Designing and Implementing Insulin Infusion Protocols and Order Sets

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Influential trials and guidelines supporting the value of glucose control in hospital settings, particularly in the intensive care and postoperative settings, has led to the widespread adoption of intravenous infusions of human regular insulin. As groups have attempted to study the outcomes or to explore improved methods for improved glucose control, a number of insulin infusion protocols (IIPs) have been reported and validated. Now, many institutions are attempting to translate this experience into clinical practice in a systematic manner. The intent of this discussion is to highlight the authors’ practical view of best practices in development and use of IIPs.

As the implementation of IIPs has progressed, it has become apparent that this is not a simple process. It requires a carefully planned, inclusive, and continuous effort striving to attain effective glucose control while avoiding severe hypoglycemia. Whereas there are limitations in the literature comparing the IIPs, we identify design elements and implementation methods that increase the chances for staff acceptance and safe attainment of glycemic goals. Most importantly, this must be a team effort with attention to the numerous potential pitfalls that can disrupt the process and place patients at risk.

In many cases, it is best to start more conservatively and methodically intensify the protocol. Continuous assessment of protocol errors, adverse events, staff satisfaction, and outcomes is vital to overall success. Journal of Hospital Medicine 2008;[5 Suppl]:42–54. © 2008 Society of Hospital Medicine.

KEYWORDS: intravenous infusion, insulin, critical care protocols, best practices.

The delayed and variable absorption of subcutaneous (SC) insulin has always provided challenges for the rapid and predictable control of hyperglycemia in the acute care setting. Conversely, intravenous infusion of human regular insulin provides a continuous and essentially immediate delivery mechanism. Once in the circulation, insulin has a very short half-life of about 5 to 7 minutes and a biological effect of about 20 minutes. Intravenous insulin infusions are well-established in several acute care settings including hyperglycemic emergencies, perioperative glucose management, and glucose control during labor and delivery.

The beneficial effects seen in early trials of strict glycemic control involving intensive care unit (ICU) patients (particularly cardiac surgery patients) and guidelines for inpatient glycemic control stimulated widespread interest in adopting insulin infusion protocols (IIPs) focused on achieving strict glycemic targets. The initial enthusiasm has been tempered by uneven results in trials of tight glycemic control, concerns about the effects of excessive hypoglycemia, and the resources needed to
implement and maintain an IIP. Although considerable controversy about the ideal glycemic target for different patient populations exists, and will likely continue for some time, this article is not a review of the evidence for supporting 1 glycemic target versus another. Regardless of the glycemic target chosen, a standardized algorithm and accompanying program of monitoring are widely endorsed for both safety and quality reasons. Most medical centers are at least attempting to implement nurse-driven protocols that have demonstrated better performance than SC regimens and physician-driven insulin infusions. In this article, we outline several variables in IIP design and implementation and endorse several aspects of design and implementation that will likely result in improved staff acceptance and, ultimately, a more safe and effective IIP.

PREPARING TO IMPLEMENT AN IIP

Building The Team
Implementing a medical center–wide standardized insulin infusion order set with supporting policies, protocols, monitoring standards, and the requisite educational programs is a major task for any hospital. This is not a simple maneuver involving only 1 or 2 interested individuals and requires much more than selecting a published protocol and disseminating it to various patient care units. Instead, to manage the full spectrum of diabetes programs and protocols, an institution must convene a multidisciplinary steering committee or task force. This should include representation from nursing, nursing administration, pharmacy, nutrition services, and the quality improvement department. Physicians should include hospitalists, intensivists, and endocrinologists but may also involve anesthesiologists and surgeons, as applicable. At times, additional members may need to be recruited according to project needs.

Identifying the Stakeholders and Current Practices
In developing or improving currently utilized IIPs, the multidisciplinary committee would benefit from careful background work before moving forward. First, administrative and institutional support must be secured to endorse uniform standards for insulin infusions, and to provide the important infrastructure needed to facilitate the work involved. Clinical and administrative stakeholders from the key departments then need to be identified.

All insulin infusion orders and policies/procedures presently used in the institution should be identified and examined. The developers and/or users of these order sets should be engaged in a dialogue and encouraged to share their experiences regarding their current practice and the attendant workflow, glucose monitoring, and data collection and reporting. Immediate concerns should be clearly addressed. Measurement systems for glycemic control, hypoglycemia, and insulin use patterns should assess current practice and the impact of subsequent modifications of the protocol or initiation of new protocols. We recommend using “glucometrics” consistent with those endorsed by the Society of Hospital Medicine (SHM) Glycemic Control Task Force elsewhere in this supplement.

