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Hemofiltration and Hemodiafiltration with On-line Prepared Fluid - Blood Purification Therapies for the Future

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Quality dialysis

Quality dialysis means optimal removal of fluid overload and uremic solutes including those of a larger molecular weight, e.g. β_2-microglobulin (β_2m). In order to improve treatment tolerance to fluid removal and to optimize the removal of larger uremic solutes more convection needs to be used in dialysis therapy.

Convective therapies

The first step to introduce more convection is to replace the standard low-flux hemodialysis (HD) membrane with a highly permeable membrane. Today 25% of all dialyzers are of high-flux type. When these membranes are used in high-flux HD, the convective transport is limited to the desired weight loss together with the excess UF which occurs in a high-flux dialyzer. This uncontrolled UF is compensated for by backfiltration of dialysis fluid. In a typical high-flux HD, maximum UF volume, from which convective clearance can be calculated, is only about 6-8 liters. To fully utilize highly permeable membranes, convective transport should be maximized. Thus, the volume of fluid driven through the membrane should be increased beyond the volumes used in high-flux HD. This is done in hemofiltration (HF) and hemodiafiltration (HDF). In HF, no dialysis fluid is used, accordingly, the only transport mechanism for solutes is convection. In conventional postdilution HF UF volumes are 25-30 litres; in modern predilution HF UF volumes are often 1-1.2 times the patient's body weight. In HDF, convection and diffusion take place simultaneously and UF volumes are traditionally 12-25 litres.

Removal of uremic solutes during convective therapies

The amount of convective transport by different therapies corresponds to UF volume. The more UF, the larger the convective transport, accordingly, more larger solutes, such as β_2 m are removed. In high-flux HD, adding a small amount of convection, there is only a minor increase in urea clearance compared with low-flux HD. However, β_2 m will be removed to some extent.
Increasing UF volume by changing to HDF, thus, adding more convection increases the removal of all solutes, the more the larger they are. The effect on smaller solutes, e.g. urea may be relatively small due to the interaction between diffusion and convection. However, according to my own experience urea reduction ratios of 0.8-0.9 can be achieved if HDF treatment is optimized with UF volumes of 30-40 litres.

In postdilution HF, urea clearance is equal to the UF rate, which in turn is about 0.3 of the blood flow rate, depending on hematocrit and protein concentration. Compared with HDF, clearance of small solutes including urea is greatly reduced, whereas larger solutes are as effectively or better removed, depending on UF volumes (Floege *et al*, 1989). Using predilution HF, the limitations as regards small solute clearance can be overcome. The clearance of urea is equal to the UF rate multiplied by the degree of dilution of the blood. The reason for the enhanced clearance of small solutes in predilution HF is an increase in filtration fraction from about 0.3 to 0.5 when the blood is diluted.

To summarize solute removal in HF, urea clearance is reduced compared with HD and HDF, especially in postdilution HF. On the other hand, with increasing UF volumes convective transport will increase and, accordingly, removal of larger solutes. The largest removal of 2m approaching estimated weekly production has been achieved with predilution HF (David *et al*, 1990).

Interesting to note, in predilution HDF urea clearance decreases as the dilution of the blood before the dialyzer reduces the concentration gradient needed for optimal diffusion (Canaud *et al*, 1994; Kiss & Halfman 1995).

Hemodynamic stability during convective therapies

Improved blood pressure stability can be achieved with postdilution HF (Baldamaus *et al*, 1982) and HDF (Wizemann *et al*, 1983). The mechanism is an increase in peripheral vascular resistance in response to fluid removal, being at least partly caused by a rise in plasma noradrenalin. Whether the hemodynamic benefits of postdilution HF are valid also with predilution HF has not been studied thoroughly. Recent reports indicate that this is the case (Altieri *et al*, 1997; Van Kuijk *et al*, 1997).

Why should convective therapies be used?

Convective therapies should be used to improve removal of larger solutes, e.g. 2 m. The clearance of small solutes will be optimal with HDF and adequate with HF, especially with predilution HF. Moreover, removal of excess fluid can take place with improved hemodynamic stability.

In addition to better intratreatment tolerance and less long-term morbidity (Quellhorst *et al*, 1985), HF has been shown to manifest better survival compared with acetate HD (Quellhorst *et al*, 1985; Schaefer *et al*, 1984). Whether this superiority in survival is maintained when HF is compared with modern bicarbonate HD needs of course to be proven.

Fluid for convective therapies

The main limitation to perform HDF or HF is the requirement of large volumes of substitution fluid free from bacteria and endotoxins. Conventional substitution fluids are available in bags, which means not only considerable cost but also work. The buffer in the fluid is lactate and the electrolyte composition is standardized. Therefore, the use of HF and HDF has been limited in the past.

Today, large volumes of iv-quality fluid can be prepared on-line, continuously by specially designed multipurpose dialysis systems in a safe, practical and cost-effective way. However, to use on-line prepared fluid there are certain important conditions which need to be fulfilled. 1) The water should be of good microbiological quality. 2) Everything added to this water must be of good microbiological quality, especially the bicarbonate component, which should come from a powder cartridge. 3) The fluid should be ultrafiltered to remove bacteria and endotoxins, and the ultrafilters should be placed in strategic positions with the final ultrafilter integrated in the infusion line and placed just before the fluid is infused into the blood. 4) The flow path should be desinfected regularly and bacterial growth must be prevented at all times, especially when the system is not in use. 5) The entire system should be maintained with microbiological awareness.

Gambro AK 200 ULTRA System

Gambro s AK 200 ULTRA System can, depending on fluid route, perform HD or HF or HDF, with the same machine using ultrapure dialysis fluid and on-line prepared substitution fluid, virtually in unlimited quantities with a fluid composition which comprises bicarbonate and which can be individualized to the patient's need.

The AK 200 ULTRA prepares the fluid from reverse osmosis water. The water is prefiltered in the first ultrafilter before entering the machine. A- and B-concentrates are added and the prepared fluid is filtered in a second ultrafilter. In HF and HDF, the amount of fluid needed as substitution fluid is pumped through a final ultrafilter before it is mixed with the patient's blood.

Choice of treatment modality

Based on the patient's individual characteristics a suitable mode of therapy can be chosen. If only small solute clearance is considered important standard HD can be used. If, however, removal of larger solutes, e.g. β_2, is also thought to be important or if the patient frequently manifests intradialytic hypotension, HF may be the best treatment modality. With HDF, optimal removal of small as well as larger solutes can be achieved together with improved hemodynamic stability.

The introduction of a specially designed multipurpose dialysis system for on-line preparation of iv-quality fluid has opened new possibilities for the use of convective therapies, such as HF and HDF, in everyday dialysis.

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