Prevention of severe hypoglycaemia in type I diabetes: a randomised controlled population study

S Nordfeldt, C Johansson, E Carlsson, J-Å Hammersjö

Aims: To investigate use of targeted self study material in type I diabetes patient education regarding dissemination, perceived patient benefit, and prevention of severe hypoglycaemia.

Methods: In a randomised 1:1:1 controlled study, 332 patients with type I diabetes (aged 2.6–18.9 years) were studied; 313 completed clinical follow up, 261 completed endpoint questionnaire. The intervention group received videotapes and a brochure designed to review skills for self control and treatment, aimed at preventing severe hypoglycaemia. Two control groups received a videotape and brochure with general diabetes information, or traditional treatment only, respectively.

Results: Yearly incidence of severe hypoglycaemia decreased from 42% to 27% in the intervention group, but not in controls. HbA1c remained unchanged. Levels of use ranged from 1 to 20 times (median 2); 40–49% had shown the materials to friends, relatives, school staff, sports coaches, etc (there was little difference between intervention and control groups). Higher benefit and learning levels resulted from the intervention material, especially in patients with severe hypoglycaemia.

Conclusions: Mass distributed pedagogical devices such as high quality video programmes and brochures may contribute to the prevention of severe hypoglycaemia. Such self study materials can reach high dissemination levels and constitute a cost effective complement to regular visits to a diabetes team and to other types of education. The findings may have implications for other topics, other ages, and other diagnosis groups.
level has been found. As a complement to traditional education methods, development of pedagogical devices and other patient education and information materials is needed. Patients may need information to help them cope, to help others understand their situation, and especially to assist them in self care, so that they can learn how to prevent further illness and complications.

Within a university hospital setting, we previously developed and evaluated for the first time a video and leaflet education material targeted at the prevention of severe hypoglycaemia. A before and after study design was used; a description of the format and contents of the material has been presented elsewhere. Our earlier findings supported the hypothesis that improved patient education aimed at the prevention of severe hypoglycaemia may reduce severe hypoglycaemia through various effects on basic knowledge and self-treatment behaviours, but controlled studies have been lacking. We therefore conducted a controlled study in a different patient population.

In the present study we tested the hypothesis that good-quality self-study material for home use would: (1) be used and disseminated; (2) be perceived as helpful in self-treatment; and (3) reduce severe hypoglycaemia without worsening metabolic control as measured by mean HbA1c.

### METHODS

The study base consisted of the 332 type I diabetes children younger than 19 years of age who lived in the catchment areas of the general hospitals in Jönköping, Kalmar, and Västervik. In accordance with the Swedish health care system, all type I diabetes patients aged 1–18 years in these areas were treated at these paediatric clinics. Table 1 presents their clinical characteristics.

The patients and clinics in this study are not those that participated in our previous uncontrolled study, nor was there any overlap. The intervention material used in the present study consisted of slightly revised versions of the videos evaluated in our earlier study and a novel self-study brochure developed and expanded from the leaflets described earlier.

### Treatment

The patients were treated with multiple insulin therapy (97% ≥ 4, 82% ≥ 5 daily doses) combined with active self control, psychosocial support, and education. The selection of insulin and regimens varied, with the aim of meeting the specific needs of the patient. All families received initial training in general management, including recognition and treatment of hypoglycaemia. Quarterly visits were aimed for, but because of limited resources the average number of outpatient visits yearly was 2.2, 2.7, and 2.9, respectively, in the three clinics.

