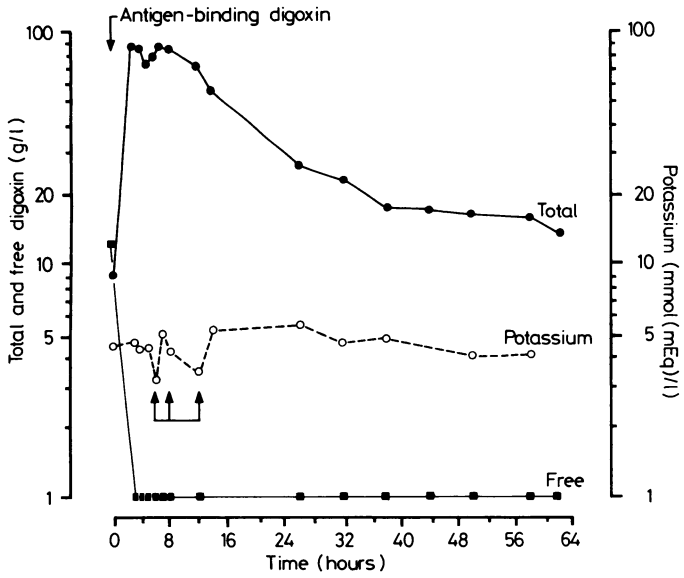
doses intradermally and then 2 mg antigen-binding fragments in saline intravenously an infusion of 200 mg in 5% dextrose was set up and given over one hour with close monitoring of vital signs. The infusion started 24 hours after ingestion. The free serum digoxin concentration fell dramatically to undetectable concentrations (< 1 ng/ml) while the total blood concentration, comprised almost solely of digoxin bound inactively to antigen-binding fragments, correspondingly rose (figure). The reduction in free



Time course of total serum digoxin concentration, free serum digoxin concentration, and serum potassium concentration immediately before and after injection of antigen-binding fragments of digoxin. Values are expressed as units on a logarithmic scale. Arrows indicate timing of infused potassium supplements.

digoxin was accompanied by a fall in serum potassium, which was corrected by infused supplements, using a total of 120 mmol. The electrocardiogram showed resolution of ectopic activity and sinus bradycardia. The coagulation disturbance was corrected using fresh frozen plasma and vitamin K.

Comment

Receptor-digoxin interaction is reversible and digoxin-specific antibodies have been shown to prevent or reverse digitalis-induced toxic arrhythmias, inotropy in isolated cardiac muscle, and inhibition of sodium, potassium, and adenosine triphosphatase in animals.[2] These antibodies, produced by immunising animals with protein-bound digoxin, have the potential to cause anaphylaxis. Antigen-binding fragments were developed that lacked the antigenicity of the intact immunoglobulin while still retaining high affinity and specificity.[3] In contrast to the parent molecule the antibody had a larger volume of distribution, equilibrated more rapidly with digoxin, and was excreted by the kidneys, taking most of the drug with it.[1 3 4] Furthermore, reversal of digoxin-induced arrhythmias in dogs was more rapid and predictable for antigen-binding fragments than for the equivalent dose of parent digoxin-specific IgG.[5]

The use of antigen-binding fragments for the successful treatment of digoxin overdose has been reported[4] but only recently has the potential importance of this mode of treatment been widely recognised. Antibody inhibition of several important drugs has been shown, but clinical use will probably be restricted to those drugs such as digoxin that are dangerous when taken in excess, in common use, and not always controlled by conventional measures.

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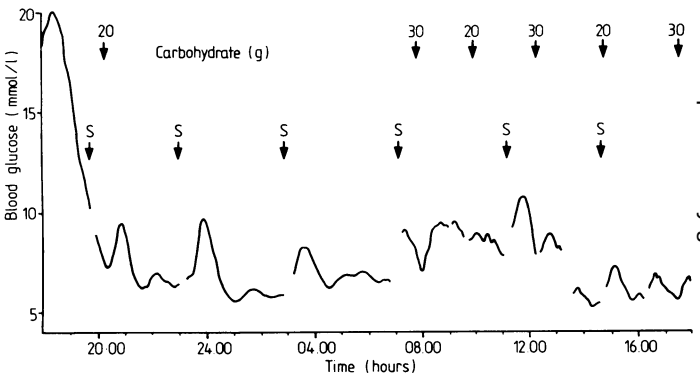
Short-term control of brittle diabetes using a Biostator

The Biostator (Miles Laboratories Ltd) is a machine which continuously samples venous blood, measures the blood glucose concentration, and then infuses either insulin or glucose intravenously. The rate of infusion is determined by an algorithm stored in the machine's computer.[1] We report the first use of this machine to control brittle diabetes (as defined by Pickup *et al*[2]) in the medical ward of a district general hospital.

