PLATELET LIFE SPAN IN URAEMIA

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Summary

Platelet life span estimated by the regeneration time of platelet cyclo-oxygenase activity after acetyl salicylic acid (ASA) intake, as measured by the malondialdehyde (MDA) production rate was 10.3±1.0 days for healthy volunteers (n=7), 6.7±1.0 days for haemodialysis patients (n=13), 8.0±1.5 days for continuous ambulatory peritoneal dialysis (CAPD) patients (n=6) and 5.0 and 4.9 days for non-dialysed uraemic patients (n=2). In uraemic patients, the platelet cyclo-oxygenase activity was significantly impaired and it correlated with the decline in platelet life span. The restoration of the platelet life span and cyclo-oxygenase activity was achieved better by CAPD.

Introduction

Uraemic patients are known to have platelet abnormalities which are usually improved by haemodialysis [1,2], but these abnormalities are thought to affect the platelet life span. Continuous ambulatory peritoneal dialysis (CAPD) is being used increasingly for treating uraemic patients. Since it has not yet been reported whether CAPD or haemodialysis is better in improving the platelet abnormalities of uraemic patients, we compared the platelet life span in CAPD patients with that in haemodialysis patients. Usually platelet life span is measured by the 51Cr-labelled technique but radioactive substances are harmful for patients, staff and examiners. In this study, we calculated the platelet life span by measuring the regeneration time of platelet cyclo-oxygenase activity after acetyl salicylic acid (ASA) intake.

Materials and methods

The study was undertaken in seven healthy volunteers, 13 haemodialysis patients, six CAPD patients and two non-dialysed uraemic patients just before starting
regular dialysis treatment. All patients had normal liver function, none had splenomegaly, and none were diabetic. None had received any blood transfusion for more than six months and none had taken any medication known to affect the platelet function for at least a week before the start of the study. The biochemistry and blood cell counts in the uraemic patients are shown in Table I.

### TABLE I. Biochemical findings and blood cell counts

<table>
<thead>
<tr>
<th></th>
<th>Haemodialysis patients (n=13)</th>
<th>CAPD patients (n=6)</th>
<th>Non-dialysed patients (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg/dl)</td>
<td>72.0 ± 18.0</td>
<td>67.6 ± 18.4</td>
<td>90.3, 122.9</td>
</tr>
<tr>
<td>creatinine (mg/dl)</td>
<td>14.6 ± 2.9</td>
<td>9.9 ± 2.1</td>
<td>11.7, 15.9</td>
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<tr>
<td>uric acid (mg/dl)</td>
<td>8.4 ± 0.9</td>
<td>8.0 ± 1.5</td>
<td>8.8, 12.3</td>
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<tr>
<td>Ca (mg/dl)</td>
<td>9.9 ± 1.4</td>
<td>8.3 ± 0.6</td>
<td>6.8, 7.8</td>
</tr>
<tr>
<td>iP (mg/dl)</td>
<td>7.2 ± 1.4</td>
<td>6.5 ± 1.6</td>
<td>7.1, 11.8</td>
</tr>
<tr>
<td>WBC (/mm³)</td>
<td>6600 ± 2000</td>
<td>5600 ± 1600</td>
<td>4500, 8300</td>
</tr>
<tr>
<td>RBC (x10⁴/mm³)</td>
<td>257 ± 57</td>
<td>312 ± 74</td>
<td>199, 188</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>8.2 ± 1.2</td>
<td>9.6 ± 1.9</td>
<td>6.4, 6.6</td>
</tr>
<tr>
<td>Platelet (x10⁴/mm³)</td>
<td>15.9 ± 4.6</td>
<td>17.1 ± 3.1</td>
<td>16.3, 27.1</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD

The platelet malonyldialdehyde (MDA) production rate was measured in all of the patients before and after ASA intake by the modified Okuma's method [3]. After venepuncture, each patient was given 660mg of ASA to inhibit platelet cyclo-oxygenase completely and irreversibly. Then the MDA was serially measured until it recovered the pre-ASA value. The time required to restore the platelet MDA production rate to the pre-ASA value is the platelet regeneration time, because only platelets formed after the effect of ASA has worn off can produce MDA. Therefore, the platelet life span can be estimated indirectly from the platelet regeneration time [4,5]. The MDA production rate was also measured in an additional 25 healthy volunteers, 17 haemodialysis patients and six CAPD patients.

