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Haemodialyser reuse: facts and fiction

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High-flux high-price dialysis: is everybody using it?

Since the advent of haemodialysis, the number of patients on haemodialysis has been growing constantly and is now increasing by 7–9% annually. Simultaneously, over the years, there has been a trend towards the use of high-flux dialysers which are much more expensive than cellulosic low-flux dialysers, albeit at different rates in different countries. In the US, the number of patients treated by high-flux dialysis, increased from 5% in 1987 to 31% in 1994. In 1994, the proportion of patients treated by high-efficiency/high-flux dialysis was 57% [1]. In 1996, in Japan, 43.5% of the patients were treated with high-flux dialysis [2]. In Australia, there has also been a movement towards more biocompatible membranes. In 1997, the most common membrane was hemophan®, used by 35% of the patients and only 6% of the patients were treated with high-efficiency/high-flux dialysers, mostly cellulose triacetate [3]. What about Europe? Data from the 1993 EDTA Registry showed that 6.8% of patients in the European Economic Community (EEC) were on high-flux techniques [4]. However, great differences were observed between countries, ranging from 0% in Denmark, Finland, Ireland and Luxembourg, to 21% in Italy. However, these figures probably do not reflect the present use of high-flux dialysers in Europe. For example, in Portugal, the number of patients treated with high-flux dialysers increased from 0.2% in 1993, to 8.1% in 1998. The present use of high-flux membranes is 40% in Germany (Dr Bommer, oral communication), 20% in Holland (Dr Leunissen, oral communication), 10% in UK (Dr Hoenich, oral communication), 20% in Spain (Dr Valderrabano, oral communication), and 20% in Italy [5].

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Reuse: a solution for the 1990s?

As the resources devoted to health care do not increase at the same rate as the cost, strategies to reduce costs are needed. Dialyser reuse has been one possible solution. In the US, because of a payment reimbursement freeze since 1982, the movement towards high-flux dialysis has been the rationale for a continued growth in reuse, which in 1996 was practised by more than 81% of centres [6]. In Australia, in 1987, 35% of the patients were treated with reprocessed dialysers [9], but more recent data are not available. Whatever the reason, Europe has shown quite a different trend. According to 1992 EDTA–ERA Registry data [7], 9% of the patients were treated with reprocessed dialysers, but there were huge differences in the prevalence of dialyser reuse. Dialyser reuse was not performed in Austria, Denmark, Finland, the Netherlands and Sweden. But reuse averaged 3% in Spain, 5% in Germany, 6% in France, 10% in the UK, and 22% in Belgium. The highest figures were in Portugal (77%), Poland (88%), and Bulgaria (100%). However, since then, three countries (Portugal, France and Spain) have prohibited the practice of reuse, and in the EEC

reuse is not performed in 8 out of 15 states. The practice of dialyser reprocessing will be debated in the near future by the EEC Commission in order to standardize legislation across all EEC states, and it is possible that a no-reuse policy will be decided for all EEC members [8]. Likewise, reuse is forbidden in Japan by health insurance regulations and cultural preferences. Canada maintains an intermediate position [10]: in 1992, 12% of the patients were treated with reused dialysers. The most common number of reuses in Europe is 3, 6, or 9 [8], which is considerably lower than that practised in the US where the average number is 16 [11], but sometimes reaching 192 [12]. Who is heading in the right direction?

Is dialyser reuse safe?

The safety of reuse has been questioned over the last 20 years with studies that show conflicting results. The first report of the long-term impact of dialyser reuse on mortality was published in 1987 by Held *et al.* [13] and showed that patients treated with dialysers reprocessed with formaldehyde had a 12% lower mortality than patients treated with dialysers that were not reprocessed.

No further outcome studies were published until 1994, when Held *et al.* [14] reported the results of a study of approximately 66 000 prevalent patients, using Health Care Financing Administration (HCFA) information on ESRD patient survival and Centers for Disease Control and Prevention (CDC) information on dialysis units' dialyser reuse practices. This study, in the main, delineated a 13% increase in mortality in patients treated with dialysers reprocessed with peracetic acid, and a 17% increase in mortality in patients treated with dialysers reprocessed with glutaraldehyde but only in freestanding units. No increased risk of death was found for patients treated with dialysers reprocessed with formaldehyde. Two years later, Feldman *et al.* reported similar results. The authors studied a non-concurrent cohort of 27 938 ESRD incident patients beginning dialysis in the US in 1986 and 1987, and found a 10% increase in mortality in freestanding facilities reprocessing dialysers with peracetic acid [15]. Nevertheless, some inconsistencies were observed in these two studies. Feldman *et al.* [14] did not find any increased mortality in hospital units reprocessing dialysers with peracetic acid or glutaraldehyde, and Held *et al.* [14], in a preliminary analysis in hospital-based units, found a 10% decrease in mortality in hospital units reprocessing dialysers with peracetic acid. These results suggest that the increased mortality is not related to the type of germicide used. The limitations of these studies included the absence of patient-level data, namely, on dialyser reprocessing, co-morbidity, quality of dialysis, nutrition and the treatment of anaemia.

