Effect of Automated Bolus Calculation on Glucose Variability and Quality of Life in Patients With Type 1 Diabetes on CSII Treatment

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ABSTRACT

Purpose: Automated bolus calculation may benefit patients with poorly controlled type 1 diabetes who are relatively new to continuous subcutaneous insulin infusion (CSII). This study investigated the effect of automated bolus calculation on glucose variability, glucose control, and diabetes-related quality of life in patients with reasonably well-controlled type 1 diabetes, accustomed to treatment with CSII for several years.

Methods: This open-label, single-center study included 32 patients (mean age, 45.9 [15.1] years; 34% male; disease duration, 27.3 [12.9] years; glycosylated hemoglobin [HbA_{1c}] level, 64.6 [12.5] mmol/mol [8.1% (1.1%)]; CSII treatment, 9.0 [7.8] years) who were randomly assigned to receive 4 months' treatment with a bolus calculator (n = 14) or continuation of standard care without a bolus calculator (n = 18). All participants received dietary counseling on carbohydrate counting. Primary outcome was glucose variability, as assessed by the SD of 7-point glucose profiles. Secondary outcomes included HbA_{1c}, rate of (severe) hypoglycemia, and diabetes-related quality of life.

Findings: After 4 months of follow-up, glucose variability had improved in the bolus calculator group compared with the control group (change, –0.8 [0.9] vs 0.1 [0.9] mmol/L; $P = 0.030$). Mean glucose levels did not change in either group (0.4 [1.1] vs 0.3 [0.9] mmol/L; $P = 0.95$). There were also no differences in change in hypoglycemia rate (–0.6 [1.6] vs –0.4 [1.6] event per patient per week; $P = 0.67$), HbA_{1c} value (–0.5 [6.6] vs –4.9 [10.6] mmol/mol; $P = 0.21$), or diabetes-related quality of life between the bolus calculator group and the control group.

Implications: Use of a bolus calculator modestly improved glucose variability in this relatively small group of patients with longstanding type 1 diabetes on CSII but did not affect other parameters of glycemic control or diabetes-related quality of life. (Clin Ther. 2018;∎:∎∎∎–∎∎∎) © 2018 The Authors. Published by Elsevier HS Journals, Inc.

Key words: continuous subcutaneous insulin infusion, bolus calculator, insulin therapy, glucose variability, type 1 diabetes.

INTRODUCTION

Various large-scale clinical trials have shown the importance of near-normalization of glucose control to reduce the risks of microvascular complications in individuals with diabetes.[1,2] Intensive insulin therapy is paramount to achieving such good glycemic control in patients with type 1 diabetes and in those with prolonged type 2 diabetes approaching the insulin-deficient state.

Optimal insulin therapy requires patients to estimate the amount of prandial insulin before each meal according to several factors, including current glucose level, anticipated carbohydrate intake, insulin-to-carbohydrate ratio (ICR), estimated insulin sensitivity, target blood glucose level, and anticipated physical activity.[3] Adjustment of the insulin dose to carbohydrate intake has shown improvement in glycemic control, treatment satisfaction, and patient's well-being.[4,5] Previous studies, however, have shown that more than one half of the patients estimate their

prandial insulin dose incorrectly,[6,7] many because they fear injecting too much insulin and causing hypoglycemia.[8] Patients with poor numeracy skills have higher glycosylated hemoglobin (HbA$_{1c}$) levels compared with patients with good numeracy skills.[9,10]

Automatic bolus calculators have emerged to aid in insulin bolus estimation, taking into account individualized ICR and insulin sensitivity factor (ISF), as well as the effect of previously administered insulin (ie, insulin on board). In daily practice, however, such bolus calculators are used by a minority of adult patients receiving CSII. There is still uncertainty about the benefit of automated bolus calculation. Some studies have shown improvements in glycemic control[11] and quality of life[3,12] in poorly controlled patients treated with CSII or multiple daily injections (MDIs),[13–18] but others have not.[17,19] In most studies, however, extensive education on carbohydrate counting accompanied the initiation of the bolus calculator, which was not routinely provided in the control situation. In addition, many participants in studies involving CSII were new to this form of treatment, and most studies excluded participants with (relatively) good glucose control.[12,16,20]

The objective of the present study was to investigate whether a bolus calculator could still benefit patients with stable CSII treatment, for whom improvement of already moderate to good glycemic control is not the primary aim of treatment. We hypothesized that in such cases, the use of bolus calculation would decrease glucose variability, reduce the hypoglycemic burden, and, consequently, improve diabetes-related quality of life without deteriorating glucose control. To test this hypothesis, we conducted a randomized controlled open-label trial in patients with diabetes treated by CSII, in which both groups received (repeated) dietary counseling at the start.

PATIENTS AND METHODS
Study Design
This 16-week, randomized controlled, single-center, open-label study was performed at the Radboud University Medical Center in Nijmegen, the Netherlands, between February 2014 and May 2016. The study was approved by the local institutional review board and performed according to the principles of the Declaration of Helsinki. All participants provided written informed consent.

Study Population
Patients with type 1 diabetes treated with CSII were recruited from the outpatient clinic. People were eligible for participation in the study when they met the following criteria: treatment with CSII for at least 6 months, age between 18 and 60 years, HbA$_{1c}$ value <86 mmol/mol (10%), disease duration >2 years, and a total daily insulin dose <1 U/kg. Key exclusion criteria were current use of a bolus calculator, inability or unwillingness to perform frequent blood glucose measurements, pregnancy or intention to become pregnant, prednisone treatment, a recent cardiovascular event, or the presence of severe microvascular complications. Although we initially invited patients with long-duration type 2 diabetes to participate, only 2 patients were enrolled, both of whom were randomized to the bolus calculation group. Because of the low numbers and this imbalance, we decided to exclude these patients from analysis.

Study Procedure
At the screening visit, participants completed various diabetes-related quality of life questionnaires (Confidence in Diabetes Self-Care scale, Hypoglycemia Fear Survey, Problem Areas in Diabetes questionnaire), and HbA$_{1c}$ levels were measured. All participants received dietary advice from a dietitian concerning carbohydrate counting and insulin bolus calculation; the knowledge thus acquired was tested by examination. When participants failed this test, they were scheduled for a second visit by a dietitian. Subsequently, participants were randomized to either the bolus calculator group or the control group. For random allocation concealment, we used opaque, sealed envelopes and blocks of 4 subjects.

The second visit occurred 2 weeks later. Participants collected 7-point blood glucose profiles for 5 days before the visit and kept a diary about their carbohydrate intake during these days. Participants randomized to the bolus calculator group were consulted by a diabetes educator to receive information about use of the bolus calculator. ICR and ISF were calculated based on the insulin total daily dose (TDD), and ratios were programmed into the bolus calculator. The ICR was calculated by using the 500 rule (ICR = 500 divided by TDD) and ISF by using the 100 rule (ISF = 100 divided by TDD).[19,21,22] Target blood glucose levels were determined individually, and insulin on board time was set at 4 hours for each