survival in elderly patients but enormously enhances the quality of remaining life. How often hypopituitarism is responsible for postural hypotension is unclear, but pointers seen in our patients included low serum thyroxine concentrations without the expected raised thyroid stimulating hormone, hyponatraemia, and disproportionately pale facies.

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Visual evoked potential and contrast sensitivity function in diabetic retinopathy

Retinopathy is a major complication of diabetes, but clinically obvious optic neuropathy is uncommon. Recent reports of abnormal visual evoked potentials in diabetics without retinopathy have been conflicting.[1][2] We therefore studied the function of the visual pathway using the visual evoked potential and contrast sensitivity function in diabetics with and without retinopathy. In the absence of ocular disease a delayed visual evoked potential indicates abnormal transmission of nerve impulses from the retina to the visual cortex. The contrast sensitivity function is a psychophysical method of detecting subtle disturbances of the visual system such as early glaucoma and lesions of the optic nerve.[3][4]

Subjects, methods, and results

We studied 22 insulin dependent diabetics aged 20-35, of whom five did not have retinopathy, 11 had background retinopathy, and six had proliferative retinopathy. The table shows the clinical details. The three groups were comparable for age and glycosylated haemoglobin concentration. All patients had a corrected visual acuity of 6/9 and J6 or better.

The visual evoked potential was recorded using a standard technique. In each patient 128 responses were averaged and the latency of the major positive peak calculated. The contrast sensitivity function was determined using a standard method based on previous work.[4] All testing was performed uniocularly. Reference values for both tests were obtained in non-diabetic controls matched for age and sex, and results were considered to be abnormal if they exceeded the mean + 2 SD in the control group. Statistical analysis was by the permutation t test.

All patients with proliferative retinopathy showed delayed visual evoked potentials, compared with only one patient without retinopathy (p < 0.001) and five with background retinopathy (p < 0.01) (table). There was no significant difference, however, between the group with background retinopathy and the group without retinopathy. There were no differences between any of the groups in the prevalence of abnormal contrast sensitivity.

Comment

Although clinically manifest optic neuropathy is uncommon in diabetes, subclinical disease might be relatively common. Our findings show that in the absence of retinopathy there is no significant increase in the proportion of diabetic patients with either an abnormal visual evoked potential or abnormal contrast sensitivity function. Although the range of severity of background retinopathy was wide, this was likewise not associated with abnormalities in these tests. There was, however, a strong correlation between prolifertive retinopathy and an abnormal evoked potential.

Neuronal degeneration in the ganglion cell and layers of nerve fibre is one of the earliest changes in diabetic retinopathy,[5] and presumably patients with proliferative changes have more extensive neuronal and vascular retinal damage than those with background retinopathy. Our findings could reflect either damage to the maculopapillary fibres in the retina or subclinical optic neuropathy. Our observations are unlikely to have been related to coagulation treatment with argon laser light as none of the patients had undergone this treatment within six months of testing. None had received retrobulbar anaesthesia or sustained vitreous haemorrhages.

These results do not agree with the previous findings of abnormal visual evoked potentials in patients without clinical diabetic retinopathy[1] and abnormalities of contrast sensitivity in patients with minimal retinopathy.[3] Our findings imply subclinical neuronal damage in the visual pathway in diabetes, affecting either the retina or the optic nerve. This seems, however, to be a feature only of patients with proliferative retinopathy.

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Effect of inhalation of corticosteroids on exercise induced asthma: randomised double blind crossover study of budesonide in asthmatic children

Corticosteroids are well established in the management of bronchial asthma and are thought to act by inhibiting the late asthmatic reaction. Whether they have any effect on immediate reactions like exercise induced asthma is controversial. Generally, they are thought to be ineffective in exercise induced asthma, whether given short or long term and orally or by inhalation,[1][2] but attenuation of exercise induced asthma has been shown during regular treatment with inhaled steroids.[3][4] I report the results of a double blind placebo controlled study in which children with exercise induced asthma received budesonide acrosol for three weeks.

