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Pharmacists' role in glycemic management in the inpatient setting: An opinion of the endocrine and metabolism practice and research network of the American College of Clinical Pharmacy

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The objective of this opinion paper was to identify and describe the role of pharmacists in ensuring safe and optimal management of patients with glycemic excursions in the inpatient setting. The role of the pharmacist includes involvement in admission medication history and reconciliation, formulary management of glucose-lowering medications and devices, individual patient medication management, discharge transition of care, and interprofessional collaboration with other health care providers. Recommendations are based on review of published guidelines and literature focusing on the management of patients with hypo- and hyperglycemia in the hospital as well as during the time of transition to and from the inpatient setting.

KEYWORDS

diabetes mellitus, hyperglycemia, hypoglycemia, inpatients, pharmacists

1 | INTRODUCTION

Diabetes mellitus (DM) is a recognized comorbidity for >25% of hospitalized patients in the United States.[1] Patients with hyperglycemia are present throughout the hospital, including units where prescribers and nurses may not be familiar with glycemic management strategies and medications. In many institutions, pharmacists play a major role in glycemic management not only in ambulatory and community settings,[2,3] but also in the hospital.[3,4] With their expertise in pharmacotherapy as well as their knowledge of pharmacokinetic and pharmacodynamic properties of medications, pharmacists can help ensure optimal outcomes for hospitalized patients with diabetes and new-onset hyperglycemia.

The Endocrine and Metabolism Practice and Research Network (PRN) is a subunit of the American College of Clinical Pharmacy (ACCP). PRN members include clinical pharmacists who practice and/or conduct pharmacotherapy research within the broad specialty of endocrinology. Authors of this paper were appointed by PRN

This paper represents the opinion of the Endocrine and Metabolism Practice and Research Network of the American College of Clinical Pharmacy. It does not necessarily represent an official ACCP commentary, guideline, or statement of policy or position.

leadership due to their extensive experience in hospital-based glycemic management. Once the paper was written, it was reviewed by PRN leadership and then the entire membership of the PRN. This article is a collective opinion of the Endocrine and Metabolism PRN regarding best practices for pharmacists who seek to ensure safe and optimized management and prevention of glycemic excursions in the inpatient setting.

2 | ADMISSION MEDICATION HISTORY AND RECONCILIATION

Prescribing errors at the time of hospital admission are frequently caused by lack of knowledge of patients' home medication lists. To our knowledge, there have been no published studies focused on the impact of a pharmacist who specifically performed admission medication histories or admission medication reconciliation in patients with DM. However, as the number of glucose-lowering medications and insulin products has increased in recent years, many health care professionals feel less confident in their knowledge of the medications available for managing hyperglycemia.[5]

When obtaining admission medication history, time should be spent determining actual medication use, barriers to adherence, baseline knowledge, and typical home glucose monitoring values, especially frequency of hypoglycemic events. Obtaining an accurate and complete list of patients' home glucose-lowering medications is more challenging than with most other medication classes. This is especially true for patients who are prescribed insulin, as they are often instructed to change their doses without generation of a new prescription. If a medication list is obtained by contacting a patient's outpatient pharmacy, for example, the dose of insulin obtained may not reflect what that patient is actually taking. The patient (or the patient's caregiver) is the most important source of information regarding how medication is taken, how often doses are missed, and the time of the last dose. Any delays in therapy while home medications are clarified may lead to missed doses of diabetes medications, and therefore hyperglycemia. In addition, patients with type 1 DM or ketosis-prone type 2 DM who miss an injection of basal insulin are at risk for developing severe hyperglycemia or diabetic ketoacidosis (DKA) within hours of a missed dose.[6] At the other extreme, if the time of a patient's last dose of basal insulin is not accurately determined, the first dose in the hospital may be scheduled too early resulting in potentially severe and prolonged hypoglycemia.

Another potential source for error upon hospital admission involves hospital-specific formulary restrictions. For example, because most common rapid-acting insulin products (insulin lispro, insulin aspart, and insulin glulisine) have similar pharmacodynamics parameters, many hospitals have only one rapid-acting insulin available on formulary. Similarly, hospitals may not carry all basal and premixed insulin agents. This can lead to patient and prescriber confusion, which is further complicated by the fact that most insulin products are included on lists of look-alike, sound-alike medications provided by the Institute for Safe Medication Practices (ISMP).[7]

3 | FORMULARY MANAGEMENT OF GLUCOSE-LOWERING MEDICATIONS AND DEVICES

Pharmacists have a responsibility to ensure the availability and appropriate use of medications in the hospital while ensuring patient safety and minimizing cost. Pharmacist contribution to development and implementation of glycemic management protocols and order sets also can help ensure patient safety. As one example, if a patient must switch insulin types upon hospital admission and/or discharge due to formulary issues, not all basal insulin products can or should be interchanged with a 1:1 dose conversion. For instance, patients typically require higher doses of insulin glargine U-300 to achieve similar glycemic control as insulin glargine U-100, and manufacturers recommend a 20% dose reduction when switching from NPH insulin to insulin glargine products. In addition, it may be prudent to apply an empiric 20% dose reduction when switching from twice daily insulin glargine or detemir to once daily insulin degludec.[8] Another example would be that because most patients with type 2 DM use one or more noninsulin agents that may not be continued during hospitalization, pharmacists should likewise contribute to protocols designed to transition patients previously taking noninsulin agents to insulin upon hospital admission.

