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Measuring glycosylated haemoglobin concentrations in a diabetic clinic

The glycosylated haemoglobin (HbA₁) concentration is a useful index of diabetic control.^{1,2} Measuring the concentration by chromatography on cation exchange columns, however, requires a skilled technician and controlled temperatures, and the result is not immediately available. We have therefore evaluated a new method (Corning Medical Ltd, Halstead, Essex) that offered accuracy, simplicity, and speed. We assessed the method in our diabetic clinic over six weeks by (a) comparing it with a chromatographic method run concurrently, (b) examining the feasibility of obtaining a result in time for the patient's consultation, and (c) estimating the value of the result.

Patients, methods, and results

On arrival all patients have their urine tested, are weighed, have their eyesight tested (yearly), and give a finger-prick blood sample for glucose and HbA₁ estimations. Often an hour or more passes after arrival before the patient sees the doctor. Some patients arrive well before the clinic starts to minimise this time, and finger-prick sampling was begun on these before 1 pm, so that the first results were available by 2 pm. Also by seeing mainly new patients first, who need more doctor-time, we hoped to achieve a good flow.

Blood obtained by finger-prick (10 µl) was haemolysed in 30 µl 0.1% saponin, 0.05% EDTA. Aliquots of haemolysate (1 µl) were analysed by electrophoresis and endosmosis on agar gels for 40 minutes and the percentage of HbA₁ determined by scanning densitometry. Standard deviation for replicate samples was 0.5%. Details of our chromatographic method have been published.³ The value of the measurements was assessed by questionnaire. After seeing each patient the doctor looked at the HbA₁ result, decided what advice to give the patient, and then answered four questions: Does this alter your management? Was the result as expected? Do you think it usefully reinforced the advice you have given? Did it alter the timing of further follow-up? Questionnaires were collected at the end of each clinic. Equipment fitted on a standard trolley, and it was found convenient to run the system in the clinic, reagents being non-toxic. The technician took about 30 minutes to learn the method.

The results were closely similar to those of chromatography (figure). In week 1 about half the results were available in time for the consultation. Week 2 was less satisfactory, but by week 3 and thereafter most results were obtained in time. A total of 259 questionnaires were answered. Haemoglobinopathy was identified in 10 cases, which we excluded from analysis. As a result of the measurements patient management was changed in 17% of cases (ranges 10-25% over the six weeks and 11-26% for the six doctors). The result was unexpected in 26% of cases (ranges 20-33% and 18-36% respectively) and was thought usefully to reinforce the advice given in 45% (ranges 38-56% and 14-75%) and to alter timing of follow-up in 12% (ranges 5-23% and 2-23%). When the first, third, and fourth questions were combined a positive answer was obtained in 135 (54%) cases.

Comment

Measuring HbA₁ by electrophoresis/endosmosis was simple, accurate, and rapid compared with column chromatography, and most results were obtained during clinic time. Nevertheless, there was some extension of waiting time and overcrowding in our just adequate waiting area, and longer term some adjustments will be necessary. Patients may need to be re-educated into considering a clinic visit as an opportunity for advice partly based on preliminary checks (including HbA₁) rather than a visit to the doctor preceded by a long wait.

As a result of measuring HbA₁ almost one-fifth of patients had their

Relation between HbA₁ concentrations measured by electrophoresis/endosmosis and our own modified Kynoch-Lehmann (K-L) columns⁴ (n=192). HbA₁ by electrophoresis = 1.10 × HbA₁ by K-L - 0.64 (—Line of identity. --- Regression line).

management changed, which is substantially more than after many tests. In over half the measurement was thought to be useful. Further studies will identify patients in whom HbA₁ measurement is most valuable.

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Spontaneous biochemical remission in parathyroid carcinoma

Spontaneous remission is an unusual but recognised feature of primary hyperparathyroidism associated with adenoma, and is then attributed to infarction of, or haemorrhage into, the affected gland. A remission seems not to have been described in parathyroid carcinoma. We describe the case of a patient with parathyroid carcinoma who had a spontaneous but temporary biochemical remission which may have been related to tumour infarction.

Case report

The patient, a man aged 60, was well until June 1976, when he developed pain in the lower lumbar region. He also noticed ankle swelling and had lost 7 lb (3.18 kg) in weight. There was no significant medical history. He was found to have hypercalcaemia and was referred to the metabolic unit, Manchester Royal Infirmary, for further investigation. Clinical examination gave normal findings apart from congenital finger clubbing. Serum concentrations were: calcium 3.75 mmol/l (15 mg/100 ml), inorganic phosphate

0.96 mmol/l (2.9 mg/100 ml), alkaline phosphatase 150 IU/l, and urea 3.8 mmol/l (23 mg/100 ml). Serum immunoassayable parathyroid hormone (iPTH) concentration was 13.1 μ g/l (normal 0.8 μ g/l). Skeletal radiographs showed subperiosteal erosions of the phalanges and a "rugger-jersey" spine. These findings indicated primary hyperparathyroidism. In March 1977 his neck was explored. A large, encapsulated, tan-coloured tumour (2.5 cm $\times$ 2 cm $\times$ 2 cm) was found in the left lower position. Three other normal-sized nodes were thought to be recognised clinically, but biopsies were not done. The tumour was composed of chief cells and, although the cells had a regular appearance, occasional mitoses were seen, suggesting the possibility of parathyroid carcinoma. He made an uneventful recovery, and the serum calcium and iPTH concentrations returned to normal.