Addressing the Burden of Change
Through this process, the committee will uncover barriers, dysfunctional and inconsistent practices, and individuals who will pose challenges. Identifying these issues should not discourage the team, but rather it should guide the interventional strategies, and help build consensus that change may be required. There must be caution not to exclude significant individuals simply because they resist changes. Indeed, if they are included and have the opportunity to contribute to the process, success is much more likely.

It is important for process leaders to understand the implications of what is proposed, particularly for nursing services. For example, it has been shown that IIPs require about 5 minutes per patient per hour for glucose monitoring and dose adjustments. Acknowledging and attempting to address this burden proactively (often well over 2 hours per day) can gain staff acceptance more effectively than a laissez faire approach. In this regard, some effort should be invested in nursing education of the benefits of tight glycemic management on critical care outcomes. The difficult-to-quantify work involved when patients’ blood glucose is not well controlled (eg, paging physicians for stat insulin orders) should also be part of this discussion.

Identifying and Addressing Barriers to IIP implementation
There are numerous potential barriers to implementation of IIPs. Table 1 identifies some of the
most frequent ones along with potential strategies or solutions. Very common barriers include skepticism surrounding the benefits of tight glycemic control, fear of hypoglycemia, and difficulty agreeing on glycemic targets.

Whereas the national guidelines call for a glycemic target in critical care areas with an upper limit of 110 mg/dL, there is room for debate, and tailoring of the glycemic target to fit individual patient circumstances is often advisable. Starting with a less aggressive glycemic target can be good politics (and perhaps good medicine as well). Once the higher glycemic targets are achieved safely, it can pave the way for a more aggressive approach.

Fear of hypoglycemia is one of the most potent barriers to intensive insulin infusion implementation. Because hyperglycemia is such a common condition in critical care units, nursing and physician staff may have developed a skewed view of the definition of hypoglycemia, at times fearing for their patient when the glucose values reach a level of 100 mg/dL or so. Polling the nurses on what they think their own fasting glucose levels are, and then actually measuring them can be an effective strategy (the nurses may be surprised that the patient’s “scary” 90 mg/dL reading is higher than their own). It should also be emphasized that properly designed and implemented protocols may actually decrease the incidence of hypoglycemia when compared to “standard care” which may involve individually and sometimes improperly adjusted intravenous (IV) insulin (discussed further below).

### CHOOSING AN IIP FOR YOUR HOSPITAL

See Table 2 for a comparison of several features identified in selected published protocols.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Strategy/Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient glucose meters to accommodate the increased testing needs</td>
<td>• Purchase additional glucose meters.</td>
</tr>
<tr>
<td></td>
<td>• Ask the vendor to provide extra on-site replacement meters at no charge until they are activated.</td>
</tr>
<tr>
<td>Nursing time requirements involved in monitoring and adjustments.</td>
<td>• Get ancillary help to check glucose values</td>
</tr>
<tr>
<td></td>
<td>○ eg, nurse assistants</td>
</tr>
<tr>
<td></td>
<td>• Make extra efforts to make protocols clear with few required calculations</td>
</tr>
<tr>
<td></td>
<td>• Avoid duplicate recording</td>
</tr>
<tr>
<td>Requirement for uncomfortable frequent sticks</td>
<td>• Utilize central lines or arterial lines.</td>
</tr>
<tr>
<td></td>
<td>○ These tend to vary by &lt; 10% from POC readings</td>
</tr>
<tr>
<td></td>
<td>○ May not be available in non-critical care settings</td>
</tr>
<tr>
<td>Staff fear of hypoglycemia</td>
<td>• Educate on the benefit of glucose control and the true definition of hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• Measure staff fasting glucose levels to demonstrate normal range.</td>
</tr>
<tr>
<td></td>
<td>• Establish metrics and publicly report hypoglycemia event rates.</td>
</tr>
<tr>
<td></td>
<td>• Pilot IIP on small scale</td>
</tr>
<tr>
<td></td>
<td>• Protocol and education for prevention of hypoglycemia.</td>
</tr>
<tr>
<td>Difficulty gaining consensus on glycemic target</td>
<td>• Compromise if needed on the glucose target</td>
</tr>
<tr>
<td></td>
<td>○ eg, start with a higher goal such as 90-140 mg/dL.</td>
</tr>
<tr>
<td></td>
<td>○ Others will be willing to lower the goal when feasibility is seen.</td>
</tr>
<tr>
<td></td>
<td>• Allow for different targets in different units if indicated</td>
</tr>
<tr>
<td></td>
<td>○ maintain consistency in other respects.</td>
</tr>
<tr>
<td>Focal points of resistance</td>
<td>• Identify a local nurse or physician champion within resistant site.</td>
</tr>
<tr>
<td></td>
<td>• Pilot the protocol in an area with least resistance</td>
</tr>
<tr>
<td></td>
<td>○ Will gain momentum with initial success and adjustments</td>
</tr>
<tr>
<td>Lack of integrated information and reporting systems</td>
<td>• Incorporate information systems personnel onto team</td>
</tr>
<tr>
<td></td>
<td>• Advocate for improved reporting capability with administrative leaders</td>
</tr>
<tr>
<td></td>
<td>• Use sampling methods to collect data until automated systems are available.</td>
</tr>
<tr>
<td>Multiple providers, hand offs, and opportunities for error and communication breakdown, diffusion of responsibility for glycemic control</td>
<td>• Involvement of varied front line providers</td>
</tr>
<tr>
<td></td>
<td>• Check lists for important items to communicate on transfer/transport</td>
</tr>
<tr>
<td></td>
<td>• Common protocols/education for similar units</td>
</tr>
</tbody>
</table>