Current guidelines recommend that insulin is the treatment of choice for most patients with hyperglycemia or known DM on admission.[9–11] The ISMP recommends that a diagnosis of DM or hyperglycemia be confirmed prior to dispensing insulin to detect erroneous orders, such as those entered for the wrong patient or involving sound alike/look alike medications.[12] At minimum, initial orders for insulin should include DM type (ie, type 1, type 2, no previous history of DM) and/or whether the patient was insulin-requiring prior to admission. This is most easily achieved with electronic insulin order sets that require indications for all ordered medications. It is important that order sets are designed and implemented in a way that standardizes care, but also allows for individualized therapy. For example, a comment such as “Hold if meal is missed” should be added to orders for rapid-acting insulin when it is used as nutritional insulin, but a comment such as “Do not hold if patient is nothing by mouth (NPO)” is appropriate when rapid-acting insulin is used as correction insulin.[13] After implementation of new order sets or protocols, it is essential that quality assurance measures are put in place to evaluate effectiveness and safety, and to address barriers to appropriate use.

Regarding maintenance of an inpatient drug formulary, there are several issues that pharmacists must consider in conjunction with their Pharmacy and Therapeutics (P&T) Committee: (1) which insulin products (and concentrations) will be stocked, (2) whether insulin will be supplied in pens or vials (or both), (3) which noninsulin glucose-lowering medications will be stocked (if any), and (4) what measures will be implemented to ensure safe usage of glucose-lowering medications.

3.1 | Analog vs nonanalog insulin

A recent literature review found shorter length of stay and lower postoperative infections rates with the use of analog compared with

non-analog subcutaneous insulin regimens in hospitalized adult patients.[14] However, the authors noted that the overall quality of available studies in this population was poor. Time of meal tray delivery is often variable in hospitals, and it is difficult to coordinate administration of regular insulin 30 to 60 minutes before a patient is ready to eat. In addition, because mealtimes are not spaced evenly throughout the day (ie, every 6 hours), there is a risk of insulin stacking (multiple doses given close together) that can lead to hypoglycemia when regular insulin is scheduled before meals.

Intermediate-acting human insulin (NPH) is useful in certain situations in the hospital, including during cycled enteral nutrition and during management of corticosteroid-related hyperglycemia. However, compared with basal insulin analogs (insulin glargine, insulin detemir, and insulin degludec), NPH has a peak that can cause hypoglycemia in the afternoon (eg, in an NPO patient receiving morning doses) or overnight (in a patient receiving evening doses without a bedtime snack).

3.2 | Concentrated insulin preparations

As the obesity epidemic in the United States continues to expand, more people with DM are requiring large doses of insulin to achieve glycemic control. Concentrated insulin is being utilized more frequently, and institutions must therefore be prepared to safely transition patients taking concentrated insulin from the ambulatory to the inpatient setting and back again. If these agents are continued in the hospital, institutional policies need to be created to ensure safe storage, dispensing, and prescribing.

Historically, concentrated regular insulin U-500 was only available in a vial. Patients were required to draw up doses with either a U-100 insulin or tuberculin syringe due to the lack of a syringe calibrated for U-500 insulin. This led to the practice of converting "syringe markings" on U-100 insulin syringes or volume measurements on tuberculin syringes into actual units of U-500 insulin (and vice-versa). These practices introduced significant potential for error when patients transitioned between hospital and home. Since approval of the U-500 insulin pen device in April 2016, which administers actual insulin units and does not require dose conversion, many health systems are placing U-500 insulin pens on formulary in place of U-500 insulin vials as a safety measure. However, health care providers must still verify how patients administer U-500 insulin at home to ensure proper in-hospital insulin dosing. In addition, U-500 insulin syringes were approved for use with U-500 regular insulin in November 2016. The ISMP strongly recommends use of the new U-500 insulin syringe for all institutions and patients who use U-500 insulin vials to reduce the potential for error.[15] However, it may be expected that some institutions will avoid using U-500 insulin syringes because they are not currently equipped with a safety needle. Finally, pharmacists should be involved in the development and maintenance of specific policies and procedures to minimize the potential for errors involving U-500 insulin.

Newer concentrated insulin formulations, including insulin lispro U-200, insulin degludec U-200, and insulin glargine U-300 are now available, although these agents have not been studied in the settings of acute illness, NPO status, or hemodynamic instability, nor do current clinical practice guidelines provide recommendations regarding their use in these settings. Nevertheless, these insulin preparations are being used with increasing frequency in the outpatient setting. As they are only available in pens, there is no need for dose conversions because pens allow dial up dosing of the actual number of units being injected. This minimizes the risk for conversion errors that have been observed with U-500 insulin, as long as providers are aware of this aspect of these products.

3.3 | Pen vs vial

Regular insulin U-100 is currently only available in vials, and some of the newer insulin products are only available in pens; however, most insulin products are available in either pens or vials. In one study, a higher percent of hospitalized patients randomized to insulin pens during hospitalization preferred to continue using insulin pens after discharge compared to the percent randomized to insulin vials that preferred to continue insulin vials.[16] The same study identified a projected cost savings associated with use of insulin pens over vials in the hospital; however, this study did not account for the availability of 3 mL vials for certain insulin products.[16] It was also noted that this cost savings would have been lower or non-existent if hospital length of stay was longer than that reported in this study (8-9 days), assuming patient-specific insulin vials and pens are dispensed.

Inpatient nurses at the same hospital reported that insulin pens were more convenient, took less time to prepare, and were an improvement over use of insulin vials and syringes.[17] However, despite training prior to the survey, only 39% felt confident that they were administering the correct dose, and less than half felt more comfortable using pens over vials, which was largely driven by nurses' reports of seeing insulin on the skin after pen administration.[17]

Since many patients who take insulin use or will use insulin pens in the outpatient setting, use of pens in the hospital provides an opportunity for patients to learn and practice the correct administration technique under supervision. If insulin pens are stocked in their hospital, pharmacists should take the lead on developing and implementing guidelines and strategies to promote safe use, including the fact that insulin pens cannot be shared between patients, and that insulin should not be withdrawn from them with a syringe.[18] For example, use of patient-specific bar codes on insulin pens can help prevent inadvertent sharing between patients. Pharmacists can also provide important safety information to patients regarding visual and administration technique differences between safety pen needles used by nurses in hospitals and pen needles dispensed by outpatient pharmacies.

3.4 | Continuous subcutaneous insulin infusion devices

In the past several years, the number of patients utilizing continuous subcutaneous insulin infusion (CSII) devices in the outpatient setting has increased dramatically, and current guidelines recommend that CSII devices be continued in the hospital in alert and willing patients.[11] However, the variety of available CSII devices and the lack of standardized components and complexity of insulin pump software

act as barriers to clinicians' knowledge and comfort with these devices.[19] In addition, there is the potential for medication errors when a patient omits doses or does not inform the nurse of doses self-administered via CSII devices.

It is recommended that hospitals adopt specific policies and procedures for continuing CSII therapy in the hospital. Recommendations include implementing processes to identify appropriate candidates for inpatient CSII self-management, developing a specific order set for in-hospital insulin pump use, delineating patient responsibilities for self-management, consistently documenting blood glucose (BG) measurements and insulin doses administered, and providing education to caregivers.[20] Other recommendations include developing "menu maps" to allow for easy navigation of CSII device menus to identify settings, and posting reminders to remove CSII devices prior to tests involving electromagnetic fields.[21] In addition, as use of continuous glucose monitors (CGMs) become more common amongst CSII device users, policies will need to include guidance on the use of CGMs in the hospital.

3.5 | Noninsulin glucose-lowering medications

Despite the growing number of noninsulin agents available, there is a dearth of literature involving their use in the hospital. The exception to this is the use of dipeptidyl peptidase 4 (DPP-4) inhibitors. Small, randomized studies have demonstrated that use of sitagliptin results in similar glycemic control as scheduled insulin in carefully selected hospitalized patients with type 2 DM, and may be associated will less glycemic variability and lower rates of hyperglycemia.[22–24] In addition, data are accumulating to support the use of glucagon-like peptide (GLP)-1 receptor agonists in hospitalized patients.[25]

Many noninsulin therapies have a delayed and unpredictable onset of action which make them less efficacious in acutely ill patients. For patients using noninsulin agents prior to hospitalization, current guidelines recommend that these agents be held in most cases due to lack of efficacy studies in the inpatient population, as well as concerns for adverse effects.[9–11] Table 1 summarizes potential risks of various noninsulin agents in the management of hyperglycemia in the hospital.[11]

Continued use of home-based noninsulin therapy may be appropriate in stable patients who are admitted with good glycemic control, expected to have a short hospital stay, and will maintain a diet similar to the one they consumed prior to admission.[10] At a minimum, pharmacists should ensure that patients are without contraindications or at high risk for poor outcomes before dispensing noninsulin therapies for management of DM or hyperglycemia.

