

# Practical implications of the revised guidelines for inpatient glycemic control

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## KEY WORDS

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## ABSTRACT

Substantial observational data has linked hyperglycemia in hospitalized patients with poor patient outcomes. While early studies suggested improved clinical outcomes with interventions targeting near euglycemia, more recent studies have yielded inconsistent results, with the suggestion of harm with more severe hypoglycemia. The American Association of Clinical Endocrinologists and American Diabetes Association published a revised consensus statement on inpatient glycemic management that takes into account this recent evidence. This statement identifies reasonable, achievable, and safe glycemic targets and describes protocols, procedures, and system improvements necessary to achieve these effectively. These modified glycemic targets promote a rational approach to inpatient glycemic management that minimizes risks associated with uncontrolled hyperglycemia and hypoglycemia. Intravenous insulin infusions are recommended for critically ill patients who experience blood glucose (BG) levels above 140 mg/dl with a target of 140 to 180 mg/dl. Lower BG targets (i.e., 110–140 mg/dl) may be appropriate for patients following cardiac or vascular surgical procedures. In noncritically ill patients, scheduled subcutaneous basal:bolus insulin is the preferred therapy for achieving fasting and preprandial BG below 140 mg/dl and random BG values below 180 mg/dl, with consideration of more or less stringent targets based on a patient's clinical status. Prolonged use of correctional insulin as monotherapy is discouraged. Oral and injectable noninsulin glucose-lowering agents have a limited role for hospital use but may be appropriate for selected noncritically ill patients. Educating personnel about appropriate inpatient glycemic management practices, obtaining reliable and reproducible measures of BG, and careful implementation of standardized protocols can help to ensure patient safety.

**Introduction** Hyperglycemia is common in hospitalized patients with and without known diabetes.<sup>1,2</sup> Illness related elevations in blood glucose (BG) occur even in patients with previously normal glucose tolerance.<sup>3</sup> These BG elevations were previously considered as part of the usual clinical course of acute illness and often not treated until levels exceeded 200 to 250 mg/dl.<sup>4,5</sup> This inattention to glycemic management changed with publication of the initial Leuven study (Leuven 1) in 2001.<sup>6</sup> This study demonstrated significant reductions in morbidity, mortality, and cost of care with intensive glycemic management in critically ill primarily surgical patients.<sup>7,8</sup> These findings were supported by other studies of intensified glycemic management, resulting

in recommendations for glycemic targets of 80 to 110 mg/dl in critically ill patient populations.<sup>9–13</sup> In the absence of randomized controlled trial (RCT) data outside critical care settings, guidelines for glycemic management in noncritically ill patients are based upon observational and epidemiologic reports of adverse outcomes with increasing BG levels.<sup>14,15</sup>

Recently, concern has been raised that BG targets of 80 to 110 mg/dl may be inappropriate.<sup>16,17</sup> Several RCTs have observed no benefit with intensive glycemic control with the suggestion of harm due to higher rates of severe hypoglycemia.<sup>18–20</sup> These contradictory reports created confusion within the medical community as to the rationale for dedicating resources to control of

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hyperglycemia in the hospital, particularly in vulnerable critically ill patients.

To address this concern, a consensus panel including representatives from the American Association of Clinical Endocrinologists and American Diabetes Association was convened to review the clinical and cost effectiveness of inpatient glycemic management, the safety of the currently available treatment protocols, and strategies for transitioning patients to outpatient care. The overall goal of this panel was to review the available literature as a way of identifying reasonable, achievable, and safe glycemic targets to guide clinicians toward rational insulin therapy while avoiding uncontrolled hyperglycemia in both critical and noncritical care areas of the hospital.<sup>1</sup>

In this review, we present a discussion of the literature that supports continued efforts to improve inpatient glycemic management, summarize the recommendations of the consensus panel, and make recommendations for clinical practice.

