Medical and psychosocial impact of acute infections in young patients

Gunnel Wiklund and Bengt Persson

Introduction

Acute infections may adversely influence the duration of clinical remission in children and adolescents with newly diagnosed type 1 diabetes mellitus. In this Swedish study, the authors set out to determine whether educating patients and families to cope with an acute infection and to maintain near-normal blood glucose levels would result in the same duration of remission in young patients with and without acute infection. They followed 39 children and adolescents with newly diagnosed type 1 diabetes and 52 controls for 2 years to investigate the impact of acute infections on duration of remission and the medical and psychosocial impact on the family.

Children and adolescents with newly diagnosed type 1 diabetes mellitus usually exhibit a period of partial endogenous insulin secretion, lasting for weeks or months. This so-called remission period (also known as the 'honeymoon period' in the UK) can clinically be defined as near-normoglycaemia, no glucosuria or ketonuria, and an insulin requirement of ±0.5 iu/kg bodyweight/24 hours.

The duration of remission increases with age at onset of the disease (Wallensteen et al, 1988). Strict blood glucose control close to the physiological range shortly after diagnosis may also prolong the remission period (Shah et al, 1989). In contrast, chronic hyperglycaemia will probably shorten the period, with significant endogenous insulin secretion.

In-vitro studies of pancreatic islet tissue indicate that elevated glucose levels not only stimulate insulin release but also increase the expression of beta-cell auto-antigens (glutamic acid decarboxylase, GAD 65), making the beta cell more vulnerable to autoimmune destruction (Björk et al, 1992; Pipeleers and Ling, 1992). Stressful events, such as acute infection, may impair glucose metabolism in type 1 patients by increasing insulin resistance. Marked hyperglycaemia with or without ketonuria may occur unless extra insulin is given to compensate for the rise in insulin resistance.

There appears to be little information regarding possible adverse effects of acute infection on the duration of remission. Since this is likely to be the case, and, more importantly, since acute infection may cause severe metabolic derangement and even precipitate ketoacidosis, much time and effort are devoted to giving the patient and family adequate guidelines for clinical management during acute infections.

This method of providing information and helping the family is well defined in the Swedish national health programme for children and adolescents with type 1 diabetes (SPRI, Vårdprogram för diabetes, 1982). In Sweden, diabetes nurses traditionally have an independent role in the diabetes team. They are readily available for advice and, because of their close contact with the family, develop a therapeutic relationship that is invaluable for the success of the continuing education of the family and the clinical management. Any acute illness that affects children and adolescents, particularly those with diabetes mellitus, may be associated with a number of practical, psychological and social problems.

However, relatively little is known about the effectiveness of this education, particularly with regard to the ability of the patient and family to cope with an acute infection and its influence on the quality of life.

We have therefore studied some short- and long-term consequences of acute infection in a consecutive series of young patients newly diagnosed with type 1 diabetes and appropriate controls.

ARTICLE POINTS

1 Children with newly diagnosed type 1 diabetes mellitus with and without acute infection had the same duration of remission.

2 The families of the diabetic children monitored blood and urine levels and adjusted the insulin dose during acute infections.

3 Control children managed to be alone more frequently than did children with type 1 diabetes.

4 The parents of the diabetic children worried significantly more than the parents of control children and did not trust anyone else to take care of their child.

5 Diabetic children needed more care than control children.

KEY WORDS

- Type 1 diabetes mellitus
- Children
- Remission
- Acute infection
- Family stress

Gunnel Wiklund is Diabetes Specialist Nurse and Bengt Persson is Lecturer at the Karolinska Institute, Stockholm, Sweden.

PAGE POINTS

1 Thirty-nine children with type 1 diabetes and 52 controls were followed up for 2 years.

2 Insulin dose, C-peptide and HbA_{1c} were monitored at regular intervals.

3 Patients and controls were interviewed every 3 months.

4 Patients monitored their blood and urine glucose levels as well as urine ketone bodies during infectious episodes.

Aims of the study

The study had two aims:

1. To analyse the impact of acute infection on the duration of remission in children with newly diagnosed type 1 diabetes.
2. To evaluate the practical management of acute infection at home, and its psychosocial effects on the family.

