Commentary

Selecting Insulin Regimens for the Management of Non-ICU Patients With Type 2 Diabetes

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The discovery of insulin at the University of Toronto in 1921-1922 is one of the most important events in the history of the treatment of diabetes. The first successful treatment of a patient with insulin, reported by Banting and Best, was on January 23, 1922, in a 14-year-old patient with blood glucose (BG) concentration of 580 mg/dL, strongly positive ketones in urine, and acetone odor on breath and close to death [1]. His clinical response was rapid, resulting in a dramatic decline of glycosuria and ketonuria by approximately 75% after a few doses of pancreatic extract injections.

Following the discovery of insulin, the recommended treatment regimen for most patients was regular insulin given by multiple injections 2 to 4 times daily. To guide insulin therapy and reduce hypoglycemic events, Elliot P. Joslin reported the use of "sliding scale" regimen in 1934 [2]. Joslin recommended giving regular insulin according to the amount of glycosuria: 5 units for "green urine," 10 units for "yellow urine," and 15 units for "orange urine." Following the introduction of glucose meters in 1970s, sliding-scale insulin using capillary BG became widely accepted by general practitioners and continues to be used in many hospitals around the world despite guidelines recommending against its use in favor of basal-bolus insulin regimen. Several randomized controlled studies and meta-analyses have reported better glucose control and reduced risk of hospital-acquired infections with basal-bolus regimen but no difference in mortality or length of hospital stay compared to sliding scale [3,4].

The basal-bolus regimen was recommended as the preferred regimen for the management of hyperglycemia and diabetes in hospital settings by the American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control in 2009. This regimen involves the administration of basal insulin given once or twice daily, along with rapid-acting insulin before meals, plus corrective doses of subcutaneous rapid-acting insulin for elevated glucose levels. Although effective in correcting hyperglycemia, the basal-bolus approach is labor intensive, requiring multiple injections per day, and is associated with increased risk of iatrogenic hypoglycemia. In controlled settings, the incidence of mild hypoglycemia with basal-bolus regimen is around 12% to 30%. For patients with decreased oral intake or undergoing surgery, a "basal-plus approach" is currently recommended by clinical guidelines [5]. This regimen consists of a single dose of basal insulin (~0.2-0.25 units/kg/day) along with corrective doses of insulin by sliding scale for hyperglycemia before meals or every 6 h (if nil by mouth) [6]. In randomized controlled trials, the use of the basal plus correction regimen resulted in glycemic control similar to a standard basal-bolus regimen and represents an effective alternative to the use of

a basal-bolus regimen for most general medical and surgical patients with type 2 diabetes [6].

Sadhu et al reported their observational study assessing different insulin strategies (sliding scale, basal bolus, and basal only) on glucose control and hospital outcomes in a large number of nonintensive care unit patients (n = 4,558) with type 2 diabetes [7]. After adjusting for multiple patient and provider variables with propensity score analysis, they report that patients treated with basal only experienced significantly lower mean daily glucose, 40% lower hyperglycemic days, and no difference in hypoglycemia compared to a basal-bolus regimen. In addition, basal only resulted in 30% lower hyperglycemic days and a 22% increase in euglycemic days compared to sliding-scale use. As expected, the basal-bolus regimen was associated with higher rate of hypoglycemia compared to a sliding-scale regimen. This single-center, real-world study supports the results of previous randomized controlled studies and current recommendations of the American Diabetes Association on the use of basal insulin or a basal plus bolus correction as the preferred treatment for noncritically ill hospitalized patients with poor oral intake [5]. An insulin regimen with basal, prandial, and correction components is indicated for patients who fail basal plus correction or in patients with good nutritional intake.

We agree with Sadhu et al [7] that the basal-bolus regimen as a single approach may not be the best strategy for all patients with diabetes. We have learned that an individualized therapy approach is the best way to obtain good glycemic control without increasing the risk of iatrogenic hypoglycemia. The treatment selection should incorporate patient characteristics, severity of illness and hyperglycemia, hypoglycemia risk, and diabetes treatment prior to admission.

Insulin-naïve patients with mild hyperglycemia (<180 mg/dL) can be initially treated with less aggressive regimens (sliding scale) or continuing oral agents (if no contraindication) to reduce the risk of iatrogenic hypoglycemia. In agreement with Sadhu et al [7], in a recent retrospective study we reported that over 80% of nonintensive care unit patients with admission BG < 180 mg/dL treated with sliding scale insulin alone achieved target glycemic control defined as mean hospital BG < 180 mg/dL without hypoglycemia during hospitalization [8]. If glycemic control is not achieved in 24 to 48 h, a basal plus correction regimen is likely to control most patients with type 2 diabetes, particularly patients with poor oral intake.

For patients with moderate or severe hyperglycemia and those who were treated with insulin prior to admission, a more intensive insulin regimens (a basal-plus or basal-bolus regimen) are indicated. Insulin-naïve patients can be treated with basal insulin starting at 0.20 to 0.25 U/kg/day plus correction or with basal-bolus regimen at a starting total daily dose between 0.3 and 0.5 units/kg, divided on a ratio of basal:bolus insulin of 50:50%. Lower doses are recommended for patients with impaired kidney function and at high hypoglycemia risk.

After 100 years of using insulin in hospitalized patients, we have not reached a consensus on best regimens or insulin formulation to manage hospitalized patients with type 2 diabetes. Clinical research focusing on individualizing therapy and determining specific glycemic goals among noncritically ill hospital patients with diabetes is needed. The evidence so far prioritizes avoiding the risk of hypoglycemia in high-risk patients and reserves more intensive therapy (basal-bolus) for patients who fail basal plus correction or with severe hyperglycemia.

Additional Information

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