#### **Hyperglycemia and patient outcomes: a review of the literature**

Hyperglycemia, defined as BG levels above 140 mg/dl, is unequivocally associated with adverse patient outcomes.<sup>1,21</sup> More severe levels of hyperglycemia (BG >150–200 mg/dl) are associated with an increased risk for infection due to altered leukocyte function, increased pathogen virulence, and glycation of immunoglobulins.<sup>21,22</sup> Other adverse outcomes associated with hyperglycemia in the hospital include an enhanced risk for cardiac arrhythmias with impairments in ischemic preconditioning and development of collateral blood flow following myocardial infarction (MI),<sup>11,23</sup> an increased risk of intensive care unit (ICU) polyneuropathy with prolongation of hospital length of stay (LOS) and need for rehabilitation services, and ultimately an increase in mortality.<sup>3,24</sup>

Implementation of protocols to control BG levels in the hospital has demonstrated significant improvements in each of these outcomes among several, but not all clinical trials.<sup>18,19,25</sup> This raises questions as to the appropriate glycemic targets as well as optimal methods for achieving these targets.

#### **Intensive glycemic control in patients following acute myocardial infarction**

The initial DIGAMI trial (Diabetes and Insulin-Glucose Infusion in Acute MI) prospectively randomized 620 patients with suspected MI and admission hyperglycemia (BG >198 mg/dl) to intensive insulin or conventional therapy. Those randomized to intensive therapy received insulin-glucose infusions for 24 h (glycemic target 126–196 mg/dl) followed by outpatient multi-dose subcutaneous insulin for 3 months or longer. The mean inpatient BG achieved was 173 and 211 mg/dl in the intensive and conventionally treated groups, respectively. While no mortality difference was observed in the hospital, significant reductions in mortality

were observed at one (26–19%,  $P = 0.0273$ ) and 3.4 years (44–33%,  $P = 0.011$ ) of follow-up.<sup>26</sup> Whether this was due to acute intravenous (IV) insulin therapy or intensification of diabetes management following discharge was not clear.

Attempts to reproduce the DIGAMI results were not as successful. DIGAMI 2 was conducted as a multicenter multinational RCT of 1253 patients with acute MI and diabetes randomized to insulin-glucose infusions (target BG 126–180 mg/dl) followed by either insulin-based long-term glucose control (fasting BG target 90–126 mg/dl, nonfasting target <180 mg/dl), or standard glucose control.<sup>27</sup> The absence of a difference in either morbidity or mortality after 2 years of follow-up was attributed in part to the inability to recruit adequate numbers of participants and to achieve glycemic separation between groups. In another study of 20,201 patients with ST-elevation MI, the group randomized to intensive therapy with glucose-insulin-potassium infusions had higher glucose levels than those who received standard care. Again, there were no group differences in patient outcomes.<sup>28</sup>

In yet another trial, a reduction in the incidence of heart failure and reinfarction was observed at 3 months in 240 subjects with diabetes randomized to receive 24 h of insulin infusion with a BG target of 72 to 180 mg/dl when compared with those receiving conventional management.<sup>15</sup> There was no early or late mortality benefit using intention to treat principles but a post-hoc analysis revealed reduced mortality at 6 months among subjects who achieved mean BG levels below 144 mg/dl during the first 24 h (2% vs. 11%,  $P = 0.02$ ).<sup>15</sup>

#### **Intensive glycemic control in patients undergoing cardiac surgery**

The strongest support for intensive glycemic control in critical illness is derived from studies performed in cardiac surgery patients. The Portland Diabetes Project is a prospective, nonrandomized interventional study of over 4800 patients with diabetes undergoing cardiac surgery.<sup>29</sup> The introduction of a continuous IV insulin infusion targeting BG levels of <150 mg/dl on the operative day through the first 2 postoperative days resulted in significant reductions in deep sternal wound infections and cardiac-related mortality.<sup>29</sup> These findings are consistent with those from other studies demonstrating reductions in complications and mortality with intensification of glycemic control to BG values below 150 mg/dl.<sup>9,11,30</sup>

Leuven 1 was a landmark study of 1 548 primarily surgical critically ill patients, 13% of whom had diabetes.<sup>6</sup> Patients randomized to intensive therapy received IV insulin for BG above 110 mg/dl to achieve and maintain BG between 80 and 110 mg/dl. Those randomized to conventional therapy received IV insulin only when the BG exceeded 215 mg/dl to maintain a glycemic range of less than 180 mg/dl. Those receiving intensive therapy experienced significant reductions

in morbidity, ICU and hospital mortality when compared to the conventionally treated patients. These benefits were observed primarily in those patients with a surgical ICU (SICU) LOS of greater than 5 days.<sup>6</sup>

