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Heparin prophylaxis of Henoch-Schoenlein nephropathy

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Eighty eight children with extrarenal manifestations of Henoch—Schoenlein purpura received 120—150 IU/kg heparin in infusion for three days at onset and at relapses. Nephropathy developed in one child (1.1%), whereas renal involvement was noticed in 14 out the 67 control patients with Henoch—Schoenlein purpura (20.9%). The difference was highly significant ($p < 0.001$).

Renal involvement has been reported in 20 to 100% of patients with Henoch—Schoenlein (H—S) purpura. Although this wide range reflects a remarkable variation in its definition, the authors agree that renal involvement is the most serious manifestation of the otherwise benign self-limited disease [1, 5, 6, 7, 10, 11, 12, 14]. Since H—S nephropathy may persist and become chronic leading to renal failure, and no effective therapy is known to alter its course, prevention of renal involvement would be highly desirable.

Considering some observations concerning the pathomechanism of H—S purpura, and the promising experience with anticoagulant therapy [2, 3, 4, 8], we have made an attempt to prevent H—S nephritis by means of low-dose heparin administration.

Subjects and Methods

From October 1, 1973, to August 31, 1984, a total of 154 children (77 girls and 77 boys) aged 3 to 13 years with H—S purpura was hospitalized in our department. The number of patients was higher in the second part of the period, because the referral region was considerably enlarged in 1978.

At admission all patients had had characteristic skin lesions, partly joint symptoms, and in 12 cases abdominal pain and/or melaena for 1 to 7 days. Isolated haematuria (erythrocyte excretion > 10/mm^3 of uncentrifuged urine) was found in 4 cases, haematuria and significant proteinuria (over 1 g/m^2/day) was observed in 3 patients, whereas haematuria + proteinuria + hypertension with decreased GFR occurred in one child. No signs of renal involvement could be detected in the remaining 146 patients.

Out of these from May 1, 1978, 88 children (48 girls and 40 boys) received 120 to 150 IU per kg body weight of heparin IV in 300 ml saline infusion through 2 to 4 hours immediately after admission. This dose was repeated on the 2nd and 3rd day under continuous control of clotting time, prothrombin level, and thrombin time, and the same procedure was performed at relapses. In addition, penicillin and vitamins C and P were administered.

A control group was built from the 49 children (27 girls and 22 boys) with H—S purpura admitted between October 1, 1973, and April 30, 1978, i.e. before the

introduction of heparin prophylaxis, including 5 patients with renal involvement. This group was supplemented by 18 cases (3 girls and 15 boys), including 3 children with initial haematuria and proteinuria, from the period after May 1, 1978, who did not receive heparin for some technical reason.

No significant difference in age distribution, history of previous infection, duration of symptoms before admission, symptomatic therapy and diet was seen between control and heparinized patients. In every case the same vitamin C + P preparation was administered.

Each of the children was followed-up for at least 6 months after the first signs of H—S purpura.

Results

In addition to the 8 children admitted with nephropathy, in 6 patients of the control group macroscopic haematuria and significant proteinuria appeared on the 3rd to 10th day of hospitalization. Thus altogether 14 nonheparinized patients developed renal complications, in 10 of whom complete recovery was found after at most 8 weeks. In 4 children, a mixed nephrotic-nephritic picture was seen, including oedema, massive proteinuria, oliguria, azotaemia and hypertension. Three of these patients were well within 4 weeks, but they had microscopic haematuria and intermittent proteinuria for 2 years after resolution of other symptoms. Chronic renal insufficiency developed in one girl. No signs of renal involvement could be traced at regular long-term urine analyses in the other 53 subjects of the control group.

Similarly, no haematuria or proteinuria developed in 87 out of the 88 children receiving heparin prophylaxis.

The girl with nephropathy in this group showed an unusually severe picture of H—S purpura. The petechiae initially seen on the lower extremities and on the buttocks appeared on the 5th day on the trunk, arms and face accompanied by joint lesions, erythema nodosum, colics and gastrointestinal bleeding. Several relapses followed each other, therefore heparin infusion was repeated 13 times during the first 29 days of her disease. In spite of the increased tendency to multifocal haemorrhages, no haematuria was observed at daily examinations during this period. After the 29th day heparin administration was stopped, and from the 34th day on the classical symptoms of nephritis developed. After nearly three years the child still has intermittent episodes of gross haematuria, proteinuria and oedema with a probably rather unfavourable prognosis.

The cumulative results are demonstrated in Table I. As shown by the figures, a highly significant difference in favour of heparin prophylaxis was found in this material.

No correlation between recurrence rate of skin lesions and nephropathy on the one hand, and between extrarenal symptoms and heparin prophylaxis, on the other hand, could be established.

No complications of the heparin treatment were seen in any of the patients.

TABLE I

Frequency of nephropathy in children receiving heparin prophylaxis and in controls with Henoch-Schoenlein purpura

	Total	Nephropathy developed	
		n	per cent
Controls	67	14	20.9
Heparin prophylaxis	88	1	1.1*

* The difference was highly significant (Fischer's exact test, $p < 0.001$)

DISCUSSION

The frequency of renal involvement in H—S purpura was approximately 20% in our control group, which corresponded to the lower limit of the range found in various surveys. Although recurrence of the original symptoms or development of nephropathy have been reported after an interval of several years [13], it seems unlikely that a significant number of renal abnormalities should appear only after the 6 to 12 months period of follow-up of our patients. This was probably the case also in the heparinized group where only a single instance of nephropathy occurred.

We are aware of the limitations of the present study. The control group did not fulfil the criteria of a double-blind study, neither detailed analyses of haemostasis nor diagnostically important examinations of the complement and immune systems [9] were performed. We could only speculate on the effect and mechanism of the low-dose heparin prophylaxis, which obviously did not affect blood coagulation. The possibility that the pattern of the disease or aetiological factors had changed after the initial five year period could not be excluded, either.

We were, however, fascinated by the significant decrease in the number of renal complications in H—S purpura after heparin infusions. A more thorough investigation of a larger material to determine the possible benefits of prophylactic heparin administration seems to be warranted.

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