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Best Practices in Fluid Management During CKRT

Announcer:
Welcome to this episode of KDIGO Conversations in Nephrology. This episode, titled Best Practices in Fluid Management During CKRT is provided by KDIGO and supported by an independent educational grant from Baxter. Here's your host, Dr. Marlies Ostermann.

Dr. Ostermann:
Hello, and welcome to another KDIGO Conversations in Nephrology. I'm Dr. Marlies Ostermann, and I am a consultant in critical care and nephrology at Guy's & St. Thomas' Hospital in London, U.K., and joining me today to discuss Best Practices in Fluid Management During Continuous Kidney Replacement Therapy is Dr. Javier Neyra. Dr. Neyra practices at the University of Alabama in Birmingham, in the U.S. He is Associate Professor of Medicine, Co-Director of Critical Care Nephrology, and also Associate Director of the Nephrology Research and Training Center. He's a renowned expert in the field of acute kidney injury and fluid management. Dr. Neyra, welcome to the program.

Dr. Neyra:
Thank you very much, Dr. Ostermann. It's really a pleasure for me to be here and to have this dialogue with you about this topic.

Dr. Ostermann:
So the focus of our discussion is fluid management, and I would like to start just asking you, what is the impact of fluid overload during critical illness?

Dr. Neyra:
Well, fluid overload has been consistently associated with increased risk of mortality, multi-organ injury and impaired organ recovery. This observation was first identified in the pediatric population but has been consistently validated in the adult critically ill population as well. Collectively these observations, of course prompt clinicians to pay careful attention to the deresuscitation phase of fluid management, which entails restriction to – of fluid intake, proper use of diuretics and of course, extracorporeal removal of fluids with kidney replacement therapies.

I would also like to highlight that the fluid overload determined before or at the time of renal replacement therapy initiation has also been associated with increased mortality, and lowered chances of kidney recovery, for example, RRT independence up to 1 year post-discharge. Therefore, I think one should consider fluid overload as a potentially modifiable risk factor in critically ill patients. While sometimes we cannot prevent the occurrence of fluid overload effectively, we still have a chance to deresuscitate fluid overload in patients, and optimizing their fluid management will be one way. In this context, key questions arise, right? When and how should we deresuscitate a patient that is fluid overloaded, and no longer fluid responsive? Those are important questions that require better evidence to guide our practice.

Dr. Ostermann:
You've already mentioned kidney replacement therapy as a therapy to address fluid overload. What exactly can kidney replacement therapy do?

Dr. Neyra:
Well let's start first for what the term "kidney replacement therapies" encompasses. This includes hemodialysis, sustained low efficiency dialysis, or prolonged intermittent renal replacement therapy – what is PIRRT, as well as continuous renal replacement therapy – we call it CRRT and lately sometimes CKRT. Additional to that, peritoneal dialysis could be a modality that can be easily implemented in some ICUs.

Now, what is the role of these therapies in fluid management – fluid overload? If we identify a patient that is no longer fluid responsive and fluid overloaded, we typically start restricting fluid intake. This includes intravenous fluids, particularly maintenance fluids, diluents in medications, and we also start using diuretics, sometimes at high doses, and even combining diuretics with different action sites in the nephron. If a patient is not responsive to diuretics, and/or we are unable to achieve a desired daily fluid balance to mitigate further fluid overload, or properly deresuscitate that patient, then we consider the initiation of kidney replacement therapies, particularly if there is a concomitant acute kidney injury that is evolving, and sometimes electrolyte acid-based derangement that can be supported by CRRT or any type of renal replacement therapy. So how we determine which modality of kidney replacement therapy to use? Well, that depends on the clinical status of the patient and the logistics available at the corresponding location. For example, for critical ill patients that are hemodynamically unstable, we prefer to use continuous renal replacement therapy – CRRT – if available. Once we initiate CRRT, we program the machine to remove fluids in an hourly manner, to achieve a desired goal of fluid balance. For example, if we want a patient to have a fluid balance of -1 liter in the next 24 hours, and the patient is projected to receive 1 liter of fluid intake in the same period of time, the total fluid removal needs to be, of course, 2 liters in 24 hours, which is equivalent to around 80 ml per hour and if the patient is 80 kilograms, this will be around 1 ml/kg per hour. Of course, many factors can affect this goal of treatment. Inadequate prescription – if the patient does not need fluid removal; ineffective delivery of the prescription – if there are treatment interruptions due to catheter issues, clotting, procedures that the patient needs to be off the room, etc.; or patient intolerance – patient needs fluid removal but cannot fully tolerate the prescription; and many other factors, of course.

