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Original Research

The Effect of Hypoglycemia on Health-Related Quality of Life: Canadian Results from a Multinational Time Trade-off Survey

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ABSTRACT

Objective: The aim of this study was to investigate the impact of hypoglycemia according to severity and time of onset on health-related quality of life (HRQoL) in a Canadian population.
Methods: Time trade-off (TTO) methodology was used to estimate health utilities associated with hypoglycemic events in a representative sample of the Canadian population. A global analysis conducted in the United Kingdom, Canada, Germany and Sweden has been published. The present Canadian analysis focuses on 3 populations: general, type 1 and type 2 diabetes. Using a web-based survey, participants (>18 years) assessed the utility of 13 different health states (severe, non-severe, daytime and nocturnal hypoglycemia at different frequencies) using a scale from 1 (perfect health) to 0 (death). The average disutility value for each type of event was calculated.
Results: Of 2258 participants, 1696 completers were included in the analysis. A non-severe nocturnal hypoglycemic event was associated with a significantly greater disutility than a non-severe daytime event (−0.0076 vs. −0.0056, respectively; p=0.05), while there was no statistically significant difference between severe nocturnal and severe daytime events (−0.0616 vs. −0.0592; p=0.76). Severe hypoglycemia was associated with greater disutility than non-severe hypoglycemia (p<0.0001). Similar trends were reported in participants with diabetes.
Conclusions: The findings presented here show that any form of hypoglycemia had a negative impact on HRQoL in a Canadian population. Nocturnal and/or severe hypoglycemia had a greater negative impact on HRQoL compared with daytime and/or non-severe events. This highlights the importance of preventing the development and nocturnal manifestation of hypoglycemia in patients with diabetes.

Mots clés :
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RÉSUMÉ

Objectif : Le but de cette étude était d'examiner les conséquences de l'hypoglycémie selon la gravité et le moment de l'apparition sur la qualité de vie liée à la santé (QdVS) d'une population canadienne.
Méthodes : La méthodologie de l'arbitrage temporel a été utilisée pour estimer les états de santé associés aux événements hypoglycémiques d'un échantillon représentatif de la population canadienne. Une analyse globale menée au Royaume-Uni, au Canada, en Allemagne et en Suède a été publiée. L'analyse canadienne actuelle met l'accent sur 3 populations : générale, diabète de type 1 et de type 2. En utilisant une enquête en ligne, les participants (> 18 ans) ont évalué l'utilité de 13 différents états de santé (grave, sans gravité, hypoglycémies diurnes et nocturnes à des intensités différentes) en utilisant une échelle de

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1 (excellente santé) à 0 (mort). La valeur moyenne de la désutilité pour chaque type d'événement a été calculée.
Résultats : Parmi les 2258 participants, 1696 personnes ayant rempli l'enquête ont été incluses dans l'analyse. Un événement hypoglycémique nocturne sans gravité a été associé à une désutilité significativement plus grande qu'un événement diurne (−0,0076 *vs* −0,0056, respectivement; p = 0,05), tandis qu'il n'y a pas eu de différence statistiquement significative entre les événements nocturnes graves et les événements diurnes graves (−0,0616 *vs* −0,0592; p = 0,76). L'hypoglycémie grave a été associée à une désutilité plus grande que l'hypoglycémie sans gravité (p < 0,0001). Des tendances similaires ont été rapportées chez les participants ayant le diabète.
Conclusions : Les conclusions présentées ici montrent que toute forme d'hypoglycémie a eu des conséquences négatives sur la QdVS d'une population canadienne. Les hypoglycémies nocturnes ou graves, ou nocturnes et graves, ont eu des conséquences négatives plus grandes sur la QdVS comparativement aux événements diurnes ou sans gravité, ou diurnes et sans gravité. Cela montre l'importance de prévenir le développement et la manifestation de l'hypoglycémie nocturne chez les patients ayant le diabète.