He remained well until June 1978, when he again developed backache. The serum calcium concentration was now raised (3.8 mmol/l), as was the serum iPTH (5.4 μ g/l). He was readmitted. The hypercalcaemia was confirmed but while an inpatient his serum calcium concentration fell spontaneously to normal. This change was accompanied by decreases in the serum iPTH and in the urinary nephrogenic cyclic AMP¹ and by an increase in the renal tubular reabsorption of phosphate (figure). This remission persisted for

Serum concentrations in case of spontaneous biochemical remission in parathyroid carcinoma (---) shows upper limit of normal range.

Conversion: SI to traditional units—Calcium: 1 mmol/l $\approx$ 4 mg/100 ml.

three weeks. In September 1978, after the return of hypercalcaemia, his neck was again explored and also the mediastinum. A biopsy specimen of tissue taken from the left upper and right lower poles of the thyroid gland showed parathyroid tissue surrounded by adipose tissue and separated by dense fibrous bands. The histology of tissue from sites in the thymic region showed further nests of parathyroid tissue insinuated between thymic lobules. There was a clump of parathyroid cells in a vein. In one of the nests of parathyroid tissue there was an area of granulation tissue containing haemosiderin pigment. The appearances were those of parathyroid carcinoma with possible tumour infarction.

He made a good postoperative recovery and the serum calcium and iPTH concentrations fell to normal. In March 1980 hypercalcaemia recurred (serum calcium 3.15 mmol/l, serum iPTH 1.3 μ g/l) and has persisted.

Comment

The clinical, operative, and histological findings confirmed that this patient had a parathyroid carcinoma. Spontaneous relapse of hyperparathyroidism was to be expected. In primary hyperparathyroidism associated with adenoma the serum calcium concentration occasionally fluctuates² and may return to normal. Much less common is spontaneous infarction of the affected gland, which may cause a prolonged biochemical remission and sometimes profound hypocalcaemia.^{3,4} The granulation tissue and haemosiderin pigment found in one of the nests of parathyroid cells suggests localised infarction of the tumour. This might explain the temporary biochemical remission. Hypomagnesaemia, which impairs parathyroid hormone secretion, was not present at any stage.⁵

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Risks from cannulae used to maintain intravenous access

Over five million intravenous plastic cannulae are used each year in Britain. Most are the Teflon Venflon type with a valved side injection port permitting convenient intermittent intravenous access. This design, however, reportedly increases the possibility of infection,¹ though evidence is lacking. We have therefore studied prospectively the risks of using the Venflon cannula for intermittent vascular access.

Materials, methods, and results

During January to March 1980 we studied 102 consecutive Venflon cannulae inserted for at least 24 hours for intermittent or emergency intravenous access in patients in two medical wards. Each entry site was examined for local inflammation (defined as the presence of two or more of noticeable tenderness, redness, swelling, and phlebitis), a skin swab taken, and the site sprayed with 0.5% chlorhexidine in spirit. The cannula was then carefully removed, the intravenous portion cut off aseptically into a dry sterile container, and a blood specimen taken for culture. The cannula tip was cultured both quantitatively by a roll-plate technique² and qualitatively in nutrient broth. Fifteen cannulae produced definite bacterial growth² on roll-plate culture, and these and an additional eight were positive on broth culture.

Cannula infection was significantly associated with positive skin-swab cultures (see table), the same micro-organism (mainly *Staphylococcus epidermidis*) always being isolated from both sites. Phage typing, biotyping, and antibiograms suggested that out of 12 paired isolates from positive cannula and skin cultures, seven were identical. One patient had *Staph aureus* grown from all specimens, including blood, and died of septicaemia and acute endocarditis. Cannula infection was not associated with local inflammation or duration of cannulation, though the second two were significantly related (table). Type of medication given through the side port

Relation between cannula infection, skin infection, local inflammation at site of cannulation, and duration of cannulation

	No of cases (total = 102)	No of positive skin cultures	Duration of cannulation (hours)	
			Mean $\pm$ SD	Range
Cannulae with positive roll-plate culture	15	13*	92 $\pm$ 59	24-243†
Cannulae with negative roll-plate culture	87	17*	83 $\pm$ 53	24-312†
Local inflammation present	35	12†	112 $\pm$ 63	39-312‡
Local inflammation absent	67	18†	68 $\pm$ 40	24-243‡

*Significant difference ($p < 0.005$; χ^2 test).

†No significant difference.

‡Significant difference ($p < 0.005$; Student's t test).