The impact of reuse practices and dialysis unit and patient characteristics on mortality were studied by Collins *et al.* [16], who studied a 10% random sample of period-prevalent haemodialysis patients from units practicing conventional dialysis (<25% high-efficiency/high-flux), and found that the mortality associated with reuse practices was not consistently different from that associated with no reuse. The authors analysed the 1989–1993 period, and showed that the reuse-associated mortality is not a generalized effect but, rather, is very specific to provider characteristics and that the effect is not consistent over time. In the 1989–1990 period, an adverse effect of peracetic acid was observed only in freestanding, for-profit dialysis units practicing manual reuse. In the 1991–1993 period, the adverse association of peracetic acid was no longer present. Furthermore, the investigators showed that the for-profit status of dialysis units adversely influences the outcome. Again, there was no data on dialysis therapy, nutrition and the correction of anaemia, three factors known to influence outcome. Recent studies by National Medical Care [17], and from Dialysis Clinics Inc [18], published only in abstract form, analysed the outcome associated with reuse, adjusted for albumin levels and dialysis therapy, and found no difference between reuse and no reuse.

Facts and fiction

Regarding reuse, some areas are a source of concern.

Reuse is associated with an increased incidence of pyrogenic reactions

In the US, over the years, units that reprocess dialysers were more likely to report pyrogenic reactions than units that did not reprocess dialysers. From a historical perspective, units that reprocess dialysers manually had more pyrogenic reactions than those using automated systems [6,12]. However, CDC investigation showed that many of these episodes were the result of inadequate reprocessing procedures, such as the use of low concentrations of the germicide and use of water that did not meet the Association for the Advancement of Medical Instrumentation (AAMI) standards (bacterial colony count <200 CFU/ml or bacterial lipopolysaccharide concentration <5 endotoxin units/ml) as a result of design flaws in the water treatment and delivery system and poor or non-existant monitoring and maintenance practices [6,19]. Furthermore, although data supporting the advantage of using more stringent guidelines than those issued by AAMI are not available, many believe that this might be necessary. In this regard, the European Pharmacopoeia guidelines for dialysate water are already more stringent than US standards (bacterial colony count <100 CFU/ml and bacterial lipopolysaccharide levels less than 0.25 endotoxin units/ml).

Polysulfone membranes reprocessed with bleach are associated with increased protein loss

In a recent publication, Kaplan *et al.* [20] showed that repetitive bleach processing of high-flux polysulfone dialysers increased permeability and caused substantial

protein losses that were related to the frequency of reuse and were of considerable magnitude after the 10th use. Other studies have shown similar results [21]. Is it acceptable to use this technique without limiting the number of uses?

Total cell volume (TCV) reuse criterion is not a well-founded practice

Worldwide, the currently accepted standards for the practice of reuse of dialysers are those issued by the AAMI. The only quantitative criterion recommended by AAMI is that the TCV should not fall bellow 80% of its original value, assuring that the urea clearance of the dialyser stands within 90–110% of the original level [22].

Is this a well-substantiated statement? Unfortunately, the answer is no. It is based only on an early study by Frank Gotch [23], which was made with a small sample of cellulosic low-flux dialysers, reprocessed manually with formaldehyde and operated at low blood flow rates (Qb 200 ml/min). Moreover, no rigorous statistical analysis of the confidence intervals was performed. No other subsequent publication has presented data establishing the validity of using 80% of the initial TCV as the criteria for acceptable dialyser reuse [24]. Is this not an important issue? Does anyone want to hold the position that the only important issue is the monthly monitoring of the delivered dose of dialysis, quantified by the removal of small solutes (Kt/V or URR)?

Reuse of dialysers may have an impact on patient outcomes

Has reuse an effect on middle-sized molecule removal? Recent studies [25–27] have shown that dialyser reprocessing with Renalin® does not restore the original β2-microglobulin clearance capabilities of high-efficiency/high-flux membranes. This decrease in β2-microglobulin clearance may be greater than 50%, while the dialyser maintains its original clearance of small solutes and a TCV above 80% of the original value. It is noteworthy that, in 1996, in the US, Renalin® was the most commonly used germicide, used by 54% of the centres [6]. In this context, is the movement towards high-flux dialysis observed in the US worthwhile? Furthermore, does this decrease in middle-sized molecule clearance have an impact on ESRD outcomes?

Hakim *et al.* [28] have shown that the use of synthetic and semi-synthetic membranes was associated with a relative risk for mortality that was at least 25% lower when compared with patients dialysed with cellulosic membranes. Preliminary data from US Renal Data System suggests that middle-sized molecule removal may explain these differences in mortality when using different types of membranes [14,29], leaving the possibility that reuse of high-flux dialysers with certain germicides may have an adverse effect on patient survival. Clearly, this is an area that needs further investigation.

In summary, dialyser reprocessing is still a controversial practice that is not without risks. Dialysis units should establish a rigorous quality assurance programme that includes the regular monitoring of the quality of the water. At least, AAMI guidelines should be followed, but it is possible that more stringent recommendations will become standard. What will be the dominant trend in the future? A movement towards no reuse which is the highest possible safety or a movement towards a continued growth in reuse under increasing economic pressure?

The impact of haemodialyser reuse on mortality is still an area of concern that needs further investigation. Ironically, it is possible that, in the meantime, there will be a trend towards no reuse under the pressure of dialyser manufacturers, which own increasing numbers of dialysis units.

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