Inpatient considerations in the management of hyperglycemia and diabetes mellitus

EMMA M. (GORMAN) STUDLACK, PHARMD, BCPS

CLINICAL ASSISTANT PROFESSOR; D'YOUVILLE UNIVERSITY SCHOOL OF PHARMACY

CLINICAL PHARMACIST, INTERNAL MEDICINE; MERCY HOSPITAL OF BUFFALO

BUFFALO, NY

Disclosures

Nothing to disclose

Objectives

- Define glycemic targets for hospitalized adults and describe the evidence supporting them
- Identify a strategy for achieving optimal glycemic control in hospitalized adults with diabetes mellitus
- Describe the management of non-insulin antihyperglycemic medications in the inpatient setting

Polling question: goal blood glucose

Background

- It is estimated that more than 10% of the US population have diabetes
  - Diabetes accounts for over 25% of hospitalized patients
- An estimated 40% of hospitalized patients experience hyperglycemia
  - Blood glucose (BG) > 140 mg/dL
- Dysglycemia (hyper- or hypoglycemia) has been associated with increased morbidity and mortality
  - Hypo- and hyperglycemia are independent predictors of in-hospital mortality

Korytkowski MT, et al. J Clin Endocrinol Metab. 2022; 107(8):2101-2128
Diabetes Care. 2022; 45(Suppl. 1):S244–S253

Background

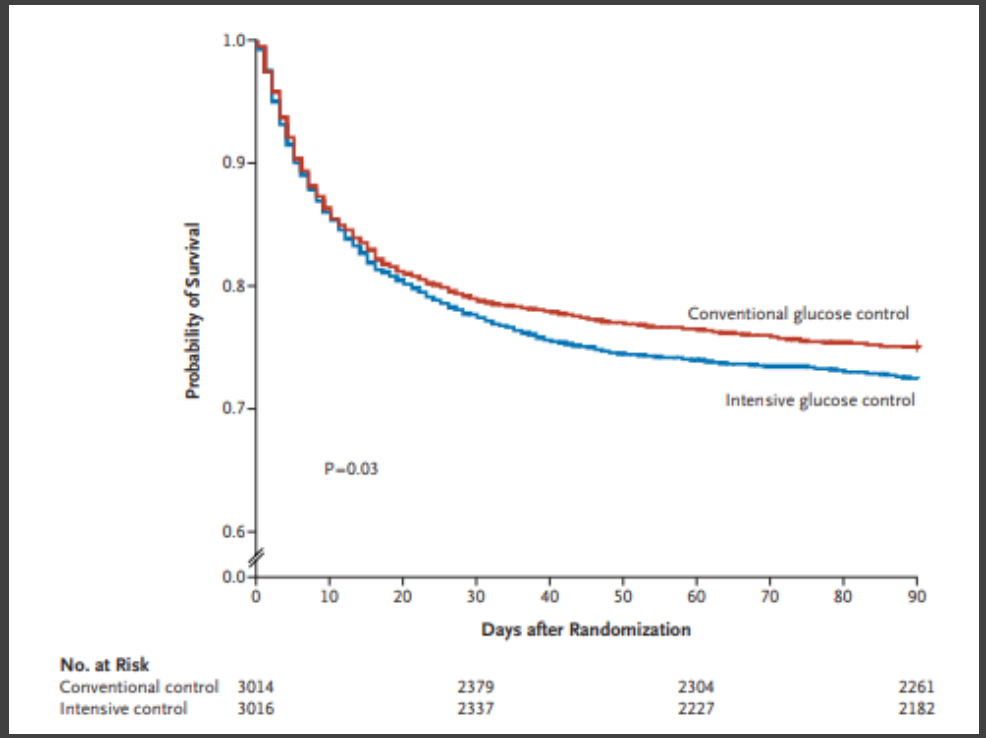
- Readmission rates for patients with diabetes are almost double of those without diabetes
- Centers for Medicare and Medicaid (CMS) is adding two new electronic clinical quality measures (eCQMs) in 2023
  - Severe hypoglycemia: proportion of patients with BG < 40 mg/dL within 24 hours of receiving antihyperglycemic agent
  - Severe hypoglycemia: number of days in which patients had a blood glucose > 300 mg/dL