4 | INDIVIDUAL PATIENT MEDICATION MANAGEMENT

Pharmacists who have additional training in inpatient glycemic management or certification in glycemic management (such as the Board Certified-Advanced Diabetes Management [BC-ADM] credential), can participate in pharmacy-specific or interdisciplinary glycemic management teams that adjust insulin orders, order A1c, and ensure patients receive appropriate post-discharge follow-up and education. Glycemic management teams that include pharmacists have been shown to improve glycemic control, reduce rates of hypoglycemia, reduce rates of post-operative infections, reduce readmissions and emergency room visits, and reduce per-patient post-discharge costs.[26–29] Alternatively, appropriately trained pharmacists can work with medical staff to create an orderable for "glucose management by pharmacy" which has also been shown to improve glycemic control.[30,31]

Pharmacists can also impact medication management and care of patients with hyperglycemia through routine participation in interdisciplinary patient-care rounds on surgical and general medicine services.[32,33] Alternatively, a centrally located diabetes stewardship pharmacist can identify patients with hyperglycemia who require intervention using an electronic medical record surveillance tool (dashboard) and communicate glycemic recommendations to pharmacists who round with each primary medical team.[34]

Pharmacists who want to establish or become involved with a glycemic management program at their hospital should consider the following steps:

1. Consider hospital type and other stakeholders. For instance, rural hospitals may not have an endocrinologist or nurse certified diabetes educator (CDE) on staff; pharmacists here may play a more significant role in glycemic management
2. Determine the target audience. For instance, hospitalists, surgeons, pulmonologists, and medical residents each have a different focus
3. Develop protocols that are supported by current guidelines and literature
4. Educate and gain buy-in of hospital leadership
5. Educate providers continually through hospital rounds, detailed pharmacotherapy notes, and case discussions.

To play a role in improving outcomes of hospitalized patients with hyperglycemia, pharmacists must be aware of available literature which guides inpatient glycemic management as summarized below.

4.1 | Initial patient assessment

Upon hospital admission, an accurate medication history (see section on Admission Medication History and Reconciliation above), admission BG, creatinine clearance, estimated glomerular filtration rate, and home glucose monitoring values (with attention to frequency of hypoglycemia) should be assessed. In addition, patients' diabetes self-management knowledge and behaviors should be assessed so that diabetes self-management education with attention to survival skills can be initiated as early as possible. Other issues to review include insulin use prior to admission as insulin requirements often differ dramatically with transitions from ambulatory to acute care settings. Hospitalized patients do not have the same meal plan or activity level, and the stress of acute or critical illness or infection can affect insulin needs. For patients with an A1c <7.5%-8%, or who are NPO or with reduced oral intake, an empiric reduction in basal insulin dose should be considered.[35]

An A1c should be obtained for all patients with known DM or hyperglycemia on admission, unless it is available within the last

TABLE 1 Risks of noninsulin agents in the management of hyperglycemia in the hospital

Noninsulin agents	Potential risks in the inpatient setting
Sulfonylureas: glyburide, glipizide, glimepiride	High risk for prolonged hypoglycemia; risk factors for hypoglycemia include age >65 years, poor nutritional status or NPO, and renal insufficiency
Biguanide: Metformin	Requires discontinuation if eGFR <30, and consideration for discontinuation if eGFR <45; temporary discontinuation of metformin is required at time of intravenous contrast dye and for at least 48 h (and until renal function is reassessed) in patients with CKD stage IV or stage V, and those who will undergo arterial catheter studies
Dipeptidyl peptidase IV inhibitors: sitagliptin, saxagliptin, alogliptin, linagliptin	Low risk of hypoglycemia when used alone; saxagliptin and alogliptin may increase the risk of heart failure, especially in setting of existing heart or kidney disease
Glucagon like peptide receptor agonists: exenatide, liraglutide, dulaglutide, lixisenatide, semaglutide	Low risk of hypoglycemia when used alone; gastrointestinal side effects, including nausea, vomiting, and anorexia, are common when therapy is started; the effect of weekly GLP-1 agonist initiation may take several weeks to be seen
Short-acting secreatagogues: repaglinide, nateglinide	Similar reported rates of hypoglycemia as sulfonylureas; require dosing with each meal and should be skipped if the meal is missed
Thiazolidinediones: rosiglitazone, pioglitazone	Discontinue in patients with or at risk for congestive heart failure or fluid overload; effect of TZD initiation or dosing change can take up to 12 weeks to be seen
Sodium-glucose co-transporter 2 inhibitors: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin	Causes polyuria and polydipsia; increased risk for genital infections, urinary tract infections, and acute kidney injury; cases of euglycemic ketoacidosis and urosepsis have been reported in patients with infection, hypovolemia, acute renal failure, hypoxemia, surgical intervention, pancreatic insufficiency, reduced food and fluid intake; discontinue SGLT2s 2-3 days prior to surgery
α-Glucosidase inhibitors: acarbose, miglitol	Gastrointestinal side effects are common; require dosing with each meal; avoid use if CrCl <25 or SCr >2

Abbreviations: CKD, chronic kidney disease; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; NPO, nothing by mouth; SCr, serum creatinine.

