



## Original Research

## Prospective Assessment of Hypoglycemia Symptoms in Children and Adults with Type 1 Diabetes

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## ABSTRACT

**Purpose:** To compare the characteristics of symptoms of hypoglycemia in children and in adults with type 1 diabetes.**Methods:** Adults with diabetes and parents of children with diabetes who were participants were asked to call a phone system to report episodes of hypoglycemia (presence of symptoms and a blood glucose <4.0 mmol/L). For each episode, blood glucose reading and a scoring of 28 symptoms on a 7-point scale (1 = not present, 7 = very intense) were collected.**Results:** Sixty six children (49.2% males, mean age = 12.1±2.4 years, mean age at diagnosis = 7.5±2.9 years) and 53 adults (41.2% males, mean age 38.7±14.5 years, mean age at diagnosis = 17.5±12.9 years) with type 1 diabetes participated. The most common symptoms in adults were hunger, sweating, trembling and weakness. The most common symptoms in children were weakness, trembling and hunger. The 2 most discriminating variables between children and adults were sleepiness and tiredness, which were more common in children (p<0.01). In a comparative factor analysis, 3 factors emerged: factor 1, autonomic and neuroglycopenic; factor 2, behavioural; and factor 3, general malaise. Factors 2 and 3 were significantly more common or intense in children than in adults; MANOVA: F(1, 113) = 6.72, p<0.05 and F(1, 113) = 4.64, p<0.05, respectively.**Conclusions:** Symptoms relating to behaviour and general malaise are more common in children than in adults with type 1 diabetes. The results of this study may assist providers in educating caregivers of children and patients with diabetes how to better recognize episodes of hypoglycemia.

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## R É S U M É

## Mots clés :

adultes  
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symptômes de l'hypoglycémie  
diabète de type 1**Objet :** Comparer les caractéristiques des symptômes de l'hypoglycémie chez les enfants et les adultes atteints du diabète de type 1.**Méthodes :** Les participants, des adultes atteints de diabète et les parents d'enfants diabétiques, étaient invités à appeler un système téléphonique pour rapporter les épisodes d'hypoglycémie (présence de symptômes et glycémie < 4,0 mmol/l). À chacun des épisodes, la lecture de la glycémie et l'évaluation de 28 symptômes sur une échelle en 7 points (1 = non présent, 7 = très intense) étaient recueillies.**Résultats :** Soixante-six (66) enfants (49,2 % de garçons, âge moyen de 12,1 ± 2,4 ans, âge moyen au diagnostic de 7,5 ± 2,9 ans) et 53 adultes (41,2 % d'hommes, âge moyen de 38,7 ± 14,5 ans, âge moyen au diagnostic de 17,5 ± 12,9 ans) atteints du diabète de type 1 ont participé. Les symptômes les plus fréquents chez les adultes étaient la faim, la sudation, le tremblement et la faiblesse. Les symptômes les plus fréquents chez les enfants étaient la faiblesse, le tremblement et la faim. Les 2 variables les plus discriminantes entre les enfants et les adultes étaient la somnolence et la fatigue, qui étaient plus fréquentes chez les enfants (p < 0,01). Dans une analyse factorielle comparative, 3 facteurs sont ressortis : facteur 1, autonome et neuroglycopenique; facteur 2, comportemental; facteur 3, malaise général. Les facteurs 2 et 3 étaient significativement plus fréquents ou intenses chez les enfants que chez les adultes; MANOVA : F(1, 113) = 6,72, p < 0,05 et F(1, 113) = 4,64, p0,05, respectivement.

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*Conclusions* : Les symptômes relatifs au comportement et au malaise général sont plus fréquents chez les enfants que chez les adultes atteints du diabète de type 1. Les résultats de cette étude peuvent aider à sensibiliser les aidants et les soignants des enfants et des patients souffrant de diabète à mieux reconnaître les épisodes d'hypoglycémie.

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## Introduction

Hypoglycemia is the most common complication in the treatment of type 1 diabetes mellitus (1,2). The Diabetes Complication and Control Trial (DCCT) has demonstrated the importance of tighter metabolic control in preventing long-term complications of type 1 diabetes (3). However, intensified diabetes management is also associated with increased frequency of hypoglycemic events, which, particularly if severe, becomes a barrier to tighter metabolic control (1,4).

Hypoglycemia is classically defined and diagnosed by a combination of symptoms and biochemical criteria known as the Whipple triad; symptoms typical of hypoglycemia are confirmed by low plasma glucose levels and are relieved by carbohydrate intake. The difficulty is in the definition of symptoms as typical. The spectrum of symptoms of hypoglycemia is broad and may vary with time or may fluctuate, often as an alteration in neurohormonal responses after preceding episodes of hypoglycemia (4).