Patients and methods

Subjects

Between November 1989 and February 1991, 42 newly diagnosed type 1 patients were admitted to St Görans Children's Hospital, Stockholm. Of these, 39 (20 boys and 19 girls; age range 2.5–15.5 years) were enrolled in the study. Two were excluded because of serious social problems and one because of inability to collect urine.

Fifty-two controls (27 boys and 25 girls) matched for age and gender were randomly chosen from the diabetic patients' school class or day care centre.

Procedure

At the time of diagnosis of diabetes, patients were admitted to the hospital for 3–4 weeks. While in hospital, all the patients and families were given intensive practical and theoretical training by the diabetes team, which included a paediatric diabetologist, a diabetes nurse and a nutritionist. Emphasis was placed on management during acute infections. Following discharge from the hospital, all patients and their parents could easily contact the diabetes team by telephone for advice in acute situations.

Body weight, height, glycated haemoglobin (HbA_{1c}) and urinary excretion of C-peptide were measured in type 1 patients at the time of diagnosis, after 1 month and every third month thereafter for 2 years. C-peptide levels were also determined during episodes of acute infections and for 1 week afterwards.

The cause and frequency of hospital admission during the study period were obtained from the medical records.

Records of acute infection

Every 3 months the parents of patients with diabetes visiting the diabetes clinic were asked about any infections the child had had. Control families were interviewed by telephone at the same intervals.

Infections were classified as: infection with fever <38.5°; infection with fever ≤38.5°; or acute gastroenteritis.

Questionnaire

One parent from each family was asked the following questions:

- How many days did the child stay at home?
- Did the child manage alone or not?
- Did you have any contact with medical care?
- What were the symptoms of infection?
- Did the child get any treatment?
- Were you worried?
- Did you have to cancel any plans?
- Did you have a babysitter?

In addition, the parents of the children with diabetes were asked if they had had any contact with the diabetes team.

The interview also included one open question: 'Did the infection have any other effect on the family?' The responses to this question were evaluated by a phenomenological method (Omery, 1983) and divided into six categories (*Table 1*). These were independently validated by two people, by testing and retesting the comments in the categories.

The diabetes patients and controls were divided into the following age-groups: 0–6 years, 7–12 years, and 13 years or older.

The degree of worry reported by the parents was graded as: not worried (worry score 1); a little worried (score 2); very worried (score 3).

Patients and controls were followed for 2 years.

Biochemical analyses

C-peptide was measured by radioimmunoassay (antiserum K6) in urine samples collected overnight. The intra- and inter-assay coefficients of variation for C-peptide determinations were 2.4% and 7.0%, respectively. HbA_{1c} was determined by high-performance liquid chromatography (Auto-A; reference values 4–6%).

All patients monitored their blood glucose levels using test strips and meters, and glucose levels and ketone bodies in urine using Keto-Diaburtest 5000.

Clinical remission was defined as HbA_{1c} ±6% and an insulin dose of ±0.5 iu/kg bodyweight/24 hours.

Table 1. Categories of response to the open question

1. Need a great deal of care
2. Feel confident about dealing with infection
3. Feel tied down
4. Emotionally difficult
5. Cause of conflict
6. No effect

Statistics

Statistical analyses were performed using the chi-squared test, except for the degree of worry, where the z-test was used.

All patients gave informed consent to participation in the study, which was approved by the Ethics Committee at the Karolinska Hospital.

Results

Demographic and clinical characteristics

The mean age at diagnosis of diabetes was 9.4 years, and the mean age of controls was 9.0 years. There was no significant difference in mean age between girls and boys in the diabetes group or in the control group.

Twelve patients had no infections during the first 12 months and 7 of these had no infections during the following 12 months.

The distributions of acute infections were similar in the two groups. The majority of subjects had mild respiratory infection without fever, of whom about one-third had fever >38.5°. Ten per cent of the infections in both groups were gastroenteritis.

Children with diabetes who experienced infections were significantly younger than those who did not (12 months $P<0.05$; 24 months $P<0.01$) (*Table 2*).

There were no significant differences in the average HbA_{1c}, C-peptide or insulin dose between patients with or without an infection after 12 or 24 months (*Table 3*).

Urine C-peptide values in type 1 children were comparable to those reported elsewhere (Knip et al, 1986). Urine C-peptide levels were approximately one-fifth to one-tenth lower than those in healthy subjects of comparable age and bodyweight (Wallensteen et al, 1988).