### Table 1: Clinical characteristics at baseline for all patients and the three treatment groups, respectively

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Intervention</th>
<th>Controls</th>
<th>Traditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>12.6 (4.1)</td>
<td>12.7 (4.1)</td>
<td>12.5 (4.2)</td>
<td>12.7 (3.9)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>12.7 (2.6–18.9)</td>
<td>13.5 (3.7–18.7)</td>
<td>12.7 (2.6–18.6)</td>
<td>12.6 (4.2–18.9)</td>
</tr>
<tr>
<td>Duration of type 1 diabetes years, mean (SD)</td>
<td>5.3 (3.8)</td>
<td>4.9 (3.5)</td>
<td>5.6 (4.2)</td>
<td>5.2 (3.6)</td>
</tr>
<tr>
<td>Age at onset (years), mean (SD)</td>
<td>7.3 (3.9)</td>
<td>7.4 (3.9)</td>
<td>7.0 (4.1)</td>
<td>7.7 (3.7)</td>
</tr>
<tr>
<td>Boys/girls proportion</td>
<td>0.83</td>
<td>0.84</td>
<td>0.81</td>
<td>0.84</td>
</tr>
<tr>
<td>No. of daily doses, mean (SD)</td>
<td>5.3 (0.9)</td>
<td>5.3 (0.8)</td>
<td>5.3 (1.0)</td>
<td>5.3 (0.9)</td>
</tr>
<tr>
<td>Insulin dose (U/kg), mean (SD)</td>
<td>1.0 (0.3)</td>
<td>1.0 (0.3)</td>
<td>1.0 (0.3)</td>
<td>1.0 (0.3)</td>
</tr>
<tr>
<td>HbA1c% (%), mean (SD)</td>
<td>7.9 (1.5)</td>
<td>7.8 (1.4)</td>
<td>7.8 (1.3)</td>
<td>8.0 (1.8)</td>
</tr>
<tr>
<td>Daily BGs, mean (SD)†</td>
<td>2.5 (1.6)</td>
<td>2.7 (1.7)</td>
<td>2.4 (1.5)</td>
<td>2.6 (1.5)</td>
</tr>
<tr>
<td>Direct acting insulin analogue (Lispro or Aspart) (n)</td>
<td>230</td>
<td>73</td>
<td>80</td>
<td>77</td>
</tr>
<tr>
<td>Pump (n)</td>
<td>21</td>
<td>7</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

†BG, blood glucose tests (self-reported average frequency).

*National standard Mono-S, on average 1.15% below DCCT level.34

### Protocol

All the clinically diagnosed type I diabetes children with a duration of diabetes >0.5 years at the start of the study in January 2000 were eligible and participated (see fig 1). They and their families were randomised to one of three groups and received:

- Two mailed videotapes and a brochure designed to review skills for self control and treatment, aimed at preventing severe hypoglycaemia (intervention group).
- A mailed videotape and brochure with general diabetes information (controls group).
- Traditional treatment only (traditional group).

### Assignment

Subjects were allocated to the three groups by a third part researcher (SN) using random numbers. Randomisation in a 1:1:1 sequence was stratified for clinic, sex, and age. The groups were equal regarding baseline clinical characteristics (table 1).

### Masking

All study participants and personnel were blinded to group assignment for the whole study period as far as possible. The groups received identical presentations of the study and of their information materials, mailed by a third part researcher (SN). Care providers received no information on the specific contents. They were instructed to discuss any clinical issue raised by the patient as usual, without trying to identify the group to which the patient belonged.

### Intervention material

Two video programmes (17 minutes + 18 minutes) were mailed in January 2000 to intervention patients. These videos consisted of interview clips of three patients aged 9–14 years and their parents regarding diabetes treatment and the prevention of hypoglycaemia, with sequences from their daily lives, and brief comments from a diabetologist. The information focused on practical aspects, with a basic optimistic attitude of support towards increasing one’s skills in self-care.

A novel self-study brochure (32 pages, 5200 words), the contents of which were related to that of the video, was mailed one month later. This brochure contained a number of frequently asked questions with answers in discussion form and related suggestions, as in the example given in table 2. The main contents covered definition and occurrence of severe hypoglycaemia, counter-regulation and warning symptoms, various aspects of prevention in practice, early symptom recognition, and early effective treatment. Separate sections dealt with use and interpretation of 24 hour profiles, urine test strips, random blood glucose, focused blood glucose, and...
HbA1c, aiming at a 24 hour blood glucose as stable and near normal as possible. Implications for particular at risk situations, such as those involving alcohol and those involving traffic were highlighted. A table of key suggestions in the material has been presented earlier.