**Intensive glycemic control in patients with critical illness** Subsequent studies were unable to reproduce the promising results of Leuven 1.<sup>18-20</sup> In the Leuven Medical ICU (MICU) study, intensive insulin therapy resulted in improvements in morbidity and ICU LOS, but not mortality.<sup>20</sup> A 6-fold increase in severe hypoglycemia (BG <40 mg/dl) was observed with intensive therapy, raising safety concerns with protocols targeting tight glycemic control.<sup>20</sup>

A higher incidence of severe hypoglycemia was observed with intensive glycemic therapy in other studies, one of which was terminated early due to safety concerns.<sup>19</sup> One study included patients with severe sepsis, who may be at higher risk for hypoglycemia at presentation.<sup>19,31</sup> The recently published Glucontrol study compared intensive insulin therapy (BG target 80–100 mg/dl) with an intermediate BG target (140–180 mg/dl) in 1101 patients in a mixed MICU/SICU.<sup>32</sup> This study was stopped prematurely due to poor compliance with study protocol. There was more hypoglycemia and no mortality benefit with intensive insulin therapy.<sup>32</sup>

The NICE-SUGAR study (Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation) is the largest RCT of intensive vs. conventional insulin therapy.<sup>18</sup> This study randomized 6104 patients with surgical or medical critical illness to glycemic targets of 81 to 108 mg/dl or 144 to 180 mg/dl. The combined results of more frequent hypoglycemia with a higher mortality at 90 days supported efforts of the consensus committee in reevaluating previously recommended glycemic targets in hospitalized patients.<sup>33</sup>

**Meta-analyses of intensive insulin therapy** There are two recent meta-analyses of intensive insulin therapy in critically ill patients.<sup>16,17</sup> In a study published prior to NICE-SUGAR, the authors concluded that intensive therapy decreased the incidence of sepsis, increased the incidence of hypoglycemia, and did not impact mortality.<sup>17</sup> A second meta-analysis that included NICE-SUGAR confirmed these findings regarding hypoglycemia risk but suggested a mortality benefit with intensive therapy in SICU patients.<sup>16</sup>

**Comparing the Leuven SICU study with subsequent studies** There are several important differences in the conduct of these recent trials that can account in part for the inability to reproduce the benefits observed with intensive insulin therapy in Leuven 1.<sup>6,34</sup> Unlike recent multicenter studies, Leuven 1 was conducted as a single center study, where nursing personnel (who are primarily responsible for implementing any IV infusion

protocol) had the opportunity to become comfortable with the insulin adjustments required to achieve specified glycemic targets. Another major difference among the studies is the source of sampling for BG measurements. In Leuven 1, all samples were obtained from an arterial line with measurement of BG values in the ICU laboratory. In subsequent studies, the source for glucose sampling was either not specified or was variably obtained from arterial, capillary or venous blood and sometimes measured using point of care (POC) meters. As discussed below, these POC meters have major limitations for use in critically ill patients with hemodynamic instability and anemia.

There are differences in the glycemic targets defined for patients randomized to conventional or standard therapy. In Leuven 1, insulin was not started until patients achieved a significant level of hyperglycemia (>215 mg/dl) while in more recent trials, insulin was started once the BG exceeded 180 mg/dl.<sup>18</sup> This resulted in less of a glycemic separation between intensively and conventionally treated subjects.

Other differences include the type of insulin infusion protocol and the specificity of instructions, the type and amount of nutritional supplementation, and differences in the duration of hyperglycemia preceding the intervention. While there is no certainty as to which of these reasons contributed to study differences, it is likely that each of these played some role.<sup>34</sup>

#### Summary of the consensus panel recommendations

There is unequivocal evidence that supports rational glycemic control management as a way of improving clinical outcomes and reducing mortality in the hospital.<sup>9,21,35,36</sup> There is a need for continued efforts to define optimal glycemic targets where these benefits can be achieved without increasing risk for hypoglycemia. The development and implementation of standardized procedures and protocols for achieving and maintaining glycemic targets is essential.<sup>37-39</sup>

Glycemic targets of 80 to 110 mg/dl can no longer be considered appropriate in the majority of critically ill patients. While many hospitals have put forth efforts to develop protocols that achieve these targets, the available evidence does not support the safety or efficacy of continuing this practice.<sup>1,33</sup> While it is possible that these glycemic targets may become acceptable in the future, current technology does not allow protocols targeting euglycemia to be safely implemented in the majority of hospitals.<sup>1,40,41</sup>

Reliable and reproducible glucose measurements are essential for ensuring the safety of any glycemic management program.<sup>40,41</sup> The currently available POC bedside meters present a major barrier to tight inpatient glycemic control. The accuracy of these monitoring devices currently varies by as much as 20% when used appropriately.<sup>40</sup> Anemia results in BG values that are falsely elevated, while polycythemia results in values that

are low. This as well as changes in perfusion and oxygenation can lead to potentially dangerous errors in insulin adjustment.<sup>40</sup> In these situations, measurement of BG in the central or other clinical laboratory provides accurate results.

With these concerns in mind, the glycemic targets recommended by the 2009 consensus panel are summarized below. These targets were selected to promote a rational approach to inpatient glycemic management that avoids a return to uncontrolled inpatient hyperglycemia and minimize risk for hypoglycemia.<sup>1</sup>

**Critically ill patients** Insulin therapy should be initiated for persistent hyperglycemia, starting at a threshold of no greater than 180 mg/dl, with a target range of 140 to 180 mg/dl for the majority of critically ill patients. Lower targets of 110 to 140 mg/dl may be appropriate for SICU patients, provided that the incidence of hypoglycemia is minimized. IV insulin infusions adjusted according to validated protocols with demonstrated safety and efficacy are preferred. Frequent glycemic monitoring guides glycemic management and minimizes risk for hypoglycemia.

**Noncritically ill patients** Recommendations are based on clinical experience and judgment. Fasting and preprandial BG targets generally should be lower than 140 mg/dl and random glucose values below 180 mg/dl. More stringent targets may be appropriate for stable patients with previous tight glycemic control, while less stringent targets may be appropriate for those with severe comorbidities or terminal illnesses.

**Applying the consensus panel guidelines to clinical practice** The relaxation of inpatient glycemic targets from 80 to 110 mg/dl to 140 to 180 mg/dl may have the paradoxical effect of actually improving glucose control in the hospital. There is often a delay between publication and implementation of any change in standard of care.<sup>42</sup> While protocols targeting tight glycemic targets of 80 to 110 mg/dl were implemented in some institutions following the publication of Leuven 1, many other hospitals felt unable to safely implement this target.<sup>43</sup> Prominent among the reasons is concern for hypoglycemia with the potential to adversely rather than favorably impact patient outcomes.<sup>38</sup> A glycemic goal range of 140 to 180 mg/dl provides a safe and achievable target as demonstrated in the conventional therapy arm of the NICE-SUGAR study where there was a low incidence of hypoglycemia and similar patient outcomes to that observed with more intensive therapy.<sup>1,18</sup>

**Patients in critical care areas** IV insulin therapy is the optimal method for achieving glycemic control in the critical care setting. Continuous IV infusions allow for timely titration of insulin in patients with changing clinical status and insulin sensitivity.<sup>31</sup> Commonly encountered situations

that affect insulin requirements include changes in nutrition, and the initiation or discontinuation of vasopressors or glucocorticoids.<sup>44,45</sup> The administration of IV insulin requires careful and frequent monitoring of BG to achieve and maintain desired glycemic targets while also avoiding hypoglycemia. For this reason, many hospitals restrict the use of IV insulin to critical care units.<sup>46</sup>

There are few comparisons of the more than 20 published IV insulin infusion protocols.<sup>47-49</sup> The majority of these protocols are outdated as the target glycemic ranges are lower than what has now been recommended.<sup>1,16,48,49</sup> In general, the safest and most effective protocols are those that take into account the current and previous BG and rate of insulin infusion to guide changes in insulin infusion rates.<sup>44,46,47,49</sup> It is important to ensure that the selected or developed protocol is easy to order and follow, achieves glycemic goals in a reasonable time period, maintains these goals with minimal risk for hypoglycemia, and includes instructions for timely adjustments with changes in nutritional intake or clinical status.<sup>1,49</sup>

**Patients in noncritical care areas** Factors to consider in determining the optimal approach to the management of hyperglycemia in noncritically ill patients include prior history of diabetes and hypoglycemic therapy, the acuity and severity of the underlying illness, the use of concurrent medications (i.e., glucocorticoids, octreotide), and nutritional status.<sup>50</sup> As a general rule, patients treated with insulin as outpatients will require this as inpatients, although the dose may require modification.<sup>51</sup>

Scheduled subcutaneous (SQ) basal:bolus insulin therapy is preferred for the majority of noncritically ill patients with hyperglycemia (TABLE). This is optimally administered as a combination of basal and nutritional or prandial insulin in combination with correction insulin, which refers to the administration of supplemental doses of short- or rapid-acting insulin for BG above desired levels.<sup>21,37,39,52</sup> The practice of discontinuing oral diabetes medications and/or insulin therapy and starting sliding scale insulin (SSI) results in undesirable levels of hypoglycemia and hyperglycemia.<sup>53,54</sup> SSI has been abandoned altogether by some institutions,<sup>55</sup> while others use correction insulin in conjunction with scheduled SQ insulin to regulate BG excursions outside desired range.<sup>37,51,52,56,57</sup>

The safety of scheduled SQ basal:bolus insulin has been demonstrated in two studies that included inpatients with type 2 diabetes.<sup>51,52</sup> In one study, glycemic control was achieved more effectively with basal:bolus insulin than with SSI in insulin-naïve patients with type 2 diabetes.<sup>52</sup> In another study comparing different basal:bolus insulin regimens in the hospital, similar levels of glycemic control were achieved.<sup>51</sup> There were no group differences in hypoglycemia in either of these reports.<sup>51,52</sup>



**TABLE** Calculating the dose of scheduled insulin therapy

obtain patient weight
multiply body weight in kg by 0.2 to 0.5 units/day to obtain total daily insulin dose
for lean patients with newly recognized hyperglycemia or with type 1 diabetes, start with the lower multiplier
for patients who are overweight with mild hyperglycemia, start with a dose of at least 0.3 units/kg/day
for obese patients with known type 2 diabetes and bedside glucose levels >140 and <240, start with 0.4 units/kg/day
for obese patients with known type 2 diabetes or patients receiving glucocorticoid therapy with confirmed bedside glucose levels >240 mg/dl, start with 0.5 units/kg/day
distribute total calculated dose as approximately 50% basal insulin and 50% nutritional insulin

Using these studies as a guide, one method for determining the starting dose of scheduled insulin therapy in the hospital is based on a patient's body weight and administered as a range of 0.2 to 0.5 units/kg as the total daily dose (TABLE). Approximately 50% of the calculated dose is administered as basal insulin and 50% as prandial or nutritional insulin in divided doses. Adjustments of insulin doses are based on results of bedside glucose monitoring to achieve glycemic targets and minimize risks for hypoglycemia. An alternative method for calculating the total daily insulin dose is based on the amount of correction insulin administered over the preceding 24 h and distributing this into basal and nutritional components.

There are few situations where correction insulin may be used as monotherapy for a short duration (<24–48 h).<sup>4,37,57</sup> This includes patients with no prior diabetes history and an elevated admission glucose, or those who begin therapy with corticosteroids, or enteral or parenteral nutrition which are known to be associated with a high frequency of hyperglycemia.<sup>15,56,58</sup> Once an insulin requirement is established, a change to scheduled basal:bolus insulin therapy is recommended.

The use of scheduled SQ insulin in specific patient populations is addressed below.

**Transitioning patients from intravenous to subcutaneous insulin** As critically ill patients begin to eat regular meals or are transferred to regular nursing units, they require transition from IV to SQ insulin to maintain reasonable levels of glycemic control.<sup>36,59</sup> The initial dose and distribution of SQ insulin at the time of transition is determined by the current IV insulin requirement with consideration of a patient's nutritional status and use of other medications.<sup>60</sup>

**Patients receiving glucocorticoid therapy** Hyperglycemia is common in patients who receive high dose glucocorticoids,<sup>58,61</sup> with the most significant effect usually on postprandial BG.<sup>58,62</sup> Glycemic monitoring for at least 48 h is recommended for all patients receiving high-dose glucocorticoids.<sup>58</sup> While the optimal management of these patients has not been clearly defined, insulin is

generally preferred, with an emphasis on adjusting doses of prandial insulin.<sup>62</sup> Insulin requirements vary among patients in response to steroid therapy. Gradual persistent adjustments in insulin according to POC BG results is recommended to avoid severe hyperglycemia and hypoglycemia.<sup>61,63</sup> Patients without insulin use may initially receive correctional insulin, with timely initiation of basal:bolus insulin based on correctional insulin requirements. For insulin treated patients, preemptive increments in total insulin doses of approximately 20% are usually safe, with ongoing adjustments according to correctional insulin requirements.<sup>63</sup> A suggested alternative emphasizes proactive use of intermediate or long-acting insulin.<sup>64</sup>

**Patients receiving enteral nutrition** Safe glycemic management of patients receiving enteral nutrition is complicated by variability in type and duration of nutrition delivery and unanticipated discontinuation of nutrition with use of basal insulins.<sup>56,57,65</sup> In one study, glargine in combination with SSI resulted in a similar level of glycemic control as SSI without an increase in risk for hypoglycemia.<sup>56</sup> Approximately 50% of patients randomized to SSI required intermediate-acting insulin to achieve glycemic control.

**Patients admitted with continuous subcutaneous insulin infusion pumps** Patients who use continuous subcutaneous insulin infusion (CSII) therapy as outpatients can be allowed to continue this in the hospital provided that they have the mental and physical capacity to do so.<sup>66,67</sup> The availability of hospital personnel who have familiarity with CSII therapy and can assist with changing insulin delivery rates is essential to an effective CSII program. Patients who are unable to continue CSII due to mental or physical impairments can be converted to basal:bolus insulin. The long- or intermediate-acting insulin dose approximates the total of all basal rates over a 24 h period. For example, a patient with an hourly CSII basal rate of 0.5 u/h would be converted to 12 units of long- or intermediate-acting insulin administered once or twice a day in divided doses. The prandial insulin dose approximates the doses administered while the patient was using CSII. If this information is not known, a weight based approximation can be made as a starting point of therapy (TABLE).

**Oral and injectable noninsulin agents** While insulin is the agent of choice for the timely management of hyperglycemia in the hospital, oral and injectable noninsulin glucose-lowering agents may be appropriate for selected noncritically ill patients, such as those who ingest regular meals and do not have contraindications.<sup>1,21</sup> In general, however, these agents have a limited role for hospital use and are limited to patients with mild hyperglycemia or those who used these agents as outpatients.<sup>21,68</sup> One reason for the insulin

preference is that time-action profiles of oral and injectable noninsulin hypoglycemic agents which do not allow rapid titration to achieve desired glycemic targets. The long half-lives of many of these agents do not allow for unanticipated changes in insulin sensitivity in acutely ill patients.<sup>1,21</sup>

Sulfonylureas (SU), which are long-acting insulin secretagogues, are associated with severe and prolonged hypoglycemia in patients with reduced or limited oral intake.<sup>69</sup> This risk is amplified in patients with renal insufficiency.<sup>70</sup> There is no data related to inpatient use of the short-acting insulin secretagogues, repaglinide and nateglinide, which may offer some advantage over the SU agents in that they are administered prior to meals and can be held in patients who are not eating. However, the risk of hypoglycemia may be similar to that with SU in the outpatient setting, suggesting caution in the inpatient setting.<sup>71</sup>

Metformin is contraindicated with any decline in renal function, such may occur with administration of IV contrast dye, which increases risk for lactic acidosis.<sup>72</sup> Risk factors for lactic acidosis in metformin-treated inpatients include cardiac disease, decompensated chronic heart failure, hypoperfusion, renal insufficiency, advanced age, and chronic pulmonary disease.<sup>73</sup> Thiazolidinediones are contraindicated in any patient with congestive heart failure or in those with hemodynamic instability.<sup>71</sup>

Pramlintide, exenatide, and the dipeptidyl peptidase inhibitors act primarily to reduce postprandial BG excursions and would not be appropriate for patients who are not eating or have reduced oral intake. Pramlintide and exenatide are administered by injection and are associated with a high frequency of nausea and vomiting.<sup>74</sup> There is limited experience, and no published data, on inpatient use of these agents.

In summary, each of the major classes of noninsulin glucose-lowering agents has significant limitations for inpatient use. Additionally, they provide little flexibility or opportunity for titration in a setting where acute changes often demand these characteristics. Therefore, insulin, when used properly, is preferred for the majority of hyperglycemic patients in the hospital setting.

### **Inpatient glycemic management and patient safety**

Hypoglycemia is the major safety concern associated with any program that intensifies glycemic management in the hospital.<sup>38,75</sup> Although it may not be possible to avoid all risk of hypoglycemia in the hospital, the risk can be reduced by coordinating premeal insulin with meals, and adjusting insulin according to changes in clinical or nutritional status.<sup>76,77</sup> The availability of nurse-directed hypoglycemic treatment protocols allow for immediate treatment of a mild event, reducing the progression to more severe or prolonged events with untoward consequences.<sup>78-80</sup>

Another aspect of safe management of inpatient hyperglycemia is directly related to the appropriate use of glucose-lowering agents and

insulin, as well as POC glucose monitoring. As discussed in the previous section, some oral and noninsulin glucose-lowering agents can pose dangers to patient safety when used in settings that enhance risk for hypoglycemia or other conditions, such as lactic acidosis or chronic heart failure.

