URÉA ET MÉtabOLiSME DU NITROGENE EN PATIENTS
TREAdé WITH HAEMOFILTRATION

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Introduction

It has been reported that fewer small molecules [1–3] but more middle molecules [1,4,5] are removed in haemofiltration (HF) as opposed to haemodialysis (HD). However, it is yet to be clarified how nitrogen (N) metabolism is changed in patients receiving HF treatment in which the removal of a great amount of small molecules such as urea in serum is inadequate. In the present study, the N metabolism of the HF patient is investigated and the treatments are compared.

Methods and materials

Sixteen regular HD patients on thrice-a-week schedule were transferred to treatment by thrice-a-week post-dilution HF. Besides the measurement of the total N, urea N, creatinine and small proteins in the dialysate or haemofiltrate, daily increments of SUN, and creatinine were determined in these patients. The ASAHI AM-10 was used as the haemodialyser; the Rhône-Poulenc RP-6 was employed as the haemofilter. The exchange volume in post-dilution HF was 20 litres.

In one female patient (case FT, 59 yrs, 34kg), the one-week nitrogen balance was investigated. Moreover, by administering 1g of 98% $^{15}$N-urea intravenously, the changes in $^{15}$N concentration in serum non-protein nitrogen (NPN), and in serum protein and its excretion into urine, faeces and dialysate (filtrate) were determined.

The auto-analyzer, JCA-H4C8R (JEOL, Japan), was used for the measurement of urea N and creatinine, and small proteins were measured by single radial immunodiffusion technique. The total N was measured by macro-Kjeldahl method, and $^{15}$N was analysed by mass spectrometer, Hitachi RMI-II type. The detailed procedure of the sample treatment and the measurement of total N and $^{15}$N were reported previously [6–8].
Results

The amounts of small proteins removed from dialysate or filtrate with one treatment in each of the 16 patients are shown in Table I, and the results of measurement of the total N, urea-N and creatinine are presented in Figure 1.

<table>
<thead>
<tr>
<th></th>
<th>HF</th>
<th>HD</th>
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<tbody>
<tr>
<td>Retinol binding protein</td>
<td>26±11mg</td>
<td>trace</td>
</tr>
<tr>
<td>α1 – Acid glycoprotein</td>
<td>trace</td>
<td>—</td>
</tr>
<tr>
<td>α1 – Antitripsin</td>
<td>trace</td>
<td>—</td>
</tr>
<tr>
<td>α2 – HS glycoprotein</td>
<td>trace</td>
<td>—</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>trace</td>
<td>—</td>
</tr>
<tr>
<td>Albumin</td>
<td>trace</td>
<td>—</td>
</tr>
<tr>
<td>Transferrin</td>
<td>trace</td>
<td>—</td>
</tr>
</tbody>
</table>

Table I. The amounts of small proteins removed from dialysate or filtrate with one treatment in each of the 16 patients

![Graphs showing removal of total-N, urea-N, and creatinine](image)

Figure 1. The removal amounts of total-N, urea-N and creatinine into filtrate (dialysate) is compared between HF and HD in one patient group
As for small proteins, whereas in the dialysate only a small amount of retinol binding protein was found, small amounts of $\alpha_1$-acid glycoprotein, $\alpha_1$-antitripsin, $\alpha_2$-HS glycoprotein, prealbumin, albumin and transferrin were identified in the filtrate, besides $26 \pm 11$mg of retinol binding protein. On the other hand, as described in Figure 1, the total N, urea-N and creatinine removed in HD was significantly greater than in HF ($p < 0.01$).

When the mean pre-dialysis SUN level was compared for the HD and HF treatment periods, the HD level was significantly lower ($p<0.01$), while the HF period showed considerably lower values ($p<0.05$) in the daily SUN increment.

Changes in pre- and post-dialysis SUN and the daily increment of SUN examined in patient FT are given in Figure 2. When the treatment was changed from HD to the lower urea N removal of HF, pre- and post-dialysis (haemofiltration) SUN levels increased but the daily increment of SUN decreased. Thus, the level of pre- and post-filtration SUN reached a plateau.

In order to investigate such change in urea metabolism, studies of N balance

![Patient F.T. 59 yrs female 34 kg](image_url)

Figure 2. Changes in the pre- and post-dialysis (filtration) SUN level and daily increment of the SUN level in case FT at HD and HF periods
Figure 3. Comparison of nitrogen balance study between HD and HF in case FT examined one week of each treatment.

Figure 4. Changes in $^{15}$N concentration in serum NPN and $^{15}$N incorporation into serum protein examined in case FT at HD and HF periods of administering 1g of $^{15}$N-urea are shown.
and $^{15}$N tracing with administration of $^{15}$N-urea were conducted at the two periods shown in Figure 2, and the results are summarised in Figures 3 and 4. As shown in Figure 3, N measurements in HD and HF were as follows: Dietary N, 9.73g/day and 7.95g/day; dialysate and filtrate N, 6.99g/day and 3.98g/day; urinary N, 0.71g/day and 1.11g/day and faecal N, 0.83g/day and 0.82g/day. The N balance in HD was found to be $+1.20g$/day and the corrected N balance in HF was $+1.70g$/day.

Changes in $^{15}$N concentration in serum NPN examined by the administration of $^{15}$N-urea and $^{15}$N incorporation into serum protein are shown in Figure 4. At 8 hours after $^{15}$N administration, $^{15}$N atom % excess in NPN was higher in HD; moreover by conducting HD(HF), $^{15}$N in NPN became lower in HD than in HF. As for the incorporation of $^{15}$N into serum protein, the highest amount in HD was 0.011 atom % excess, whereas that in HF was 0.036, or three times the HD level. The recovery percentages of $^{15}$N removed one week after administration, were 59.3% (urine 4.8%, faeces 0.8% and dialysate 53.7%) in HD, and 52.4% (urine 12.8%, faeces 1.5% and filtrate 38.1%) in HF.

**Discussion**

In HF using 20 litres of replacement fluid, the removal of urea N, creatinine and the total N was apparently lower than in conventional dialysis. Although the SUN levels of patients treated with HF were higher than in the HD treatment period, the level reached a plateau without further elevation.

On the other hand, the daily increment of the SUN level was lower in the HF period than in the HD one, suggesting that metabolic changes suppressed the accumulation of urea. In our previous works on the 10- and 30-litre dialysate delivery systems, similar results were obtained [7,9,10], namely the stabilisation of the SUN level at a certain level was considered to be the result of an increase in faecal N.

In the present study on HF treatment, an increase of urea-N recycling into protein synthesis, an increase of urinary N and a reduction of dietary N intake were considered as the cause of the decrease in the daily increment of the SUN level. The reasons for the increase in urea-N recycling into protein synthesis can be considered to be the higher protein turnover with removal of small proteins and increased urease activity of intestinal bacteria due to an elevation in the SUN level. Furthermore, there is a possibility that protein synthesis is enhanced by the increased removal of middle molecules, and this also has to be carefully evaluated. The increase in urinary N was caused not only by the elevation of the SUN level but also by an increase in the urinary volume.

If HF patients with less removal of total N take in the same amount of protein as in those on HD, we could expect a considerable increase in body protein resulting in a gain in the net body weight or a remarkable accumulation of N compounds. In the present study, however, no such evidence was observed. N intake, as seen in patient FT, seemed to lower with the elevation in the SUN level.

We conclude from these observations that all the factors, recycling of urea-N, a decreasing tendency in the intake of dietary N and an increase in urinary N, contribute to the maintenance of a slightly positive N balance in HF patients.
References