3 months.[11] This A1c can help guide both inpatient insulin use and the decision to initiate, intensify, or de-escalate the outpatient regimen upon discharge. Pharmacists should note situations when A1c obtained in the hospital may not be reliable. Some laboratories use an assay method that is inaccurate in patients with sickle cell trait, other hemoglobin variants, or those with elevated fetal hemoglobin (HbF).[36] In addition, A1c results may not be accurate in patients who receive blood transfusions and in patients with anemia, heavy bleeding, kidney failure, or liver failure.

As noted above, patient's type of DM should be assessed and documented. Patients with type 1 DM or ketosis-prone type 2 DM require basal and nutritional insulin throughout their hospitalization. For other hospitalized patients, the American Diabetes Association (ADA) recommends initiating scheduled insulin therapy when the BG is ≥180 mg/dL. The recommended BG target is 140 to 180 mg/dL for most hospitalized patients.[11] Since more stringent goals may be appropriate for younger and healthier patients, and higher BG ranges may be acceptable in patients with multiple diabetes-related complications or severe comorbidities, the ISMP recommends that the patient-specific BG targets be documented in the medical record.[12]

4.2 | Initiating subcutaneous insulin

Table 2 provides initial insulin dosing recommendations for hospitalized patients with either known DM or new hyperglycemia upon hospital admission. Current practice guidelines recommend proactive means of controlling BG in the hospital, as opposed to reactive measures such as sliding scale insulin (SSI).[9,11] Correction (or supplemental) insulin is different from SSI because it refers to use of additional doses of a rapid-acting or regular insulin to control hyperglycemia that occurs despite use of scheduled insulin. Correction insulin is not recommended as insulin monotherapy for >24 to 48 hours, and is never appropriate as monotherapy in patients with type 1 DM. Monotherapy with correction insulin may be appropriate in mildly hyperglycemic patients who do not have known insulin requirements.[10] However, if more than two doses of correction insulin are required within a 24 hours period, then scheduled subcutaneous insulin should be initiated.

Scheduled subcutaneous insulin includes basal insulin, with or without nutritional insulin, plus correction insulin.[37–39] A randomized, controlled trial in previously insulin-naïve patients with type 2 DM on nonsurgical units demonstrated that basal plus nutritional and correction insulin resulted in significant improvement in glycemic control without increasing the incidence of hypoglycemia when compared with SSI alone.[37] A similar trial in the surgical population found that a basal plus nutritional and correction insulin improved glycemic control and reduced hospital complications compared with SSI alone, although at the expense of higher rates of hypoglycemia, which may have been related to NPO status and/or poor appetite.[38] Finally, the Basal-Plus study demonstrated that medical and surgical patients with type 2 DM who were previously managed with diet, noninsulin agents, or low-dose insulin (≤0.4 units/kg/day) had similar improvements in glycemic control and hypoglycemia when treated with basal plus correction insulin compared with basal, nutritional, and correction insulin.[39] We recommend basal plus correction insulin as the initial regimen in patients who only use basal insulin or are insulin-naïve prior to hospitalization.

4.3 | Daily review and insulin adjustments

After insulin is first prescribed in the hospital, a patient's glycemic patterns must be reviewed on a daily basis, and dose adjustments made if the patient is not meeting glycemic goals. Patients who commonly require frequent changes in insulin dose include those who require

TABLE 2 Initiation of subcutaneous insulin in the hospital

Patient's regimen prior to hospitalization	Recommendation for initiation of subcutaneous insulin
Basal and nutritional insulin	Order home insulin regimen but consider reducing doses by ≥20%[a] (unless home BG always high)
Pre-mixed insulin	Order 50%-60%[a] of patient's total daily insulin dose at home as long-acting insulin. Order the other 40%-50% as nutritional insulin (rapid-acting insulin), divided into three pre-meal doses which can be held if patient is made NPO
Basal insulin (with or without noninsulin agents)	Order 60%-80%[a] of the home basal insulin dose plus correction insulin.[b] Add nutritional insulin if required[c]
No insulin	Order correction insulin.[b] if patient requires >2 doses in 24 h, then add weight-based basal insulin.[d] Add nutritional insulin if required[c]

Abbreviations: BG, blood glucose; DM, diabetes mellitus; NPO, nothing by mouth.

