Pediatric Therapeutic Plasma Exchange: Coming of Age?

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Therapeutic plasma exchange (TPE), an extracorporeal procedure that uses a medical device to replace plasma with colloids and/or crystalloids, is performed in various diseases to remove pathological substance(s) from plasma, such as autoantibodies, immune complexes or cryoglobulins, and/or replenish deficient components, e.g., complement factors or ADAMTS13 protein [1]. Based on the quality and robustness of evidence to favor benefit over harm, the American Society for Apheresis (ASFA) rates the indications from category I, i.e., first-line therapy, to category IV, wherein apheresis is deemed ineffective or harmful [1]. Despite emerging availability of specific therapies for certain conditions, this relatively nonspecific therapy remains a crucial adjunct to managing several diseases. Membrane filtration TPE (mTPE) utilizes conventional hemodialysis machines in ‘bypass’ mode with filters of larger pore size (0.2–0.5 μm) than those used for hemodialysis. Centrifugal TPE (cTPE) uses dedicated apheresis devices that allow precise calibration, slower flow rates, and additional therapies (e.g., cytapheeresis). The choice between modalities is chiefly dictated by the provider and location; while mTPE is typically performed in dialysis units and is popular in Europe and Japan, cTPE is conventional in transfusion medicine services and is popular in North America [1, 2].

Pediatric TPE constitutes less than one-twentieth of all apheresis procedures, with publications limited to case reports or retrospective series [2, 3]. TPE in children is challenging for various, often nonmodifiable, factors, and lacks evidence-based guidance. Currently available apheresis machines and disposables are designed for adult patients. Hence, TPE entails large extracorporeal volumes that risk hemodynamic instability unless the circuit is primed with blood or colloid solution.

Due to organ system immaturity or liver cell failure in sick young children, there is delay in metabolism of the citrate infused continuously to anticoagulate the circuit during cTPE, leading to high risk of hypocalcemia, acidosis, dyselecrolytemia, and bleeding. Other challenges in pediatric patients are the inability to secure adequate size vascular access, circuit clots due to slow flow rates, risks of hypothermia, dysglycemia and adenine or mannitol toxicity, fluid overload or iatrogenic anemia following ‘rinse-back’ or improper priming, inability to self-report symptoms, and complications associated with sedation in uncooperative patients [2, 3].

Available reports from India describe TPE in anecdotal cases or single-center series of specific illnesses; large series describing mTPE or cTPE are uncommon [4, 5]. In this issue of the Journal, Hans et al. report a retrospective audit of the indications and safety of cTPE at a single tertiary care center in North India [6]. During 2001–2019, they performed 672 procedures on 99 patients weighing 5–45 kg for diverse indications, chiefly hematologic, neurologic, and renal conditions. The indications were preponderantly ASFA categories I and II, similar to that reported by others. Complement-mediated thrombotic microangiopathy (atypical hemolytic uremic syndrome) was the most common indication, as reported previously in the region [4]. The study reports only a few children with neurological illnesses (e.g., acute inflammatory demyelinating polyneuropathy), due to access to IV immunoglobulin and preference for mTPE in older children. Centrifugal TPE was performed using three of the five commonly used centrifugal instruments available in India, including a newer option that permits smaller extracorporeal volumes and has a wide range of pump rates that might be safer for use in small children. Techniques such as immunoabsorption or low-density lipoprotein (LDL) apheresis were not reported. As compared to previous studies [4, 5, 7, 8], the authors report low rates of complications in a younger age group, potentially because of the exclusion of large volume cytapheeresis procedures, prophylactic use of calcium infusion, uniform use of blood prime, and use of packed red cells free of saline-adenine-glucose-mannitol additive. Expectedly, adverse events correlated inversely with body weight, and positively with extracorporeal

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volume, number of procedures, and use of fresh frozen plasma as replacement fluid.

Overall, the findings reaffirm the satisfactory experience with TPE in pediatric patients through a comprehensive audit over two decades. The study is a valuable addition to data on safety and efficacy of cTPE in children in a field where the evidence base cannot yet rely on clinical trials. The findings underscore the technical difficulties faced during pediatric TPE using adult equipment and calls for action from industry and experts to devise apheresis machines and disposables suited to meet these challenges [9]. Meanwhile, such case series highlight the feasibility of pediatric TPE at experienced centers, indicating the need for prompt referral when the procedure is indicated.

Declarations

Conflict of Interest None.

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