EDITORIAL

Renal Replacement Therapy in Pregnancy-related Acute Kidney Injury: Getting the Timing Right

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Abstract

Recent trials have failed to show a survival benefit from the early initiation of dialytic therapies in acute kidney injury (AKI), but the problem has not been studied in pregnancy-related AKI. While the KDIGO criteria have not been validated in pregnancy-related acute kidney injury (PRAKI), additionally both fetal and maternal outcomes require to be studied. The short observational study by Banerjee et al. contains some interesting observations.

Keywords: Fetal loss, Pregnancy-related acute kidney injury, Renal replacement therapy.

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Broad consensus exists that patients with acute kidney injury who have hyperkalemia, metabolic acidosis, volume overload, blood urea nitrogen >100 mg%, pericarditis, or encephalopathy need renal replacement therapy.[1] All of these are now regarded as complications of AKI, and several trials have focused on achieving homeostasis by an earlier initiation of RRT at KDIGO stages 2 or 3 without complications. Initiation of RRT in the AKIKI STAART AKI[2] and IDEAL ICU studies was considered to be delayed if the above complications were present. These three recent multicenter randomized controlled trials accounting for a total of 4,035 patients in either early or delayed strategies have shown no difference in the primary outcomes of 60- and 90- day mortalities, but revealed that 38–49% of patients randomized to a delayed strategy never received RRT. Additionally, the early strategy was associated with a three times higher risk of catheter-related bloodstream infection,[3] hypotensive episodes,[4] longer duration of RRT or dialysis dependence,[3] and hypophosphatemia.[4] These studies and an earlier RCT from India[5] appear to establish an absence of benefit of an early initiation of RRT strategy and a signal of harm, although the study from KEM, Mumbai, was not carried out in an ICU but a ward where the patient and illness profile are very different. Importantly, 80% of the patients in AKIKI and all those in IDEAL-ICU had sepsis, while the population in STAART AKI was large enough and heterogeneous enough to allow for a subgroup analysis. The majority of evidence therefore appears to be stacked up against an early start.

Now Banerjee et al.[6] in this issue of the journal presented an evidence that fetal outcomes may be improved with the early initiation of RRT in pregnancy-related acute kidney injury (PRAKI). There are multiple important implications of this study, which differ from the multiple high-quality trials. In the first place, the AKIN and KDIGO criteria for the classification of AKI, universally used in all the above trials, have not been validated in PRAKI. This group of patients may therefore behave differently and have special requirements, which have not been studied and need to be elucidated. Indeed, it is common for many studies to exclude pregnant patients from initial studies. Macedo and Mehta[7] have suggested that the kidney possesses a finite capacity to support other organ systems and RRT should be viewed as a support to meet a supply–demand mismatch that exists in AKI. This problem may be particularly evident in PRAKI as all systems including the renal are already working at the maximum capacity of their functional reserve.[6,8] Thus, any compromise may result in an inability to accommodate an increased metabolic and volume load. In fact, stable chronic patients on maintenance dialysis (MHD) require an increased dose of dialysis (20 hours per week) to successfully carry a pregnancy to term.[9] The only study to show a benefit of early initiation, the ELAIN trial[10] was a single-center study mainly in cardiac surgery patients, suggesting that different patient populations may have different needs and outcomes.

The second important message of this study is that it focuses on an important subclass of patients in India where 25% of critical care AKI patients requiring RRT may be pregnant women[6] as opposed to developing countries where this subgroup is smaller.

The third unique aspect of PRAKI in general and in this study is that both maternal and fetal outcomes need to be measured. Because a large number of PRAKI are expected to improve with delivery, the impact of dialysis upon maternal rather than fetal outcomes is assessed. In this study, the authors show that maternal outcomes were not impacted, in line with the results of the other RCTs in adults, but a significantly better fetal outcome was observed in patients who received an early RRT.

This study has the above mentioned strengths, but also has several limitations. It is a single-center study with a small number of patients, an expected result as improved obstetric care has

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decreased the number of PRAKI. It may therefore contain a significant alpha error and, in the light of contrasting evidence from very high-quality multicenter studies, clearly needs validation in a multicenter randomized trial. Single-center studies have frequently been noticed to inflate an effect even in randomized trials as seen in the ELAIN study, which actually compared very early (KDIGO stage 2) with early (stage 3) AKI, and interestingly, 75% of the stage 3 patients had complications, such as pulmonary edema. With the demonstration that a significant number of patients may actually recover from AKI without RRT, given time, the impact of such a delayed strategy on fetal outcomes needs to be studied in an RCT with well-defined criteria. Another limitation of this study was that the initiation of RRT was driven by the preference of the primary care physician. This, however, may reflect the widespread practice where despite the evidence from trials, clinicians frequently take a more arbitrary decision on initiation,[11] especially to control volume overload in anuric patients with a large mandatory projected intake in the ICU. The need for a randomized trial is again underlined by the fact that the two groups differed very significantly in blood pressure, anemia, sepsis, oliguria urea, and creatinine. It appeared that the early initiation group were clearly sicker and would have definitely had a worse outcome if the RRT had been delayed, another similarity with the ELAIN trial.[11] Finally, the entire cohort was extremely heterogeneous with the etiology of AKI, including sepsis, malaria, and snake bite, which while characteristic of AKI in a developing country do not strictly merit consideration as a PRAKI. The results of this study therefore may not be applicable to a more classic cohort of PRAKI.

In conclusion, two important questions therefore still confront the community of intensivists, nephrologists, and obstetricians in India. They need to validate the KDIGO criteria of AKI in PRAKI, and a randomized multicenter study of timing of RRT in PRAKI that evaluates both maternal and fetal outcomes is urgently needed.

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