SHORT REPORTS

Somatic growth in girls receiving low dose prophylactic co-trimoxazole

Recurrence of urinary tract infection is common in childhood and indicates some impairment of the defences of the bladder. Provided that there is no outflow obstruction, reinfections of the urinary tract may be effectively prevented by using an appropriate prophylactic antibacterial agent until the underlying cause resolves or is corrected.¹ Co-trimoxazole has been used effectively in low dosage for this purpose but, in view of experimental evidence suggesting that high dose co-trimoxazole might interfere with normal somatic growth,² we studied the growth velocity and longitudinal growth of girls receiving prophylactic co-trimoxazole over long periods.

Methods and results

A total of 114 girls aged 2-12 years were given continuous low dose co-trimoxazole (about 10 mg sulphamethoxazole and 2 mg trimethoprim/kg/day) for between six months and six years after a urinary infection. Their heights and weights were measured accurately and the urine was cultured every three months. The intravenous urogram and micturating cystourethrogram were normal in 54 girls; abnormalities included vesicoureteric reflux in 51 girls, with renal scarring in 12 and miscellaneous lesions in nine (scars four, duplex systems two). Girls with neuropathic bladder or outflow obstruction were excluded. Height and weight velocities were calculated over six month periods randomly distributed over the calendar year. Velocities were grouped in one year age groups according to the age at the start of the period of prophylaxis.

Growth velocities obtained in 114 girls both while they were having and were not having co-trimoxazole prophylaxis were first compared with standard growth velocity curves.³ No deviation from the normal in weight or height was found in either of the samples (figure). Two way non-orthogonal

Height velocity curves in 114 girls, during (▲) and before and after (●) co-trimoxazole prophylaxis calculated over six month periods compared with standard height velocity.³

analysis of variance with age group and treatment group as main effects was then used to assess the effect of treatment.⁴ There was a significant effect of age on both height and weight, but when allowance was made for this there was no overall difference between treatment groups (with or without prophylaxis). There was, however, a barely significant effect ($p < 0.05$) on growth velocity in early adolescence, when growth was slightly faster in girls receiving co-trimoxazole.

Data from a further subset of 53 girls, where a six month growth velocity was calculable both before and immediately after a change in treatment, were analysed with a crossover design.⁵ Some 29 girls changed from no treatment to co-trimoxazole prophylaxis and 24 changed the reverse way. No significant interaction was found between weight or height velocity and whether treatment was given or not apart from the inevitable one of slight difference of age between the two groups, indicating that the order in which treatment was given was unimportant as regards growth. Thus growth velocities over six month periods were satisfactory during co-trimoxazole prophylaxis even in 51 girls with vesicoureteric reflux and 16 with renal scarring.

The effect of duration of co-trimoxazole prophylaxis on growth was further studied in 46 girls with vesicoureteric reflux with or without renal scarring who received continuous prophylaxis for two to five years. They

were divided into three cohorts according to the duration of prophylaxis: 46 girls had at least two years of treatment, 35 at least three years, and 22 at least four years. Because of the wide age variation heights were expressed as standard deviation scores. No significant change in height status from the start to the end of co-trimoxazole prophylaxis occurred during or between any time periods.

Six children developed a single asymptomatic reinfection without any effect on growth.

Comment

From our results we may conclude that during low dose co-trimoxazole prophylaxis of urinary infection growth velocity remains normal. Normal somatic growth may also be expected during long periods of treatment with low dose co-trimoxazole in girls without urinary outflow obstruction, including those with vesicoureteric reflux.

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¹ Smellie JM, Katz G, Grüneberg RN. Controlled trial of prophylactic treatment in childhood urinary tract infection. *Lancet* 1978;ii:175-8.

² Udall V. Toxicology of sulphonamide-trimethoprim combinations. *Postgrad Med J* 1969;45, suppl:42-5.

