An Analysis of “No Effect of Insulin Pen with Memory Function on Glycemic Control in a Patient Cohort with Poorly Controlled Type 1 Diabetes: A Randomized Open-Label Study”

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Abstract

Missing meal bolus and nonadherence is an important barrier to achieving glycemic goals in type 1 diabetes (T1DM). In this issue of Journal of Diabetes Science and Technology, Danne and coauthors reported the results of a 24-week randomized-controlled study designed to evaluate if using an insulin pen with memory function, the HumaPen® Memoir™, might improve injection compliance and, therefore, overall glycemic control in T1DM. Patients treated with the pen device with memory function improved, albeit nonsignificantly, their mean HbA1c by 0.43%. Among the reasons to justify why this study was not positive, the most important is the high proportion of adult patients included in the study (87.9%)—children and adolescents being under-represented. I am convinced that pen devices with memory function might be helpful for forgetful patients (children, adolescents), as suggested in another recent study.


INTRODUCTION

Intensive insulin therapy prevents the onset or delays the progression of microvascular and macrovascular complications in type 1 diabetes mellitus (T1DM)1,2. However, poor adherence to insulin treatment has been reported as one of the major factors that contribute to long-term poor glycemic control, diabetes ketoacidosis, and brittle diabetes in adolescents and young adults with T1DM.3 In addition, in a survey on insulin-treated patients, mostly with type 2 diabetes, 33.2% of patients reported insulin omission/nonadherence at least 1 day in the past month.4 For young patients using continuous subcutaneous insulin infusion (CSII), missed mealtime insulin boluses have been recognized as a major cause of suboptimal glycemic control.5 Patients who missed <1 bolus per week achieved a mean hemoglobin A1c (HbA1c) lower (~0.8%) than those who missed ≥1 bolus per week.5 A trend was found, albeit not significant, between lesser incidents of missing bolus and more self-monitoring of blood glucose (SMBG) tests per day.5 The consequences of missing bolus in adolescents with T1DM wearing insulin pumps are devastating. An audit in Sweden showed ~40% of adolescents missed >15% of doses on the previous day.6 These patients had higher HbA1c, took fewer SMBG measurements, were less satisfied with their treatment, and perceived medical treatment more negatively.6
The impact of poor adherence on insulin treatment efficacy has been quantified in some clinical scenarios. In adolescents using CSII, it has been calculated that HbA1c decreased by 0.2% for each additional SMBG \((p = .001)\) and for each bolus event \((p < .001)\).\(^7\) In addition, if patients took ≤2 meal boluses per day ≥1 day per fortnight, then HbA1c increased by 0.8% \((p = .001)\).\(^7\) Reviewing medical literature, Randløv and Poulsen\(^6\) in a simulation study, suggested that forgetting 2.1 meal-related injections per week would increase HbA1c by at least 0.3–0.4%, confirming that missing injections are one of the main reasons for suboptimal treatment.

Regarding causes for insulin omission or nonadherence, the five most common reasons, as indicated by patients and providers in a survey, were as follow: too busy, travelling, skipped meals, stress or emotional problems, and/or public embarrassment.\(^4\) Insulin omission or nonadherence were more frequent among patients who were male, younger, had type 2 diabetes or more frequent hypoglycemia, were less successful with other treatment tasks, regarded insulin adherence as less important, had more practical/logistical barriers and difficulties with insulin adherence, were concerned that insulin treatment required lifestyle changes, or were dissatisfied with the flexibility of injection timing.\(^9\)

Recognizing that missing meal bolus and nonadherence is an important barrier to achieving glycemic goals, different strategies have been tested with different success. In youth with T1DM wearing insulin pumps, Chase and coauthors\(^10\) evaluated if the use of meal bolus alarms would result in fewer missed boluses per week. Although the number of missed meal boluses significantly decreased after 3 months (from a mean of 4.9 to 2.5 missed meal boluses per week; \(p = .0005\)) and, therefore, HbA1c declined (from 9.32% to 8.86%; \(p = .0430\)), this beneficial effect of meal bolus alarms was not sustained after 6 months.\(^10\) The number of missed meal boluses increased by a mean of 0.8 per patient week between 3 and 6 months.\(^10\) The reasons for the weaning beneficial effect of the meal bolus alarms in these patients remain speculative.

For patients using insulin pens, other tools have been developed for increasing patient compliance with insulin injections. In this issue of *Journal of Diabetes Science and Technology*, Danne and coauthors\(^11\) reported the results of a 24-week randomized controlled study designed to evaluate if using an insulin pen with memory function, the HumaPen® Memoir™, might improve injection compliance and therefore overall glycemic control in a broad age range sample of inadequately controlled patients with TIDM (baseline HbA1c ≥ 8.0%). The HumaPen Memoir is a pen with memory function that records dose, date, and time of the past 16 injections.\(^12\) Although patients treated with the pen device with memory function improved their mean HbA1c by 0.43%, there was not a significant difference from the decrease observed in the control group.\(^11\) No differences were also found regarding hypoglycemic episodes or treatment satisfaction.\(^11\)

There are several reasons to justify why this study was unable to demonstrate superiority of the pen device with memory function against the conventional pen. Most of the arguments have been discussed by the authors in the original manuscript. In principle, such a device will be of most profit for forgetful patients, mostly youths, who sometimes do not inject the insulin before meals and then, when they remember, administer the bolus after meals. However, the majority of patients in this study were adults (87.9%), with a mean age of 39.8 years, with children and adolescents underrepresented. Although the reasons for poor diabetes control may be diverse, it could be assumed that adults with poor diabetes control (HbA1c = ~9.1%) may also be too noncompliant to administer insulin after meals. In addition, there was no information about the overall number of missed bolus injections, the number of corrective actions based on the memory, and, also importantly, blood glucose profiles, essential information to understand exactly the causes for the unexpected results. It is plausible that either corrective insulin injections started too late after a forgotten preprandial injection or there were, in fact, too few to have an impact on overall glycemic control.

Adolfsson and coauthors\(^13\) evaluated safety and patient perception of a new insulin pen with simple memory function in a sample of children and adolescents with TIDM. The tested pen device showed only the last dose and was able to deliver insulin in 0.5 U steps. They found that this new pen device increased the proportion of children who injected insulin themselves, missing fewer injections and reporting greater confidence in managing their insulin injections.

In conclusion, missed meal boluses or insulin injections occurs frequently, especially in pediatric patients, and are a major cause of poor glycemic control in these patients. Therefore, any strategy designed to increase compliance in these patients is welcome. Pen devices with memory function might be helpful for forgetful patients, mostly...
children and adolescents, as shown by Adolfsson and coauthors. Consequently, there is still a need for more studies with such devices with memory function to establish their value in selected populations.

References:


