A New Antithrombotic Agent in the Treatment of Acute Renal Failure Due to Hemolytic-Uremic Syndrome and Thrombotic Thrombocytopenic Purpura

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Dear Sir,

The hemolytic-uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP) share many common features including microangiopathic hemolytic anemia, thrombocytopenia, and renal involvement. Prolonged anuria, severe hypertension and marked neurological manifestations are signs of poor prognosis for both the recovery of renal function and patient's survival. The etiology and pathogenesis of the two conditions are still unclear. It has been suggested [1] that a process of intravascular coagulation plays a role in the development of renal lesions, and thrombotic lesions are seen in the glomeruli and vessels up to the arcuate arteries. These findings have prompted numerous therapeutic attempts using heparin, urokinase, streptokinase, and platelet aggregation inhibitors, but the efficacy of these approaches is difficult to assess. On the other hand such therapies are not without considerable morbidity and mortality. Recent studies [2] suggest the hypothesis that a deficiency of plasma factor(s), which normally modulate vascular PGL $\cdot$ synthesis and release, have some role in the pathogenesis of HUS and TTP.

In the last year we treated 5 patients (3 children and 2 adults) affected by HUS or TTP with a new antithrombotic agent (Defibrotide). This drug is a polydeoxyribonu-cleotide [3], extracted from mammalian organs, which has been demonstrated to increase the generation of PGI $_2$ from vascular tissue, and displays considerable fibrino-lytic and antithrombotic activity. Clotting investigations did not indicate that Defibrotide has any significant heparin-like activity.

All patients were anuric on admission. Serum creatinine ranged from 5.3 to 8.7 mg/dl; platelet count was low (from 11,000/mm 3 to 35,000/mm 3); circulating fibrin degradation products (FDP) were found to be raised in all patients. Severe neurological involvement was present in 3 of them. All patients required dialysis treatment.

Defibrotide was administered by intravenous infusion at a dosage of 10 mg/kg/day. Treatment was started 16–28 h after admission, and was continued for an average of 14 days (range from 9 to 21). All patients showed a rapid decrease of circulating FDP associated with an increase in platelet count. Diuresis increased and serum creatinine concentration decreased in 4 patients, with a complete recovery of renal function within 12–47 days. In the 5th patient, who presented severe neurological involvement and hypertension at the admission, Defibrotide administration was followed by a rapid disappearance of neurological manifestations, and normalization of

blood pressure, while renal function did not show any improvement. The use of Defibrotide was not associated with relevant side effects.

On the basis of these preliminary results we suggest that this new antithrombotic agent might be considered as a valuable drug in the treatment of acute renal failure due to HUS and TTP.

References

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