Ultrapure Dialysis Fluid - is it Important?

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Dialysis fluid is in contact with blood via a thin, semipermeable membrane and all substances dissolved or dispersed in the fluid that can pass through the pores of the membrane can also reach the blood. Although dialysis fluid is considered as a drug in many countries, there is no requirement on sterility. As long as acetate was used as buffer source the degree of microbial contamination was usually limited, but the widespread introduction of bicarbonate in dialysis has lead to increased risk of bacterial and endotoxin contamination. In combination with the growing use of highly permeable membranes, there may be reasons for concern about the microbiological quality of dialysis fluid and the effect on the patient.

Practical guidelines for dialysis usually contain sections on the quality of water and dialysis fluid, advising on methods for testing and recommending maximum target levels. The quality term "ultrapure" was introduced a couple of years ago; it means practically free from bacteria and endotoxin. In quantitative terms it is defined as $<10^{-1}$ CFU/mL and <0.03 EU/mL.

Ultrapure dialysis fluid can be prepared from standard quality dialysis fluid by a single step of controlled ultrafiltration. One additional step of controlled ultrafiltration will turn ultrapure dialysis fluid into sterile fluid, that can be used for infusion. The need for large volumes of sterile infusion solution, such as in the convective therapies hemofiltration and hemodiafiltration, is a strong motivation for preparing ultrapure dialysis fluid. However, there are also clinical benefits associated with the use of ultrapure dialysis fluid in conventional hemodialysis that are starting to be perceived.

The literature contains a large number of reports of in vitro experiments testing the permeability of dialysis membranes to microbiological contaminants in the dialysis fluid.

Different results can be obtained depending on the choice of bacterial strain, membrane, result parameter and experimental set-up, but the general impression from these studies is that bacterial products in the dialysis fluid can have an effect on blood components during dialysis.

The most common indicator of this is activation of monocytes and release of proinflammatory cytokines into the blood.

The next question is whether this has any relevant impact on the patient. Several clinical studies are now appearing showing that the use of ultrapure dialysis fluid makes a difference for patients in terms of less inflammation as indicated by lower CRP values, lower β_2-microglobulin levels and less frequent occurrence of CTS, reduced need for EPO, better nutritional status and even better preservation of residual renal function. However, there are also studies showing that the use of standard or ultrafiltered dialysis fluid has little impact on the inflammatory status; in fact it appears to be of less importance than the choice of dialysis membrane or the occurrence of infectious episodes. All these studies are generally retrospective, small or non-randomized. There are many possible explanations to the controversial results because large natural variations

have been found in all parameters involved - endotoxin potency, patient immune response and CRP levels.

Thus, the benefits of using ultrapure dialysis fluid are not yet unequivocally shown, and this issue is going through the same stages of looking for evidence as we experienced 10-15 years ago concerning the benefit of using biocompatible membranes. From a logical and a physiological point of view there is no doubt that using non-complement-activating membranes and ultrapure dialysis fluid is better than exposing dialysis patients to repeated challenges of the immune system, but the hard evidence for both is lacking. Still, we should let our conviction guide us towards a more physiological dialysis at the pace that technical innovation makes possible and society can afford.

REFERENCES

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