Clinical details of patients and results of tests of visual function

Retinopathy	No of patients	Mean (SD) age (years)	Mean (SD) duration of diabetes (years)	Mean (SD) glycosylated haemoglobin (%)	No of eyes tested	No with abnormal visual evoked potential	No with abnormal contrast sensitivity function
None	5 (4M, 1F)	25·4 (3·9)	8·8 (1·0)	10·8 (1·8)	10	1	
Background	11 (6M, 5F)	27·9 (2·8)	15·0 (4·1)	10·5 (1·5)	22	5	
Proliferative	6 (4M, 2F)	27·8 (5·0)	15·2 (4·4)	12·5 (2·5)	12	12	3

Patients, methods, and results

Sixteen children aged 8 to 15 (mean 10·9) years with perennial asthma were selected on the basis of >20% decrease in lung function after exercise. None had received corticosteroids within the past three months. Sodium cromoglycate was stopped 24 hours before the study and inhaled B_2 agonists eight hours before visits.

The study consisted of two three week treatment periods separated by a fortnight's wash out; during each treatment period participants received 200 μg budesonide aerosol twice daily through a 750 ml cone spacer or a placebo with a double blind randomised crossover protocol. Immediately before and at the end of each treatment period the children performed an exercise test and delivered a 24 hour urinary sample for analysis of cortisol. The exercise challenge consisted of five or six minutes of continuous running on a treadmill at individually adjusted, submaximal workloads. Heart rate was measured by radiotelemetry, and all subjects wore a nose clip during exercise. The absolute humidity was recorded.

Forced expiratory volume in one second was recorded on a dry spirometer (Vitalograph) before exercise (baseline) and three or five, 10, and 20 minutes after exercise. Results were expressed as the maximal percentage fall from the baseline value. Urinary cortisol was measured by radioimmunoassay. Two

Individual percentage falls in forced expiratory volume in one second induced by exercise before and after three weeks' treatment with budesonide aerosol and its placebo. Means (SD) are shown.

way analysis of variance and t tests for paired comparisons (two tailed, 5% level) were performed.

Fourteen children completed the study. Mean (SD) baseline forced expiratory volume in one second (% predicted) improved from 84 (17)% to 94 (16)% (p<0·02) during treatment; placebo showed no effect. Budesonide reduced the mean fall in forced expiratory volume in one second from 45 (16)% to 17 (14)% (p<0·001) (figure). No carryover effect from the treatment was detected after wash out. No significant changes occurred in the test conditions (absolute humidity, final heart rate, and workload). The mean 24 hour urinary free cortisol excretion was 94 (55) nmol/l (3·4 (2·0) μg/100 ml) and 116 (55) nmol/l (4·2 (2·0) μg/100 ml) before treatment and 96 (34) nmol/l (3·5 (1·2) μg/100 ml) and 85 (34) nmol/l (3·1 (1·2) μg/100 ml) after placebo and budesonide, respectively (F= 1·64; df 3·44, NS). One case of hoarseness during budesonide treatment was the only side effect reported.

Comment

Budesonide given by inhalation for three weeks afforded significant protection against exercise induced asthma in most children without appreciable suppression of adrenal function. Improvement in baseline airway function cannot explain the effect of budesonide on exercise induced asthma.[4] Normal 24 hour urinary free cortisol excretion cannot exclude more subtle degrees of adrenal suppression.

The present results and the finding that the immediate reaction induced by allergen was blocked after a week's treatment with prednisone[5] show that regular steroid treatment attenuates some immediate asthmatic reactions. The pathogenesis of exercise induced asthma and the precise modes of action of steroids, however, are incompletely understood. It is generally accepted that the airway cooling that occurs during exercise initiates the bronchoconstriction, but the mechanism is unknown. The decrease in bronchial reactivity during steroid treatment might result from decreased mucosal inflammation, reflex activity, or mediator release.