Korytkowski MT, et al. J Clin Endocrinol Metab. 2022; 107(8):2101-2128
Diabetes Care. 2022; 45(Suppl. 1):S244–S253

Glycemic targets and technology

NICE-SUGAR

- Compared strict and conventional glucose control in critically ill patients
  - Strict glucose control = 81-108 mg/dL
  - Conventional glucose control = < 180 mg/dL
- Primary outcome was all-cause mortality at 90 days
- Intensive glucose control was associated with higher all-cause mortality and higher rates of severe hypoglycemia (blood glucose < 40 mg/dL)
  - All-cause mortality; 27.5% vs 24.9%, p = 0.02
  - Severe hypoglycemia; 6.8% vs 0.5%, p<0.001



N Engl J Med. 2009; 360:1283-1297

Glycemic targets

- Data from the NICE-SUGAR trial has historically been extrapolated to non-critically ill patients
- The American Diabetes Association and the Endocrine Society endorse a target blood glucose of 140-180 mg/dL for most non-critically ill patients
- Guidelines also recognize that stricter blood glucose goals may be acceptable for some patients (such as those undergoing cardiothoracic surgery) and that more lenient blood glucose goals may also be acceptable for others (those at increased risk for hypoglycemia)
  - Clinical judgement should be employed for these special circumstances

Korytkowski MT, et al. J Clin Endocrinol Metab. 2022; 107(8):2101-2128
Diabetes Care. 2022; 45(Suppl. 1):S244–S253

Point-of-care testing

- The American Diabetes Association recommends that bedside point-of-care (POC) blood glucose testing be performed before meals or every 4-6 hours for those not eating
- Limitations to POC testing include
  - Variability in measurement compared to blood draw (plasma)
    - Post-prandial capillary blood is typically higher in glucose than venous blood
  - Interference from comorbid conditions
    - Dehydration, hypoxemia, hypotension, anemia

Polling question: CGM

Continuous Glucose Monitoring

- Continuous Glucose Monitoring (CGM) provides frequent interstitial glucose levels
- Data supports use of CGMs in the outpatient setting for patients on multiple daily injections or continuous subcutaneous insulin
- Data supporting use of CGM inpatient is limited
  - In a study by Holzinger et al in 124 critically ill patients receiving mechanical ventilation, CGM was associated with lower rates of severe hypoglycemia and an absolute risk reduction of 9.9%
- In the era of Covid-19, CGM may provide an opportunity for reduced staff exposure risk and use of personal protective equipment (PPM)

Holzinger U, et al. Diabetes Care. 2010; 33(3):467-472
Gothong C, et al. Curr Opin Endocrinol Diabetes Obes. 2022; 29:1-9

Use of insulin therapy in the inpatient setting

Inpatient insulin use

- The American Diabetes Association makes the following recommendations regarding insulin therapy in the inpatient setting
  - Insulin is the preferred agent for management of hyperglycemia in hospitalized patients
  - Insulin therapy should be initiated for patients with *persistent hyperglycemia*
    - *Persistent hyperglycemia* is defined as a blood glucose $\geq$ 180 mg/dL on more than one occasion
  - Use of bolus correction insulin (sliding scale) only is strongly discouraged
    - Patients with poor oral intake or those who are taking nothing by mouth should receive basal insulin or basal + bolus correction insulin
    - Patients with good oral intake should receive basal, prandial (nutritional), and correction insulin

Korytkowski MT, et al. J Clin Endocrinol Metab. 2022; 107(8):2101-2128
Diabetes Care. 2022; 45(Suppl. 1):S244–S253

Inpatient insulin use

- The Endocrine Society makes the following recommendations regarding insulin therapy in the inpatient setting
  - Insulin is the preferred agent for management of hyperglycemia in hospitalized patients
  - Scheduled insulin therapy should be initiated for patients with *persistent hyperglycemia*
    - *Persistent hyperglycemia* is defined as a blood glucose $\geq$ 180 mg/dL on more than one occasion
  - Correctional insulin can be initiated for patients with mild hyperglycemia (< 180mg/dL)

