IMPROVEMENT OF BLEEDING TIME, PLATELET AGGREGATION AND PLATELET COUNT DURING CAPD TREATMENT

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Summary

Mean bleeding time in 11 uraemic patients improved from 11.2 (range 3.5—20) before to 5.8 (range 2.5—20) minutes during CAPD treatment (p < 0.025). Bleeding time became normal in six out of seven patients with a prolonged bleeding time prior to CAPD. There was a concomitant improvement in platelet aggregation. Mean platelet count rose from 195 (range 117—414) to 311 (148—522) x 10^9/L (p < 0.01).

A significant correlation was found between the change in bleeding time and in platelet aggregation induced by ristocetin, but not between the change in bleeding time and the platelet count. Our results suggest that CAPD treatment improves the uraemic bleeding tendency, even in patients on previous haemodialysis treatment.

Introduction

An enhanced bleeding tendency is one of the complications of uraemia. Impaired platelet function is probably one of the major causes of this phenomenon [1]. Haemodialysis and peritoneal dialysis may improve bleeding time and platelet function [2], probably by removing uraemic toxins [3]. Several investigators have shown however that in patients treated with haemodialysis, in contrast to those treated with intermittent peritoneal dialysis, platelet aggregation is still abnormal [4,5]. Others showed that the bleeding time does not always improve on haemodialysis treatment [6].

In this report we present the results of our investigations of the bleeding time, platelet aggregation and the platelet count in patients treated with CAPD.

Methods

Eleven patients, five female and six male, age 30—61 years, were studied before and during CAPD treatment. Eight were on regular haemodialysis treatment
previously, while three did not receive renal replacement therapy.

Determinations of bleeding time, platelet aggregation and platelet counts were done both before and one week to 14 months (median three months) after the beginning of CAPD treatment. Bleeding time was performed with a Simplate II (General Diagnostics) bleeding time device (Mielke).

Platelet-rich plasma, obtained from venous blood, was anticoagulated with trisodium citrate 3.8% (1/10) and centrifuged at 180g for 15 minutes. Platelet aggregation (Born) was investigated in a dual Payton aggregation module with a bar speed of 900rpm at 37°C. Presented is the percentage of aggregation four minutes after the addition of one of the following aggregating agents: ADP in a final concentration 2.3μM (Sigma), ristocetin 1.2mg/ml (Lundbeck), adrenaline 270μM (Hospital Pharmacy) and collagen 20μg/ml (Hormonchemie).

Normal values for platelet aggregation tests were obtained from 20 healthy persons, nine females and 11 males, with ages between 25 and 54 years. Before the studies both patients and normal subjects had not used any medication that could influence platelet aggregation or bleeding time, for at least 10 days.

For statistical analysis the Wilcoxon signed rank test (paired observations) and the Wilcoxon-Mann-Whitney signed rank test (unpaired observations) were used. The Spearman rank test was used for correlations.

Results

Table I and Figure 1 show the results of the platelet aggregation studies. The platelet aggregation in the patient group before CAPD therapy induced by ristocetin and collagen was significantly less than in 20 normal subjects. During CAPD

### Table I. Haemostatic parameters (mean and range) in uraemic patients before and during CAPD treatment and in 20 normal subjects

<table>
<thead>
<tr>
<th></th>
<th>Bleeding time n = 11</th>
<th>Platelet count n = 11</th>
<th>Percent platelet aggregation induced by: n = 9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ADP</td>
</tr>
<tr>
<td>Before</td>
<td>11.2 (3.5–20)</td>
<td>195* (117–414)</td>
<td>61</td>
</tr>
<tr>
<td>During</td>
<td>5.8† (2.5–20)</td>
<td>311*† (148–522)</td>
<td>69</td>
</tr>
<tr>
<td>Controls</td>
<td>236 (168–330)</td>
<td>72 (34–85)</td>
<td>89</td>
</tr>
</tbody>
</table>

