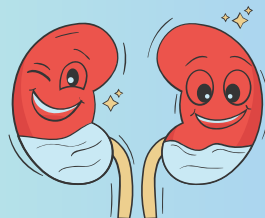
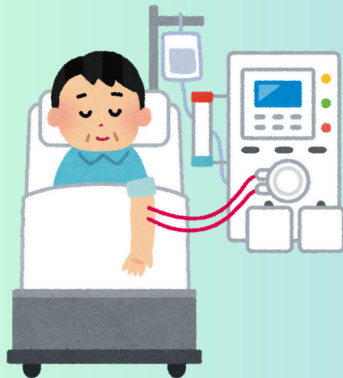


HEMODIAFILTRATION ADVANCEMENTS IN PEDIATRICS

MEDigest

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HDF: A NEW ERA IN PEDIATRIC KIDNEY CARE

The first section of this newsletter will focus on Hemodiafiltration (HDF) as a promising treatment for children with stage 5 Chronic Kidney Disease (CKD) with technical specifications.

CLINICAL OUTCOMES IN PEDIATRIC HDF



The second section will highlight some of the clinical studies showcasing the HDF outcomes in pediatric CKD population and discuss the future implications.



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HDF: Introduction

Advancements in technology have propelled HDF forward, with innovations such as improved high-flux dialyzers, ultrafiltration, and more efficient machines (1). Increasing evidence suggests that HDF with a high convective volume of ≥ 23 L/session/ 1.73m^2 of body surface area (BSA) per session, may improve individual survival rates while lowering cardiovascular risks (2). Several clinical benefits of HDF have a significant impact on patients' cardiovascular health and general well-being (3). By combining the best of hemodialysis (HD) and hemofiltration (HF), HDF offers a powerful solution for toxin removal, especially targeting middle molecular weight uremic toxins that traditional HD cannot eliminate. Some other potential advantages of HDF in adults are mentioned in Figure 1B.

HDF in CKD-stage 5 children

Pediatric HDF has been gaining momentum in treating young CKD patients [>5 years] (4). Similar to HDF in adults, the three prerequisites to perform HDF in children include high-flux dialyzers, dialysis machines that permit precise control of ultrafiltration (UF), and "ultrapure" water as a replacement fluid (5) (Figure 1A). One of the limitations with the currently available dialysis machines for HDF is that the current ones are only suitable for children weighing >10 Kgs in Europe and Australia, >20 Kgs in Japan and >40 Kgs in Canada (6). Hence technological advancements for the younger and most vulnerable patients would be beneficial.

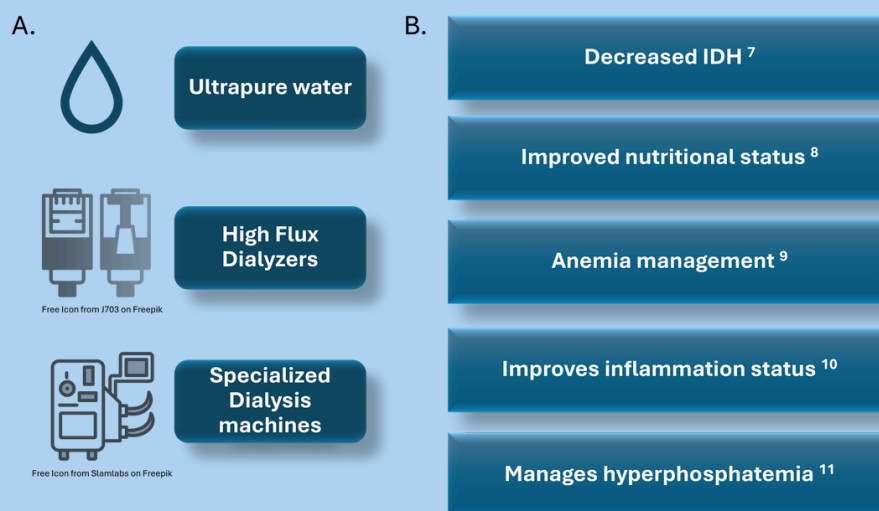


Figure 1: HDF and its clinical benefits. A. HDF technical requirements. B. Some clinical advantages of HDF in adults.

The Hemodiafiltration, Heart and Height (3H) study, the first prospective, observational, multicenter study with 190 children from 10 countries in Europe and North America, assessed the clinical benefits of HDF in children compared to HD in a 1 year follow up. The HD group had a mix of low/mid and high flux, with $>70\%$ on high flux. The study showed that high convective volumes of $12\text{-}15$ L/ m^2 BSA that equates to $20\text{-}23$ L/session in adults, could be achieved in children (4). To attain the maximum convective volume, clinicians can aim for the ideal dialyzer surface area, blood flow, and dialysis duration (12). The blood flow of children in the 3H study was ~ 200 ml/min and they had dialysis for 12 hours/week in both HD and HDF group (4).

Post-dilution HDF is performed in most pediatric centers, but hemoconcentration at high UF rates leading to clotting of the extracorporeal circuit is a potential disadvantage. Pre-dilution HDF, on the other hand may reduce the efficiency of both the diffusive and convective component by hemodilution (5), but might be helpful with high hematocrit patients (12).

Since some of the early studies demonstrated the benefits of HDF in children, some pediatric dialysis units worldwide, have implemented it, with 58% of children being in the Western Europe and from International pediatric Hemodialysis Network (IPHN) data, only 15% of children are on HDF globally (12).

