

The effect of convection on the nutritional status of haemodialysis patients

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Abstract

Malnutrition, defined as insufficient protein-calorie intake, is highly prevalent in haemodialysis (HD) patients. It is commonly associated with decreased body weight, depleted energy stores (fat tissue) and loss of somatic proteins. It has been suggested that there may be at least two fundamentally different types of malnutrition in HD patients. The first is related to low protein and energy intake. This type of malnutrition may be amenable to adequate nutritional and dialysis support. In contrast, the second type of malnutrition is associated with inflammation and atherosclerotic cardiovascular disease (MIA syndrome). This type of malnutrition is much more difficult to reverse with nutritional support and dialysis therapy, unless the underlying co-morbid conditions and chronic inflammatory response are treated adequately. There is no single measurement which can be used to determine the presence of malnutrition. Therefore, a panel of measurements is recommended, including a measure of body composition, a measure of dietary protein intake and at least one measure of serum protein status. Therapeutic interventions in malnutrition of HD patients include dietary prescription, correction of metabolic acidosis, therapeutic intervention for co-morbidities, an adequate dose of dialysis and finally interventions on dialysis techniques, membrane and dialysate quality. It is a widespread belief that convective treatments give a clinical advantage over standard diffusive HD, when considering the physiological outcomes, such as haemodynamic instability. Since convective treatments are usually performed utilizing synthetic biocompatible membranes, it is very difficult to separate the effects of convection from those of biocompatibility on a given outcome, e.g. the nutritional status of HD patients. There are, to date, no prospective randomized clinical trials with sufficient power in which the effects of convective

therapies on the nutritional status of HD patients were compared with those of other dialysis modalities. Morbidity and mortality of HD patients are strictly associated, but not necessarily linked by a cause–effect relationship to some nutritional parameters, notably serum albumin levels. Thus, as the presence of malnutrition is one of the strongest predictors of mortality, the crucial point is to demonstrate the superiority of convective treatments over standard diffusive HD on hard outcomes: morbidity and mortality. Even though almost all available studies support the hypothesis that convection and high-flux biocompatible membranes are associated with reduced morbidity and mortality risks, there is, to date, no absolute proof showing a cause–effect relationship between convection and high-flux biocompatible membranes and the outcome of HD patients. In conclusion, convective therapies offer the opportunity for as yet unrivalled small and/or middle molecular clearance. Regarding short-term complications, there is ample evidence for the fact that haemodynamic stability is better maintained during haemofiltration than during standard HD. Although a beneficial effect of convective therapies was suggested mainly in uncontrolled studies, as far as the nutritional status, the morbidity and the mortality of HD patients are concerned, there appears to be a shortage of well-controlled prospective randomized clinical trials with sufficient power assessing the potential merits of convection.

Keywords: biocompatibility; convection; haemodiafiltration; haemofiltration; high-flux haemodialysis; malnutrition

Introduction

Both malnutrition, defined by insufficient protein-calorie intake (the so called protein-energy malnutrition), and cachexia, defined by defective food assimilation or utilization in the presence of hypercatabolism

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and systemic inflammation, are highly prevalent in haemodialysis (HD) patients [1]. Malnutrition is commonly associated with decreased body weight, depleted energy stores (fat tissue) and loss of somatic proteins. Recently, malnutrition criteria have been found in 20–36% of 7123 French HD patients in a cross-sectional study [2]. Both malnutrition and cachexia are due to uraemia itself (loss of appetite), dialytic treatment (loss of amino acids and proteins, bioincompatibility of treatments, quality of the dialysate), as well the premature ageing of HD patients and the increased burden of co-morbidity factors [3].

The pathogenesis of malnutrition in HD patients: are there two types of malnutrition in chronic uraemia?

It has been suggested that there may be at least two fundamentally different types of malnutrition in HD patients [4]. The first is related to low protein and energy intake. In this context, co-morbid conditions are uncommon and serum albumin may be normal or only slightly decreased. This type of malnutrition may be amenable to adequate nutritional and dialysis support. In contrast, the second type of malnutrition is associated with inflammation and atherosclerotic cardiovascular disease (MIA syndrome). Co-morbid conditions are common and serum albumin levels are usually decreased. This type of malnutrition is much more difficult to reverse with nutritional support and dialysis therapy, unless the underlying co-morbid conditions and chronic inflammatory response are treated adequately [4]. Obviously, these two types of malnutrition are often combined in the clinical setting [5].

Methods to assess nutritional status in HD patients

There is no single measurement which can be used to determine the presence of malnutrition. Therefore, a panel of measurements is recommended, including a measure of body composition, a measure of dietary protein intake and at least one measure of serum protein status.

- (i) History and physical examination: the history and physical examination (symptoms, psychosocial issues, assessment of the 'dry weight') can often provide important clues for malnutrition.
- (ii) Food intake: a food diary is very useful; dietary protein intake can also be estimated by calculating the protein catabolic rate (PCR) utilizing kinetic modelling.
- (iii) Anthropometry: anthropometric measurements (skin fold thickness at the triceps or subscapular area, mid-arm circumference) provide a rapid, non-invasive and reproducible method for evaluating body fat and muscle mass.

- (iv) Bioelectric impedance analysis (BIA).
- (v) Dual-energy X-ray photon absorptiometry (DEXA).
- (vi) Subjective global assessment (SGA) of nutritional status is a method based on the combination of history and physical examination.
- (vii) Serum markers: (a) correlated to both malnutrition and inflammation: albumin, pre-albumin, insulin-like growth factor-1 (IGF-1) and transferrin; (ii) correlated to inflammation: main proteins of the acute phase [C-reactive protein (CRP), serum amyloid A], secondary proteins of the acute phase (fibrinogen, ferritin, complement), cytokines [interleukin-6 (IL-6), tumour necrosis factor- α].