Symptoms of hypoglycemia, when classically defined and confirmed through principal component analysis, have been divided into 3 categories: autonomic, neuroglycopenic and general malaise. Autonomic symptoms include sweating, palpitations, shaking and hunger. Neuroglycopenic symptoms include confusion, drowsiness, speech difficulty and odd behaviour. Finally, general malaise includes nausea and headaches (4–7). Deary and his group studied hypoglycemic symptoms in adults with type 1 diabetes using factor analysis and have shown very good segregation of symptoms into the autonomic or neuroglycopenic categories. These autonomic and neuroglycopenic symptom groups were associated with different glycemic thresholds, depending on the severity of the episode (7).

The results of the DCCT showed a 3-fold increased relative risk for severe hypoglycemia (3) with intensive diabetes management. The DCCT included a subgroup of 195 adolescents (13 to 18 years of age), which allowed comparison of this age group with the adult participants. In both the conventional and the intensified diabetes management groups, the adolescents had significantly higher rates of hypoglycemia compared to the adults (8,9). Although some studies (10–12) suggest differing presentation of symptoms of hypoglycemia in children and in adults, to our knowledge, there is no published study specifically designed to compare symptomatology in adults and children. This may be an important distinction because children are at increased risk for hypoglycemia (13,14) and because the ability of children and their parents to detect symptoms of hypoglycemia has been reported as being poor (15). An understanding of these differences in symptomatology is needed to better educate caregivers and patients with type 1 diabetes and to improve their abilities to recognize and treat hypoglycemia. Therefore, we conducted this study to report and compare the symptoms of hypoglycemia in children and adults.

## Methods

This study was approved by the Conjoint Health Research Ethics Board at the University of Calgary. Subjects were recruited from patients aged 6 to 18 years of age who had type 1 diabetes and were followed at the Alberta Children's Hospital and from adult subjects

with type 1 diabetes attending the Calgary Health Region Diabetes, Hypertension and Cholesterol Centre. Individuals were excluded based on the following criteria: inadequate proficiency in English; physical or intellectual barriers to completion of study; use of medication interfering with ability to perceive hypoglycemia symptoms (e.g. beta-blockers, oral corticosteroids, etc); and other concomitant medical problems requiring ongoing treatment other than controlled asthma, celiac disease, hypothyroidism, hypertension or hyperlipidemia.

Once informed consent had been obtained, the subjects and 1 parent were asked to complete a validated 28-item questionnaire on hypoglycemia symptoms (16) at baseline (retrospective symptom report). Children completed the survey with a research assistant, and the parents of pediatric subjects completed their versions in a separate room. Adult participants completed the questionnaire on their own during the initial meeting with the research assistant. For each symptom, a score from 1 to 7 could be assigned (1 = symptom not present to 7 = very intense). Symptoms were divided into 3 main groups: autonomic, neuroglycopenic and general malaise. Thereafter, subjects were asked to call a specialized automated phone system to report each episode of hypoglycemia (symptoms of hypoglycemia and blood glucose <4.0 mmol/L on monitoring) for a 4-week period following their enrolment. Date, time, level of blood glucose and rating for each of the 28 items on the hypoglycemia questionnaire were collected from each call. For younger children, the parents were instructed to have the child rate each symptom, even if the parent was phoning in for them. To help with interpretation of the results, the following information was obtained from the patient or the patient's medical chart: date of birth, date of diagnosis, gender, past history of severe hypoglycemia and ability to tell whether having hypoglycemia (single question with a 6-point Likert scale: 1 = always to 6 = never). The patient was also asked to obtain an A1C result if this result had not been obtained in a 3-month period prior to enrolment. At the end of the study, subjects were asked to fax or mail a copy of their logbooks for 4 weeks of the study. For the 66 subjects for whom a logbook was available (42 children and 24 adults), 31 had good concordance between the reported frequency of hypoglycemia, whereas 35 had discrepancies of more than 1 episode between the logbook and the phone system; 26 had more episodes reported by phone than in the logbook. Therefore, compliance with the system was good or very good in 86% (57/66) of subjects.

## Data Analysis

Comparisons of retrospective and prospective data (between adults and children with type 1 diabetes) for each of the 28 individual symptoms were conducted using analysis of variance (ANOVA) to compare adults to children and repeated ANOVA measures to compare retrospective to prospective data within each patient group.

A discriminant function analysis was conducted using all 28 symptoms for children and for adults so as to determine which combination of the symptoms best discriminated between adults and children. The percentage of adults correctly classified as adults and the percentage of children correctly classified as children were reported. In order to avoid interference by varying numbers of

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