Figure 1 shows the frequency of clinical remission and average HbA_{1c} values in the diabetes group (n=39) over the study period.

Clinical remission

Children with diabetes were in remission for an average of 121 days (Range 0–630 days). Girls had a shorter (though not significantly) remission period than boys.

Twelve boys and 7 girls were in remission after 3 months, and 8 boys and 5 girls after 6 months (ns). The girls in remission after 6 months were younger than the boys (6.1 *vs* 11.69 years, $P<0.01$). Two boys and three girls were in remission for more than 12 months. The boys were older than the girls (14 *vs* 7.5 years, $P<0.001$).

Urinary excretion of C-peptide during infections increased or decreased without any consistent pattern. An individual increase in urinary C-peptide excretion during acute infections was not associated with a longer remission period.

Self-care

Most of the families monitored blood glucose and urine levels at home. They increased the dose of insulin during infection according to the test results (*Table 4*).

Two of the 39 patients did not increase the insulin dose because of low blood glucose values, and a further two because they did not understand that they should. The frequency of home monitoring of blood glucose level varied from 3 to 6 times/day.

The children stayed home from school or the day-care centre for an average of 3.5 days in the diabetes group and 3.6 days in the control group, weekends not included.

No difference was found between the

(Continued on page 48)

PAGE POINTS

1 No difference was seen in the length of remission between the diabetes group and controls.

2 Most of the families monitored blood glucose and urine levels at home.

3 The families of children with diabetes increased the insulin dose during infection according to the test results.

Table 2. Mean ages (in years) of the children with type 1 diabetes at 12 and 24 months following onset of diabetes mellitus

	At 12 months	At 24 months
With infection	9.4 (SD 3.8)	10.6 (SD 3.9)
Without infection	12.4 (SD 3.7)	14.8 (SD 2.9)

Table 3. Mean values and ranges of HbA_{1c}, C-peptide excretion and insulin dose in children with type 1 diabetes with or without acute infections at 12 (n=12) and 24 (n=7) months following onset of diabetes

		With infection	Without infection	P†
HbA_{1c} (%)	12 months	6.8 (4.8–8.9)	6.8 (4.7–10.2)*	ns
	24 months	7.4 (5.5–9.3)	7.0 (5.6–8.6)	ns
C-peptide (nmol/kg bw and hrs x 10^{-3})	12 months	2.41 (0–10.9)	2.22 (0–10.5)	ns
	24 months	0.94 (0–4.1)	3.4 (0–16.6)	ns
Insulin dose (iu/kg bw/24h)	12 months	0.64 (0.25–1.17)	0.65 (0.4–0.9)	ns
	24 months	0.73 (0.27–1.15)	0.71 (0.45–0.95)	ns