There has been no RCT on pediatric HDF as of now, but the 3H study (4) and a few more have indicated that HDF can improve cardiovascular risk profile, growth, and quality of life as well as reduce inflammation, endothelial dysfunction, and oxidative stress in children (12,13). Some key findings from the 3H study and others comparing HDF vs HD in children are listed below and in Figure 2.

1. **Cardiovascular outcomes:** The 3H study showed an attenuated progression of carotid intima-media thickness-standard deviation score (CIMT-SDS) in the HDF group, while the HD group showed a +0.47 increase after the follow-up ($p=0.02$); similarly the mean arterial pressure SDS change in the HD cohort was 0.65 higher than HDF group ($p=0.01$) (4). Moreover, inflammatory markers such as C-reactive protein (CRP) [2.86 in HD vs 2.03 in HDF; $p=0.02$] and uremic toxins such as asymmetric dimethylarginine (ADMA), an endothelial dysfunction marker [1.16 in HD vs 0.85 in HDF; $p=0.007$] and, Beta-2 microglobulin [40.5 in HD vs 24.5 in HDF; $p=0.005$] were reduced in children switching from HD treatment to HDF in 3 months (13).

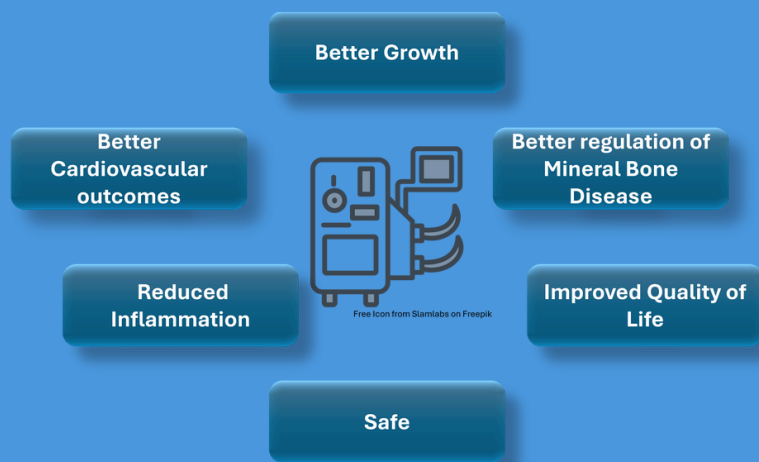


Figure 2: Benefits of HDF in children. Adapted from (3)

2. **Bone health:** The 3H study showed that the parathyroid hormone (PTH) levels declined significantly in the HDF cohort ($p=0.004$) after one year compared to the static levels in the HD group ($p=0.13$) (4). Furthermore, Fibroblast growth factor-23 (FGF-23) was increased by 109% in the HD group, while it was relatively unchanged in the HDF group (14).

3. **Growth and nutrition:** The 3H study showed a significant increase in the height SDS change of HDF group compared to the HD ($p=0.04$) (4).

4. **Safety:** A stable albumin level and a lower inter-dialytic weight gain ($p=0.04$) was noted in the HDF group in the 3H trial indicating fewer adverse symptoms (4,12) and therefore making it safe for children.

5. **Quality of life (QoL):** HDF improved the QoL by reducing cramps, headaches, and post-dialysis recovery times, leading to improved school attendance and physical activity (4).

Future implications

The existing literature shows that HDF is safe, practical and well-tolerated treatment in children, although it still require RCTs to confirm its potential clinical benefits such as better cardiovascular outcomes, BP control, improved bone health and growth among others (5,12). An active clinical trial aiming to compare pre and post-HDF may contribute to define an optimum modality for children (15). As technology continues to advance and research provides deeper insights, HDF may become the cornerstone of pediatric renal care, improving both the quality and longevity of life for children with severe kidney conditions especially those in the long waiting list of transplantation.

Therefore, along with RCTs investigating a series of important clinical outcomes, integration of patient-reported outcomes, economical and sustainability factors are needed to further convince the wider application and utilization of HDF into pediatric care (12).

References:

1. Maduell F, *Semin Dial.* 2018;31(6):625-632. [PubMed](#).
2. Peters SA, et al. *Nephrol Dial Transplant.* 2016;31(6):978-84. [PubMed](#).
3. Maduell F, et al. *J Clin Med.* 2024;13(4):1110. [PubMed](#).
4. Shroff R, et al. *J Am Soc Nephrol.* 2019;30(4):678-691. [PubMed](#).
5. De Zan F, et al. *Semin Dial.* 2022;35(5):427-430. [PubMed](#).
6. Ranchin B, et al. *Kidney Int.* 2023;103(6):1038-1040. [PubMed](#).
7. Locatelli, et al. *J Am Soc Nephrol.* 2010;21:1798-1807. [PubMed](#).
8. Savica, et al. *J of Renal Nutrition.* 2006;16(3):237-240. [PubMed](#).
9. Bonforte G, et al. *Blood Purif.* 2002;20:357-363. [PubMed](#).
10. Pedrini, et al. *Nephrol Dial Transplant.* 2011;26:2617-2624. [PubMed](#).
11. Davenport, et al. *Nephrol Dial Transplant.* 2010;25:897-901. [PubMed](#).
12. Ahlmann C, et al. *Pediatr Nephrol.* 2024;39(9):2611-2626. [PubMed](#).
13. Ağbaş A, et al. *PLoS One.* 2018;13(6):e0198320. [PubMed](#).
14. Fischer DC, et al. *Kidney Int. Reports.* 2021;6:2358-2370. [PubMed](#).
15. Shroff R, et al. *NCT04210154.* (2021 Feb- 2024 Dec). [CTG](#)