Pediatr Nephrol (2015) 30:701–702
DOI 10.1007/s00467-014-2998-x

EDITORIAL COMMENTARY

The complexity of dialytic therapy in hyperammonemic neonates

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Received: 16 October 2014 / Revised: 17 October 2014 / Accepted: 22 October 2014 / Published online: 7 March 2015

Abstract The utilization of renal replacement therapy (RRT) in the setting of hyperammonia is a rare and complicated occurrence. Data demonstrate that the quicker the ammonia level is normalized, the better the neurological outcome. The optimal form of RRT is often decided by local practice. The recent work by Picca and colleagues details a larger series of children who underwent RRT for hyperammonia and adds some credence to the use of peritoneal dialysis (PD) in this population. While these authors conclude that PD is not optimal, they do note that the use of PD may be an option when other forms of RRT are not available. The results reinforce the general maxim that you should continue to do that which you do well and often, which in this context refers to continuing to use your form of RRT until alternative modalities are available.

Keywords Infant · Inborn error of metabolism · Renal replacement therapy

The recent paper by Picca and colleagues identified a series of 45 neonates over a 21-year span who underwent extracorporeal therapy or peritoneal dialysis (PD) for hyperammonemia due to an inborn error of metabolism (IBM) [1]. One of the aim of the authors was to examine the question of whether PD can play a role in hyperammonemia therapy and if so, then how does PD compare to either hemodialysis (HD) or continuous renal replacement therapy (CRRT) in the form of continuous venovenous hemofiltration or continuous venoarterial hemofiltration. The latter modalities have been referred to as extracorporeal therapy.

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In their article, the authors point out that PD is easy to initiate and that it can be performed at the vast majority of centers throughout Italy. They also point out that fewer centers provide extracorporeal therapy and therefore there may be a delay in initiation of HD or CRRT, making short-term PD a viable option. The crux of their study is that both early intervention with PD and later invention with extracorporeal therapy result in a similar outcome neurologically but not in a similar outcome hemodynamically. The authors also point out that the clearance and decay of ammonia are greatest with HD, less with CRRT, and least with PD.

Although PD is not believed to be the therapy of choice for the patient with an IBM, evaluation of the question of the benefits of PD reveals three potential benefits of this therapeutic modality in this population. These are:

1. PD is easy to administer and can be rapidly initiated at most centers with expertise.
2. The glucose load from glucose-based PD solutions may contribute to PD patients being less likely to go into a catabolic state. Catabolism in the patient with an IBM favors the stimulation of ammonia production. Therefore, it is not unusual that glucose infusions are given to the PD patient. It is also possible that the use of intraperitoneal glucose in the form of PD is beneficial to the infant in terms of minimizing the catabolic effect.
3. Children on PD may enter, in both the short term and long term, into a negative nitrogen balance. Protein loading in the patient with an IBM has the potential to stimulate ammonia production to the detriment of the infant. It is also known that amino acids and albumins are cleared in patients on PD, resulting in these patients being more likely to be in a negative nitrogen balance. The theory of using PD to induce a negative nitrogen balance may be beneficial to the patient as a way to minimize the risk of ammonia production.

In terms of extracorporeal therapy, Picca and colleagues identified patients who were treated with HD or CRRT. They make the point that due to the variable prescribing behavior at the different centers, independent of the form of dialysis, it was difficult to make a direct comparison of ammonia clearance. They also note that the decay rate of ammonia was greatest in patients on HD, as previously mentioned, and that there was an increase in the odds ratio for death associated with the use of extracorporeal therapy as compared to PD therapies. This increased odds ratio is possibly due to the complexity of administering extracorporeal therapy to infants or perhaps because the children were subjected to a delay in the initiation of dialytic therapy, making them more hemodynamically unstable. It is known that the longer such patients are acidotic and catabolic, the higher the risk of their hemodynamics being compromised. The issue of why there was a higher risk of death with extracorporeal therapy is not adequately addressed in this paper and can only be speculated upon. In addition, the authors failed to address the possibility of a hybrid option of sequential HD followed by CRRT or PD, as we have previously reported [2].

In terms of the relative risk of neurologic sequelae in patients on PD versus those on extracorporeal dialysis, the authors found the risk to be essentially equal with both modalities.

In patients on PD or extracorporeal therapy, the authors began medical intervention with the use of arginine, carnitine, sodium benzoate, phenylbutyrate, hydroxocobalamin, and biotin prior to initiation of extracorporeal therapy. This is consistent with work performed in other laboratories [2, 3] and indicates that use of these medications prior to the initiation of therapy may be beneficial and is certainly not detrimental, even though these medications will be cleared on dialysis [2, 3].

Whereas the authors cannot conclude that one form of therapy is better than the other, I suggest that the conclusion to be drawn from their results is that the earliest medical intervention possible, be it medical therapy, protein restriction, prevention of catabolism, initiation of dialysis, or a combination of these, is in the child's best interest. The authors point out that if extracorporeal therapy is unavailable in the immediate future, then a reasonable option is to initiate PD until extracorporeal therapy can be commenced. They showed that the initiation of PD at an average of 10 h after IBM diagnosis versus initiation of extracorporeal therapy 20 h after the onset of hyperammonemia resulted in no difference in neurologic sequelae of these patients. I also suggest that the conclusion should be that PD is only a stop gap measure in most patients and should not be considered as the sole dialytic therapy [4].

In summary, the article by Picca and colleagues reinforces the maxim guiding many medical decisions: whatever you do well and do all the time is what you should do.

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