[a] Greater reduction is usually appropriate in patients with type 2 DM who will be NPO or whose dose of basal insulin is much greater than 50% of their total daily dose of insulin.[35]

[b] Correction insulin is rapid-acting insulin given in response to an elevated BG before meals (if patient is eating) or every 6 hours (if patient is NPO or on continuous nutrition).

[c] After basal insulin is titrated to a fasting BG <180 mg/dL, and patient is eating consistently with pre-meal or bedtime BG out of range, adjust or add nutritional insulin (rapid-acting insulin). The total daily dose of nutritional insulin is generally equal to the total daily dose of basal insulin, divided into three pre-meal doses.[35,37,38]

[d] Initial dose of basal insulin is determined after considering patient's A1C, body mass index, and current risk factors and tolerance for hypoglycemia. The recommended starting dose for basal insulin, based on the doses used in randomized clinical studies in the inpatient setting, is 0.15 to 0.25 units/kg/day.[37–39]

medications known to affect glycemic control (such as corticosteroids) and those whose infections or other acute disease states worsen or improve. Multiple fasting BGs >140 mg/mL or random BGs >180 mg/dL may suggest a need for an increase in insulin dose.[9–11] In addition, changes to a patient's insulin regimen should be made prior to any anticipated change in nutritional status. Specific interventions for adjusting insulin therapy in patients receiving enteral and parenteral nutrition have been reported in the literature.[40] As patients transition to different levels of care in the hospital, such as transfer to or from a critical care area, glycemic management orders must be re-assessed to ensure they remain safe and appropriate.

4.4 | Management of hyperglycemic crises

Pharmacists can improve outcomes of patients with hyperglycemic crises by ensuring compliance with published recommendations for DKA and hyperglycemic hyperosmolar state (HHS) management.[6,41] One key aspect includes ensuring an adequate amount and rate of intravenous (IV) fluid resuscitation and potassium replacement prior to insulin initiation. Continuous IV insulin infusions are indicated for management of most patients with hyperglycemic crises, but subcutaneous rapid-acting insulin plus aggressive fluid management may be appropriate for some patients with mild or moderate DKA managed in emergency department or step-down units.[42] If IV insulin is used, protocols that prompt nurses to add dextrose to IV fluids when the BG drops less than 250 mg/dL should be initiated. Protocols that instruct nurses to stop insulin therapy when specific BG thresholds are reached should not be utilized in this population because insulin must be continued until acidosis (in DKA) or mental status change (in HHS) have resolved.

4.5 | IV insulin infusions

In addition to management of hyperglycemic crises, IV insulin infusions are indicated for the management of persistent hyperglycemia in critically ill patients.[10,11] Many published protocols of IV insulin titration exist, and it is important for hospitals to select a validated insulin titration program that targets an evidence-based goal, avoids hypoglycemia, and minimizes glycemic variability.[43] Pharmacists can help ensure safe use of IV insulin infusions by establishing house-wide standardized insulin concentrations and smart pump guardrails and alerts.

4.6 | Transitioning from IV to subcutaneous insulin

Patients with hyperglycemic crises and those with a history of insulin-requiring DM on IV insulin require transition to basal plus nutritional subcutaneous insulin. In addition, patients with type 2 DM requiring >0.5 unit/hour of IV insulin, and those with stress hyperglycemia requiring >1 unit/hour require transition to subcutaneous insulin.[43] Given the rapid (<10 minutes) half-life of regular insulin when administered intravenously, and the delayed onset of subcutaneous insulin, the first dose of basal insulin must be given at least 2 to 4 hours before discontinuation of IV insulin. Failure to overlap IV and subcutaneous insulin will result in rebound hyperglycemia and potentially DKA. See Table 2 for suggested starting doses of subcutaneous insulin in patients not previously on insulin. Otherwise, subcutaneous insulin doses should be based on the patient's current IV insulin requirements and carbohydrate intake.

There is no single best transition protocol, but studies have shown that in an NPO patient, 60%-80% of a patient's total daily dose of IV insulin, based on mean hourly dose for the prior 6 hours, can be used to estimate basal insulin requirements.[43] In patients who are eating when on IV insulin, it may be prudent to schedule pre-meal subcutaneous doses of rapid-acting insulin (ie, nutritional insulin) while the patient is receiving an IV insulin infusion. This may avoid covering nutritional insulin requirements with IV insulin and will allow for more accurate estimates of basal insulin requirements.

