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Convection vs Diffusion - What is the Difference?

Ingrid Ledebo, Ph.D.

Gambro Corporate Research, Lund, Sweden

Hemodialysis, the major dialysis therapy for 40 years, is based on blood purification by diffusion through a tight cellulosic membrane. However, diffusion removes mainly small solutes in response to the concentration gradient provided by the dialysis fluid. Many large solutes normally cleared by the kidneys are retained in uremia and exert negative effects on cells and tissue.

Today there is a trend towards using more permeable membranes in dialysis, making it possible to apply convective transport, on its own or in combination with diffusion.

Convection is driven by the flow of ultrafiltered fluid that carries across the membrane all solutes that pass through the pores. Thus, optimal convection requires a high ultrafiltration rate and sterile fluid to replace the excess volume, in addition to an open membrane.

The major characteristic of convection compared to diffusion is thus the potential to clear a wide range of solutes, and the literature contains evidence of removal of uremic retention solutes, such as phosphate, homocystein, β_2-microglobulin, leptin and factor D, with convective therapies. Comparisons are made between hemodialysis with high-flux membranes, in which the convective component is limited, and hemodiafiltration, in which convection can be fully utilized provided on-line prepared substitution fluid is available, and clearly demonstrate the superior solute removal capacity of hemodiafiltration, qualitatively as well as quantitatively.

Convective therapies in general and hemofiltration in particular are associated with improved hemodynamic stability. It is well documented that a physiological increase of peripheral resistance in response to fluid removal is seen during isolated ultrafiltration and hemofiltration, but rarely so during hemodialysis. The mechanism for this is still not understood, but a difference in energy balance seems to play a role; hemofiltration leading to less heat gain and therefore more vasoconstriction. Removal of a large vasoactive molecule has also been hypothesized. Irrespective of the mechanism, convective therapies provide improved hemodynamic stability and facilitated blood pressure management.

The application of convection in modern dialysis implies the use of high-quality components - the required high-flux membrane is usually synthetic and biocompatible, the necessary infusion solution is prepared on-line which provides the potential for it to be individualized, contain bicarbonate and as freshly prepared have a high microbiological quality. When hemodialysis is made with similar membranes and similar fluid quality there is no major difference in biocompatibility. However, while modern convective therapies require these components, contemporary hemodialysis is still frequently performed with standard membranes and standard fluid quality. When evaluating the impact of convective therapies on important outcome parameters this difference in biocompatibility - regarding the membrane as well as the fluid quality - should not be disregarded.

In order to practice evidence-based medicine we need proof that the extended solute removal, enhanced hemodynamics and improved biocompatibility of convective therapies lead to a survival benefit for patients treated with these therapies. There are single-center reports of patients treated with different modes of renal replacement therapy that show a clear advantage for hemofiltration. There are also single-center reports of entire patient populations treated with hemodiafiltration showing mortality data that is widely superior to registry data. A registry report of patients treated with convective therapies found a non-significant survival benefit and a significant morbidity benefit, in terms of less interventions for β_2m-amyloidosis.

As there are no long-term controlled studies of patients on convective therapies, we may have to extrapolate from data for patients treated with high-flux membranes. Again, there are a number of registry reports and retrospective single-center observations showing improved survival for patients treated with high-flux, synthetic membranes. However, this provides no proof of causality, only of association. A recent study, designed to provide evidence for a possible advantage of dialysis with high-flux membranes, the HEMO study, showed no overall survival benefit but did find that some patient categories - e.g. patients who have been on dialysis for a long time - have a significantly lower mortality when treated with high-flux membranes. Still, further evidence is needed.

With increasing awareness of the wide variety of uremic solutes that accumulate in patients with chronic kidney disease and are associated with long-term complications, we need to adapt our methods for blood purification. Convective transport is a useful tool, since it removes not only small solutes but solutes over a large molecular weight spectrum. Solute removal as well as hemodynamic stability are related to the degree of convection, which is controlled by the amount of ultrafiltration applied. Modern applications of convective therapies are inherently biocompatible and as such provide patient benefits that can not be separated from those of the transport mechanism. A large spectrum of subjective and objective patient benefits have been documented with convective therapies, but survival advantages remain to be shown.

REFERENCES

1) Ledebo I : Principles and practice of hemofiltration and hemodiafiltration. *Artif Organs* **22**:20-25, 1998
2) Ledebo I : On-line hemodiafiltration : technique and therapy. *Adv Ren Repl Ther* **6**:195-208, 1999
3) Ledebo I : Does convective dialysis therapy applied daily approach renal blood purification. *Kidney Int* **78**:S286-291, 2001