

Drug points

High dose inhaled corticosteroids and dose dependent loss of diabetic control

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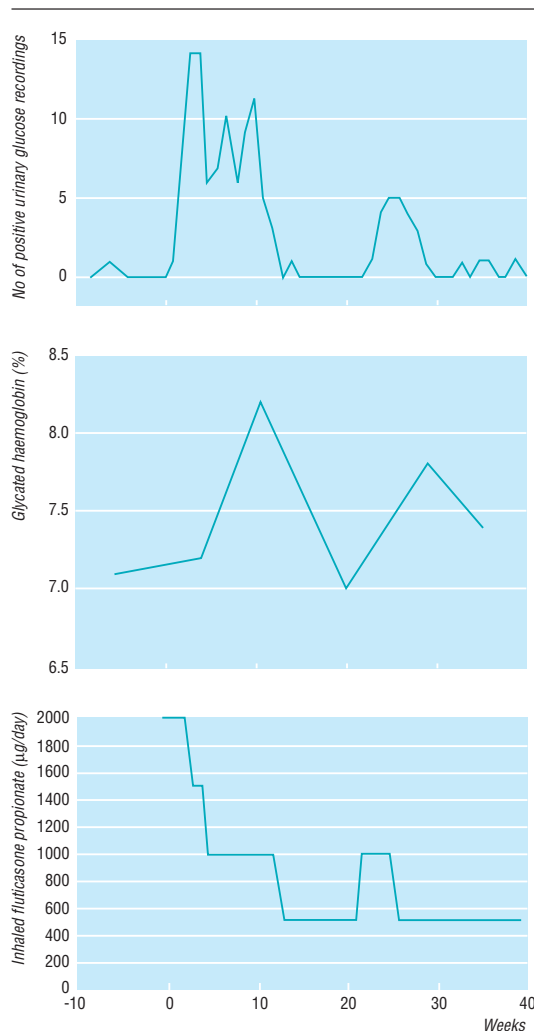
We report a case of loss of diabetic control in a patient given high doses of inhaled fluticasone propionate for asthma.

A 67 year old man who had had asthma for 10 years was referred for respiratory assessment. He had had non-insulin dependent diabetes mellitus for 40 years and was taking glibenclamide 5 mg and metformin 1700 mg daily. Glycaemic control was monitored every six weeks in an outpatient clinic using the percentage of glycated haemoglobin (haemoglobin A_{1c}) (Corning-Drew Glycomat low pressure chromatography system).¹ The normal range is <6% and the within batch coefficient of variation is 2.6% and 1.5% for concentrations of 7% and 10% respectively. During the previous year he had had only occasional trace glycosuria (<2 positive urinary glucose readings a week) and glycated haemoglobin concentrations (measured every 8 weeks) ranged from 7.0% to 7.3% (data not shown). His asthma treatment comprised ipratropium bromide 0.5 mg and salbutamol 5 mg by nebuliser four times daily. Computed spirometry (12 hours after his last nebuliser) showed that forced expiratory volume in 1 second was 1.48 litres (45% of predicted values) and 1.98 litres 30 minutes after bronchodilatation (Morgan plethysmograph). He had taken no other drugs and no oral corticosteroids in the previous 6 months. He did not drink alcohol or smoke. He was meticulous in taking his treatment and in recording his peak expiratory flow rate twice daily (morning and evening before treatment using a hand held mini-Wright meter) and urinary glucose measurements (Baker Diagnostics).

At week 0 he started treatment with inhaled fluticasone propionate 2000 µg per day by metered dose inhaler through a Volumatic spacer device (figure). During the next 30 weeks of monitoring he did not take oral corticosteroids, his diabetic treatment and strict diet and exercise regimens remained unchanged, and his weight remained stable. After starting inhaled fluticasone propionate subjective breathlessness and wheeze improved and average weekly peak expiratory flow rate increased from 410 l/min to 440 l/min, but he developed persistent glycosuria during week 3. All 28 urinary glucose measurements were positive for glucose in weeks 3 and 4 and the dose of inhaled fluticasone propionate was thus reduced in a stepwise fashion to 500 µg per day in week 14.

To our knowledge, deterioration in diabetes has not been documented with the use of inhaled corticosteroids.^{2,3} Furthermore, tolerance to the hyperglycaemic effect of systemic corticosteroids might have explained the subsequent improvement in diabetic control between weeks 15 and 24.⁴ With his consent we rechallenged him (single blind fashion) by increasing his daily dose of inhaled fluticasone propionate from 500 µg to 1000 µg in week 25. Within a week he developed glycosuria (from week 24 to 28, 21 out of 70 urinary readings were positive for glucose). Glycosuria resolved after reducing the dose of fluticasone propionate.

In this case the administration of high dose inhaled fluticasone propionate was matched by both a rise in glycated haemoglobin concentration (8.2% after 2000 µg per day; 7.8% after 1000 µg per day) and a worsening glycosuria (figure). Chronic use of high dose inhaled fluticasone propionate has been associated with adrenal suppression.⁵ On the basis of these data, the possibility of impaired diabetic control should be considered with high doses of inhaled fluticasone propionate.



Effect of inhaled fluticasone propionate on glycaemic control

- 1 Koenig RJ, Peterson CM, Jones RJ. Correlation of glucose regulation and hemoglobin A_{1c} in diabetes mellitus. *N Engl J Med* 1976;295:417-20.
- 2 Barnes PJ. Inhaled glucocorticoids for asthma. *N Engl J Med* 1995; 332:868-75.
- 3 Kruszynska YT, Greenstone M, Home PD, Cooke NJ. Effect of high-dose inhaled beclomethasone dipropionate on carbohydrate and lipid metabolism in normal subjects. *Thorax* 1987;42:881-4.
- 4 Conn JW, Fajans SS. Influence of adrenal cortical steroids on carbohydrate metabolism in man. *Metabolism* 1956;5:114.
- 5 Clark DJ, Lipworth BJ. Adrenal suppression with chronic dosing of fluticasone propionate compared with budesonide in adult asthmatic patients. *Thorax* 1997;52:55-8.

Correction

Cross sectional longitudinal study of spot morning urine protein:creatinine ratio, 24 hour urine protein excretion rate, glomerular filtration rate, and end stage renal failure in chronic renal disease in patients without diabetes

An editorial error occurred in this paper by Ruggenti and others (14 February, pp 504-9). In the second section of the results, in relation to figure 2, the decline in glomerular filtration rate in the lowest third of the population was wrongly given as -0.31 (0.21) ml/min/1.73 m²/month. It should have read -0.13 .