Inhaled B_2 agonists are the most effective drugs against exercise induced asthma, though the duration of action of bronchodilators is short and the effect sometimes insufficient, especially in severe cases. Additionally, children often forget to use or refrain from using prophylactic medicine when necessary. The present results suggest

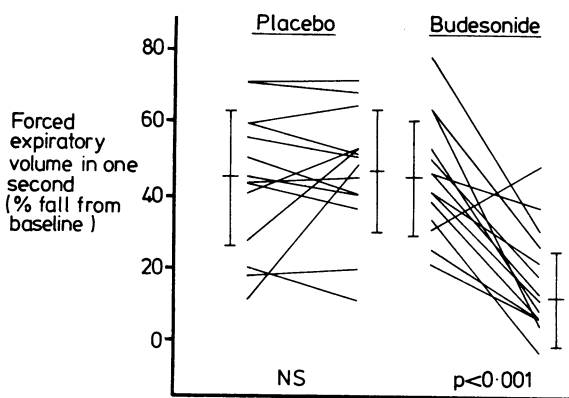inhaled steroids may be valuable in managing troublesome exercise induced asthma.

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Fatal exacerbation of systemic lupus erythematosus after treatment with griseofulvin

Most cases of systemic lupus erythematosus pursue a chronic relapsing course. Some drugs that are commonly prescribed and considered to be fairly safe can exacerbate existing disease, unmask a lupus diathesis, or produce a drug induced lupus syndrome. Awareness that drugs can adversely alter the course of systemic lupus erythematosus could prevent morbidity and death. We report a fatal exacerbation of systemic lupus erythematosus presumed to be due to griseofulvin.

Case report

A 22 year old woman with a six year history of systemic lupus erythematosus was admitted after one month of malaise, sweating, and fever. The diagnosis had initially been made on the basis of fever, lymphadenopathy, Raynaud's phenomenon, digital vasculitis, photosensitivity, and butterfly rash. Antinuclear and native double stranded deoxyribonucleic acid (DNA) antibodies were present in considerable but varying titres. She subsequently developed proteinuria. Renal biopsy showed focal proliferative glomerulonephritis; cerebral lupus was presumed to be present because of changes in personality and an electroencephelogram showed diffuse slow wave activity. She was given maintenance treatment of prednisolone 7 mg on alternate days.

Over the month before admission her general practitioner had prescribed ampicillin and erythromicin for a presumed respiratory tract infection. Griseofulvin had been prescribed seven days before admission; although the precise amount was unknown, the total dose could not have exceeded 1 g.

On admission she looked unwell and had a fever of 38·7°C, pulse rate 110 beats/min regular, and blood pressure (supine) 120/100 mm Hg. Results of examination were otherwise normal with no cutaneous signs of systemic lupus erythematosus and no obvious source of sepsis. White cell count was $3·9 \times 10^9$/l, haemoglobin concentration 10·5 g/dl, and erythrocyte sedimentation rate 121 mm in the first hour; C reactive protein was absent, and blood, sputum, and urine cultures yielded negative results. Renal function, electrolyte concentrations, and results of a short Synacthen test were normal. Liver enzyme activity (aspartate transaminase, alanine transaminase, and γ glutamyl transferase) and bilirubin concentrations were normal, as was a chest x ray film. DNA binding was 41% (normal <30%). She was presumed to have an exacerbation of her disease rather than infection, and prednisolone was increased.

On the second day in hospital she developed symptoms of a peripheral, sensory polyneuropathy and left lateral popliteal nerve palsy. Examination of cerebrospinal fluid showed a normal cell count and protein concentration. Results of gram staining and culture were negative. An intravenous bolus of methylprednisolone 1 g was given with symptomatic benefit. Further neurological signs did not develop, but nausea and a low intake of fluid necessitated intravenous fluids.

On the fourth day a further 1 g methylprednisolone was given for weakness. Objective and biochemical evidence of myositis was absent. Urea and creatinine concentrations had risen to 16 mmol/l (96 mg/100 ml) (normal 2·5-8·0 mmol/l (15-48 mg/100 ml)) and 180 μmol/l (2·0 mg/100 ml) (normal 40-130 μmol/l (0·5-1·5 mg/100 ml)) respectively. Intravenous fluids were increased to maintain a positive fluid balance.