Other sources of information were also suggested. As described previously, the material was developed in association with patients and parents, and was based on specific questions raised by them, the best evidence from the literature, relevant guidelines from the International Society for Pediatric and Adolescent Diabetes (ISPAD), and 20 years of clinical experience with intensive treatment by the diabetes team that produced the material. Other sources of information were also suggested. A group of other medical, psychological, and pedagogical advisors contributed. A psychologist with extensive experience with diabetes families checked the language and content in order to prevent imposing guilt feelings.

**Control material**

In January 2000 a videotape (13 minutes) containing general information on type I diabetes for children and families was mailed to controls. It consisted of interview clips regarding clinical experience with intensive treatment by the diabetes team that produced the material. A group of other medical, psychological, and pedagogical advisors contributed. A psychologist with extensive experience with diabetes families checked the language and content in order to prevent imposing guilt feelings.

**Table 2** Example of question and answer from the intervention brochure

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Suggestion</th>
</tr>
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<tbody>
<tr>
<td>Can you get serious insulin reactions from exercise?</td>
<td>Occasional hard exercise or a great deal of exercise without eating extra energy/food and without decreasing your dose of insulin a little can give you a lower blood sugar during the time you are exercising, and many hours after that. You can get a severe insulin reaction a long time after hard exercise, and even during the night or the morning after!</td>
<td>Extra energy is usually needed both before/during exercise as well as afterwards. The nighttime insulin dose often needs to be temporarily decreased a little after activities like long walks, a disco, sports day, or a football match. With greatly increased exercise you always have to pay extra attention to your blood sugar and insulin doses. This also applies to winter sports holidays/skiing holidays, when sports training gets underway, and especially when spring comes and you are out and more active in the evenings. Then it’s especially important to do 24-hour profiles and adjust your insulin. One or more doses might need to be decreased during the spring and early summer. A new adjustment period comes at the end of the summer and this requires extra attention. Sometimes certain doses need to be increased.</td>
</tr>
</tbody>
</table>
diabetes with a patient at the age of 10 and then 19 years and his parents, sequences from their daily lives, and brief comments from a diabetologist. A self study brochure containing related material (16 pages, 800 words) was mailed one month later. This material projected a basically optimistic attitude towards living a good life with diabetes without discussing in detail any concrete issues of self care.

**Access to video players**

Patients receiving videos were informed that a video player was available at the outpatient departments if needed. Based on earlier Swedish population data, it was expected that approximately 95% of the families would have a video player at home.

**Primary outcomes**

The yearly incidence of severe hypoglycaemia was obtained from postal surveys at the start of the study in January 2000 regarding 1999 (baseline), and one year later regarding 2000. These surveys were conducted by the independent Center for Medical Technology Assessment at Linköping University. Patients were informed that individual patient data would not be reported to the diabetes team. The specific question was: “Did you experience episodes of severe hypoglycaemia (needing assistance) during the last 12 months? Yes/No.” This was registered without other inclusion or exclusion criteria. Local routine methods for HbA1c determination, calibrated to the national standard method Mono-S, were utilised.**10** Since 1997 a national recalibration to the Mono-S standard has resulted in a yearly mean that is on average 1.15% below the level in the Diabetes Control and Complications Trial (DCCT).**11**

**Secondary outcomes**

Patient attitudes and level of use regarding the intervention and control materials, respectively, were evaluated after one year with the postal questionnaire method mentioned above. Open questions combined with visual analogue scales were mailed to patients under 20 years of age who at this time had had experience with diabetes for at least 18 months.

**Analysis**

We used intention to treat analysis for primary outcomes. For statistical analysis, StatView 5.0.1 software (SAS Institute Inc.) was used. As planned, the \( \chi^2 \) test was used for incidence in proportion of patients, and the non-parametric Mann-Whitney U test for HbA1c and for visual analogue scale readings; \( p \) values \( < 0.05 \) were regarded as significant. Mean values (1 SD) are given.

