Patient reactions to long-term outpatient treatment with continuous subcutaneous insulin infusion

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Abstract

Fourteen of the first 15 insulin-dependent diabetics to be treated in our unit by three weeks or more of outpatient continuous subcutaneous insulin infusion with a portable syringe pump completed a questionnaire about their reactions to the system. Motivation was more important to a favourable response than occupation or intelligence. Most patients thought that diabetic control was better with the pump than conventional injection treatment and several felt subjectively better. Features such as the greater flexibility of diet and insulin delivery rates during continuous subcutaneous infusion were appreciated.

The most consistent adverse criticism was about the size of the device used, nearly all patients thinking that smaller and lighter infusion systems should be developed. Psychological reactions to the infusion and difficulties with interpersonal relationships were identified; these must be clearly appreciated and discussed with patients and family before and during treatment. Nine of the 14 patients said they would undertake continuous subcutaneous infusion for one year and a further two said they would do so if the infuser was smaller.

These results provide guidance on future technological development of continuous subcutaneous insulin infusion and indicate that the major constraint to long-term trials of the present system is the size of the pump.

Introduction

We developed the technique of continuous subcutaneous insulin infusion¹⁻⁶ as a means of achieving near-normoglycaemia in insulin-dependent diabetics for periods long enough to test the hypothesis that strict metabolic control may slow, prevent, or reverse the progress of diabetic microvascular disease. Other workers recently confirmed the inpatient and outpatient efficacy of the system in small groups of diabetics.⁷⁻¹¹

A randomised, controlled, prospective trial of the effect of diabetic control on complications requires a large number of patients studied for prolonged periods, perhaps many years. It is therefore important to establish the tolerance to outpatient treatment with continuous subcutaneous insulin infusion in patients with a wide range of occupations, life styles, intelligence, and clinical features of diabetes. Their response to the "first-generation" insulin infusion pumps may also provide valuable guidance on future technological developments and indicate the constraints of long-term trials.

We therefore report the responses elicited by a questionnaire sent to diabetics treated at home by continuous subcutaneous infusion for three weeks or more.

Methods and results

The figure shows the questionnaire, which was sent to the first 15 insulin-dependent diabetics who had been treated as outpatients with continuous subcutaneous insulin infusion for three weeks or more. Table I shows the clinical features and occupations of the patients. One patient did not return the questionnaire.

We need to find out people's reactions to wearing the insulin pump and it would be a great help if you would answer the questions set out below. All of the answers will be treated as strictly confidential. We would appreciate it if you would complete and return this questionnaire as soon as possible in the envelope enclosed.

- (1) How old are you?
- (2) What is your occupation?
- (3) How old were you when your diabetes was diagnosed?
- (4) How did you feel about the period of pump treatment? (Please mention any advantages or disadvantages you recall—inconveniences, embarrassments, fears, restrictions to your life, insulin reactions, etc)
- (5) Could you contemplate "settling down" with the pump for a period as long as one year?
- (6) How did the period on pump treatment compare with life on ordinary insulin injections?
- (7) Did you feel that you understood the pump?
- (8) What advice do you have for us on the future use of the pump (that is, ways of making it more acceptable for long-term use)?

Thank you very much for your help.

The questionnaire.

TABLE I—Clinical features and occupations of diabetics treated by long-term continuous subcutaneous insulin infusion

Case No	Age (years)	Sex	Duration of diabetes (years)	Occupation
1	28	F	24	Telephonist
2	39	M	11	Messenger
3	26	F	14	Housewife
4	41	M	24	Computer programmer
5	45	M	32	Manager
6	49	M	24	Docker
7	18	F	12	Clerk
8	21	M	10	Hospital administrator
9	52	M	6	Bank official
10	24	F	1	Musician
11	24	F	2	Sales administrator
12	23	M	2	Building worker
13	31	M	26	Accountant
14	31	F	5	Clerical officer

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The procedures for the infusion were as described previously.^{4,6} Two models of the Mill Hill infuser were used: either the 1001 series specially adapted to deliver at two rates (a basal rate of 50 μ l/h and a preprandial rate of 400 μ l/h for 17 minutes) or the commercially available 1001 HM series, in which there is metered manual advance of the lead screw, giving variable boluses of insulin for meals. The

delivery cannula was either a fine nylon cannula (Portex Ltd, Hythe, Kent) implanted subcutaneously in the abdominal wall using local anaesthetic¹ (cases 1, 2, 4, 7, 8, 10, 11, 12) or a 25-gauge butterfly needle (Abbott Laboratories, Queenborough, Kent) implanted without local anaesthetic by the patient himself (cases 3, 5, 6, 8, 9, 13, 14). All patients monitored their blood glucose concentrations at home using Dextrostix glucose oxidase reagent strips, usually four or more times daily, reading the results on a reflectance meter (Hypocount, Hypoguard Ltd, Ipswich). The pump was worn either on a belt around the waist or fitted into a special shoulder harness, and its batteries were changed each week.