³ Tanner JM, Whitehouse RH, Takaishi M. Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965 -I and -II. *Arch Dis Child* 1966;41:454-71, 613-35.

⁴ Finn JD. *Multivariates: univariate and multivariate analysis of variances, covariance and regression*. Ann Arbor, Michigan: National Education Resources, 1972.

⁵ Hills M, Armitage P. The two-period cross-over clinical trial. *Br J Clin Pharmacol* 1979;8:7-20.

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Stump pemphigoid: a new complication of the amputee

Skin problems affecting the stump of the leg amputee are common, and diabetic patients have additional factors which may cause complications during rehabilitation. We report a case of a diabetic amputee who developed a previously unreported skin complication—localised bullous pemphigoid.

Case report

A 66 year old man presented to his general practitioner with a three month history of an infected ulcer on the great toe of the right foot. This developed without blistering and was consistent with the ulceration classically seen in the diabetic foot. He was noted to have glycosuria on routine urine examination, and the blood glucose concentration was 22 mmol/l (400 mg/100 ml). He was started on a carbohydrate restricted diet and referred to hospital as the ulcer failed to heal.

Examination showed a deep ulcer on the great toe with spread to the underlying bone. There were no pulses palpable below the right femoral artery but he had no evidence of peripheral neuropathy. Ultrasound investi-

gation disclosed an ankle pressure index of 0.7, indicative of peripheral vascular disease. This index is a ratio of the systolic pressure of the posterior tibial artery at the ankle to that of the brachial artery and is normally greater than 1.0. There was no history of any skin disorder. Results of investigations were: haemoglobin concentration 11.6 g/dl, normochromic normocytic pattern; erythrocyte sedimentation rate 83 mm in the first hour; blood glucose concentration 14.3 mmol/l (257.4 mg/100 ml); and normal urea and electrolyte values. He was started on glibenclamide 5 mg daily and referred for surgical treatment.

The great toe was amputated but, unfortunately, this failed to heal and he had a below knee amputation three weeks later. He made a good postoperative recovery and underwent early rehabilitation with a prosthesis, which is the policy for diabetic amputees. He continued with glibenclamide and was given no other medication. Two months postoperatively and after several weeks of active rehabilitation he developed a blistering eruption over the amputated stump (figure). These clear, tense blisters developed on normal skin. Biopsy

Appearances of stump (below knee) two months after amputation.

showed a large subepidermal blister with a strong inflammatory component including numerous eosinophils. Direct immunofluorescence showed deposition of IgG along the basement membrane extending into the roof of the blister. These are the findings of bullous pemphigoid, but circulating ant basement membrane antibody was not detected on two separate occasions. The patient responded to rest and topical steroid treatment with clobetasol propionate ointment, and mobilisation was recommended. This caused a recurrence of the blistering eruption, remaining localised to the amputated stump, and final control was achieved only with oral prednisolone 15 mg daily. At no time did the eruption become generalised.

Comment

There are many skin problems which can affect the amputee who wears a prosthesis. The skin is exposed to frictional trauma and the tightly fitting socket of the prosthesis prevents air circulating, trapping perspiration. These factors increase the likelihood of skin complications, and contact dermatitis, eczemas, epidermoid cysts, bacterial and fungal infections, chronic ulcers, and verrucous hyperplasia have been reported.¹ The diabetic patient has additional hazards: there is an increased susceptibility to infection, and below knee amputations heal less well than above knee amputations.²

Localised bullous pemphigoid has been reported occurring around the scar of a previous injury to the leg,³ and some cases of bullous pemphigoid have been observed to start with a localised group of blisters before the generalised eruption.⁴ There is no increased incidence of bullous pemphigoid in diabetes, however, and there have been no previous reports of the eruption confined to the skin of the amputated stump. The aetiological relevance of trauma is difficult to assess, but blistering due to trauma alone results in skin separation in the granular zone of the epidermis without positive immunofluorescence findings.⁵

We thank Dr J D Ward for permission to report this case.

