



Managing Hyperglycemia in the Hospital Setting

Sliding scale insulin, a standard practice in hospital settings for over 70 years fails to provide physiologic insulin coverage to hospitalized patients. Consensus statements from the American Diabetes Association and American College of Endocrinology stated in 2004 that the “use of ‘sliding scale’ insulin alone is discouraged; evidence does not support this technique, because it has resulted in unacceptably high rates of hyperglycemia, hypoglycemia, and iatrogenic diabetic ketoacidosis in hospitalized patients. The use of standardized protocols that are developed by multidisciplinary teams is associated with improved glyce-mic control and lower rates of hypoglycemia.”¹ A multidisciplinary team worked together at the Alaska Native Medical Center (ANMC) to put these recommen-dations into practice. This issue of the Diabetes Dispatch will review manage-ment of hyperglycemia in hospital settings and lessons learned during protocol implementation at ANMC.

An important first step is to recognize the targets of hyperglycemia management in the inpatient setting. Table 1 reviews these targets.²⁻³ The management of diabetes in the hospital setting is generally considered secondary in importance to the condition that prompted admission. With the recognition that hospital costs for patients with diabetes were about 2.1 times higher than costs for peo-ple without diabetes this focus is beginning to change.⁴ The adverse effects of

	American Diabetes Association	American College of Endocrinology/ American Association of Clinical Endocrinologists
ICU or critically ill patients	As close to 110 mg/dl as possible and <180 mg/dl	<110 mg/dl
Non-ICU or non-critically ill patients	Pre-prandial 90-130 mg/dl Post-prandial <180mg/dl	Pre-prandial <110 mg/dl Post-prandial <180 mg/dl

hyperglycemia on patient outcomes have been documented in a variety of hos-pital settings and types of patients, including general medical and surgical pa-tients, patients with acute myocardial infarction, patients undergoing cardiac sur-gery and patients with strokes. Effective management of hyperglycemia has been associated with a reduction in the risk of multi-organ failure, systemic in-fections, and decreased length of hospitalization.^{1,4} Insulin is the most effective agent to gain immediate control of hyperglycemia in hospitalized patients.

Oral antihyperglycemic agents are sometimes used in the hospital setting for non-critically ill patients who received these agents as outpatients, were well controlled on the oral regimen, and who are expected to eat normally during their hospital stay. However, no large, well designed clinical studies have been

continued on page 4

Inside this issue:

A Review of the RABBIT 2 Trial-More Support for Basal-Bolus Insulin	2
Example Adult Subcutaneous Insulin Order Set	3
Managing Hyperglycemia in a Hospital Setting	4

Goal.

- The goal of the Diabetes Dispatch is to increase the reader's knowledge of diabetes treatments and technologies and to provide the most current information on new drugs, therapies, and devices.
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A Review of the RABBIT 2 Trial– More Support for Basal-Bolus Insulin

By Amy Yoo, PharmD Candidate

Hyperglycemia in the intensive care unit has been related to poor clinical outcomes and possibly increased mortality. Studies have shown the benefit of tight glycemic control for these patients, including decreased complications, length of stay, and overall cost.¹ Continuous insulin infusions are the most effective means to obtain goal blood glucose levels. As a result, several hospitals have adjusted their insulin protocol for the critical care setting. What about the patients admitted to the general medicine floor? Are they deemed severe enough to warrant continuous infusions or are the common sliding scale (SSI) regimen appropriate? Results from a recent prospective, randomized study suggest that a change in acute care insulin protocol may be needed.