Now in the case of hemodialysis, we typically will prescribe 3-4 hours of treatment, and the withdraw filtration will range from 1-3 liters, as tolerated by the patient. But we certainly need to limit the withdraw filtration to around 10 mls/kg per hour to avoid complications. So renal replacement therapies are very critical for patients that are in the ICU, but our goal of course, is to deliver these therapies in a timely, effective, monitored and hopefully safe way.

Dr. Ostermann:
Dr. Neyra, you mentioned effective and safe fluid removal and you highlighted the importance. But why is it so challenging to remove fluid effectively and safely during kidney replacement therapy?

Dr. Neyra:
This is a key question, right? First, we need to recognize that fluid management in a critical ill patient is a dynamic target, and of course, this applies to a scenario in which patients are already receiving kidney replacement therapy. Second, we need to standardize the way we prescribe fluid removal in patients on RRT in the ICU. My personal choice here is to prescribe fluid management based on a desired fluid balance, and use fluid removal or net ultrafiltration rate as a vehicle to achieve this goal. Third, we need to standardize ways to monitor fluid removal during CRRT in the ICU. We need to create flow sheets, if possible electronic flow sheets, that can assist bedside nurses with adjustments of fluid removal targets on the machine. Sometimes, these flow sheets even can be automated, and have embedded calculations to determine the fluid removal target that the nurse need to insert in the machine according to the current fluid balance of the patient, and also incorporating any residual deficit from prior hours. So we really can construct this ecosystem that can assist the bedside delivery of the treatment.

Finally, we need to appraise current literature and understand its valuable points, and also the limitations. For example, if we summarize some of the recent literature, observational data from Raghi Murugan and colleagues have highlighted that net ultrafiltration rates more than 1.75 ml/kg/hour, compared to less than 1.01 ml/kg/hour, can be associated with increased risk of mortality. So the attributable mortality here could be multifactorial, including cardiovascular complications. Nonetheless, when cohorts are restricted to only patients that are fluid overloaded, or in whom clinicians want to achieve a negative fluid balance, higher net ultrafiltration rates are associated with lower risk of mortality. Now while this could seem as a paradox, this could also reflect the effect of patient tolerance to fluid removal, when they are fluid overloaded.

While observational studies are subject to indication and selection biases, we still recognize key elements or lessons from this study. Number one is that one size does not fit all, and we should personalize fluid removal rates in critical ill patients requiring RRT in the ICU, and the second one is that we should have safety limits when prescribing net ultrafiltration rates. Perhaps the cutoff of 1.75 ml/kg/hours, at least for some patients should be used, as suggested by current evidence. So as I mentioned before is that CRRT is not the only type of RRT we can do in the ICU. So in the case of hemodialysis, for example, I recommend to limit ultrafiltration to 10 ml/kg/hour to avoid intradialytic hemodynamic complications that can affect kidney and cardiovascular outcomes, at least as extrapolated from the end-stage kidney disease population.

Dr. Ostermann:
For those just tuning in, you're listening to KDIGO Conversations in Nephrology. Today's episode is on Best Practices in Fluid Management During Continuous Kidney Replacement Therapy. I am Dr. Marlies Ostermann, and I'm here with Dr. Javier Neyra.

Dr. Neyra, you mentioned the importance of monitoring, and the importance of getting the prescription right. How do you, in your clinical practice, determine the fluid removal prescription during continuous renal replacement therapy?

