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On-line Hemodialysis & mixed HDF

Mi Jung Lee
Bundang CHA Medical Center, Korea, Republic of

Hemodiafiltration (HDF) is a combined form of renal replacement therapy, which utilizes diffusive and convective solute removal in a single therapy. HDF requires a high-flux hemodialyzer and a sterile nonpyrogenic substitution fluid infusing system for maintaining fluid balance. On-line HDF enables to obtain large volume of substitution fluid by online filtration of standard dialysate through a series of bacteria- and endotoxin-retaining filters. Filtered dialysate is infused as a substitution solution directly into the patient's blood. According to the location of administration of substitution solution, on-line HDF is categorized into pre-dilution, post-dilution, mid-dilution, and mixed dilution. Among them, the post-dilution method involves a dilution of blood by infusing substitution solution after ultrafiltration, leading to the highest solute clearances for the lowest convection volume. However, post-dilution approach may be challenging in patients with high predialysis hematocrit levels or low vascular access blood flow. Hemoconcentration and hyperviscosity coupled with increased shear stress is a known risk factor for red cell damage and reduced dialysis efficiency.

To date, several large randomized controlled trials and pooled analysis have suggested that HDF is associated with improved clinical outcomes, when it achieved adequate convection volume. The CONvective TRAnsport STudy (CONTRAST) and the Turkish HDF study (THDFS) showed a modest, non-significant effect of HDF on all-cause mortality, but the Spanish Estudio de Supervivencia de Hemodiafiltracion On-Line (ESHOL) study indicated a reduced mortality in HDF. Of note, *post hoc* analysis of all three studies demonstrated that patients treated with the highest convection volumes had a significantly lower mortality risk. Furthermore, individual participants data (IPD) analysis of the CONTRAST, THDFS, ESHOL, and the French HDF study also revealed that patients with achieved convection volume over 19 L/session had a significantly reduce risk of all-cause and cardiovascular mortality, supporting the importance of high convection volume in the HDF treatment.

However, not all patients are suitable to achieve effective convection volume in the post-dilution methods due to high blood viscosity or low vascular access blood flow. Mixed HDF may be helpful to increase convective volume in these patients group. Mixed dilution provides substitution fluid to both pre- and post-dialyzer. Automatic transmembrane pressure (TMP) feedback is applied to adjust the ratio of pre- and post-dilution substitution to obtain the maximal filtration fraction within safe pressure and hydraulic conditions. In terms of clinical relevance, mixed HDF showed a benefit in beta 2 microglobulin removal and anemia management compared with post-dilution HDF, but evidence is not sufficient. Future studies are needed to provide additional evidence on the potential benefit of mixed HDF.

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