*n = 12; †level of significance $P<0.005$; ns = not significant

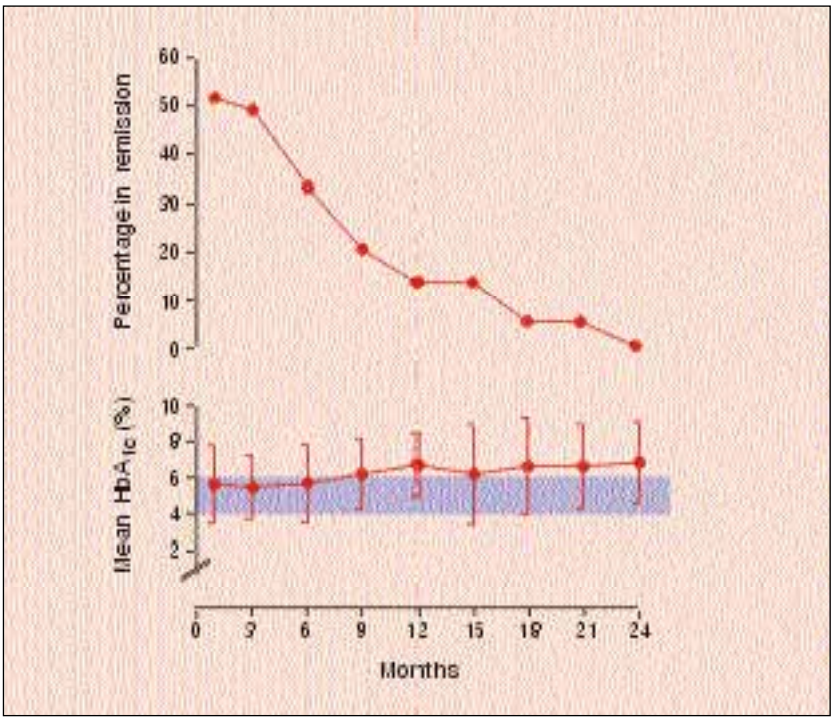


Figure 1. Mean values of HbA_{1c} in relation to the percentage of children in remission in 39 children with type 1 diabetes 0–24 months after the diagnosis of diabetes mellitus.

Table 4. Percentages of parents initiating measures during episodes of acute infections (n=72)

	Yes	No	No information
Monitoring of blood glucose levels	66%	6%	28%
Monitoring of urine for glucose and ketones	81%	3%	16%
Extra insulin	63%	12%	25%

(Continued from page 45)

two groups regarding which parent stayed at home with the child. In both groups the mother stayed at home during episodes of infection in the child in 80–90% of cases.

During acute infections, control children managed to be alone more frequently than did the diabetic children ($P<0.01$, *Figure 2*).

Children with diabetes and controls used primary care to the same extent. In addition, parents of the diabetic children were in frequent telephone contact with the diabetes team.

During the study, 7 of the children with diabetes were admitted to hospital for a total of 41 days, of which 25 days (mean 5.9 days) were due to diabetes.

The reasons for hospitalization were:

1. Collum fracture (girl aged 10 years; 10 days)
2. Hypothyroidism, non-infectious gastritis (girl aged 15 years; 6 days)
3. Asthma, virosis, gastroenteritis (girl aged 4 years; 10 days)
4. Placed on insulin pump (girl aged 17 years; 3 days)
5. Hypoglycaemia x 2 (girl aged 4 years; 5 days)
6. Poor metabolic control (boy aged 7 years; 4 days)
7. Poor metabolic control (girl aged 11 years; 3 days)

Effects on the family

The parents of children with diabetes worried significantly more ($P<0.001$) than did parents of control children (*Figure 3*).

The worry score was about the same in the diabetes group at 12 and 24 months. There was no difference in score between boys and girls or between children above and below 12 years of age. Parents reported significantly more worry when the children developed ketonuria during an infection ($P<0.05$). High blood or urine glucose values did not affect the worry score.

When evaluating the answers to the question 'Did the infection have any other effect on the family?' cases and controls were subdivided into three age groups: 0–6 years, 12 children with diabetes and 12 controls; 7–12 years, 15 children with diabetes and 21 controls; ≤13 years, 5 children with diabetes and 12 controls

The answers were subdivided as follows:

1. Need a great deal of care: In the diabetes group a high level of care included home monitoring of blood glucose level, changes in insulin dose and medical decisions. Two parents felt that they could not cope with the situation alone. In one case both parents had to stay home from work; in the other case the mother had to leave a younger brother, who was also sick, with the grandmother.

The parents of children with diabetes looked after the child more frequently during the night than did parents in the control group. In the latter group, parents were worried that the child might infect other persons in the family or the close environment. This problem was not mentioned by parents of children with diabetes.

2. Feel confident about dealing with infections: In the diabetes group, this

meant that the parents managed to give the appropriate doses of insulin. They felt able to handle the situation. In the control group the parents felt that the child could manage alone with the help of a babysitter.

3. Feel tied down: Parents in the diabetes group did not trust anyone else to take care of their child. Parents in the control group felt tied down because they had to cancel their plans.

4. Emotionally difficult: Infections in diabetic children younger than 13 years led to feelings of guilt, inability to control the situation, failure, and fear of a low blood glucose level in their families. Worry in the control group was related to the infection itself, whereas in the diabetes group the parents were entirely preoccupied by the metabolic balance.

5. Cause of conflict: The few comments given by the control group concerned conflict about staying home from work. In the diabetes group, there was sometimes conflict between the parents about the insulin doses and with the child about carrying out blood glucose tests.