### Table 3 Incidence of hypoglycaemia

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Intervention group (n=111)</th>
<th>Control group (n=111)</th>
<th>Difference unadjusted for baseline % (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1999</td>
<td>2000</td>
<td>1999</td>
<td>2000</td>
</tr>
<tr>
<td>Responders</td>
<td>92</td>
<td>82</td>
<td>92</td>
<td>89</td>
</tr>
<tr>
<td>Severe hypoglycaemia, n (%)</td>
<td>38 (42)</td>
<td>35 (27)</td>
<td>31 (34)</td>
<td>33 (37)</td>
</tr>
<tr>
<td>Difference before-after, % [95% CI]</td>
<td>-15 (-1 to 29)</td>
<td>0.0394</td>
<td>+3 (-11 to 17)</td>
<td></td>
</tr>
</tbody>
</table>

VAS, visual analogue scale. Exact questions used:

*Getting this video/brochure was of: no use at all = 0 mm, greatest possible help = 100 mm.*

†Did you learn anything that is useful for the treatment: nothing at all = 0 mm, a lot = 100 mm.

### Ethics

The study was approved by the Ethics Committee for Human Research at the Faculty of Health Sciences at Linköping University, Linköping, Sweden.

**RESULTS**

A total of 261 of 332 subjects responded to the questionnaire in 2001 (278 at baseline in 2000); 37% (32%) were teenagers responding themselves and 37% (42%) answered with some help from their parents. Of the respondents, 97% had a video player at home.

**Severe hypoglycaemia and HbA1c**

After the intervention, the incidence of severe hypoglycaemia during 2000 was reduced in the intervention group from 42% to 27% compared with 1999 (risk difference 15%, 95% CI 1% to 29%, \( p = 0.0394 \)), but was not reduced in the control and traditional groups. Controls did not differ from traditional. Table 3 gives absolute figures.

Including only those patients responding both at baseline and after one year, the incidence of severe hypoglycaemia during 2000 was reduced in the intervention group from 45% to 28% compared with 1999 (risk difference 17%, 95% CI 1% to 32%, \( p = 0.0369 \)).

There were no differences in yearly mean HbA1c levels compared with control and traditional groups or compared with baseline.

**Reading and viewing levels**

Twelve months after distribution the intervention brochure had been read in the family a median of two times (range 1–20) and the control video viewed a median of one time (range 1–20). The control brochure had been read a median of two times (range 1–20) and the control video viewed a median of one time (range 1–20).

Furthermore, 40% of the intervention subjects (43% of controls) had also shown the brochure to others, mainly relatives, friends, school staff, and sports coaches, and 47% of intervention subjects (49% of controls) had shown the video to similar persons.

Fifty nine per cent of the intervention subjects (51% of controls) anticipated future use of the brochure, and 60% of the intervention subjects (47% of controls) anticipated future use of the video.

**Perceived benefit**

Within wide ranges, the intervention material was perceived after one year as being of at least some benefit to most patients, as shown in table 3, with higher benefit compared to
controls from the brochure \( p = 0.0283 \). A greater proportion of intervention subjects than controls indicated that they had learnt something useful from the hypoglycaemia prevention video \( p = 0.0075 \) and the brochure \( p = 0.0049 \).

Intervention subjects with severe hypoglycaemia during 2000 indicated greater benefit from receiving the brochure \( p = 0.0126 \) and the video \( p = 0.0100 \) than those without severe hypoglycaemia. Moreover, a greater proportion of those with severe hypoglycaemia indicated that they had learnt something useful from the brochure \( p = 0.0301 \) and the video \( p = 0.0178 \), respectively. No such differences were found in controls.

**DISCUSSION**

Ever since it was first used, individuals treated with insulin have needed detailed practical information/education on the prevention of severe hypoglycaemia. This randomised controlled study shows that the incidence of severe hypoglycaemia (reported as needing assistance by another person) may be reduced with good quality patient education materials.

It also shows that such pedagogical devices may reach high reading, viewing, and dissemination levels at a low cost. This was so even when they were distributed without selection to a geographical population including older adolescents with a long duration of diabetes and those who never experienced severe hypoglycaemia. The levels of use and perceived benefit of the materials illustrate a general need for good patient/consumer education materials about diseases, treatment options, self-care, and prevention of further illness and complications. Such communication should deal with important issues and risks, with the aim of reducing uncertainty. To produce good patient information/education materials, collaborative efforts by people with a range of expertise in the fields of medicine, psychology, pedagogy, and the media, and also including patients/consumers in the process, are important. Careful attention to patient needs and concerns is essential. Patients prefer facilitative, honestly optimistic, structured, and concise information.