Tables II and III show the responses of the patients to questions 4, 5, 6, and 8 on the questionnaire. In reply to the question "Did you feel that you understood the pump?" (question 7) all patients answered yes.

TABLE II—Responses of patients to question 4: How did you feel about the period of pump treatment?

Case No	Comments
1	Aware of pump motor; others treated me as a robot at first; appreciated "time off" pump—for example, bathing
2	Harness uncomfortable
3	Happy most of time; liked meal-time flexibility; size of pump a disadvantage; sex life disturbed; sleeping sometimes uncomfortable
4	Appreciated not having to inject; size awkward; care needed when mixing solutions; restrictive during sex; others sometimes embarrassed by pump
5	Less regimentation of meals; disliked inserting butterfly needle; disadvantage at night
6	Easy to live with pump; slight initial inconvenience with manual work
7	Restrictive with clothing; worried about cannula kinking (nylon); felt insecure when removing pump for baths, etc; not keen on blood sugar monitoring; liked not having to give injections
8	Felt better; enjoyed greater flexibility; generally no problems
9	Pump bulky; welcomed flexibility, especially at meals
10	Adapted well; manual work slightly difficult; occasionally embarrassed by people staring at pump
11	Regarded pump at first as a novelty; clothes needed altering; would think that sexual relationships sometimes difficult in some pump wearers
12	Liked flexible diet; physically restraining; reassured by good control
13	Felt better; uncomfortable at night; restricted type of clothing; minor hypoglycaemic feelings only
14	Happy and content. No inconvenience or embarrassments; no hypoglycaemic reactions

TABLE III—Responses of patients to questions 5, 6, and 8

Comment	Case No
Question 5: Could you contemplate "settling down" with the pump for a period as long as one year?	
Yes	1, 2, 4, 5, 6, 8, 9, 10, 14
No	7, 11, 12
No, but would if pump smaller	3, 13
Question 6: How did the period on pump treatment compare with life on ordinary insulin injections?	
Better control	1, 5, 6, 7, 8, 10, 12, 13
Same or similar	2, 11
More flexible or improved life style	4, 8, 9, 10, 12
More aware of diabetes	3, 10
More thought required	12
No local skin reactions	14
Liked pump more than injections	11
Question 8: What advice do you have for us on the future use of the pump?	
Smaller or lighter pump needed	1, 3-13
Improve harness, attachment to body	2, 4, 11
Variable basal rates needed	1, 8
Quieter pump needed	1
Easier changing of insulin reservoir needed	4
Improve cannula insertion, design	10, 12
Permanently implanted cannula needed	5
None specifically	14

Discussion

The diabetics in this survey represented patients with a wide range of ages (18-52 years), duration of diabetes (1-32 years), and occupations. Although we did not formally estimate their intelligence, we gained the impression that motivation was more important than IQ in coping with the pump. All of the occupations were compatible with long-term continuous subcutaneous infusion, though manual jobs (such as dock or

building work) obviously presented more difficulties, more because of the bulk of the system than because of exercise-induced hypoglycaemia. Such hypoglycaemia, in fact, is rarely noted during continuous subcutaneous insulin infusion and seems to be much less common than during conventional treatment by insulin injection.^{6, 12}

It was encouraging that almost all of the patients thought that diabetic control was better during treatment by continuous subcutaneous infusion than injections, and several felt better in themselves while receiving the infusion. The increased flexibility of diet and insulin regimens was often commented on—that is, the facility to delay or even omit meals altogether on occasions, to alter the basal insulin infusion rate independently of the timing and size of the prandial insulin boost, and to vary the boost with the expected size of the meal.

