and 5 Fr catheters, maximal blood flows within safe circuit pressures (+100 and -100 mmHg) can be set at the values of 13 and 29 mL / min, respectively, when a small pediatric pump is used. Differently, when using adult roller pumps, only maximal flows of 10 and 20 mL / min are reached.

In clinical practice, these results showed that the 4 Fr 5 cm catheter with a flow of 13 mL / min should be used for a small preterm patient (i.e., below 3 kg), whereas the 5 Fr 5 cm (29 mL / min) for a bigger patient (i.e., above 3 kg) may ensure an adequate clearance.

Conclusions

This study showed that with adequate technical equipment (miniaturized roller pump), 4 Fr and 5 Fr catheter could be reliably used in small infants to obtain conceptually adequate flows.

The interaction between patient weight and available RRT devices could be considered as the basis of a simple rule for clinicians to follow in the moment of selecting the dialysis catheter.

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Disclaimer

Carpediem™ machine is an active, non-invasive, class IIb medical device CE0123 manufactured by Bellco S.r.l.
BD Plastipak syringe is a medical device manufactured by Becton Dickinson S.A.
They are included in the Carpediem procedure pack 0075.

Carpediem preassembled devices 015 and 025 are non-active, non-invasive, class IIb medical device CE0123 manufactured by Bellco S.r.l.
BD Plastipak syringe is a medical device manufactured by Becton Dickinson S.A.
They are included in the Carpediem procedure packs 015 and 025.

Please refer to the devices and procedure pack Instructions for Use for complete instructions, contraindications, warnings and precautions.

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Mozarc Medical
EMEA Regional Headquarters
Via Varesina, 162
20156 Milano (MI), Italy

emeacontactus@mozarcmedical.com
mozarcmedical.com
LinkedIn

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