



COMMENTARY

## Inpatient Use of Computer-Guided Insulin Devices Moving into the Non-Intensive Care Unit Setting

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**B**ASAL-BOLUS INSULIN THERAPY is recommended as the preferred regimen for management of hyperglycemia in non-critically ill hospitalized patients with diabetes.<sup>1</sup> Basal-bolus insulin regimens with basal insulin analogs or intermediate-acting insulin given once or twice a day, in combination with short- or rapid-acting insulin administered prior to meals, has been proven an effective and safe strategy for glycemic management in non-critically ill patients.<sup>2,3</sup> Additionally, in non-cardiac general surgery patients, basal-bolus regimens are also shown to reduce the risk of complications, especially surgical-site infections.<sup>3</sup> Unfortunately basal-bolus therapy is associated with high rates of hypoglycemia, especially when meal insulin and food intake do not match. In several observational and randomized control trials in non-intensive care unit patients, the rate of hypoglycemia has ranged between 5% and 32%,<sup>2-4</sup> which is a concern because hypoglycemia in non-intensive care unit settings has been associated with increased length of stay, hospital complications, and mortality.<sup>5,6</sup>

Despite well-outlined recommendations, basal-bolus therapy is perceived to be complex and therefore inadequately adopted for hyperglycemia management in all areas of the hospital. Issues identified for underutilization include a fear of hypoglycemia, which leads to insufficient starting doses of insulin and inertia in routinely titrating them as is needed by the changing requirements of a hospitalized patient.<sup>7</sup> Many insulin protocols have reported success in improving glucose management in the hospital including standardized basal-bolus paper-based or electronic order sets, as well as education programs for providers, residents, and medical students,<sup>8-10</sup> but no simple fix has yet been identified.<sup>11</sup> Some commercial computer-guided insulin administration programs are now available to guide basal-bolus insulin therapy in patients with type 1 and type 2 diabetes (Glucomanager™ [Glytec, Greenville, SC], EndoTool System® [MD Scientific LLC, Charlotte, NC], and GlucoStabilizer® [Medical Decision Network, Charlottesville, VA]). These devices may be especially useful in hospitals with no diabetes management teams or diabetes experts on staff; however, some are at a considerable financial cost to the institution.

In this issue of the journal, Neubauer et al.<sup>12</sup> present the results of an open label uncontrolled intervention study introducing a mobile device, the GlucoTab® (Joanneum Research GmbH [Graz, Austria] and Medical University of Graz [Graz]) system, which standardizes glycemic management using a computerized decision support system for patients with type 2 diabetes. This device provides dual functionality including real-time guidance on insulin dosing for both providers and nurses. In addition, a screen interphase displays current glucose values, glucose trends, and past administered insulin doses, while allowing the capability to change insulin orders.

The GlucoTab system was evaluated in four wards in the tertiary-care Graz hospital using varied hospital patients, including cardiology, endocrinology, nephrology, and plastic surgery. Patients differed significantly in their levels of insulin resistance, and the providers differed in their knowledge of basal-bolus insulin therapy. Providers were educated in the basics of insulin treatment and the device prior to the study start. Standard published basal-bolus algorithms from previous randomized controlled prospective trials were used in the GlucoTab system, with total daily starting insulin doses of 0.3 or 0.5 units/kg/day, depending on the renal function of patients.<sup>2,3,13</sup> Normal basal bolus ratios are approximately 50% basal and 50% bolus, with bolus doses further divided somewhat equally among three meals. In this study (device) Neubauer et al.<sup>12</sup> evaluated a modified bolus dose algorithm that split the bolus dose into 45% of bolus dose at breakfast, 25% at lunch, and 30% at dinner. This modification from the standard protocols came about after the observation of higher caloric intake or higher postprandial glucose excursion after breakfast compared with other meals during the day.

This higher requirement may be due to a combination of factors, including a large carbohydrate load at breakfast frequently provided in hospitals, the dawn phenomenon, or a late breakfast with delayed insulin administration. The GlucoTab system algorithm using the variable bolus dose worked well and allowed over 50% of their patients to reach a glucose goal of 70–140 mg/dL, with low levels of hypoglycemia.

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Percentages of patients in the study of Neubauer et al.<sup>12</sup> reaching glucose goals varied among the different ward specialties, with cardiology and nephrology being the lowest. Acute cardiology patients had higher glucose levels and probably represent the most insulin resistant of the study group. In contrast, the nephrology group was treated as the most insulin sensitive and initiated with a lower starting dose of insulin at 0.3 units/kg/day, and fewer patients reached goal glucose levels. Because patients were varied in renal function, reason for admission, and nutritional support, the GlucoTab algorithm may perform better with several different starting insulin doses, but unfortunately this may complicate use of the device by nondiabetes experts. Regression analysis performed to analyze this diverse patient population identified four predictors of poor glycemic outcome: insulin treatment prior to admission, higher pre-admission glycated hemoglobin levels, higher starting insulin doses in the hospital, and acuity of admissions.

Even with these few limitations, it is encouraging that the GlucoTab system in the hands of nondiabetes experts allowed the target mean blood glucose of 70–140 mg/dL (mean achieved value,  $154 \pm 35$  mg/dL) to be reached in a large percentage of patients compared with prior clinical trials of basal-bolus therapy performed by expert trained providers (66% in RABBIT 2<sup>2</sup> and 52% in RABBIT 2 Surgery<sup>3</sup>). This was accomplished with a similar or slightly lower risk of hypoglycemia and no episodes of severe hypoglycemia compared with RABBIT 2 Surgery.<sup>3</sup>

Many factors may have contributed to the low hypoglycemia rates. The insulin on-board calculator, a safety feature in insulin pumps, seems to perform an important function for the GlucoTab system. It tracks insulin doses, calculates the active insulin remaining from the patient's last injection, and provides guidance on reducing insulin doses at administration time. This adjustment is not intuitively made when a provider orders or a nurse administers insulin and is of particular importance in hospitals with meal service, where food and insulin are not given in the traditional 4–6-h intervals. Another important aspect of hypoglycemia prevention may have been the timing of administration of long-acting insulin (glargine). The study dosed glargine in the afternoon after rounds, allowing providers to evaluate the 24-h response to the last insulin dose before modifying it and also reducing the dose if the injection was delayed. In our experience hospitalized patients, especially those with renal failure, are very insulin sensitive overnight and have less hypoglycemia with daytime basal insulin administration.

Computer-guided devices are an evolving and welcome technology in the diabetes field and may facilitate glucose control and reduce hypoglycemia, especially when no diabetes teams or experts are available to direct insulin therapy. This trial introduces an efficacious device, which potentially can simplify glucose management in hospitalized patients. The GlucoTab system has a fine-tuned algorithm and design interphase that was well accepted by staff and allowed a significant number of patients to reach goal even in the hands of teams not expert in basal-bolus insulin therapy. As a clinical tool this device would be significantly more powerful if it could be integrated into an electronic medical record system as a basal bolus calculator for ordering insulin.

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