In the Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients with Type 2 Diabetes (RABBIT 2 Trial),² patients were randomized to receive either a basal-bolus insulin regimen or the SSI. Patients in the basal-bolus regimen received 0.4 units/kg/day if their blood glucose was 140-200 mg/dL upon admission or 0.5 units/kg/day if their blood glucose was 201-400 mg/dL. Half the dose was insulin glargine (Lantus®) and the other half was insulin glulisine (Apidra®). Glulisine is a rapid acting insulin analog with a time profile similar to insulin aspart (Novolog®) or insulin lispro (Humalog®). Insulin glargine was given once daily at the same time each day, and the insulin glulisine was given in three divided doses before each meal. If the patient was unable to eat, the dose was held. If the patient had glucose levels >140 mg/dL, supplemental (or correction) insulin glulisine was given. Patients in the sliding scale insulin regimen received a dose of regular insulin before each meal and at bedtime. They were then supplemented with regular insulin in either the “usual”, “insulin sensitive”, or “insulin resistant” scale. (Figure 1)

Figure 1:²

Blood glucose (mg/dL)	Insulin Sensitive	Usual	Insulin Resistant
>141-180	2	4	6
181-220	4	6	8
221-260	6	8	10
261-300	8	10	12
301-350	10	12	14
351-400	12	14	16
>400	14	16	18

Both groups had 65 previously diagnosed patients with no significant differences in baseline characteristics. The ultimate goal of the study was to compare the safety and efficacy of each therapy in maintaining glucose levels <140 mg/dL. Despite similar glucose levels upon admission, the basal-bolus insulin therapy had a significantly lower mean fasting glucose, random glucose, and overall glucose level during the hospital stay. The SSI group had 38% of their patients at target levels of <140 mg/dL compared to 66% of patients receiving basal-bolus insulin. For those patients who remained >240 mg/dL with the SSI, glycemic control was obtained by switching to the basal-bolus insulin. Hypoglycemia occurred in two patients from each group, which was immediately corrected and none were associated with adverse events. With these results, the investigators concluded that the basal-bolus insulin regimen should be preferred over SSI alone in non-critically ill patients with Type 2 diabetes.

The Rabbit 2 Trial is one of the more recent studies published in support of a basal-bolus approach for the inpatient management of hyperglycemia. This continues to build our confidence that a proactive approach with basal bolus insulin delivered subcutaneously is more effective than a reactive sliding scale insulin regimen in maintaining glycemic control.

References

1. Inzucchi SE. Management of Hyperglycemia in the Hospital Setting. *N Engl J Med.* 355;1903-11. 2006.
2. Umpierrez GE, et al. Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients with Type 2 Diabetes (RABBIT 2 Trial). *Diabetes Care.* 30;2181-2186. 2007.

CLINICAL RECORD

ASAP Order

DOCTOR'S ORDERS

(sign all orders)

Adult Subcutaneous Insulin Orders –

****Patient Eating a Diet or Receiving Bolus Tube Feeds****

STEP 1: ASSESS ORAL ANTI-HYPERGLYCEMIC AGENTS

*(**Recommendation to Stop ALL Oral Anti-Hyperglycemic Agents**)*

STEP 2: PROVIDER TO ASSESS TOTAL DAILY INSULIN NEEDS

- If patient is already on an insulin regimen:
 Total daily insulin dose = _____ units/day
OR
- If patient is newly diagnosed or was on oral anti-hyperglycemic agent(s):
 Patient's weight (kg) _____ x 0.4 units/kg = _____ units/day
OR
- If patient is transitioning from IV insulin drip to subcutaneous insulin:
 Total # of units given over last 8 hours _____ x 3 = _____ units/day

Patient Weight (kg): _____

-Consider reducing the total daily insulin dose by ~20-25% for patients in acute renal failure, who are tremulous or hypoglycemia-prone, or will be reducing their caloric intake.
 -Insulin requirements will change during hospitalization. Re-assess every 24-48 hours.