¹ Levy SW. Skin problems of the leg amputee. *Prosthet Orthot Int* 1980; 4:37-44.

² Steinberg FU. Rehabilitation of the diabetic amputee. In: Levin ME, O'Neal LW, eds. *The diabetic foot*. 3rd ed. St Louis: C V Mosby Co, 1983:303-29.

- ³ Sparrow GP, Moynahan EJ. Localised pemphigoid. *Br J Dermatol* 1976; 95, suppl 14:27.
- ⁴ Sneddon IB, Church RE. Diagnosis and treatment of pemphigoid. Report on 22 cases. *Br Med J* 1955;ii:1360-3.
- ⁵ Sulzberger M, Cortese TA Jr, Fishman L, et al. Studies on blisters produced by friction. *J Invest Dermatol* 1966;47:456-65.

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Asthma associated with N-acetylcysteine infusion and paracetamol poisoning: report of two cases

Intravenous infusion of *N*-acetylcysteine has been shown to be effective and safe for paracetamol poisoning. Side effects are said to be few and serious complications rare.¹⁻³ We, however, describe two patients with a history of asthma in whom an asthmatic reaction occurred after treatment.

Case reports

Case 1—An 18 year old woman was admitted to the emergency centre after having swallowed over the previous seven hours 65 tablets of Di-gesic containing a total of 21 g paracetamol and 2.1 g propoxyphene. She had a history of frequent "bronchitic" cough and hay fever and had been taking antihistamines by mouth and beclomethasone and cromoglycate by inhalation. Physical examination elicited only general weakness and tiredness. Intravenous infusion of *N*-acetylcysteine was begun according to a standard protocol.¹ After infusion of 9 g over 15 minutes she developed increasing tachypnoea, central cyanosis, and diffuse bilateral wheezing. Peak expiratory flow rate was 180 l/min and arterial blood gas values (pH 7.43) were: oxygen pressure 10.2 kPa (77 mm Hg), carbon dioxide pressure 4.4 kPa (33 mm Hg), bicarbonate concentration 22 mmol (mEq)/l, and base excess -1.0 mmol (mEq)/l. The infusion was stopped and the patient responded to intravenous aminophylline infusion and salbutamol inhalation. She remained well over the next three days and was discharged. Her serum paracetamol concentration on admission was 84 mg/l, which fell further after admission.

Case 2—A 16 year old girl weighing 91 kg was admitted to the emergency centre one and a half hours after swallowing 50 tablets of Panadol, which contained a total of 25 g paracetamol. She had a history of asthma as a child and had been treated with salbutamol and beclomethasone inhalation. Infusion of *N*-acetylcysteine was instituted according to the usual protocol. After receiving 13.5 g over 15 minutes she had a severe attack of bronchial asthma. The infusion was stopped and she responded to intravenous aminophylline infusion. After a week of observations in the ward (during which time no clinical or biochemical evidence of liver dysfunction appeared) she was transferred to the psychiatric service. Her serum paracetamol concentration on admission and two and a half hours later were 203 and 125 mg/l respectively.

Comment

Paracetamol, singly or in combination with other drugs in proprietary preparations, is one of the most popular and easily available analgesic and antipyretic agents, and accounts for an increasing number of attempted suicides in Australia and Britain.³ Hepatotoxicity is the most serious complication and a major cause of morbidity and mortality in these cases.⁴ In recent studies Prescott *et al* have shown *N*-acetylcysteine to be effective and safe in the treatment of this condition.¹ Intravenous administration is preferred to the oral route, which has the disadvantage of unreliable absorption due to the use of oral activated charcoal and to vomiting. Vomiting often occurs in such cases as a result of other drugs ingested or is induced as a therapeutic measure.

N-Acetylcysteine is now available for intravenous use. The indications and methods of administration have been described¹ and are adopted in this hospital. Prescott and colleagues recommended