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This is not a comprehensive list of all protocols found in the literature. Rather, the authors consider it representative of the various types of IIPs.
<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>IIP Description</th>
<th>Patient population</th>
<th>Glucose Target (mg/dL)</th>
<th>Mean Glucose (mg/dL)</th>
<th>Time to Reach Target Hypoglycemia</th>
<th>Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van den Berghe7/21</td>
<td>Initial and subsequent rates based on BG • Nurses had latitude • TPN standard with IIP</td>
<td>Surgical ICU</td>
<td>80-110</td>
<td>6 AM glucose 103 ± 19</td>
<td>Not reported</td>
<td>5.1% of patient &lt; 41 mg/dL</td>
</tr>
<tr>
<td>Van den Berghe21</td>
<td>Initial dose determined by BG and type of DM • Changes based on present BG and last change • Relatively complex</td>
<td>Medical ICU</td>
<td>80-110</td>
<td>6 AM glucose 105</td>
<td>Not reported</td>
<td>19% of patients &lt; 41 mg/dL</td>
</tr>
<tr>
<td>Furnary22 (2001-2003 version)</td>
<td>Initial dose determined by BG and type of DM • Changes based on present BG and last change • Relatively complex</td>
<td>CABG</td>
<td>100-150 (there is a newer protocol with lower targets)</td>
<td>Not mentioned. Appears to be &lt; 150</td>
<td>&quot;94% within 3 hours&quot;</td>
<td>0.5% &lt; 60 (% of readings?) Not reported with any specificity</td>
</tr>
<tr>
<td>Goldberg23</td>
<td>Dosing based on: • Current BG • Velocity of glucose change</td>
<td>MICU</td>
<td>100-139</td>
<td>Not specified</td>
<td>10.1 hours</td>
<td>0.3% of readings &lt;60 BG &lt;60 in 5.4% of patient days</td>
</tr>
<tr>
<td>Goldberg24</td>
<td>Infusion rate • Uses 3 tables • Relatively complex</td>
<td>CT Surgery</td>
<td>100-139</td>
<td>122 ± 17 Once target attained.</td>
<td>5 hours</td>
<td>0.2% of all BGs &lt; 60 mg/dL &lt; 60 in 2.9% of patient days</td>
</tr>
<tr>
<td>DeSantis25</td>
<td>Initial dose based on BG • Changes based on present glucose and rate of change • IV bolus used with changes.</td>
<td>Mostly surgical ICU and CVICU (75% surgical)</td>
<td>80-110</td>
<td>135 ± 49 (higher in SICU and CVICU alone)</td>
<td>10.6 hours</td>
<td>1.5% of readings &lt; 60 mg/dL (lower for CVICU &amp; SICU alone)</td>
</tr>
<tr>
<td>Braithwaite26</td>
<td>6-column method</td>
<td>Trauma ICU</td>
<td>&lt;110 mg/dL</td>
<td>129 ± 25</td>
<td>16.7 hours</td>
<td>2.4% of readings &lt; 70 mg/dL</td>
</tr>
<tr>
<td>Davidson27</td>
<td>Computer-directed algorithm (similar to column method)</td>
<td>Full spectrum</td>
<td>Varied by year and situation</td>
<td>Not reported (approximately 125 mg/dL when stable)</td>
<td>90% &lt; 150 mg/dL in 3 hours</td>
<td>0.6% of readings &lt;50 mg/dL 2.6% of patients</td>
</tr>
</tbody>
</table>
or best recognized IIPs in the literature. Note that there is variability in study population, the glucose targets, hypoglycemia, the time to reach the target, and the time spent in the target range. Other practical factors to consider in reviewing the literature and selecting an IIP design are the complexity of the protocol, the required process steps or calculations, the evidence for staff acceptance, and the level of resources supporting the published protocol.