4.7 | Perioperative management of patients with diabetes

Management of pre-, peri-, and post-operative hyperglycemia in surgery patients often needs to be individualized. However, general

guidelines and protocols have been established to achieve optimal glycemic control while minimizing hypoglycemia.[44,45] In general, noninsulin glucose-lowering medications should be avoided on the day of surgery, and may be resumed postoperatively once the patient resumes eating adequately and tolerates oral medications. In addition, doses of nutritional insulin are held when the patient is NPO, and doses of basal insulin may require reduction during periods of NPO or reduced oral intake.

4.8 | Management of Corticosteroid-related Hyperglycemia

The prevalence of corticosteroid-related hyperglycemia in hospital is 20%-50% among patients without a previous history of DM.[46,47] Corticosteroid type and duration of action must be taken into consideration when choosing an appropriate insulin regimen.[11] For longer acting corticosteroids like dexamethasone, use of basal insulin is appropriate. For prednisone scheduled once daily, administering NPH with the corticosteroid may be considered, because onset and duration of NPH mimics glucose-raising effects of prednisone, and use of long-acting insulin can result in nocturnal hypoglycemia.[48] While most inpatient glycemic control guidelines suggest insulin regimens to be given as 40%-50% basal insulin and 50%-60% nutritional insulin, a 3 years retrospective study showed that non-critically ill patients with hyperglycemia receiving corticosteroids require a higher percentage of their total daily dose insulin therapy as nutritional to achieve target glycemic levels.[46] In addition, it is important to decrease the insulin regimen when corticosteroids are being tapered to prevent hypoglycemia.

4.9 | Hypoglycemia management

Hypoglycemia requiring intervention is defined by the ADA as a BG <70 mg/dL.[11] Changes in mental status, nutritional intake, and daily routine while a patient is hospitalized may complicate identification and treatment of hypoglycemic episodes.[49] In addition, various concomitant medical conditions may predispose patients to experiencing hypoglycemia, including renal or hepatic failure, malnutrition, heart failure, sepsis, and malignancy. Pharmacists can play a role in preventing hypoglycemia by identifying these risk factors and recommending adjustment of glucose-lowering medications and insulin before hypoglycemia occurs.

Hypoglycemia management protocols should encourage use of the oral route in patients who are alert, can swallow, and who are not at risk for aspiration. Unless contraindicated, the same agents used in the outpatient setting (ie, carbohydrates, glucose tablets and/or gel) can be used in the hospital. Use of dextrose-containing IV fluids should be reserved for patients who are critically ill and/or who cannot tolerate management via oral or enteral routes. When dextrose-containing IV fluids are required in a patient who cannot swallow, 25 to 50 mL (ie, 12.5-25 g) of 50% dextrose can be administered into a large vein followed by a saline flush. Larger volumes of less concentrated dextrose in IV infusions (eg, 250 mL of 10% dextrose) may be used to minimize irritation and risk for extravasation. Following an episode of hypoglycemia, pharmacists should recommend reduction or discontinuation of noninsulin glucose lowering medications and/or insulin doses to prevent recurrence, keeping in mind that basal insulin should never be discontinued in a patient with type 1 DM or ketosis-prone type 2 DM.

5 | PREPARING A PATIENT WITH HYPERGLYCEMIA FOR HOSPITAL DISCHARGE

Patients with DM who are not at goal A1c should have their regimen intensified at discharge, while considering the importance of avoiding hypoglycemia.[50] It is also important to note that in-hospital use of insulin does not necessitate insulin use following discharge.[50] Pharmacists should refer to published guidelines for management of type 2 DM when recommending discharge medications.[51] For patients who do require insulin at discharge, all insulin doses and BGs during the hospitalization should be considered when designing the discharge regimen, keeping in mind that the hospital's formulary insulin may not be covered by the patient's prescription insurance provider. Also, any changes to a patient's anticipated glycemic control, such as resolution of infection or tapering of steroids, should be considered. Importantly, therapeutic interchanges made during hospitalization for formulary reasons must be reconciled with the patient's pre-admission medication list upon discharge.

Potential barriers to a successful transition to home, including financial restraints, lack of an outpatient diabetes provider, transportation issues that impact attendance at appointments, and medication access issues should be addressed prior to discharge. Some hospitals provide patients with a supply of medications at discharge.[52] If this is not possible, pharmacists should work with the patient's outpatient pharmacy to assess ability to pay for new prescriptions. It is important to note that patients who have health insurance may still have high out-of-pocket costs for certain medications or insulin types (vial vs pen). If cost is prohibitive, pharmacists can recommend or procure an alternative therapeutic option that would be more cost-effective. As an example, insulin regular, NPH, and mixed insulin may be initiated upon discharge if a patient is unable to afford a more expensive analog insulin.