* normal laboratory values < 7 minutes and † 150–400 x 10⁹/L
* p < 0.05 compared to before CAPD
† p < 0.05 compared to 20 normal subjects

treatment only the mean platelet aggregation induced by collagen was different from the normal controls. With the institution of CAPD a significant increase was found in the platelet aggregation induced by ristocetin (p < 0.01) and adrenaline (p < 0.05).
Figure 1. Platelet aggregation induced by ADP, ristocetin, adrenaline and collagen in nine CAPD patients. Results are presented as the percentage of platelet aggregation four minutes after the addition of the aggregating agent. (−) indicates mean values, (♀) indicates patient 1 (see text).
Figure 2. Individual values of bleeding time, ristocetin induced platelet aggregation and platelet count. Patients 2, 3 and 8 did not receive renal replacement therapy before CAPD, the other patients were on chronic haemodialysis. The points on the left side of each panel indicate the values before CAPD, on the right side after CAPD treatment.
Table I and Figure 2 (individual data) show the results of bleeding time, platelet aggregation induced by ristocetin, and platelet count. Mean bleeding time improved from 11.2 (range 3.5—>20) minutes before to 5.8 (range 2.5—>20) minutes during CAPD treatment (p < 0.025). In six out of seven patients the prolonged bleeding time became normal. Mean platelet count increased from 195 x 10^9/L (range 117—414) before to 311 x 10^9/L (range 148—522) during CAPD therapy (p < 0.01). The increase occurred in 10 out of 11 patients.

The decrease in bleeding time correlated with the increase in platelet aggregation induced by ristocetin (p < 0.025 r = -0.76), but not with the change in platelet count or haemoglobin level. The change in platelet count did not correlate with the change in platelet aggregation.

Only patient 1 showed an abnormal bleeding time and platelet aggregation (Figures 1 and 2) during CAPD treatment. However it later became apparent that heparin had been administered (by accident) to this patient several hours before the determinations were done. These were not repeated because the patient had a successful kidney transplantation soon afterwards.

After one year of CAPD therapy, patient 4 (Figure 2) was re-transferred to haemodialysis. Bleeding time and platelet aggregation again became abnormal in this patient.

Discussion

Although at present only a limited number of observations are available, the results of this study suggest that CAPD treatment may cause improvement of both bleeding time and platelet aggregation. This may be clinically important because a relationship has been demonstrated in uraemic patients between clinical bleeding tendency and a prolonged bleeding time [1]. In addition, these results are comparable with the findings in patients on intermittent peritoneal dialysis, as improvement of both bleeding time and platelet aggregation has been reported in these patients [4,5,7].

It is unlikely that the somewhat low number of platelets in the patients prior to CAPD treatment was the cause of either the prolonged bleeding time or the disturbance in platelet aggregation, because in normal subjects these determinations are within normal limits, provided the platelet count is above 100 x 10^9/L [7,8].

The improvement in platelet aggregation by peritoneal dialysis may be the consequence of the better removal of middle molecules by this form of treatment. However, haemodialysis with removal of only low molecular weight substances has also been reported to cause an increase in platelet aggregation [2]. Assuming that both low molecular weight substances and middle molecules play a role in decreased platelet function [3,9] this might explain the further improvement in platelet aggregation when haemodialysis treatment is changed to CAPD treatment.

An alternative explanation for the improvement of these patients could be that they are not subjected to the toxic effects of haemodialysis. This procedure may cause a decrease in platelet aggregation induced by ADP [4], a rise in beta-thromboglobulin level and a slight decrease in platelet count [10]. It may well be that
heparin, used for anticoagulation during haemodialysis, is partially responsible for these adverse effects of haemodialysis. In normal persons heparin may produce a prolongation of the bleeding time [11]. Platelet aggregation induced by ristocetin in heparin anticoagulated platelet-rich plasma is strongly inhibited [12].

Only one patient (Figure 2) had a prolonged bleeding time during CAPD treatment. Because this patient had received heparin several hours before the determination of the bleeding time, the effect of heparin was tested in two other uraemic patients. One hour after the administration of heparin (100 U/kg) bleeding time had increased from four to 18 minutes in one patient on CAPD treatment, while in another patient on haemodialysis therapy an increase was seen from 10 to more than 20 minutes.

The increase in platelet count in 10 of the 11 patients is a remarkable finding. No relationship was found between the increase in platelet count and the change in haemoglobin concentration. The rise in the platelet count may be related to the removal of middle molecules by CAPD, or to a toxic effect of either heparin or some other factor in the haemodialysis procedure.

In conclusion, CAPD treatment improves the uraemic bleeding tendency probably by improving platelet function and possibly by a rise in platelet count. The role of heparin as a causative agent of the uraemic bleeding tendency in haemodialysis patients needs further investigation.

References

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