Selected Summary

Haemodiafiltration or haemodialysis in kidney failure

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SUMMARY

This paper reports on the findings of a pragmatic, open-label, randomized controlled trial called the CONVINCE trial which aimed to compare the survival benefits of high-dose haemodiafiltration (HDF) versus conventional high-flux haemodialysis in patients with kidney failure. The trial, conducted across 61 centres in 8 European countries, enrolled 1360 patients who were candidates for HDF, providing a real-world perspective on the efficacy of this treatment. The primary outcome was death from any cause, and key secondary outcomes included cause-specific mortality, cardiovascular events, hospitalizations and infection related admissions. Over a median follow-up of 30 months, wherein majority of patients received the prescribed dose of high flux dialysis and HDF, the group receiving high-dose HDF had a significantly lower risk of all-cause mortality (hazard ratio [HR] 0.77 with 95% confidence interval [CI] being 0.65–0.93), than conventional high flux haemodialysis.

COMMENTS

Regular maintenance haemodialysis is the commonest modality of treatment for end-stage kidney disease (ESKD), the others being peritoneal dialysis and kidney transplant. Kidney transplant provides much better outcomes and quality of life, but only a minority of ESKD patients receive a kidney transplant for a variety of reasons.

Haemodialysis involves using an artificial kidney (dialyzer) to remove uraemic toxins and extra body fluid/volume by physical principles of diffusion and ultrafiltration. The standard prescription of haemodialysis involves 4 hour sessions done thrice per week with a typical ultrafiltration volume 2000 to 3500 ml (approximately 5% of body weight). The pore size of the dialyzer decides and also limits diffusive clearance and the body's homeostatic limitations cap the maximum ultrafiltration rate or fluid removal rate. Over the decades, dialyzers with larger pore size (high flux dialyzers) with higher clearance than low flux dialyzers came into use. Uraemic toxins comprise molecules that span a wide range of size, charge and protein binding properties. The clearance of larger molecules, typically represented by beta-2-microglobulin is better achieved with convection (ultrafitration across large pore sizes) than by standard diffusion. HDF addresses this limitation of conventional haemodialysis by ultrafiltering large volumes by convection (>20% of blood volume processed to achieve convective clearance; exceeding 23 L per session in this study) and replacing this ultrafiltrate by online generation of ultra-pure, non-pyrogenic, compatible replacement fluid and finally it's infusion into the patient's blood. Thus, HDF represents the progressive evolution of renal replacement therapy modalities from low flux haemodialysis to high flux haemodialysis and then HDF.[1]

The complexity of ESKD patients and the increasing utilization of HDF by many centres across the world, underlines the importance for evaluating its utility in real life. As per a recent report, even a decade ago more than 100 000 patients were already on regular HDF mostly in Europe and Asia–Pacific where the growth rate of HDF is 2–3 times the growth rate of the conventional dialysis population.[2] There have been a few earlier studies on HDF[3] each with its own limitations but with a definite signal for improved outcomes in ESKD patients creating the right setting for this elegant CONVINCE trial. The study design and methodology used in this trial are robust, with a good sample size, and adhere to established clinical research standards. It's pragmatism, with minimal exclusion criteria, supports generalizability to a broader population of patients with ESKD.

The key features of this study need to be mentioned. Previous studies have suggested that an ultrafiltration/convection volume of 23 L is necessary to reap the benefits of HDF. The CONVINCE study achieved this goal in 92% sessions of the study arm. The median vintage of patients was 35 and 30 months in the study and control arm, respectively, though patients who had been on dialysis for at least 90 days were included. This would have definitely enriched the cohorts with healthier subjects because ESKD patients experience disproportionate mortality in the initial few months of initiation of dialysis. Though the benefits of HDF were seen in all-cause mortality, patients with diabetes or with known cardiovascular disease (CVD), which comprise a substantial proportion of prevalent ESKD patients, did not have a survival benefit. Also the risk of death due to CVD, the dominant cause of mortality

in the dialysis population was similar in both groups. These findings would definitely impact as well as help in defining the best candidates for HDF. It is also possible that initiating HDF earlier in the course of maintenance dialysis might deliver better outcomes, before the uraemic pathophysiology has taken a stronghold while the patient is on conventional haemodialysis. Moreover, the absence of data on race or ethnic background limits the generalizability of the findings to non-white patients.

Applicability and relevance to healthcare in India

While the study primarily focuses on European patients, its findings have broader implications for treatment of kidney failure worldwide, including India. The relevance of the CONVINCE trial to Indian healthcare is multi-fold:

1. *Increasing incidence of kidney failure*: ESKD is a growing global health concern, and its incidence is on the rise in India due to factors such as an aging population, changing lifestyles, and the increasing prevalence of type 2 diabetes and hypertension. The findings of this study can provide insights into improving the treatment of kidney failure patients in India.
2. *Comparative data*: The study provides valuable comparative data on two different dialysis methods. All societies face resource constraints in delivering healthcare and this is more acute for renal replacement therapy. Hitherto access to dialysis itself was a major challenge in many parts of low-middle income countries (LMIC). India has mix of private and public healthcare. In the past decade India has executed a laudable initiative in providing dialysis to all economically challenged sections of society. The Pradhan Mantri National Dialysis Programme (PMNDP) was launched in 2016–17 to provide free dialysis to deserving beneficiaries.[4] As of 2023, 1442 dialysis centers with 9807 machines have been established and more than 2.1 million patients have benefited. In the Indian subcontinent's context, where access to quality healthcare, especially for chronic diseases, remains a challenge, any treatment modality that improves survival rates is of great importance.
3. *Survival benefits and cost-effectiveness*: The finding of a lower risk of death among patients receiving HDF needs to be contextualized for India and LMIC at large, where access to advanced medical care can be limited or heterogenous. The visible cost of HDF is at least two or four times that of conventional haemodialysis and it needs stringent quality control of the processes. Understanding whether HDF is not only more effective but also cost-effective can inform healthcare policy and resource allocation.

Limitations and future research

The study's limitations of including the somewhat healthier trial population, the absence of race and ethnicity data, and the lower-than-expected overall risk of death, should be acknowledged. To put it in a different perspective, at least 48 patients need to be on HDF for one year to save one life. But the study also opens up some key questions regarding its lack of benefits in the subset of ESKD patients with pre-existent co-morbid conditions.

In conclusion, the CONVINCE trial offers valuable insights into the treatment of ESKD patients with high-dose HDF, with clear survival benefits to ESKD patients who don't have diabetes or known CVD. Future research and adaptation to local contexts are essential. Initiatives could focus on expanding the investigation to more diverse patient groups, and then exploring the long-term implications of HDF. Additionally, studies that directly examine the applicability and efficacy of such treatments in the Indian healthcare context would be invaluable.

Conflicts of interest. None declared

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