STEP 3: ORDER BASAL AND PRE-MEAL SCHEDULED INSULIN

- Notify Dietary via RPMS that patient is on insulin as "additional order"

For Type 1 or Type 2 Diabetes or Hospital-related Hyperglycemia:

- Glargine (Lantus®) x 50% of total daily dose (Step 2) = _____ units SQ QHS
- + Pre-meal Aspart x 1/6 of total daily dose (Step 2) = _____ units SQ before each meal AND Correction Insulin (Step 4)

HOLD Aspart if Blood Glucose <70 mg/dl* *Inject Aspart 10-15 min before meal & tray should be in room* *No food, No Aspart

STEP 4: ORDER GLUCOSE MONITORING AND CORRECTION INSULIN

Capillary Blood Glucose check before each meal while patient is eating a diet or receiving bolus tube feeds.

Correction Insulin: Administer **Aspart Insulin** (Novolog®) SQ according to the table below:

Blood Glucose	<input type="checkbox"/> <70 kg or Very Insulin Sensitive	<input type="checkbox"/> 70-130 kg or Usual Insulin Sensitivity	<input type="checkbox"/> >130 kg or Very Insulin Resistant
<51	Dextrose 50% (25gm) 50mL IV x1. Recheck Blood Glucose after 15 minutes.		
51-70	No action if about to eat. If not, give Orange Juice 120ml PO or Dextrose 50% (25gm) 50mL IV x1.		
71-149	No additional action necessary.		
150-199	1 unit	2 units	4 units
200-249	2 units	4 units	8 units
250-299	3 units	6 units	12 units
300-349	4 units	8 units	16 units
350-399	5 units	10 units	20 units
≥ 400	6 units	12 units	24 units

- Notify provider if 2 or more Blood Glucoses are above 200mg/dl in a 24-hour period.

Provider Signature

Date

Patient Identification Sticker

Approved HRC 03/27/07, Pharmacy

Managing Hyperglycemia in the Hospital Setting, continued

conducted to demonstrate a favorable impact on outcomes from oral agents. Additionally, the usefulness of oral agents is limited by difficulty titrating dosage and promptly achieving near normal blood glucose concentrations. The sulfonylureas have a long duration of action. Sulfonylureas also can cause hypoglycemia in patients with limited food intake. Metformin is contraindicated in many critically ill patients because of the increased risk for lactic acidosis. Thiazolidinediones increase intravascular volume which could cause problems for patients with heart failure or alter the patient's hemodynamics.¹ Insulin is the most clinically effective and cost-effective therapy for managing hyperglycemia in the hospital setting. Proactive strategies for glycemic management attempt to mimic normal physiologic patterns of insulin secretion. This can be accomplished using a combination of human insulin and insulin analogues. (Table 2)

In order to mimic physiologic insulin patterns, a basal insulin is used to simulate a background level of insulin. Basal insulin administration prevents gluconeogenesis (the liver making glucose) and ketogenesis (breaking down fat for energy). Prandial (meal related) insulin doses are given around meals to assist muscle and tissue uptake of glucose into the cells where it will be used for energy. Additional corrective insulin is also recommended by those who advocate a basal-bolus approach to inpatient hyperglycemia management. Corrective doses of rapid or short acting insulin are added to the meal time insulin to compensate for elevated blood glucose values. Essentially a corrective insulin dose administered along with the bolus dose of insulin overcomes the high blood glucose value and the glucose consumed during the meal.

Type of Insulin	Insulin Product	Time to Onset of Action (hr)	Time to Peak Effect (hr)	Duration of Action (hr)
Rapid acting	Insulin aspart, lispro, glulisine	≤0.5	0.5-3	3-6
Short acting	Regular human insulin	0.5-1	1-5	6-10
Long acting	Insulin glargine and detemir	1-2	Not applicable (has no peak)	~24 for glargine ~6-23 for detemir

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A proactive basal-bolus approach to inpatient hyperglycemia management was piloted at ANMC beginning in April 2007. The current order set can be seen on page 3 (Figure 1). The new protocol was implemented hospital wide in February 2008. Challenges the steering committee did not fully anticipate included the coordination of meals and medication, the staff fear of hypoglycemia, initially being very conservative on weight based dosing of insulin 0.2 units/kg/day versus 0.4 units/kg/day. It is critical to monitor for hypoglycemia and to provide education on what blood glucose is too low. Such a large change in culture, i.e. removing sliding scale insulin protocols from the floors and implementing a basal-bolus approach, requires a significant dedication to provider, nurse, dietary, and pharmacy education.