Physical reactions to the infusion system centred mostly on the size of the pump (the Mill Hill infuser measures 7 × 14.5 × 2.3 cm). Several patients found it uncomfortable at night and awkward to secure to the body, particularly in a harness. Women remarked on the restrictions and alterations sometimes necessary with fashionable clothing. One patient was conscious of the noise of the pump motor, although generally we find that this quickly becomes unnoticed by the wearer.³

All patients considered that they understood the principle and the operation of the pump system, indicating that the present controls are adequately simple.

Psychological reactions were notable. Many patients remarked that the treatment made them more aware of being a diabetic, which they usually regarded unfavourably. Partly this was because others noticed the device, were curious about it, and might embarrass the patients. The increased attention to and supervision of these diabetics probably also highlighted their condition.

Reliance on a mechanical device for life-supporting drug delivery might be expected to produce considerable unease. Some patients were thought of by others, or even themselves, as "robots," at least at first, but it is surprising that the patients did not express more anxiety about system failure. None asked for audible warnings of possible events such as battery discharge or other pump malfunction, although several new pump designs will incorporate these features.

Sexual relations and sporting activities might be restricted when the pump is being worn, and it is obviously important that full discussion with the patient and patient's spouse or partner takes place before treatment begins. After deliberate removal of the infusion pump blood glucose concentrations remain stable for about one hour before beginning to rise.¹³ Patients should be advised that disconnecting the system for bathing, sexual intercourse, etc, is perfectly safe for this period.

Despite the above strictures nine patients indicated that they would undertake continuous subcutaneous infusion for one year and a further two that they would do so if the infuser were smaller. Almost all the patients agreed that the infuser should be smaller, emphasising that future work should be directed towards miniaturising the infuser. In our laboratory we have developed a prototype pump about one-third the size and weight of the Mill Hill infuser, and other small second-generation devices are currently undergoing clinical trials elsewhere. Other suggestions for future development such as separate and easily variable day-time and night-time basal infusion rates have been incorporated in new prototype pumps. These new pumps should greatly improve the long-term acceptability of continuous subcutaneous infusion. Though this questionnaire was sent to only the first 15 patients who received prolonged outpatient treatment with this method, we are continuing to elicit patient responses as pump technology and infusion techniques improve.

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References

- ¹ Pickup JC, Keen H, Parsons JA, Alberti KGMM. Continuous subcutaneous insulin infusion: an approach to achieving normoglycaemia. *Br Med J* 1978;i:204-7.
- ² Pickup JC, Keen H, Parsons JA, Alberti KGMM. Continuous subcutaneous insulin infusion: good blood glucose control for up to 4 days. *Diabetologia* 1979;16:385-9.
- ³ Pickup JC, Keen H, Parsons JA, Alberti KGMM, Rowe AS. Continuous subcutaneous insulin infusion: improved blood glucose and intermediary metabolite control in diabetics. *Lancet* 1979;i:1255-8.
- ⁴ Pickup JC, White MC, Keen H, Kohner EM, Parsons JA, Alberti KGMM. Long-term continuous subcutaneous insulin infusion in diabetics at home. *Lancet* 1979;iii:870-3.
- ⁵ Pickup JC, Keen H. Continuous subcutaneous insulin infusion: a developing tool in diabetes research. *Diabetologia* 1980;18:1-4.
- ⁶ Pickup JC, Keen H, Viberti GC, et al. Continuous subcutaneous insulin infusion in the treatment of diabetes mellitus. *Diabetes Care* 1980;3:290-300.
- ⁷ Tamborlane WV, Sherwin RS, Genel M, Felig P. Reduction to normal of plasma glucose in juvenile diabetes by subcutaneous administration of insulin with a portable infusion pump. *N Engl J Med* 1979;300:573-8.
- ⁸ Tamborlane WV, Sherwin RS, Genel M, Felig P. Restoration of normal lipid and amino acid metabolism in diabetic patients with a portable insulin-infusion pump. *Lancet* 1979;i:1258-61.
- ⁹ Tamborlane WV, Sherwin RS, Genel M, Felig P. Outpatient treatment of juvenile-onset diabetes with a preprogrammed portable subcutaneous insulin infusion system. *Am J Med* 1980;68:190-6.
- ¹⁰ Champion MC, Shepherd GAA, Rodger NW, Dupré J. Continuous subcutaneous insulin infusion in the management of diabetes mellitus. *Diabetes* 1980;29:206-12.
- ¹¹ Raskin P, Pietri A, Unger R. Changes in glucagon levels after four to five weeks of glucoregulation by portable insulin infusion pump. *Diabetes* 1979;28:1033-5.
- ¹² Pickup JC, Keen H, White MC, Kohner EM, Parsons JA, Alberti KGMM. Perfusions sous-cutanées d'insuline chez les diabétiques: résultats cliniques. *Journ Annu Diabetol Hotel Dieu* 1980;17-22.
- ¹³ Pickup JC, Viberti GC, Bilous RW, et al. Metabolic and hormonal decompensation after deliberate withdrawal of prolonged subcutaneous insulin infusion. *Diabetologia* (in press).