A protocol for ordering diabetes supplies during the discharge process should be made available. Diabetes supplies include a glucose meter, testing supplies such as lancets and glucose test strips, and insulin pen needles or syringes if insulin or an injectable GLP-1 is prescribed. Where possible, the specific brand of glucose meter/strips should not be specified on the prescription so that the outpatient pharmacist can supply the insurer's preferred brand of testing supplies. Patients with Medicare Part B require an ICD-10 diagnosis code on all prescriptions for diabetes testing and injection supplies.

Pharmacists should be involved with educating patients on basic diabetes survival skills, especially those related to medication use.[52,53] Ideally, pharmacists who are CDEs can be responsible for diabetes-related patient education, but the CDE credential is not required to provide patients with clear and easy to follow instructions on name(s), dose(s), and administration time(s) for all diabetes medications, as well as information about which medications taken prior to admission

should be stopped or changed. Medication education, including instructions on how to administer insulin or noninsulin injectables, is best started early in the hospitalization. In addition, early assessment of a patient's cognitive ability, vision, manual dexterity, and numeracy skills is important for patients who will take insulin after discharge so that there is time to develop a plan to successfully transition the patient from the hospital.[50]

6 | INTERPROFESSIONAL COLLABORATION

Pharmacists in the hospital must work in collaboration with physicians, physician extenders, dietitians, nurses, and case managers. When each health care discipline understands and capitalizes on the expertise of the others, patient outcomes are improved. Pharmacists are valuable members of the interdisciplinary glycemic management committee at many hospitals. These oversight committees develop policies, procedures, and protocols for safe and effective management and prevention of inpatient hyper- and hypo-glycemia.[54–56] The Joint Commission (TJC) requires inclusion of a pharmacist on such teams if the hospital desires Inpatient Diabetes Certification.[57] At some institutions, pharmacists serve as chairs or leaders of the local glycemic control improvement team.[55]

Pharmacists can educate prescribers about newly approved agents used for glycemic management during daily provider conferences such as noon conferences, grand rounds, and other in-service opportunities. Pharmacists can reduce prescribing error rates by providing formalized, face-to-face feedback to prescribers regarding reported prescribing errors identified during the hospitalization and discharge process. At one hospital, pharmacists review of orders on a structured insulin order set helped to reduce the percentage of patients prescribed SSI without basal insulin, which led to a reduction in hyperglycemia.[58]

Bedside nurses play an important role in inpatient glycemic management by adopting patients' home self-management tasks during hospitalization. When paired with other urgent tasks, glycemic control often falls behind on the priority list. Pharmacists must be sensitive to the task lists of nurses and contribute to development and maintenance of glycemic management protocols that ease the burden on nursing and allow for time-sensitive glycemic control. To successfully collaborate with nurses, pharmacists should partner with nursing leadership to determine best practices. Pharmacists should volunteer to educate the hospital's core group of nursing educators and become involved with new-hire nurse education classes that cover hospital protocols and patient safety cases. Important topics related to in-hospital hyperglycemia include differences in treatment of patients with type 1 and type 2 DM, inpatient glycemic targets, insulin action and administration, importance of coordination of timing of diabetes care, and prevention and treatment of hypo- and hyperglycemia. Perhaps the most important piece of information to cover during nurse in-services is prevention of insulin-related medication errors, including omission, improper dose/quantity, and improper use of protocols which may result in labile glycemia and poor outcomes.[18] Because nurses often provide discharge medication education and assist with discharge needs of patients, such as making requests for diabetes supplies, pharmacists must engage nurses to ensure they are prepared to take on this challenging role.

Dietitians are also essential partners in hyperglycemia management teams. Pharmacists can rely on a dietitian's expertise in setting carbohydrate limits for inpatients, teaching of carbohydrate counting, dietary restrictions, and cultural and religious practices. Pharmacists should collaborate with dietitians to ensure a connection between nutritional intake and glycemic control. For example, recommendations should be made to administer nutritional insulin at the time of food intake rather than at a standardized time. In addition, glucose monitoring should be timed prior to meals, if the patient is eating, to avoid hypoglycemia related to inappropriate correction of a postprandial BG.

7 | CONCLUSION

Hospital pharmacists can play a role in preventing and managing glycemic excursions by obtaining accurate and complete admission medication histories, participating in formulary management of glucose-lowering medications and devices, recommending appropriate inpatient glycemic management strategies such as avoidance of SSI monotherapy, and addressing barriers to a successful discharge. In addition, inpatient diabetes pharmacist specialists with advanced training or certification can take a leadership role in their hospital's interdisciplinary glycemic management oversight committee (as required for TJC certification) and participate as members of glycemic management patient care teams. In all these activities, pharmacists can improve glycemic safety and outcomes.

Conflict of interest

Alicia Abla is on the Speaker's Bureau of Novo and BI. Raja Hanania is on the Speaker's Bureau of Novo. None of the other authors have any conflicts to disclose.

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