Hyperglycemia in critically ill and postoperative patients with and without diabetes increases mortality, morbidity, and costs. Correction of hyperglycemia in these patients reduces mortality, the risk of infections, and other adverse outcomes. Proactive management of hyperglycemia is needed to achieve and maintain glycemic control. Administering insulin by basal-bolus plus correction subcutaneously is safe and effective to meet glycemic goals in hospitalized patients.¹⁻⁵

References

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ALASKA NATIVE DIABETES PROGRAM



Objectives.

1. Become familiar with inpatient management of hyperglycemia
2. Recognize the results of the Rabbit 2 Trial
3. Describe the goals of blood glucose control based on patient type, general floor versus critically ill

Continuing Education Quiz

Diabetes Dispatch: Spring 2008

1. According to the American Diabetes Association what is the target blood glucose concentration for patients who are not critically ill?

- a. As close to 110 mg/dl as possible and < 180 mg/dl
- b. Pre-prandial 90-130 mg/dl
Post-prandial <180 mg/dl
- c. <110 mg/dl
- d. Pre-prandial <110 mg/dl
Post-prandial <180 mg/dl

2. According to the American College of Endocrinology what is the target blood glucose concentration for patients who are critically ill?

- a. As close to 110 mg/dl as possible and <180 mg/dl
- b. Pre-prandial 90-130 mg/dl
Post-prandial <180 mg/dl
- c. <110 mg/dl
- d. Pre-prandial <110 mg/dl
Post-prandial <180 mg/dl

3. What type of inpatient would be considered a good candidate to continue oral antihyperglycemic agents?

- a. the patient is non-critically ill
- b. the patient was well controlled on oral agents when an outpatient
- c. the patient is expected to eat normally during hospitalization
- d. all of the above

4. What is the most effective agent to gain immediate control of hyperglycemia in hospitalized patients?

- a. metformin
- b. glyburide
- c. insulin
- d. pioglitazone

5. What is the time to onset of action of rapid acting insulins?

- a. ≤ 0.5 hours
- b. 1-2 hours
- c. 3-6 hours
- d. ~ 24 hours

6. What is the duration of action of insulin glargine?

- a. ≤ 0.5 hours
- b. 1-2 hours
- c. 3-6 hours
- d. ~ 24 hours

7. True or False

Uncontrolled hyperglycemia in hospitalized patients increases mortality, morbidity, and costs.

8. During the Rabbit 2 Trial what dosing would a provider use for a patient randomized to the basal-bolus group with a blood glucose of 150 upon admission?

- a. 0.2 units/kg/day
- b. 0.3 units/kg/day
- c. 0.4 units/kg/day
- d. 0.5 units/kg/day

8. During the Rabbit 2 Trial what percentage of patients in the basal-bolus group reach the blood glucose goal <140 mg/dl

- a. 66%
- b. 38%
- c. 50%
- d. 100%



LESSON EVALUATIONS

To obtain C.E. credit for this lesson you must answer the questions on the quiz (70% correct required) and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. In May and

November of each year we will mail a statement of credit, unless otherwise arranged with the AkPhA office.

This program furnishes 1.0 credit per lesson.

EXPIRATION FOR CREDIT: Pharmacist and technicians may receive credit for completing this course if returned by May 14, 2011. The ALASKA PHARMACISTS ASSOCIATION is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

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Circle one: Pharmacist Technician

	Poor			Excellent
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3) Author's knowledge of topic	1	2	3	4 5
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