The statistical analysis was done by the unpaired Student's 't' test.

**Results**

Table I indicates the biochemical findings and blood cell counts in the three patient groups. The platelet counts were comparable between the haemodialysis and CAPD patients. The platelet MDA production rate (pre-ASA value) was 13.3±2.0nmol/10⁹ platelets for the 32 healthy volunteers, 8.3±2.0nmol/10⁹ platelets for the 30 haemodialysis patients and 9.6±1.2nmol/10⁹ platelets for the 12 CAPD patients (Figure 1). It was significantly lower in uraemic patients.
than the healthy volunteers and was also lower in haemodialysis patients than in CAPD patients.

The recovery time of the platelet MDA production rate after ASA intake or the platelet life span in the seven healthy volunteers, 13 haemodialysis patients, six CAPD patients and two non-dialysed patients was 10.3±1.0 days, 6.7±1.0 days, 8.0±1.5 days and 5.0 and 4.9 days, respectively (Figure 2). The platelet life span in uraemic patients was significantly shorter than that in healthy volunteers. Furthermore, it was significantly shorter in haemodialysis patients than in CAPD patients.

In all of the healthy volunteers and uraemic patients, there was a significant correlation between the platelet MDA production rate and its life span.

Discussion

The platelet life span was found to be significantly shorter in uraemic patients than in healthy volunteers. There may be many reasons for the shortening of the platelet life span in uraemic patients, such as platelet dysfunction, uraemic toxins and excess consumption of the platelet, but it had not been clarified.

Among uraemic patients, the haemodialysis patients who received extracorporeal circulation had significantly shorter platelet life spans than the CAPD patients. Serum beta-thromboglobulin and platelet factor 4 increases after haemodialysis [6], which may be due to platelet agglutination or aggregation. Platelet counts decrease at the start of haemodialysis, but later recover to their former value [7]. CAPD patients do not need extracorporeal circulation and the platelets are therefore not at risk. In other words, there is a great difference in platelet stress between haemodialysis and CAPD. However, Levin et al reported that many platelets are not destroyed during haemodialysis [8]. We have also shown that platelet MDA production rate is the same before and after haemo-
Figure 2. Regeneration time of the platelet cyclo-oxygenase activity after ASA intake (platelet life span) for healthy volunteers (open circles), non-dialysed (squares), haemodialysis (triangles) and CAPD patients (closed circles). Values represent mean ± SD. There were significant differences between the healthy volunteers and the haemodialysis (p<0.001) and CAPD patients (p<0.01) and between the haemodialysis and CAPD patients (p<0.05).

dialysis regardless of ASA intake. Therefore, platelets may not have been consumed by the extracorporeal circulation and the platelet life span may have been shortened by other causes.
In the non-dialysed uraemic patients, bleeding tendencies are observed as a symptom of uraemia. Nasal and gingival bleeding is seen after ASA intake, which may shorten the platelet life span even further. Because of this, it is difficult to obtain, with this method of measurement, the actual platelet life span in patients with bleeding tendencies.

Platelet cyclooxygenase activity is significantly impaired in uraemic patients. Therefore, the platelet itself and plasma factors may have been the causes of the low MDA production rate. Remuzzi et al have reported that the cause of the impairment in the cyclooxygenase activity in uraemic patients is in the plasma, presumably uraemic toxins [9]. Haemodialysis patients have a significantly lower platelet MDA production rate than CAPD patients which seems to be due to differences in the method of blood purification. The platelet MDA production rate had a statistically significant correlation with the platelet life span in all of the healthy volunteers and uraemic patients. Therefore, it can be said that the plasma factor or the uraemic toxins was one of the factors that affected the platelet MDA production rate and subsequently the platelet life span.

In conclusion, the platelet life span was shortened and its MDA production rate decreased in uraemic patients, but they were improved by dialysis. However, CAPD was able to restore them more significantly than haemodialysis.

References
2 Jorgensen KA, Ingeberg S. Nephron 1979; 23: 233
3 Okuma M, Steiner M, Baldini M. J Lab Clin Med 1971; 77: 728