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Correspondence to Dr Edith Schober, Department of Paediatrics, University of Vienna, Währinger Gürtel 74-76, A-1090 Vienna IX, Austria.

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Successful use of danazol for hereditary angio-oedema

C RAJAGOPAL AND J R HARPER

General Hospital, Northampton

SUMMARY A 10-year-old boy with severe hereditary angio-oedema was given danazol, 200 mg each day. There was a pronounced reduction in the frequency and severity of oedema.

Danazol (17 α -Pregna-2,4-dien-20-yno[2,3-*d*]isoxazol-17-ol) is an orally active pituitary gonadotrophin inhibitory agent, without oestrogenic or progestational activity. It does not appear to affect other pituitary endocrine axes and its effect on gonadotrophins is reversible. Since its introduction to the UK in 1974 it has been used in adults for endometriosis and breast disorders.¹ It has been successfully used in children with precocious puberty.²

We report here the successful use of danazol for the prevention of hereditary angio-oedema.

Case history

The boy's parents came from St Helena. He was first admitted at age 3 years with painless oedema of one hand. Examination showed no other abnormality. A diagnosis of hereditary angio-oedema was confirmed on estimation of C1 esterase inhibitor levels, which were not detectable. His father also suffers from hereditary angio-oedema, with episodes of oedema and, occasionally, airways obstruction.

Since his original presentation he has been admitted with episodes of varying severity ranging from oedema of limbs or face to obstruction of the upper airways. Acute symptoms on these occasions were treated with fresh frozen plasma and aminocaproic acid. To try to quantitate the effects of

prophylactic treatment, his symptoms were graded according to severity: grade 1, swelling of the extremities or scrotal swelling; grade 2, facial swelling, abdominal pain with or without vomiting, swollen tongue; grade 3, upper airways obstruction manifesting as stridor or dyspnoea.

During the last four years he has been admitted to hospital about 6 times a year with symptoms of grade 1 severity. In addition to this, he has had four episodes of grade 3 severity. He has been treated with aminocaproic acid during this time, but his frequent absences from school and his frequent hospital admissions have been causing concern. At age 9 years 10 months it was decided to start him on danazol 100 mg twice daily. Before starting the drug, basal studies on puberty, growth, estimates of complement activity and testosterone levels were carried out, and were normal.

During 10 months of treatment with 100 mg danazol twice daily, he has had only two episodes of grade 1 symptoms and none of grades 2 or 3. He has

Figure Facial swelling during a bout of angio-oedema.

not missed a single day of school since starting danazol. He has maintained a normal growth velocity and has shown no androgenic or other side effects.

Discussion

Hereditary angio-oedema is characterised by oedema of the face, airways, extremities, and gut wall. The consequences may be life threatening, particularly if it affects the larynx and trachea.³⁻⁴

It is inherited as an autosomal dominant, the essential lesion being a qualitative or quantitative deficiency of C1 esterase inhibitor. Under normal circumstances C1 inhibitor exerts a halting influence on the C1 component and stabilises the complement system.⁵ Many drugs have been tried in the treatment of this condition. Inhibitors of serine proteases—for example aminocaproic acid—were the first to be tried, followed by tranexamic acid. While these agents are useful in acute attacks, danazol has been found effective in prevention. It has been shown that danazol induces C1 esterase inhibitor activity and thus prevents attacks.⁶ We feel that the use of danazol is justified. Arguments against its use in children are mainly based on fears that it suppresses growth and gonadal function. These theoretical complications may be acceptable if there are frequent hospital admissions and the child and the parents are in constant fear of severe airways obstruction. In

our patient a significant reduction in symptoms occurred on a dosage of danazol that did not cause any rise in serum testosterone level. After discussion with the boy and his parents we felt that it was correct to continue treatment, but his endocrine function is being closely monitored.

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Correspondence to Dr C Rajagopal, Department of Paediatrics, Duchess of Kent Military Hospital, Catterick, North Yorkshire.

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Value of the gastric aspirate shake test

M L SMITH, D CURNOCK, AND F FORSHAW

Neonatal Unit, City Hospital, Derby

SUMMARY The results and predictive value of the gastric aspirate shake test are reviewed in 432 preterm babies admitted to a neonatal unit during a 3-year period. It is concluded that the degree of prematurity is a better indicator of the chance of developing idiopathic respiratory distress syndrome than the test itself.

Respiratory distress syndrome (RDS) still continues to be a common neonatal problem and is all too frequently a cause of neonatal death. The deficiency of surfactant can be predicted antenatally by measuring the lecithin-sphingomyelin ratio in

amniotic fluid.¹ A simple method (the shake test), also carried out on amniotic fluid, was described by Clements *et al.*² This test has been used by others³⁻⁶ on gastric aspirate and the results showed that a negative result correlated well with the development of RDS. It has been suggested that the results of a shake test might help to decide whether a preterm baby should be transferred to a regional centre;³ it also differentiates RDS from other causes of neonatal respiratory problems.⁷

Patients and methods

Since 1976 each preterm baby admitted to the