Dr. Neyra:
This is a very important question, and I want everybody to recognize that fluid overload is one of the most common indications of continuous renal replacement therapy, particularly those patients that are critically ill – that are hemodynamically unstable, and in the ICU. We – we mentioned before that fluid overloads contributes to mortality, and also could be a potentially modifiable risk factor, if we mitigate its consequences through extracorporeal removal of fluids when the native kidneys cannot do the job, and in some cases, using a device for CRRT. Now, while multiple studies have suggested that fluid overload associated with adverse outcomes, there are also studies that were completed in the last 3-4 years, most of them post-hoc analyses of their renal trial and all the cohorts in Australia and New Zealand, in which the authors identified that also higher rates of fluid removal, specifically net ultrafiltration rates, were associated with higher mortality. And we discussed that cutoff, right? 1.75 ml/kg/hour. Therefore, literature is telling us that fluid overload could be detrimental for the patient, but also the way we remove fluids from the patients could cause harm, particularly if this is done too fast.

There are many physiological reasons for these, right? So, we can have patients that have already weak heart, and rapid removal of fluid could induce myocardial stunning, and all the hemodynamic complications affecting other organs. But at the same time, we need to recognize that leaving that – that worsening fluid overload without intervention could also be detrimental. So how to find that sweet spot? And how to determine the right fluid removal prescription for the patient? Those are key questions. And I think the answer here, at least in my view, is to assess and reassess, and also reassess how the patient is tolerating the fluid removal prescription. And perhaps use trends of noninvasive hemodynamic monitors and also bedside ultrasonography to be more precise in our fluid management. A simple way to reassess is to track the percentage gap in the prescription versus achievement of fluid balance, at least in 12 or 24 hour intervals. This could force us really to determine goals of treatment according to the varying course of the critical illness in our patient.

And there are many tools these days, to help you in the prescription of fluid removal with CRRT. For example, noninvasive hemodynamic monitoring of cardiac output and stroke volume, bedside ultrasonography to quickly assess the lungs, the heart or the IVC. The combination of tracking fluid removal prescription – the gap between what you prescribe and you achieve, and the dynamic adjustment of fluid balance goals based on this information, plus adjuvant tools such as POCUS, right? Could really improve the precision in fluid management with CRRT. This implies periods of timing which being more conservative or more aggressive is potentially most beneficial for patients. So I think we need to improve on personalize this intervention. Certainly, we can do it better than we currently do.

It doesn't matter exactly what you use, but your ability to reassess and adjust the prescription to the individual needs of the patient. You should use what's available at your hospital – a tool that you feel most comfortable using, a tool that has good reproducibility among operators in the ICU. But the most important thing is the trend of the parameters you are tracking. The trend of how your intervention – in this case, fluid removal – is changing that parameter that can help you adjust and personalize the treatment. Maybe the prescription should be kept the same, we should increase the fluid removal rate if the patient is tolerating it, and showing signs of hemodynamic improvement, or the opposite – backing down on the fluid removal rate if that is necessary.

Dr. Ostermann:
And how do you judge whether a patient is tolerating fluid removal or not?

Dr. Neyra:
So, in our practice, the way we do this, we set up a goal of fluid balance in 24-hour cycles, and then we reassess how close or far we are from that goal. Let's say my goal today is that the patient is -1 liter in the next 24 hours, and then when we are rounding the next morning, we recognize the patient never achieved that negative fluid balance of 1 liter that we prescribed. Patient is then still in positive fluid balance – let's say, 0.5 liter positive. This represents about 150% of gap between the prescription and the current fluid balance. It is at this time that we reassess. What's going on here? So first, we determine if the treatment was interrupted for any reason, such as clotting or a catheter problem – very often in the ICU. Did the patient leave the room for a procedure or imaging study? There are plenty of possibilities to determine if the treatment interruption, if any, was unintended or intended. Then we determine if there was a clinical event that required a change in prescription overnight? For example, stopping fluid removal by the night team, or if the patient had an overnight complication that required fluids or blood products. We need to keep in mind that critical ill patients in the ICU can easily become septic for multiple reasons, and/or can develop bleeding or ischemic episodes that may change their overall clinical status, precluding fluid removal. For example, inability to tolerate fluid removal coupled with worsening solute control – let's say, worsening metabolic acidosis, hyperlactatemia may represent at the novel, ischemic or septic event. Finally, if we do not identify a reasonable cause of the gap, we talk with the bedside nurse, to ascertain the causes of turning down the fluid removal rate or not keeping up with the hourly flow sheet that yields an hourly fluid removal rate, or net ultrafiltration rate target on the machine. So sometimes, when you