Due to risk for significant harm when used incorrectly, insulin is considered a high-alert medication by the Institute for Safe Medication Practices.<sup>37</sup> There are steps that hospitals can take to promote safe use of insulin. These include standardizing concentrations for all IV insulin infusions prepared by the hospital pharmacy and educating hospital personnel about appropriate inpatient glycemic management practices.<sup>1,77,81</sup>

Safe inpatient glycemic management cannot be accomplished by an individual physician, nurse or pharmacist. It is important that hospitals provide support for the formation of a multidisciplinary committee dedicated to guiding glycemic management protocols that are specific to an institution.<sup>38</sup>

**Conclusions** Hyperglycemia in hospitalized patients is common and associated with adverse outcomes. While early studies suggested improved clinical outcomes with protocols targeting near euglycemia, the consistency of more frequent hypoglycemia in more recent RCT resulted in modification of glycemic goals to more moderate BG targets of 140 to 180 mg/dl. This represents a safe and achievable target that minimizes risk associated with uncontrolled hyperglycemia and hypoglycemia. Insulin administered as IV infusions in critical care or SQ basal:bolus therapy in noncritical care areas is the preferred method for achieving desired glycemic targets. Proper education, the ability to obtain reliable and reproducible BG measurements, appropriate administration of insulin, and careful implementation of standardized protocols are essential elements of an inpatient glycemic management program.

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# Praktyczne implikacje nowych wytycznych dotyczących kontroli glikemii u chorych hospitalizowanych

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## SŁOWA KLUCZOWE

cukrzyca, hiperglikemia, insulina, pacjenci hospitalizowani, szpital

## STRESZCZENIE

Dane obserwacyjne potwierdzają niekorzystne skutki hiperglikemii u hospitalizowanych pacjentów. Początkowe badania rekomendowały poprawę punktów końcowych u tych pacjentów poprzez osiągnięcie stanów bliskich euglikemii. Ostatnie badania dają odmienne wyniki – zwracają uwagę na niebezpieczeństwo ciężkich hipoglikemii wskutek powyższego postępowania. Mając to na uwadze, The American Association of Clinical Endocrinologists i American Diabetes Association opublikowały konsensus dotyczący postępowania z hospitalizowanymi pacjentami z hiperglikemią. W konsensusie tym określono rozsądne, osiągalne i bezpieczne wartości docelowe glikemii, i przedstawiono protokoły leczenia. Pozwalają one zminimalizować ryzyko towarzyszącej leczeniu niekontrolowanej hiper- i hipoglikemii. Rekomendowane są dożylnie infuzje insuliny u pacjentów w stanie ciężkim, z glikemią > 140 mg/dl. Celem leczenia są wartości glikemii z zakresu 140–180 mg/dl. Niższe zakresy docelowe glikemii (np. 110–140 mg/dl) mogą być odpowiednie dla pacjentów po zabiegach kardiochirurgicznych. U pacjentów niebędących w ciężkim stanie zalecaną formą leczenia hiperglikemii jest insulinoterapia podskórna. Celem leczenia są wartości glukozy we krwi na czczo i przedposiłkowe < 140 mg/dl, ze średnimi glikemiami < 180 mg/dl. Docelowe wartości glikemii mogą być niższe lub wyższe, w zależności od stanu klinicznego pacjenta. Nie zaleca się długiego leczenia korekcyjnymi dawkami insuliny stosowanymi wyłącznie w przypadku znacznych hiperglikemii. Inne środki hipoglikemizujące (poza insuliną) mają ograniczone znaczenie w terapii szpitalnej i mogą być stosowane u pacjentów w dobrym stanie. Edukacja personelu medycznego na temat właściwego leczenia stanów hiperglikemii w warunkach szpitalnych, osiąganie wiarygodnych, powtarzalnych pomiarów glikemii, ostrożne wprowadzanie w życie przyjętych protokołów leczenia pomogą zapewnić bezpieczeństwo terapii.

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