Case report

A 13-year-old girl (weight 55 kg) usually achieved satisfactory control using subcutaneous Actrapid insulin delivered by a Mill Hill infuser[2] (average daily dose 60 units). Three or four times each year she used to become resistant to doses of more than 500 units of subcutaneous and intramuscular insulin and rapidly became ketoacidotic. Control was usually re-established without difficulty using intravenous insulin (60-120 units daily), which was continued for 1-2 weeks until the resistance to subcutaneous insulin settled spontaneously.

On 27 December 1981 she was admitted to hospital because of resistance to subcutaneous insulin, and for the first time it was impossible to achieve stable control with intravenous insulin although blood samples were taken every 1-2 hours by day and at night. Blood glucose concentrations were measured using BM-Test-Glycemie 20-800 strips (Boehringer-Mannheim Corporation) and fluctuated rapidly between 1 and 44 mmol/l (18 and 792 mg/100 ml). Between 26 and 30 January 1982 her diabetes was controlled using a Biostator. The constants used to determine the infusion rates of insulin or glucose were those preprogrammed into the computer,[1] except that the variance, which determines the response rate to a change in blood glucose concentration, was increased from 100% to 200% during the first 24 hours. Blood glucose concentrations during the second and third days of this treatment are shown in the figure. Lack of suitable veins for the sampling cannula, which had to be replaced three times, resulted in the treatment being stopped after four days, during which time the blood glucose



Blood glucose concentrations during the second and third days' treatment with the Biostator. The record begins after a two-hour interruption due to a blocked cannula. Arrows marked S indicate gaps for standardisation; unmarked gaps are due to cannula blockages.

Conversion: SI to traditional units—Blood glucose concentration: 1 mmol/l ≈ 18 mg/100 ml.

concentration was 7·9 ± 2·6 mmol/l (142·2 ± 46·8 mg/100 ml) (mean ± SD, n = 3871), range 4·4 to 20·2 mmol/l (79·2 ± 363·6 mg/100 ml). In the four days before treatment with the Biostator the blood glucose concentration was 14·9 ± 8·9 mmol/l (268·2 ± 160·2 mg/100 ml) (n = 61) and the range 1-44 mmol/l (18-792 mg/100 ml).

After this period of relative stability it was much easier to control her diabetes with intravenous and then subcutaneous infusions of insulin, and she went home on 5 February 1982 taking her usual subcutaneous dose.

Comment

We have shown that the Biostator can be used on a general medical ward to control brittle diabetes in the short term. Major advantages for the patient were the abolition of hypoglycaemia and the freedom from fingerprick blood samples, which allowed regular sleep. The absence of hypoglycaemia may have contributed to the improved diabetic stability when conventional insulin infusions were restarted. This improvement was only temporary and by May 1982 there had been three further episodes of insulin resistance.

It was not possible to compare insulin dosages delivered by the Biostator with those by conventional means because of an intermittent leak on the poorly designed connector joining the infusion tubing to the infusion cannula and because we took no precautions to prevent adsorption of insulin to plastic. The glucose analyser and computer functioned perfectly but the double lumen sampling cannula was not satisfactory. It is 5·3 cm long and can therefore only be used in peripheral veins, which are often scarce in patients who have had repeated episodes of ketoacidosis. The inner lumen is only 0·51 mm in diameter so the limb must be firmly splinted if the cannula is near a joint. A longer cannula which could be placed in a central vein is needed and would have the added advantage of allowing the patient greater mobility.

We estimate that a biochemistry technician is needed for at least 20 hours each week to run the machine. Extra work for medical staff was caused mainly by the flushing or replacing of blocked cannulas and was very time consuming in this case. The nursing staff standardised the analyser every four hours and soon became familiar with the machine. The extra nursing time involved was probably no greater than the time previously spent on taking fingerprick blood samples and treating hypoglycaemia. Brittle diabetes is a rare and dangerous illness.[2] Its treatment with the Biostator in a district general hospital stretches resources to the limit, and we could not have sustained the necessary effort for more than a week.

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Mid-arm circumference as simple means of identifying malnutrition in Crohn's disease

Malnutrition is common in patients with Crohn's disease.[1] Weight loss is widely used as a simple means of identifying patients at risk of malnutrition, but it may be an unreliable indicator if it depends on the patient's memory and if oedema occurs as a result of hypoalbuminaemia. Moreover, the importance of weight loss may be considerably greater in thin subjects than in obese ones. Measurement of mid-arm circumference has been used as a simple method of objectively assessing nutritional state among children.[2,3] We performed a study to determine whether this measurement was of value in predicting which adult patients with Crohn's disease were at risk of malnutrition.