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HLA-DR patterns in pernicious anaemia

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Abstract

The pattern of HLA-DR antigens was studied in a group of 66 patients with Addisonian pernicious anaemia, comprising a subgroup of 18 patients with associated endocrine disease and a subgroup of 48 patients with no associated endocrine disease. Compared with a control group of 120 subjects all 66 patients showed an increase in HLA-DR2 and DR4 and a decrease in DR3 ($p < 0.02$). Significant differences were also found between the endocrine and non-endocrine subgroups for patterns of HLA-DR antigens ($p < 0.005$) and for pairwise combinations of HLA-DR antigens ($p < 0.01$). Relative to controls, the endocrine subgroup showed an increase of HLA-DR3/DR4 (relative risk 4.0), contrasting with an increase of HLA-DR2/DR4 (relative risk 6.85) and DR4/DR5 (relative risk 5.38) in the non-endocrine subgroup.

These observations suggest that HLA-DR antigens or closely linked genes may interact to influence susceptibility to pernicious anaemia (or endocrine disease, or both). Thus interactive effects related to HLA-DR2/DR4 and DR4/DR5 may predispose to pernicious anaemia without endocrine disease, whereas interactive effects related to HLA-DR3/DR4 may predispose to pernicious anaemia in association with endocrine disease.

Introduction

We have documented significant heterogeneity in HLA-B patterns in clinical subgroups of patients with Addisonian pernicious anaemia. In patients without endocrine disease

pernicious anaemia was associated with HLA-B7 and B12, whereas in patients with coexistent endocrine disease pernicious anaemia was associated with HLA-B8, B15, and B18.¹

The purpose of the present study was to test for associations between pernicious anaemia and HLA-DR antigens and to determine what bearing these might have on the pathogenesis of pernicious anaemia and its relation to autoimmune endocrine disease.

Patients and methods

We studied 66 unrelated Caucasians with pernicious anaemia who attended this hospital for treatment or review during 1979-80. They comprised 25 men and 41 women aged 20 to 94 years (mean age 66.5 years) who satisfied the standard diagnostic criteria for Addisonian pernicious anaemia.² All had impaired vitamin B₁₂ absorption, shown by a Schilling test result of 0-5%. Serum antibodies to human parietal cells were present in 60 patients and to intrinsic factor in 31.

Of the 66 patients, 48 (17 men and 31 women) were clinically free of endocrine disease ("non-endocrine" subgroup), while 18 (eight men and 10 women) had known endocrine disease ("endocrine" subgroup). Three of these patients (including one diabetic) had thyrotoxicosis due to Graves's disease, five had primary myxoedema, one (a diabetic) had idiopathic Addison's disease of the adrenals, one had myasthenia gravis, and 10 had diabetes mellitus (seven were dependent on insulin).

TABLE 1—Prevalences of HLA-DR antigens in 66 patients with pernicious anaemia with and without associated endocrine disease and 120 healthy controls. Figures are numbers of subjects (percentages in parentheses)

HLA antigen	Patients with pernicious anaemia			Controls (n = 120)
	Total (n = 66)	With endocrine disease (endocrine group: n = 18)	Without endocrine disease (non-endocrine group: n = 48)	
DR1	13 (19.7)	3 (16.7)	10 (20.8)	24 (20.0)
DR2	29 (43.9)	2 (11.1)	27 (56.2)	31 (25.8)
DR3	14 (21.2)	8 (44.4)	6 (12.5)	39 (32.5)
DR4	29 (43.9)	10 (55.5)	19 (39.6)	34 (28.3)
DR5	14 (21.2)	4 (22.2)	10 (20.8)	25 (20.8)
DRW6	5 (7.6)	2 (11.1)	3 (6.2)	22 (18.3)
DR7	14 (21.2)	4 (22.2)	10 (20.8)	25 (20.8)

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