Korytkowski MT, et al. J Clin Endocrinol Metab. 2022; 107(8):2101-2128
Diabetes Care. 2022; 45(Suppl. 1):S244–S253

Insulin Pharmacokinetics*

	Onset	Peak	Duration
Rapid-acting			
Insulin lispro	Within 15 minutes	~ 1 hour	3-4 hours
Insulin aspart	Within 15 minutes	1-3 hours	3-5 hours
Insulin glulisine	15-30 minutes	30-60 minutes	3-5 hours
Short-acting			
Regular insulin	~ 1 hour	2-4 hours	5-8 hours
Intermediate-acting			
Insulin NPH	1-2 hours	4-10 hours	14+ hours
Long-acting			
Insulin detemir	3-4 hours	6-8 hours+	Up to 20-24 hours
Insulin glargine	1.5 hours	Flat	24 hours
Ultra Long-acting			
Insulin degludec	1 hour	9 hours	Up to 42 hours

Feingold KR, et al. Endotext [Internet].

* Not all-inclusive + Relatively flat

Correctional insulin

- Also known as “sliding-scale insulin” or “rainbow coverage insulin”
- The use of rapid-acting or regular insulin based on preprandial blood glucose readings, or every 4-to-6 hours for patients who are nil per os (NPO)
- A 2011 study by Umpierrez and colleagues found reduced rates of hospital complications in patients with Type 2 Diabetes undergoing general surgery who were treated with basal-bolus insulin compared to sliding-scale insulin (n=211)
  - Also, increased rates of hypoglycemia
- A 2018 Cochrane review found that basal-bolus scheduled insulin therapy was associated with a lower average blood glucose compared to sliding-scale insulin
  - But, basal-bolus scheduled insulin was associated with a longer length of stay and increased ratesof hypoglycemic episodes

Umpierrez GE, et a. Diabetes Care. 2011; 34(3):256-261
Colunga-Lozano LE, et al. Cochrane Database Syst Rev. 2018 Nov; 2018(11): CD011296

Selecting an insulin dose

- For patients previously requiring insulin, who are well-controlled, and who are expected to continue eating a normal diet
  - Continue outpatient insulin regimen
  - Consider dose reduction of 10-20% in patients who are on a “basal heavy” insulin regimen
    - Requiring > 0.6 units/kg/day of basal insulin
  - Consider a dose reduction of 25-50% to account for reduced nutritional intake in patients who are at risk for hypoglycemia
- For patients who previously did not require insulin therapy, or who have poorly-controlled diabetes despite outpatient insulin use
  - A weight-based ***total daily dose*** of insulin should be calculated for patients requiring insulin therapy

Guidelines for inpatient diabetes management. Diabetes Institute. University of Pittsburgh.
Inzucchi SE. Diabetes facts and guidelines. Yale Diabetes Center, 2011.

Selecting an insulin dose

- Divide total daily insulin dose
  - 50% as basal therapy
  - 50% as pre-prandial bolus therapy divided into 3 meals

Clinical Characteristics	Total daily dose
Lean, elderly, advanced kidney or liver disease	0.2-0.3 units/kg
Normal BMI	0.3-0.4 units/kg
Obese/Overweight	0.4-0.5 units/kg

Guidelines for inpatient diabetes management. Diabetes Institute. University of Pittsburgh.
Inzucchi SE. Diabetes facts and guidelines. Yale Diabetes Center, 2011.

Titrating insulin

- If fasting blood glucose > 180 mg/dL
  - Increase basal insulin by 10-20% every 2-3 days
- If post-prandial blood glucose > 180 mg/dL
  - Increase prandial insulin by 1-2 units/dose every 1-2 days
- If any blood glucose < 80 mg/dL
  - Reduce total daily insulin dose by 20%

Guidelines for inpatient diabetes management. Diabetes Institute. University of Pittsburgh.
Inzucchi SE. Diabetes facts and guidelines. Yale Diabetes Center, 2011.