6. No effect at all: The parents said that the infection did not affect the family.

Of the comments received in the diabetes group, 60–70% concerned the extent of care needed or emotional difficulties, compared with 20–30% in the control group. In the control group, 40–60% said that the infection had had no effect on the family, compared with 10% in the diabetes group.

There were no differences between the groups concerning feelings of confidence, being tied down, or conflict. In the age group ≤13 years, there were very few comments. This group is not included in *Table 5*.

Discussion

The mean age at onset of diabetes was slightly lower than that reported by the Swedish national register. As expected, the group with acute infections was significantly younger than the group without infection. It is well recognised that young age *per se* is accompanied by a shorter remission period (Wallensteen et al, 1988).

Around 50% of children with diabetes in the present study experienced a clinical remission (arbitrarily defined as normal HbA_{1c} (±6.0%) and an insulin dose of ±0.5 iu/kg bodyweight). Knip et al (1986) reported a somewhat longer average remission period of 203 days in their children with type 1 diabetes. These authors defined clinical remission as absent or minimal glycosuria and a daily insulin dose of 0.5 iu/kg bodyweight. These differences in results are probably due to differences in the criteria used to define a clinical remission.

The results of the present study indicate that acute infections have no effect on the duration of clinical remission in children and adolescents with type 1 diabetes. The findings also demonstrate that, even if the patients did not achieve a normal or near-normal blood glucose level during the infection, the long-term glycaemic control was still excellent 2 years after the onset of diabetes. In the infection group, the average HbA_{1c} value was 7.4%, i.e. about the same as in the group without infections (7.0%).

Björk et al (1992) reported a strong dose-related stimulating effect of glucose on insulin release by islets from human pancreatic tissue in vitro. It is well known that infections with fever may lead to insulin resistance and an increased demand for insulin. Hence blood glucose levels should rise during an acute infection, leading to increased insulin secretion and thus increased C-peptide values.

The majority of patients had hyperglycaemia during periods of infections which were frequently (60%) compensated for by extra insulin injections. Infections were not consistently associated with increased urinary C-peptide excretion. It may be that determining urinary C-peptide excretion overnight does not measure variations in endogenous insulin secretion adequately, or that hyperglycaemia did not

PAGE POINTS

1 The parents of children with diabetes worried more than the parents of control children.

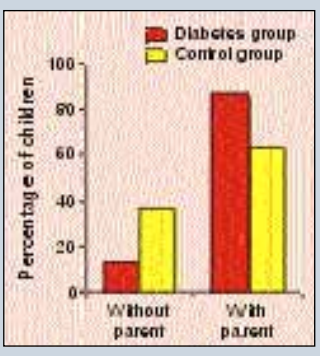
2 The parents of children with diabetes did not trust anyone else to take care of their child.

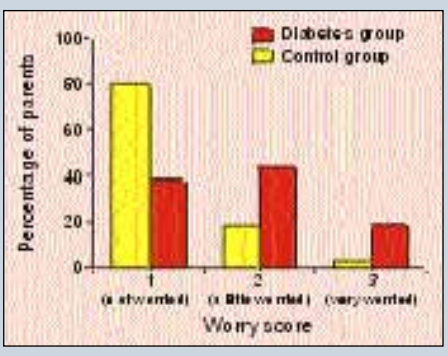
3 The parents of children with diabetes had to make difficult medical decisions.

4 The families of children with diabetes need a lot of support from the diabetes team.

Figure 2. (left below) Percentage of children staying home with or without parent during an acute infection.

Figure 3. (right below) Degree of worry (graded on a scale of 1–3) reported by the parents of children in the diabetes and control groups.





Publisher's note: The images are not available full resolution in the online version.

Table 5. Consequences of acute infection reported by parents of children with type 1 diabetes and parents of controls (frequency of answers to open question in the questionnaire)

	Diabetic group (%)	Control group (%)
Age group 0–6 years		
1. Need a great deal of care	37	15
2. Feel confident about dealing with infections	7	2
3. Feel tied down	5	7
4. Emotionally difficult	35	12
5. Cause of conflict	7	12
6. No effect	10	60
Age group 7–12 years		
1. Need a great deal of care	30	10
2. Feel confident about dealing with infections	8	17
3. Feel tied down	12	15
4. Emotionally difficult	30	10
5. Cause of conflict	8	9
6. No effect	10	40

persist for long enough.