Introduction

In 2011, it was estimated that 6.8% of the Canadian population (>12 years of age) had either type 1 or 2 diabetes (1). Hypoglycemia is recognized as a limiting factor in the glycemic management of these individuals and a major cause of morbidity and mortality (2–4). The incidence of severe hypoglycemia in the Canadian population with diabetes is estimated to be ~1.9 and 2.6 episodes per patient per year in patients with type 1 and 2 diabetes, respectively, while the incidence of non-severe hypoglycemia is estimated to be 102 and 66 episodes per patient per year (5). Moreover, the incidence of severe hypoglycemia reported during sleep is estimated to be 0.5 and 0.2 episodes per patient per year in patients with type 1 and 2 diabetes, respectively (5). Other studies have shown that more than half of severe hypoglycemic events may occur during the night (6). Nocturnal hypoglycemic episodes are often asymptomatic due to a reduced autonomic response to hypoglycemia during sleep (7) and recurring episodes may contribute toward cognitive impairment, and more seriously toward "dead-in-bed" syndrome (8), which is responsible for ~6% of all deaths in patients with diabetes <40 years of age (9).

Patient-specific factors that impact health-related quality of life (HRQoL) are becoming increasingly important in the clinical decision-making process that underpins the provision of optimal diabetes treatment (10). Acute hypoglycemia symptoms have significant effect on a patient's overall well-being; however, the *total* impact of hypoglycemia needs to account for potential behavioural changes (avoiding exercise, overeating and reluctance to intensify therapy), impaired awareness of hypoglycemia (IAH) and fear of future hypoglycemic events, which are all likely to complicate glycemic control and diminish treatment effectiveness (11). HRQoL can be quantified using health utility values — single summary measures typically between 0 (death) and 1 (perfect health) that describe the impact of an intervention or health state on HRQoL from a patient's perspective (12). Health utility values can help quantify the overall impact of hypoglycemia on patients' HRQoL with respect to individual events. Although several studies have measured hypoglycemia utility values, these studies were small in scale and had various limitations (4,13–15). One study investigated the HRQoL impact in a Canadian population and showed a utility loss associated with non-severe hypoglycemia, but did not distinguish between diurnal and nocturnal events (16).

The time trade-off (TTO) method, which is a health utility estimation approach that was partly developed in Canada, is recommended by healthcare agencies, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) and the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom. These utility values can be used to calculate quality-adjusted life-years (QALYs) (17,18) for cost-effectiveness analyses, and could potentially be used to help optimize diabetes treatment algorithms, particularly when utility instruments such as EuroQoL (EQ-5D) or Health Utilities Index (HUI) are unavailable. The results from the primary study demonstrate the negative effect of hypoglycemia, particularly nocturnal hypoglycemia, on respondents' HRQoL in a large multinational cohort (19). The primary aim of this Canadian subanalysis was to assess the impact of hypoglycemia on HRQoL according to severity and time of onset, using a rigorous patient-based TTO utility approach in a large Canadian population of subjects with or without type 1 or 2 diabetes.

Methods

A cross-sectional survey was carried out across a representative sample of the Canadian general population (≥18 years of age). This sample was one of several populations pertaining to a global study, which included participants from Germany, Sweden, United States and United Kingdom (19). Participant details were provided through marketing research company Gfk Custom Research (New York, NY), where anonymity was preserved throughout the process. All participants had previously agreed to take part in Internet-based surveys and several tools (web banners, telephone and personal interviews) were used to ensure a representative population was chosen. Participants were offered incentive "points" (a total corresponding value of 1.50 to 3.00 CAD$) to participate in the survey, which could then be redeemed against a selection of commodities. Three specific study populations were selected: general population, type 1 and type 2 diabetes. Deciding which is the most suitable study population (general or patient) for this type of analysis is a contentious topic, but this decision should be informed by the downstream application of the results (20–23). The inclusion of a general population sample is recommended by CADTH Guidelines for the Economic Evaluation of Health Technologies (24), given that the general population are the ultimate payers of the publicly funded health care system. In addition, those subjects of the general population that had diabetes were identified and included in both the general population and diabetes groups.

The full methodology of the global TTO study has been published elsewhere (19). Briefly, respondents were asked via an Internet-based survey (SurveyXact) to "trade-off" a defined portion of their remaining lifespan for a different health state (see 'Health States' below). This returned a utility value between 0 (death) and 1 (perfect health). To ensure the trade-off values were as accurate and "real" as possible, the time horizons used in the survey were based on each respondent's projected life expectancy (calculated using WHO life tables (25) and respondent demographics [age and gender]). The TTO score was determined using the point of indifference (12). To identify the point of indifference with regard to a TTO question (where both answers are equally acceptable), respondents were asked the same question repeatedly, varying only the number of years living in full health each time. This