Special populations

Corticosteroid use

- A reported 30-80% of hospitalized patients receiving supraphysiologic doses of glucocorticoids (GC) experience glucocorticoid-induced hyperglycemia
- Patients with glucocorticoid-induced hyperglycemia have higher rates of mortality, cardiovascular events, and infection
- NPH Insulin is an option for management of GC-induced hyperglycemia for patients receiving intermediate-acting corticosteroids (prednisone, prednisolone, methylprednisolone)
  - Similar onset and duration of action
- Intensified insulin regimens must be adjusted as glucocorticoids are tapered or discontinued

Aberer F, et al. J Clin Med. 2021; 10:2124

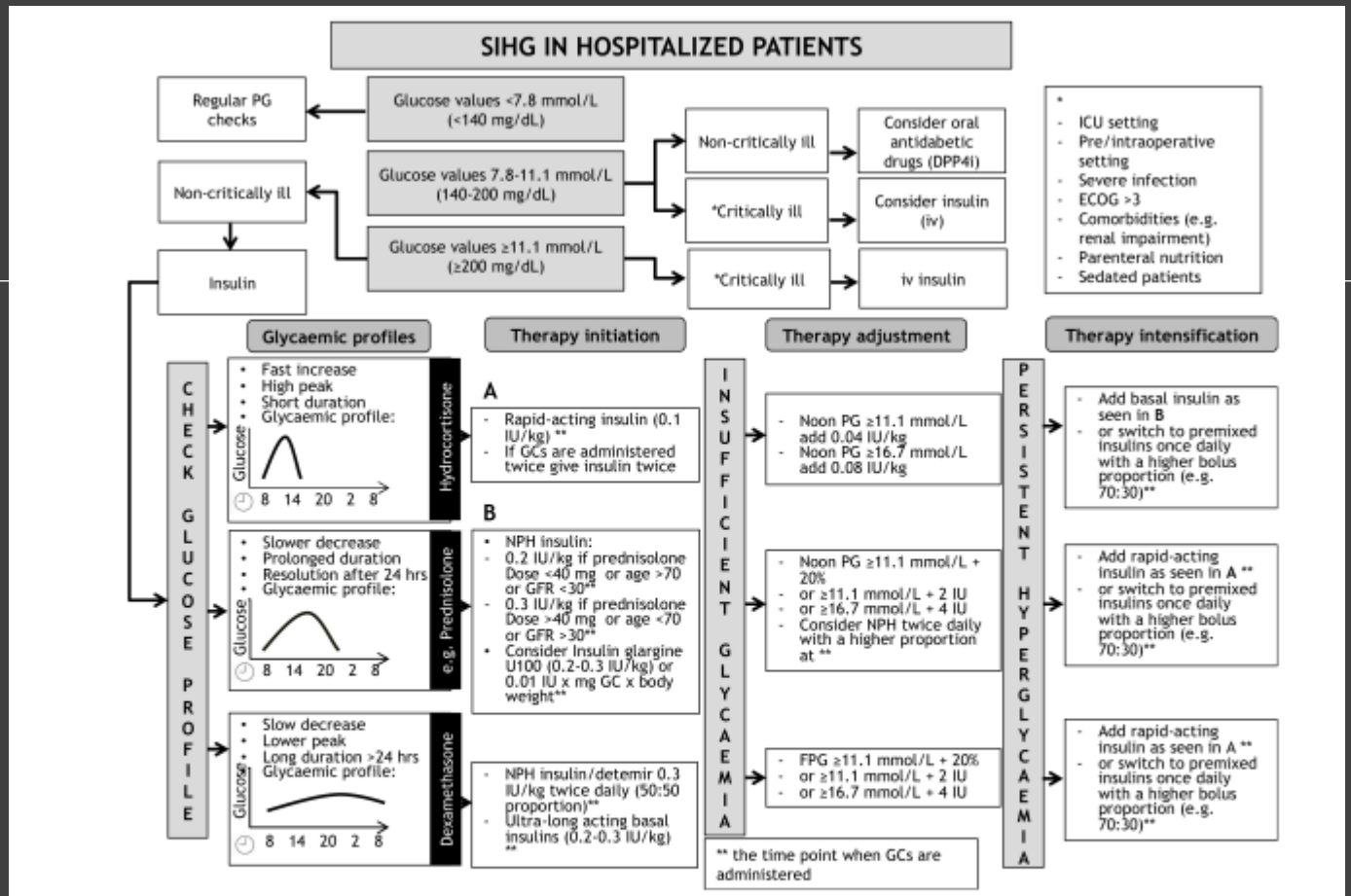


Figure 1. Opinion-based schematic algorithm for initiation, adjustment and intensification of insulin therapy for treatment of SIHG. DPP4i = Dipeptidyl-Peptidase4-inhibitor, ECOG = Karnofsky index, FPG = Fasting plasma glucose, GC = Glucocorticoid, ICU = Intensive Care Unit, IU = International Units, NPH = Neutral Protamine Hagedorn, SIHG = Steroid induced hyperglycaemia. * = definition of critical illness, ** = indicating the time point when glucocorticoids are administered. (**A**) indicates recommendations for initiation of rapid-acting insulin. (**B**) indicates recommendations to initiate basal in-sulin.

Continuous subcutaneous insulin

- I.e. Insulin pump therapy
- Patients who receive continuous subcutaneous insulin infusions via insulin pumps should continue therapy in the hospital whenever able
- In patients where continuation of the subcutaneous pump is not feasible, these patients should be transitioned over to basal-bolus subcutaneous insulin
  - Patients with the inability to adjust pump settings, patients who are critically ill, and others
- An effort should be made to determine the patient's total daily insulin requirements to assist in creation of an appropriate basal-bolus insulin regimen
- Institutions should have policies and procedures in place for patients who are maintained on insulin pump therapy

Patients that are nil per os (NPO)

- Patients that are not eating should have their blood glucose monitored every 4-to-6 hours
- Nutritional insulin should not be administered
- Correctional and basal insulins should continue
- Basal insulin should not cause hypoglycemia
  - Consider a 25% dose reduction for patients at risk of hypoglycemia