As stated earlier, increased functional activity of beta cells may stimulate the expression of beta-cell autoantigens (Björk et al, 1992). Administration of extra insulin during an infection, leading to normoglycaemia, might diminish the autoimmune attack. One could speculate that the good metabolic control maintained by our patients probably explains why the remission periods were of equal duration in children with and without acute infection.

Our programme of education for children with type 1 diabetes has not previously been evaluated. This study shows that most of the families were able to cope with an acute infection. During more than 60% of the infections the parents performed frequent blood glucose tests, and in 80% of them they tested the urine for glucose and ketones. Most parents (63%) also increased the dose of insulin during the infections. Only a few children developed ketonuria during infections, indicating that the treatment given at home was appropriate.

It was also reassuring that only two patients needed hospital admission during the study for an acute infection (gastroenteritis and viral infection) and hypoglycaemia. Both patients were below 3 years of age. The number of days in hospital with diabetes as a co-factor was very low: only 0.6 days/patient over the 2-year period.

The finding that most infections could be managed at home, with support from the diabetes team, accords with the findings of Hoffman et al (1978) and Hardie et al (1979). Thus a children's diabetes clinic that offers clinical support and an education programme reduces the number of hospital admissions for acute complications.

Instructing families and patients about acute complications of diabetes may increase their worry. For instance, the administration of extra doses of insulin is frequently associated with fear of hypoglycaemia. However, this worry may be of value by initiating practical activities such as monitoring of blood and urine glucose levels. A high 'worry score' among parents when detecting ketonuria during an episode of infection probably stimulates them to act, indicating that they understand the severity of this condition.

This study also clearly demonstrates that during an acute infection in children with type 1 diabetes, the families spend additional time on various measures and are frequently preoccupied with medical decisions.

The responses to the open question in the interview increase our knowledge of the psychological effects on the families. The qualitative method is a valuable complement to quantitative methods. ■

Björk E, Kämpe O, Karlsson A et al (1992) Glucose regulation of the auto-antigen GAD65 in human pancreatic islets. *Journal of Clinical Endocrinology and Metabolism* **75**(6): 1574–6

Bojestig M, Arnqvist H, Hermansson G et al (1994) Declining incidence of nephropathy in insulin-dependent diabetes mellitus. *New England Journal of Medicine* **330**:15–18

Funell M (1994) Role of nurses in the implementation of intensified management. *Diabetes Reviews* **2**(3): 322–8

Hardie J, McPherson K, Baum JD (1979) Hospital admission rates of diabetic children. *Diabetologia* **16**: 225–8

Hoffman W, O'Neill P, Khoury C et al (1978) Service and Education for the insulin-dependent child. *Diabetes Care* **1**(5): 285–8

Knip M, Ilonen J, Mustonen A et al (1986) Evidence of an accelerated B-cell destruction in HLA-Dw3/ Dw4 heterozygous children with type 1 (insulin-dependent) diabetes. *Diabetologia* **29**: 347–51

Omery A (1983) Phenomenology: a method for nursing research. *Advanced Nursing Science* **January**: 49–63

Pipeleers D, Ling Z (1992) Pancreatic beta cells in insulin-dependent diabetes. *Diabetes/Metabolism Reviews* **8**(3): 209–27

Rudberg S, Ullman E, Dahlquist G (1993) Relationship between early metabolic control and the development of microalbuminuria – a longitudinal study in children with type 1 (insulin-dependent) diabetes mellitus. *Diabetologia* **36**:1309–14

Rudberg S, Dahlquist G (1996) Determinants of progression of microalbuminuria in adolescents with IDDM. *Diabetes Care* **19**(4): 369–71

Shah S, Malone J, Simpson N (1989) A randomized trial of intensive insulin therapy in newly diagnosed insulin-dependent diabetes mellitus. *New England Journal of Medicine* **330**: 550–4

SPRI Report 104 (1982) *Vårdprogram för Diabetes.* Swedish National Program

Wallensteen M, Dahlqvist G, Persson et al (1988) Factors influencing the magnitude, duration, and rate of fall of B-cell function in type 1 (insulin-dependent) diabetic children followed for two years from their clinical diagnosis. *Diabetologia* **31**: 664–9