assess all these trajectories, you see that some patients – they were tolerating fluid removal for certain hours, and then their hemodynamics started to change, to the point that the nurses start backing down on fluid removal, and even sometimes giving back fluids.

So those are the patterns we need to recognize. So perhaps in that particular patient, the initial fluid removal rate was too high, and we need to decrease it to allow more sustained fluid removal that translates into a desired negative fluid balance during a prespecified interval of time. I always tell my colleagues in the ICU, fluid removal with CRRT is a monitor, not a spring. So what matter is the overall goal of reaching back euvolemia. This is particularly important, as some patients, while still fluid-overloaded, can be vasoplegic, and only able to tolerate gentle fluid removal, sometimes even with adjuvant low-dose pressures. Certainly, if the conclusion is that patient is unable to tolerate fluid removal, while still having signs of fluid overload, bedside ultrasonography or other tools can be very helpful to reassess the goals of treatment.

Dr. Ostermann:
Thank you, that's very clear. Dr. Neyra, you are very research active in this field. What do you think are the ongoing gaps in knowledge that need to be addressed in future studies?

Dr. Neyra:
Well, we definitely need to do more research about fluid deresuscitation, right? And when we are talking about patients with AKI requiring kidney replacement therapy, certainly we are talking about mechanical deresuscitation. I definitely think we need interventional studies to address this important aspect of care. A lot of recent data about rates of fluid removal with CRRT or net ultrafiltration rates, while very informative about the recognition that too fast fluid removal may be detrimental for the patient, are still observational data, with some limitations in terms of selection and indication biases. So we need interventional studies – clinical trials in which we need to test different strategies of fluid deresuscitation. Mechanical fluid deresuscitation. But, we need to also learn from prior experiences. We know one size does not fit all, so perhaps what we need now are smarter trials, that have some type of enrichment targeting populations with fluid overload, at high risk of adverse outcomes. Who are those patient phenotypes, that typically struggle with fluid overload? So those are the patients we need to consider on this type of studies.

And then, we need to pragmatically test interventions, right? Not necessarily based on the rate of fluid removal with CRRT, but on fluid balance perhaps, as a goal, and the ability to adapt that goal according to the evolving needs of the patient. So we need to test enhanced processes of fluid deresuscitation, in addition to fluid balance, conservative versus more aggressive goals. Perhaps for this, adaptive trial design platforms could be useful. Yes, we can do this. We have much better tools for pragmatic trials these days, and we should not forget that we can incorporate a lot of data coming from the electronical record, and also from the device itself. If we integrate these data, we can create certain algorithms that can amend clinical decisions at the bedside.

So I think, overall, these are exciting times, because there are many bioinformatics and computational tools that could be used, in research and in practice. I think we need to create a collective platform for collaborations in critical care nephrology, and advance the field, with developing much-needed evidence to really inform best practices, and fluid management with CRRT is certainly an area in need. So the time is now. We need to develop evidence to best inform effective and safe fluid removal in critically ill patients on CRRT.

Dr. Ostermann:
Well, that brings us to the end of our conversation. I want to thank our audience for listening in, and I want to thank you, Dr. Neyra, for joining me and for sharing all your valuable insights. It was a pleasure speaking with you.

Dr. Neyra:
Thank you very much, Dr. Ostermann, and it has been my pleasure.

Dr. Ostermann:
I am Dr. Marlies Ostermann. To access this and other episodes in our series, please visit KDIGO on Spotify, or kdigo.org/podcasts. Thank you for listening.