Structural Differences in Protocols
Protocols that vary by level of insulin sensitivity generally use column methods with the individual columns representing different categories of insulin sensitivity, placing the most sensitive category on the left with the highest level of insulin resistance on the far right. These methods use a multiplier to adjust for sensitivity. They are constructed according to the “rule of 1500, 1700, or 1800,” thereby adjusting for changes in insulin sensitivity that follow surgery or other changes in physiologic stress in the acute setting. “Rate of change” is addressed by shifting to the right if correction of hyperglycemia is too slow and to the left if the glucose is dropping too rapidly.

Most institutions using the column/insulin sensitivity method, implement “paper” orders as first published by Markovitz. The same concepts have been used to develop computer-assisted insulin infusion protocols. One published method is the Glucommander, but a number of institutions are using similar computer-assisted methods developed locally.

Other methods use the present glucose and change from last glucose to constantly adjust to any situation. They usually involve 2 or 3 steps and often require more calculations by the nurse. These methods are purported to be more agile or flexible but there have been no direct comparisons with the column methods looking at effectiveness, nursing errors, or hypoglycemic risk. The “Yale Protocol” and the “Portland Protocol” are 2 prominent examples of this type of protocol. Adjustments are defined as units, percent change, or a combination of both.

Limitations of the IIP Literature
There had been few published insulin protocols aimed at reaching specific glucose goals when the Leuven surgical ICU experience was published in 2001. These early publications featured algorithms that adjusted insulin infusions solely on the basis of glucose level, and did not take the velocity of change, direction of change, proximity to glycemic target, or different insulin sensitivities into account. Also, the targeted glucose goals in those reports were not consistent with the present standards. Other published protocols featured glucose-insulin-potassium infusion (GIK) protocols that focused on the amount of insulin administered and failed to attain appropriately defined glucose targets. These publications offer no real guidance in crafting a modern glycemic target-oriented protocol.

Whereas more than 20 modern IIPs directed at glycemic targets have been published, many of the published protocols represent local modifications of ones previously published elsewhere, and no published, prospective, head-to-head comparisons of the best-known IIPs are available.

Several reviews of previous published reports include comparisons of IIPs with varied areas of emphasis. The reliability of such comparisons is limited by the inconsistency in methodology between studies and the different populations studied. For example, medical populations are generally harder to control and are more prone to hypoglycemia than surgical populations, and some studies include only patients with diabetes. In addition, definitions of hypoglycemia and methods of analyzing glycemic control are highly variable, making comparisons of IIPs challenging. As a result, attempts to compare published IIP results without consideration of the population studied could lead to erroneous conclusions.

In spite of the aforementioned limitations, there are several lessons we can learn from the IIP literature and accumulated clinical experience at a variety of centers.

Glycemic Targets and Other IIP Features Can Evolve over Time
Revisions of protocol details, including glycemic targets, often evolve over time. This deliberate approach can facilitate staff acceptance by demonstrating safe achievement of higher glycemic targets. The Yale team initially selected a conservative glycemic target of 100-139 mg/dL, as depicted in Table 1. They subsequently low-
erected the target range to 90-119 mg/dL and increased the initial insulin bolus amount by 40%.\textsuperscript{50} The modified protocol displayed improved performance and yet retained safety, with only 1 glucose reading < 40 mg/dL in 101 patients over 117 runs of insulin infusion.

The Portland Protocol, used primarily in cardiac surgery patients, has also evolved over time. This group has altered the IIP in a number of ways at least 4 times. These protocols, including the most recent protocol targeting glucose levels of 70-110 mg/dL, is found at www.portlandprotocol.org.\textsuperscript{4,5,55,56}

\textbf{Medical and Surgical Patients Are Different}

The most convincing evidence for stringent glycemic control evolved from studies of surgical patients.\textsuperscript{4,5,7} Acknowledging this fact, along with the greater degree of difficulty in achieving glycemic targets safely in critically ill medical patients, have led many to endorse higher glycemic targets for certain populations than others.\textsuperscript{57} Although we generally favor a uniform glycemic target for a unit serving a particular patient population, adopting a less stringent glycemic target for a unit serving a particular patient population, several different IIP regimens have frequently achieved identical or very similar glycemic control with less than 5% of the patients experiencing severe hypoglycemia.\textsuperscript{27,50,62} Although implementation factors, severity of illness, and other population factors play some role, some protocols have an inherent structural propensity to produce more hypoglycemia than others. In the case of the Leuven protocol, there is more of a role for clinician adjustment, and the written protocol itself does not call for much active adjustment as the patient enters into the hypoglycemic range.\textsuperscript{52} In contrast, more sophisticated and complicated regimens adjust more aggressively in this range and consistently induce less hypoglycemia.

Local Factors and Implementation Methods Matter

The success or failure of a protocol likely depends on local factors and implementation methods as much as it does on the structure of the protocol itself. IIP development and implementation is a process that must be approached systematically and with attention to detail.\textsuperscript{19} Errors in approach can delay or abort the implementation, or potentially lead to an ineffective or unsafe protocol for the institution.

The Yale experience again provides us with a salient example.\textsuperscript{58} Initial efforts to implement an IIP failed due to a number of factors: a complicated protocol, insufficient nursing involvement, and inadequate training and education led to incomplete buy-in, and nursing concerns over “hypoglycemia” that actually was within the goal range of the protocol. Successful implementation was not achieved until the leaders learned from their mistakes. Nurses and other clinical allies were involved and educated. Important stakeholders, who were not included earlier, were now involved, and front-line nursing staff were engaged in proactive troubleshooting.

In another example, multisite studies like VISEP\textsuperscript{59} and Glucontrol\textsuperscript{9} have tried to adapt the Leuven protocol, only to struggle with excessive hypoglycemia and an inability to replicate the tight glycemic control enjoyed by van den Berghe and colleagues.\textsuperscript{7,21} The Leuven care team augmented the performance of the IIP by their experience with the protocol, physician involvement, and adjustments made by the nursing staff.

\textbf{Some IIPs Have Lower Hypoglycemia Rates than Others}

Recent articles have highlighted the association of intensive insulin treatment, hypoglycemia, and mortality in the medical ICU population.\textsuperscript{60} Concerns that excessive hypoglycemia could reduce or reverse the overall benefits of intensive insulin therapy has led some to call for moderation of critical care glycemic targets.\textsuperscript{61} Comparisons of IIPs\textsuperscript{52-54,61} that include information about the propensity of the IIP to produce hypoglycemia are therefore important.

The Leuven IIP has been reported to yield high rates of hypoglycemia with almost 20% of patients suffering from severe hypoglycemia (glucose < 40 mg/dL) in some studies.\textsuperscript{9,21,59} By way of contrast, several different IIP regimens have frequently achieved identical or very similar glycemic control with less than 5% of the patients experiencing severe hypoglycemia.\textsuperscript{27,50,62} Although implementation factors, severity of illness, and other population factors play some role, some protocols have an inherent structural propensity to produce more hypoglycemia than others. In the case of the Leuven protocol, there is more of a role for clinician adjustment, and the written protocol itself does not call for much active adjustment as the patient enters into the hypoglycemic range.\textsuperscript{52} In contrast, more sophisticated and complicated regimens adjust more aggressively in this range and consistently induce less hypoglycemia.

\textbf{Successful Methods to Manage the Complexity of an IIP}

Many modern IIPs use bolus insulin to expedite control and adjust the infusion rate based on the velocity and direction of glucose change, not just the glucose value.\textsuperscript{52} Insulin resistance is taken
into account in some models, and multiple calculation steps are required in several reported protocols.\textsuperscript{52} The improved automation and control refinements come at a cost of increased complexity.

Intensive implementation efforts and strong leadership can overcome some issues, as demonstrated by the Yale experience, but 2 other strategies have commonly demonstrated success. First, focused expert glycemic management teams that directly oversee many aspects of the IIP, or even assume direct management roles, can be quite effective,\textsuperscript{25} especially during early implementation.

Automation of calculations and computerization is another method to consider, and many recent reports involve applications of web-based or other computerized models.\textsuperscript{27,40,42,43,46,48,63} Comparisons of computerized versus manual methods, computerized versus column methods, and a computerized nomogram-versus-chart method are now available.\textsuperscript{42,45,46,48,62} Computerized protocols show significant promise and would be expected to reduce dosing errors. These instruments generally present the nurse with a specific infusion rate after each monitored glucose and then recommend an interval for the next glucose determination. In direct comparisons, they tend to perform as well or often better than conventional methods. For example, in the most recent randomized trial comparing the Glucommander to a paper-based column method in an ICU, Newton and colleagues found the computerized method reached the goal more rapidly and reached a lower mean glucose without increasing the rate of severe hypoglycemia (< 40 mg/dL).\textsuperscript{62} Computerized methods also facilitate data collection for analytical purposes.

Computerized systems (both commercial and home-grown versions) are becoming more common and appear to hold significant benefits as long as they are backed by a validated algorithm. Whereas many institutions are not yet in a position to integrate such protocols into their standard or electronic record systems, we expect the trend for increased implementation to continue.

**ENHANCING THE DESIGN OF YOUR IIP**

Once the improvement team has identified and examined current order sets and protocols in the context of the literature, we encourage consolidation of institutional insulin infusion orders into a common basic structure. This basic structure should be enhanced by incorporating a variety of elements designed to enhance the reliability of use and safety of the IIP. These design features are outlined in Table 3. Randomized trial evidence of the effectiveness of these design features are largely lacking, but they are well grounded in reliability principles and common experience, and have also been recommended by others.\textsuperscript{10–13,58}

The orders should require a single physician signature and limited physician choices as the vehicle initiating the nurse-driven protocol. The glycemic target range should be explicitly identified, and guidance for calling the physician and how to handle interruptions in nutrition should be embedded in the order set. Frequent monitoring of glucose levels is necessary for the safe infusion of insulin. Guidance for how often the monitoring is required must be explicit and included in the infusion order set, and standardization of documentation of the infusion rates and glucose values is highly desirable. IIPs that adjust based on the velocity of glucose change and insulin sensitivity are desirable. Certain elements may be more appropriate for some institutions than others, partly based on previous protocols and methods of practice. For example, the hypoglycemia protocol may be embedded or referred to as a separate standard of care with clear presence in the chart. The intended timing of conversion from IV to SC insulin should be included, but the actual method may be the subject of a separate order set. At other times, the conversion formula will be part of the initial intravenous order set.

![Table 3](image-url)

**Table 3**

<table>
<thead>
<tr>
<th>Ingredients for Insulin Infusion Protocol Orders</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Identifies the glycemic target range</td>
</tr>
<tr>
<td>□ Includes clear dosing instructions with acceptable calculation requirements for nurses</td>
</tr>
<tr>
<td>□ Incorporates glucose monitoring expectations</td>
</tr>
<tr>
<td>□ Easy physician ordering, check box simplicity</td>
</tr>
<tr>
<td>□ Criteria for calling the physician</td>
</tr>
<tr>
<td>□ Includes guidance on steps to follow for interruption of nutrition</td>
</tr>
<tr>
<td>□ States guidelines on when to initiate the infusion and when to stop</td>
</tr>
<tr>
<td>□ Defines the insulin concentration clearly and consistently</td>
</tr>
<tr>
<td>□ Considers changing insulin sensitivity as well as the current glucose value and rate of change in attempting to reach goal and avoid hypoglycemia</td>
</tr>
<tr>
<td>□ Includes or refers to a standardized hypoglycemia treatment protocol and prevention protocol</td>
</tr>
<tr>
<td>□ Incorporates guidelines and cautions for transition to subcutaneous insulin</td>
</tr>
<tr>
<td>□ Ideally adaptable outside of critical care unit—clear definition of locations where order set is to be used</td>
</tr>
</tbody>
</table>

\[<40 \text{ mg/dL}\]
IMPLEMENTATION: ADDRESSING SAFETY ISSUES

The use of insulin infusions comes with several potential hazards. Many of these potential complications can be proactively addressed, thereby minimizing accidental injuries to the patient on an insulin infusion.

Standardizing Insulin Infusion Preparations and Priming New Tubing

Varied concentrations or types of insulin for insulin infusions can lead to serious errors. Insulin infusions should generally be centrally prepared with a standard concentration of regular insulin in the pharmacy (usually 1 unit/cc), and the infusion concentration should be included in your infusion order set. Insulin binding to IV tubing can lead to false elevation of insulin requirements, potentially followed by serious hypoglycemia. When nurses change IV tubing or initially set up an insulin drip, education/instructions on priming new tubing with a small amount of insulin infusion to saturate the binding to the polyvinyl chloride tubing should be incorporated into their routine. Although 50 mL has often been recommended for priming, a recent study found that 20 mL of insulin infusion is enough to reach the saturation point.

Avoiding Over-Reliance on the Insulin Protocol

Nurse-driven insulin infusion protocols automate frequent insulin adjustment and reduce unnecessary calls to the physician. Although this is generally a decided advantage, the care team can be lulled into a sense of false security by the presence of orders that allow for such adjustment. Increasing the rate of an insulin infusion without thoughtful attention to factors that may be playing a role in this increased requirement (such as developing sepsis, other medical decompensation, steroid boluses, or an increase in carbohydrate intake) can have serious consequences. By the same token, an unanticipated rapid decrease in insulin requirement should lead to a reassessment of the infusion, and an inquiry about cessation of glucocorticoid therapy or nutrition. Rarely, a pharmacy or nursing error may induce a pseudo-change in insulin requirements. The protocol should lead the nurse to seek advice and alert the physician to review potential causes of dramatic changes in insulin requirements, rather than simply adjusting insulin or nutrition to correct the present abnormal value.

Interruption of the Insulin Infusion

Interruption of insulin infusions may occur for many reasons, either intended or unintended. At times, the doctors or nurses may temporarily stop the protocol to allow for delivery of blood products or medications when IV access is limited. Infusions may mistakenly not be restarted, or deliberate discontinuation may not be adequately communicated, potentially leading to worsening hyperglycemia or even the development of ketoacidosis, and other adverse clinical outcomes. Therefore, the algorithm should have clear orders for the nurses to contact the ordering physician if the infusion is stopped for any reason, other than protocol-driven cessation due to falling blood glucose concentrations.

Interruption of Nutrition, Field Trips, and Communication

Insulin infusion commonly provides both basal and nutritional insulin requirements. Interruptions in nutritional intake are extremely common in the inpatient setting, with a potential to cause serious hypoglycemia. Feeding tubes are often pulled out without warning; enteral nutrition may also need be halted if high gastric residuals are noted or during certain diagnostic tests. At times, IV carbohydrate sources (dextrose, partial parenteral nutrition, total parenteral nutrition) may be interrupted as well. In some cases, “field trips” out of the critical care units to the operating room, imaging studies, or other hospital locations add another layer of challenges to managing the IIP. Staff in these various areas may not be familiar with the IIP or monitoring standards and techniques, and potentially may not even be aware that the patient is on an insulin infusion. It is therefore crucial to anticipate these pitfalls and develop effective institutional procedures for addressing them. For example, many institutions use D10 solution to replace the carbohydrate calories that are lost when tube feedings have to be interrupted in a gram-per-gram fashion. Patients should be clearly identified as being on an insulin infusion. The requirement for consistent glucose monitoring, hypoglycemia recognition and treatment, and insulin infusion adjustment requires either critical care nurse care of the patient on the field trip, or training in the same skills in areas such as endoscopy, interventional radiology, and operating rooms including the preoperative and postoperative care units. In any case, all services should be
involved in crafting solutions that will ensure a consistent approach to glycemic control as the patient travels off-unit. Monitoring and treatment equipment needs to be readily available in all sites, and hypoglycemia protocols need to be distributed and supported in all areas.

Preventing and Treating Hypoglycemia
Some hypoglycemia will occur with infusion protocols, no matter how carefully a protocol is crafted and how well it is administered. Hypoglycemia protocols should therefore be incorporated directly into an infusion order set. Treatment of hypoglycemic events with a full 50 mL of D50 solution is equivalent to 25 g of carbohydrate, which will raise glucose levels in the average patient by 125 mg/dL. Many institutions discourage the overcorrection of hypoglycemic events by encouraging giving lesser aliquots of D50 based on the degree of hypoglycemia.

Preventing hypoglycemia by recognizing hypoglycemia risk factors, proper monitoring, and anticipating reductions in insulin requirements from decreasing severity of illness, nutritional intake, or steroid dosing can also reduce the frequency of hypoglycemic events.

IMPLEMENTATION: EDUCATING AND ENGAGING NURSING AND PHYSICIAN STAFF
Nursing staff generally bear the brunt of the burden on the front line of implementing intensive IIPs. Educational efforts for nurses should include the rationale for intensive insulin therapy and use of an IIP. Additionally, detailed, case-based instruction on utilization of the IIP is required. Properly educated, nursing staff often become the strongest advocates of the IIP. In addition, they can frequently provide important input when situations arise that require troubleshooting. Regular feedback sessions early in implementation that address ease of use, clarity of orders, and difficulties encountered by nurses can be invaluable. Improvement teams need to provide frequent in-service training and updates on the IIP selected after implementation. This is imperative to promote nursing acceptance and adherence to the IIP chosen, particularly with consideration for traveling nurses. The importance of nursing champions to design and carry out this work cannot be overstated. Educational programs focusing on the physician staff can also be very useful, particularly when focused on high-volume physicians and influential thought leaders.

IMPLEMENTATION: ADDRESSING COMMON CLINICAL SITUATIONS

Steroids
Steroid boluses are commonly an integral part of regimens targeting a variety of conditions, such as transplant rejection, reactive airways disease, certain infections, cancer, and a variety of autoimmune disorders. This can lead to glycemic excursions and rapidly varying insulin requirements. Educational efforts and treatment regimens should address the disproportionate impact that steroids have on postprandial glycemic excursions. To minimize the glycemic impact of glucocorticoid therapy, a team should investigate promoting the use of steroid infusions in situations when a bolus is not absolutely necessary.

Dealing with the Eating Patient and Other Sources of Carbohydrate-Induced Glycemic Excursions
Glucose levels can be difficult to control in patients who are eating while on insulin infusion, because the infusion “chases” the glycemic excursions through frequent adjustments, often with a late overshoot and inappropriate reduction in dose. We instead recommend providing bolus nutritional insulin to cover the expected glycemic excursion caused by carbohydrate ingestion. Carbohydrate counting and using a unit of insulin for each 10-15 g of carbohydrate consumed can smooth out the rapid fluctuations in glucose. Guidance for this should be incorporated into the order set.

Transition Off of Insulin Infusion
Rational strategies for dealing with this transition are covered in detail elsewhere in this supplement.65 Guidance for managing this transition should be integrated into your insulin infusion and SC order sets. The transition to SC insulin may represent a separate order set but is sometimes best integrated into the IV insulin infusion order set itself.