Therapeutic interventions in malnutrition of HD patients

- Dietary prescription
- Correction of metabolic acidosis
- Therapeutic intervention on co-morbidities
- Adequate dose of dialysis
- Interventions on dialysis techniques, membrane and dialysate quality. It is a widespread belief that convective treatments, such as high-flux haemodialysis, haemodiafiltration, on-line haemodiafiltration, haemofiltration and on-line haemofiltration, give a clinical advantage over standard diffusive HD, when considering the physiological outcomes, such as haemodynamic instability.

Convective treatments and malnutrition in HD patients

The membranes used in convective treatments are high-flux, semisynthetic and synthetic. Characteristics of these membranes are their high permeability, which allows convective removal of water and electrolytes and a higher clearance of middle and larger molecular weight solutes, and their high biocompatibility, which minimizes the 'inflammatory response' secondary to interactions between blood and the artificial material of the HD system [6].

Since convective treatments are usually performed utilizing synthetic biocompatible membranes, it is very difficult to separate the effects of convection from those of biocompatibility on a given outcome, such as the nutritional status of HD patients.

A role for the membrane material as a whole (biocompatibility and/or convection) in protein malnutrition has been suggested in healthy volunteers [7]. It has been suggested that biocompatible high-flux membranes can positively affect the relationship between dietary protein intake (measured as PCR) and dialysis dose (expressed as Kt/V) [8], i.e. that HD with a biocompatible high-flux membrane results in higher protein intake at every level of Kt/V. However,

Table 1. Impact of dialysis membrane and flux on patient mortality

Authors and reference	Comparison	Relative risk of death (reference = 1)/statistical significance
Hornberger <i>et al.</i> [15]	High-flux <i>vs</i> conventional membranes	0.24/ $P < 0.001$
Hakim <i>et al.</i> [16]	Synthetic <i>vs</i> cellulose membranes	0.74/ $P < 0.002$
Koda <i>et al.</i> [17]	High-flux <i>vs</i> conventional membranes	0.61/ $P < 0.05$
Bloembergen <i>et al.</i> [18]	Synthetic <i>vs</i> cellulose membranes	0.82/ $P < 0.002$
Leypoldt <i>et al.</i> [19]	High-flux <i>vs</i> low-flux membranes	0.95/ $P < 0.0001$
Locatelli <i>et al.</i> [20]	Convective <i>vs</i> diffusive treatments	0.90/NS
Woods <i>et al.</i> [21]	High- <i>vs</i> low-flux polysulfone	0.30/ $P < 0.001$
Port <i>et al.</i> [22]	Synthetic <i>vs</i> cellulose membranes	0.82/ $P < 0.002$
Eknoyan <i>et al.</i> [23]	High-flux <i>vs</i> low-flux membranes	0.92/NS

it must be noticed that these studies present major methodological drawbacks [6].

Concerning the nutritional status in HD patients, no clear changes were found when comparing convective *vs* diffusive therapy, although body composition was not assessed in detail [9–11].

Locatelli *et al.* [12] did not demonstrate an influence of the dialysis membrane and convection on any of the variables related to the nutritional status (body weight, serum albumin, transferrin, triglycerides and cholesterol, skin fold thickness at the triceps and subscapular area, mid-arm circumference). Similarly, a correlation between Kt/V and PCR was not found. Lastly, Schiff *et al.* [13] found that the shift from a conventional to an ultrapure dialysis fluid was able to reduce significantly the serum levels of IL-6 and CRP and to increase significantly dry body weight, serum albumin, IGF-1 and leptin concentrations, PCR and mid-arm circumference after 12 months.

To summarize this issue, there are, to date, no prospective randomized clinical trials with sufficient power in which the effects of convective therapies on the nutritional status of HD patients were compared with those of other dialysis modalities.

Convective treatments and mortality in HD patients

Morbidity and mortality of HD patients are associated, but not necessarily linked by a cause–effect relationship to some nutritional parameters, notably serum albumin levels [14]. Thus, as the presence of malnutrition is one of the strongest predictors of mortality, the crucial point is to demonstrate the superiority of convective treatments over standard diffusive HD on hard outcomes such as morbidity and mortality.

A detailed discussion of the studies [15–23] dealing with this issue is beyond the scope of the present paper. They are summarized briefly in Table 1. Here, we want to stress only the results of the paper published very recently by Eknoyan *et al.* on behalf of the Hemodialysis (Hemo) Study Group [23]. It was a randomized clinical trial involving 1846 patients undergoing thrice weekly dialysis, using a 2×2 factorial design to assign patients randomly to a standard or high dose of

dialysis and to a low-flux or high-flux dialyser. The primary outcome, death from any cause, was not significantly influenced by the dose or flux assignment; the relative risk of death in the high-flux group as compared with the low-flux group was 0.92 (95% confidence interval, 0.81–1.05, $P = 0.23$) [23].

To summarize this issue, even though almost all available studies support the hypothesis that convection and high-flux biocompatible membranes are associated with reduced morbidity and mortality risks, there is, to date, no absolute proof showing a cause–effect relationship between convection and high-flux biocompatible membranes and the outcome of HD patients.

Conclusions

Convective therapies offer the opportunity for as yet unrivalled small and/or middle molecular clearance. As far as short-term complications are concerned, there is ample evidence for the fact that haemodynamic stability is better maintained during haemofiltration than during standard HD. Although a beneficial effect of convective therapies was suggested, mainly in uncontrolled studies, as far as the nutritional status, the morbidity and the mortality of HD patients are concerned, there appears to be a shortage of well-controlled prospective randomized clinical trials with sufficient power assessing the potential merits of convection [24].

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