    - Elderly, significant renal or liver impairment, and those with a basal-heavy regimen

Non-insulin antihyperglycemics

Polling question: non-insulin antihyperglycemics

Dipeptidyl peptidase-4 (DPP-4) inhibitors

- Reduce post-prandial glucose by enhancing endogenous prandial insulin secretion and inhibiting glucagon secretion
- Associated with relatively low rates of hypoglycemia
- A study by Umpierrez and colleagues compared sitagliptin alone, sitagliptin + insulin glargine, and traditional basal-bolus insulin in 90 hospitalized patients with a history of type 2 diabetes
- The authors found no difference in outcomes (incidence of hyperglycemia), but patients received less subcutaneous injections

Umpierrez GE, et al. Diabetes Care. 2013 Nov; 36(11): 3430–3435

Glucagon-like peptide 1 agonists (GLP-1)

- Trials have suggested a modest decrease in hypoglycemia with GLP-1 agonists compared to traditional basal-bolus therapy in hospitalized patients
- One study by Fayfman and colleagues compared exenatide, exenatide plus basal insulin, and basal-bolus insulin in 150 hospitalized patients
  - They found that exenatide alone or in combination with basal insulin resulted in a higher proportion of patients reaching target blood glucose
- Implementation may be limited by the significant increase in gastrointestinal side effects secondary to GLP-1 agonist therapy

Fayfman M, et al. Diabetes Care 2019;42:450–456

Opportunities for pharmacists

Opportunities for pharmacists

- Inpatient hyperglycemia team
- Pharmacy to dose/adjust insulin
- Transitions of care

Conclusions

- Inpatient dysglycemia is a common occurrence and has significant potential ramifications, including increased in-hospital mortality
- Inpatient dysglycemia may also impact reimbursement of your institution
- Insulin remains the standard of care for management of inpatient hyperglycemia
- Point-of-care blood glucose testing remains commonplace, but we may see implementation of CGM in the inpatient setting in the future
- Pharmacists are uniquely qualified to assist in management of these complex patients and medication regimens

Inpatient considerations in the management of hyperglycemia and diabetes mellitus

EMMA M. (GORMAN) STUDLACK, PHARMD, BCPS

CLINICAL ASSISTANT PROFESSOR; D'YOUVILLE UNIVERSITY SCHOOL OF PHARMACY

CLINICAL PHARMACIST, INTERNAL MEDICINE; MERCY HOSPITAL OF BUFFALO

BUFFALO, NY