Patients, methods, and results

We studied 106 outpatients with Crohn's disease (age range 18-72 (mean 41) years); diagnoses were based on conventional criteria. Height, weight, mid-arm circumference (MAC), and triceps skinfold thickness (TSF) were measured in the standard way.[4] Mid-arm muscle circumference (MAMC) was calculated from the formula MAMC = MAC − 0·314 TSF.[4] Results were expressed as a percentage of ideal standards.[4]

There was a strong positive correlation between weight and mid-arm circumference, both expressed as a percentage of the ideal standard ($r = 0·872$, $p < 0·001$, $n = 106$). Forty-eight patients were taking prednisolone, with 40 receiving long-term treatment with a mean daily dose of 8 mg. The correlation coefficient in this group between weight and mid-arm circumference was also strongly positive ($r = 0·889$, $p < 0·001$, $n = 48$). Mid-arm circumference at the 90% standard (26·4 cm in men, 25·7 cm in women) appeared useful as a reference point as all 39 patients whose mid-arm circumference was less than 90% of the ideal were below ideal weight, including 21 patients who were more than 10% below ideal weight.

Seventy patients with Crohn's disease were then arbitrarily divided into those undernourished with mid-arm circumference less than 90% ideal and those well nourished with mid-arm circumference greater than 90% ideal. Weight, mid-arm muscle circumference, and laboratory variables were compared between these two groups and also with results obtained from patients with ulcerative colitis and healthy subjects. Serum albumin concentration (normal range 35-50 g/l) was measured by SMA plus autoanalyser, serum prealbumin concentration (normal range 200-500 mg/l) by radial immunodiffusion, and haemoglobin concentration by Coulter counter. Creatinine height index (normal range 1·0 ± 0·1) was based on mean daily urine creatinine excretion estimated from two consecutive 24-hour urine collections. This index gave a measure of lean body mass.

For each variable studied the groups were well matched in terms of numbers, age, and sex. The site of Crohn's disease was classified as diffuse small bowel, ileocaecal, ileocolonic, colonic, or anorectal. There were more patients with diffuse small-bowel disease and fewer with colonic and anorectal disease in the undernourished group with Crohn's disease compared with the well-nourished group ($\chi^2 = 10·622$, $p < 0·05$). Sixty per cent of undernourished patients with Crohn's disease were taking steroids compared with 43% of well-nourished patients; this difference was not significant.

The table shows the results. For every variable patients with Crohn's disease with mid-arm circumference less than 90% ideal had values significantly below those in patients with mid-arm circumference greater than 90% ideal, who in turn were no different from the control groups. Creatinine height index (mean ± 1 SD) in 20 patients with Crohn's disease with mid-arm circumference less than 90% ideal (0·71 ± 0·17) was also significantly lower than that in 18 patients with mid-arm circumference greater than 90% ideal (0·89 ± 0·18) and in 22 healthy individuals (1·10 ± 0·21) $p < 0·01$.

Anthropometric and laboratory measurements in patients with Crohn's disease and ulcerative colitis and normal subjects. Values are means ± 1 SD

	Patients with Crohn's disease		Patients with ulcerative colitis (n = 30)	Normal subjects (n = 30)
	Mid-arm circumference < 90% ideal (n = 30)	Mid-arm circumference > 90% ideal (n = 30)		
Weight:				
Mean % of ideal	86·7 ± 7·1*	108·2 ± 16·1	117·3 ± 17·1	110·7 ± 11·9
No with < 90% ideal	19	1	1	1
Mid-arm muscle circumference:				
Mean % of ideal	82·3 ± 7·0*	100·2 ± 9·8	102 ± 10·4	97·2 ± 9·0
No with < 90% ideal	25	3	4	7
Serum albumin concentration:				
Mean (g/l)	36·6 ± 5·7*	43·2 ± 3·7	43·8 ± 3·1	45·2 ± 3·3
No with < 35 g/l	12	1	0	0
Serum prealbumin concentration:				
Mean (mg/l)	215 ± 76*	290 ± 62	277 ± 55	297 ± 47
No with < 20 mg/l	15	1	1	0
Haemoglobin concentration:				
Mean (g/dl)	11·9 ± 1·5*	13·5 ± 1·3	13·6 ± 1·7	14·1 ± 1·5
No with < 11 g/l	9	0	2	0

*Comparison with three other groups: $p < 0·001$ (Student's t test).

Comment

Patients with Crohn's disease with a mid-arm circumference less than 90% of the ideal standard had appreciably reduced laboratory and anthropometric variables compared with well-nourished patients whose mid-arm circumference was greater than 90% of the ideal standard. The impaired nutrition probably reflects more extensive small-bowel disease. Well-nourished patients with Crohn's disease were in turn similar to the two control groups. There was no significant difference in steroid treatment between the two groups with Crohn's disease, so that any steroid effect would not invalidate the result.