Normal Response of Uraemic Platelets to Thromboxane A₂ Agonist

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Dear Sir,

Bleeding tendency in uraemia is ascribed mainly to impaired platelet adhesiveness [7] and aggregation [3]. At present it is assumed that there are three independent pathways of platelet aggregation: mediated by ADP, arachidonic acid (AA) and the platelet activating factor [8]. In uraemia the arachidonate-dependent pathway has been the most extensively investigated. Most of the aggregating agents act through that way.

A biphasic response of uraemic platelets to increasing concentrations of AA has been described [4]. At low concentrations their aggregation is increased, whereas it decreases in response to higher concentrations of AA. The behaviour of AA-induced platelet malondialdehyde production was similarly biphasic. Reduced malondialdehyde formation after thrombin stimulation [5], decreased production of thromboxane A₂ (TXA₂) [6], and lowered cyclo-oxygenase activity [2] in uraemic platelets has been reported. The reactivity of the uraemic platelet to TXA₂ is unknown. If it is increased the net platelet response may be virtually unchanged even if TXA₂ production is lowered.

We investigated the aggregation of platelets in platelet-rich plasma of uraemic patients induced by U46,619 (Upjohn, Kalamazoo, Mich.), which is a stable agonist of the TXA₂ receptor [1]. We studied 9 uraemic patients on chronic haemodialysis (6 males and 3 females aged 22 to 65 years, mean 36 years; 3 of them were HBsAg-positive) and 9 healthy volunteers (3 males, 6 females, aged 20 to 40 years, mean 28 years). All the subjects took no drugs which influenced platelet function for at least 10 days before testing. Threshold aggregating concentration of U46,619, defined as the smallest concentration of the agent which produced irreversible aggregation within 3 min, was determined using an Elvi 840 aggregometer. Statistical analysis was performed using Student's t test. The results are shown in figure 1.

Control ($\pi = 9$)

Uraemic ($\Pi = 9$)

Fig. 1. Threshold aggregating concentrations of U46,619 in control and uraemic platelet-rich plasma.

No significant differences in threshold aggregating concentration between the uraemic platelets and those of the control group were observed. This suggests that the platelet TXA₂ receptor is not affected in uraemia. Therefore low production of TXA₂ may indeed be responsible for the impaired platelet aggregation observed in uraemia. It is interesting that the lowest threshold aggregating concen-

tration of $LUe_{\beta i\theta}$ was observed in the HBsAg-positive patients, but this requires confirmation in a larger group of patients.

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