**The intervention method**

We have discussed the strengths and limitations of this kind of intervention elsewhere. Distributing a pedagogical device is simple and inexpensive, and dissemination to persons other than close family, which is also important for the child, may occur in many cases. It is easy to show a videotape and then discuss it together. A combination of pedagogical methods may enhance learning. The combination of a pedagogical device for home use and regular follow up visits offers possibilities for fruitful discussions. Another option is to view and discuss this material with groups of patients and parents and then to give participants their own copies for home use and further dissemination. Opinions differ on diabetes treatment, and group discussions may stimulate learning.

**Strengths and limitations of the study**

With a complete geographical population of this size and a randomised controlled design, an adequate base for studying real world effectiveness is created. Our consistent blinded endpoint registration method in a closed cohort is another strong point. However, at least quarterly prospective registration of severe hypoglycaemia would also be valuable in future studies.

Clinically useful prevention strategies need to minimise severe hypoglycaemia without compromising metabolic control.\(^{13,14,15}\) As was done in this study. Using prospective registration and a longer follow up period, it would be worth examining whether this method might contribute to improved self control, reduction of acute complications, and/or a larger knowledge base.

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**What this paper adds**

**What is already known on this subject?**

- Severe hypoglycaemia remains a serious problem in modern insulin treatment.
- The risk can probably be reduced with improved education and information, but population studies are lacking.
- Patient information materials in general are often incomplete regarding risks and complications.

**What does this study add?**

- This randomised controlled study shows that the major side effect of insulin treatment, severe hypoglycaemia, can be reduced with good quality education materials containing targeted information on the prevention of such acute complications.
- Targeted diabetes education that deals with such risks and complications can be perceived as more useful than general diabetes information.
- Mass distributed good quality education materials may reach high reading, viewing, and dissemination levels at a low cost.

**Costs**

As described earlier, the cost for the intervention was estimated at €1000 per 100 patients. The yearly socioeconomic cost for severe hypoglycaemia per 100 diabetes patients at a Swedish clinic has been conservatively estimated at €17 440, but costs for possible traffic accidents and other material damage, disablement or premature deaths, effects from worsened control because of uncertainty after events, and consumption of people’s leisure time and other intangibles were not included in that figure.\(^{30}\)

As this method substantially reduced severe hypoglycaemia, the cost for severe hypoglycaemia was correspondingly reduced, resulting in cost savings; the method is therefore cost effective for society. It is also likely to contribute to improved quality of life.\(^{31}\)

**Future approaches to prevention of severe hypoglycaemia**

From a clinical point of view, there is a need for novel approaches to prediction and prevention of severe hypoglycaemia.\(^{32}\) The multifactorial aetiology of severe hypoglycaemia offers several possibilities for prevention in the future. More physiological insulin preparations and regimens, new glucose sensors and alarms, and other improved technologies may contribute to prevention of hypoglycaemia.\(^{33,34}\) Genetic predictors combined with earlier known determinants might prove useful to identify certain patients with a need for more intensive assessment and support (in press). However, intensified education and training in the prevention of severe hypoglycaemia without worsened metabolic control is probably an essential intervention at the present time.\(^{35}\)

**Conclusions**

We found that a pedagogical device for home use that supports diabetes self care and is especially targeted at the prevention of severe hypoglycaemia may contribute to a decrease in severe hypoglycaemia without worsened metabolic control. When mass distributed, such self study materials can be widely disseminated at a low cost. This method may be used as a complement to regular visits to the diabetes team and other types of education.

The level of use and patient preferences suggest that there is a great need for good quality patient/consumer education materials dealing with aspects of general management and risk prevention in diabetes treatment. The findings may also have implications for other topics within diabetes education, other ages, and for other diagnosis groups.
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Authors’ affiliations
S Nordfeldt, Division of Child and Adolescent Psychiatry, Division of Pediatrics and Center for Medical Technology Assessment, Linköping University, Linköping, Sweden
E Carlsson, Department of Paediatrics, Hospital of Kalmar, Sweden
J-Å Hammersjö, Department of Paediatrics, Hospital of Västervik, Sweden

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