SUMMARY

Assessment of the different types of dialyzer membranes for ESRD

Until relatively recently the standard hemodyalizer membrane type has been a cellulose derivative, notably the cupramonium regenerated cellulose (ie Cuprophan). It still is but several innovations have been recently introduced in the market, due partially because of basic inmunology based promising developments. Among these innovations are other cellulose derivatives and a variety of polymers.

Here, like in other medical practice areas, there are significative scientific uncertainties which result in the lack of consensus among professionals on usage criteria for specific dyalizers which could explain the variability pattern for them both domestically and internationally.

The assessment of the effectivenes of ESRD hemodyalisis therapy as in any other therapeutic device should be measured in the outcome parameters fo survival (mortality), morbidity and quality of life. The level of success in each parameter is the result of a combination of a variety of elements, present for the duration of patient treatment. In general these factors are:

- Specific condition of patient, like age and comorbility.
- Specific dialysis procedure and protocol (time of exposure, type of dyalizer, monitoring, technique).
- Intensity and quality of medical procedures.
- Intensity and quality of nursing procedures.
- Social and family situation and support.

Thus a specific type of dyalizer is only one factor or only one variable in a multifactorial process —the dialysis— which affects the outcome. The contribution that the specific type of dyalizer membrane makes to this outcome is difficult to identify and measure.

Practice has shown that it is particularly difficult to design (and more to conduct) a study with proper control of all relevant intervening factors to assess the comparative merits of the dialyzing element. This difficulty could be insurmountable if the timeframe is to be long term (more than 3 years). There is no published evidence of reasonable large controlled clinical trial with random allocation of dyalizer membranes for long term treatment. In consequence there is no solid, well established evidence in support of the use on any tipe of dyalizer membrane over the others on a outcome basis or ineffectiveness on the overall treatment of ESRD.

However there are some retrospective, observational, or partially experimental studies which albeit not conclusive may legitimally be interpreted as indicating that some benefits can be obtained from the use of high permeability membranes. Namely that they could be more efficient, better tolerated during procedures, and induce less changes on biological parameters like complement activation, $ß_2$-microglobuline, coagulation, lipids. Yet the real clinical significance of these alterations is not well established.

Furthermore since there is substantially less cumulative experience on the use of these membranes, some aspects related to their specific functional characteristics are still sources of concern and raise questions not yet satisfactorily answered. Retrofiltration is one of them.

The specific characteristics of efficiency performance and biocompatibility are often independent from each other; a given membrane has a specific behaviour for each thus arising a wide gamut of combinations of binomia efficiency-biocompatibility in today´s dializer marketplace: high efficiency , high efficiency-high biocompatibility, low biocompatibility, etc. In addition to these are relevant manufacturing-related parameters like sterility procedures.

In addition to the lack of well established risk, benefit and overall effectiveness evidences other factors appear to account for the variation of utilization patterns: economic considerations. In Spain this is shown by the scarce utilization of «special» (id est, expensive) dyalizers by external contracted providers as opposed as national health system owned and operated ones. That reflects the different economic constrains and operational contexts.

RECOMMENDATIONS

After discussing the clinical well established factual evidence and from all other considerations identified as relevant for this repport it is concluded that hemodialysis practiced by means of conventional (regenerate cellulose) membranes is considered appropriate practice.

However there are selected patient categories where, on indirect evidence, additional benefits could reasomably be presumed for treatment by synthetic membrane dyalizers. These patients may be grouped in the following categories.

A) Patients who have comorbidity on the dialysis admission time, specifically:

- Severe chronic obstructive lung disease.
- Severe myocardial dilatation.
- Progressing malnutrition.
- Repeated infection.
- Polineuropathy.
- Amyloidosis.

B) Patients developing the same stated comorbidities once having started therapy by conventional membrane dialysis, but after having dealt with all other relevant causal factors unrelated to dyalizer.

C) Patients under hemodialysis excluded from transplant waiting lists for definitive medical reasons, whom are expected to be under long term dialysis.

D) Patients suffering from acute kidney failure.

There are substantial prize differences between conventional membrane dialyzers (like Cuprophan) and some of the newer including «special» membranes. That is particularly the case when for polymeric membranes (PAN, polysulphone, polymetacrilate, polyamide). The difference may triplicate or even quadriplucate the individual cost of the dialysis component and can have an import economic impact on the overall dialysis programs, depending on the proportion of cases being elected for this specific membranes. In Spain this would be a 20% increase of the overall program cost (from 4.2 million pesetas to 5.0).

This prize difference may have been explained in this past on grounds of the limited volume of dispensation of special membranes, but it has remained or even increased even tough the number of patients currently being on special membranes treatment has increased. If the lack of correlation of cost increases and potential clinical benefits are taken on consideration on a hypothetical widespread adoption of special membranes situation, two recommendations appear. The first a recommendation for selective use of these filters, under a restrictive condicion list. The second is a management policy oriented to prize control. On grounds of component cost control there are proven policies not yet available in Spain to be considered including dyalizer reutilization.