IIPs Outside of the Critical Care Setting
IIPs are most commonly used in the critical care setting. In some institutions, IV insulin protocols are safely and effectively employed outside the
ICU. Obviously, the number of nurses and other personnel who must be familiar with such protocols is much higher outside the ICU, and protocol errors are therefore likely to be somewhat higher. In addition the nurse-per-patient ratio is usually lower outside of the critical care setting. As a result, suggestions for safe implementation of insulin infusion regimens outside of the critical care setting include:

- Choose an infusion protocol with a higher glycemic target.
- Limit the medical and surgical units where this expertise will be developed.
- Consider simplified infusion protocols but stay consistent with format.
- Automated or computerized assistance of calculations may reduce human error and nursing burden.

ASSESSING THE IMPACT OF YOUR EFFORTS: FOLLOW-UP AND FOLLOW-THROUGH

Monitoring, Recording, and Analyzing Glycemic Control Data

Once the IIP is implemented, it is critical that the impact on glycemic control, hypoglycemia, insulin use, and other factors be analyzed and used for improving the IIP and care delivery. Frequent monitoring of glucose levels is necessary for the safe infusion of insulin. Guidance for how often the monitoring is required must be explicit and included in the infusion order set. Intermittent auditing for compliance with the frequency of glucose testing and appropriate dose selection is good practice. Attention should be paid to how the glucose level is obtained, recorded, and made available to the health care team in your institution. All glucose readings should be recorded electronically for ongoing analyses and retrieval, and ideally, this could be done in an automated or single-step method. Try to eliminate duplication of effort, such as asking the nurse to record the glucose level and their reaction to it on paper and again in an electronic format. Your team should also provide guidance about the potential problems of using point-of-care glucose testing in settings with hypotension, sepsis, pressor use, and other conditions that may impair the accuracy of capillary glucose readings.

Reports on the time to reach the glycemic target, glycemic control while on infusion, and the incidence of hypoglycemia should be reviewed by the multidisciplinary steering committee. The Society of Hospital Medicine Glycemic Control Task Force recommends analysis by patient – day and by patient – stay (or insulin infusion run) as preferred methodologies for analysis of glycemic control and hypoglycemia rates over the method of using each individual glucose reading as the unit of analysis. (The latter tends to under-value the frequency of hypoglycemia.) Detailed practical recommendations for analyzing and summarizing glycemic control data are available elsewhere in this supplement. These data should drive decisions on modification of glycemic targets and the protocol structure. Patients meeting prespecified criteria should be referred to the improvement team for review. For example, patients who experience any glucose readings of ≤ 40 mg/dL, or who take more than 12 hours to reach the upper limit glycemic target should be referred to the team for a case review.

Assessing Adherence to the Protocol and Ease-of-Use Issues

Focused audits in the pilot and early implementation phases should look for nonadherence to the protocol. Deviations should be evaluated according to the patterns identified. For example, variation in application in some cases is specific for an individual and in others is characteristic of a specific group or the whole. Accordingly, this may point to gaps in education or attitudes about the importance of this endeavor. Front-line staff may deviate from the protocol because they find it ineffective, unsafe, or impractical for certain situations or specific patients. Many IIPs are the subject of nursing errors related to the knowledge and acceptance of the nurse but also the complexity of the protocol. Appropriate modifications to the protocol based on these cases can frequently improve the ease of use and effectiveness of the protocol. The ongoing review process should identify issues that must be addressed with permanent solutions rather than accepting frequent individual alterations to meet goals. Revisions require supplementary education and rapid and wide dissemination. Although educational efforts and monitoring are often most intense in the early implementation phase, periodic retraining should continue to achieve optimal results and safety. Educational tools must consider nursing time commitments and will often include an interactive
web-based module that gives more flexibility for trainers and clinical nurses alike.

**CONCLUSIONS**

Insulin infusions are a powerful clinical tool in the inpatient setting to maintain glycemic control. Many IIPs have been developed and used successfully. The institutional challenge is to select, modify, and implement the IIP to reduce hyperglycemia and improve outcomes without excess hypoglycemia. In order to accomplish this goal safely and efficiently, standardized processes and collaboration between physicians, nurses, and pharmacists are needed. The keys to minimizing errors include developing a culture of safety and cooperation, back-up checks, standardization, automation, and robust training for all those who are involved in the care of a patient on an insulin infusion. Although we encourage standardization and the use of protocols, providers always need to consider the unique clinical circumstances and potential problems presented by each individual patient. It is important to recognize the many barriers to successful implementation of an IIP, but strategies exist to overcome these. Finally, remember that the process does not end with the development phase. Continued review is paramount to success. Note variations in use, analyze them, and learn from them, in order to continually improve the process of care.

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Received 7 January 2008; revision received 14 August 2008; accepted 14 August 2008.

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