Management of Inpatient Hyperglycemia and Diabetes in Older Adults

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Adults aged 65 years and older are the fastest growing segment of the U.S. population, and their number is expected to double to 89 million between 2010 and 2050. The prevalence of diabetes in hospitalized adults aged 65–75 years and over 80 years of age has been estimated to be 20% and 40%, respectively. Similar to general populations, the presence of hyperglycemia and diabetes in elderly patients is associated with increased risk of hospital complications, longer length of stay, and increased mortality compared with subjects with normoglycemia. Clinical guidelines recommend target blood glucose between 140 and 180 mg/dL (7.8 and 10 mmol/L) for most patients in the intensive care unit (ICU). A similar blood glucose target is recommended for patients in non-ICU settings; however, glycemic targets should be individualized in older adults on the basis of a patient's clinical status, risk of hypoglycemia, and presence of diabetes complications. Insulin is the preferred agent to manage hyperglycemia and diabetes in the hospital. Continuous insulin infusion in the ICU and rational use of basal-bolus or basal plus supplement regimens in non-ICU settings are effective in achieving glycemic goals. Noninsulin regimens with the use of dipeptidyl peptidase 4 inhibitors alone or in combination with basal insulin have been shown to be safe and effective and may represent an alternative to basal-bolus regimens in elderly patients. Smooth transition of care to the outpatient setting is facilitated by providing oral and written instructions regarding timing and dosing of insulin as well as education in basic skills for home management.

The global burden of diabetes has increased significantly during the past two decades and is expected to affect more than 642 million adults by 2040, with the majority of patients having type 2 diabetes (1). In the U.S., the Centers for Disease Control and Prevention has estimated that 9.3% of the total population has diabetes (2) and forecasted that the incidence will double by 2050 (3). Diabetes disproportionally affects the elderly, as more than 25% of the U.S. population older than 65 years of age has diabetes (4). For those aged 65–74 years, the rates doubled from 10.1 to 21.5% between 1993 and 2014, and for those aged 75 years or older, the rate increased from 8.0 to 19.2% between 1990 to 2014 (5). Patients with diabetes are more likely to require hospital admissions compared with individuals without diabetes. Results from the National Hospital Discharge Survey (NHDS) estimated that ~250,000 hospitalized patients had diabetes as a first-listed diagnosis in 2010, with a more than three times higher rate for individuals aged 65 years and older (48.9 per 10,000 population) compared with patients younger than 45 years (13.3 per 10,000 population) (6).

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Several observational and prospective randomized trials have reported a strong association between inpatient hyperglycemia and poor clinical outcome with regard to mortality, morbidity, length of stay, infections, and overall complications (7,8). In addition, substantial evidence indicates that correction of hyperglycemia reduces infections, hospital complications, and mortality (9–11). Few prospective studies, however, have focused on the management of elderly patients in the inpatient setting. This review will examine the prevalence, diagnosis and monitoring, and available recommendations on the hospital management of hyperglycemia and diabetes in the elderly population.

PREVALENCE

The overall prevalence of inpatient hyperglycemia and diabetes in elderly patients is not known. Cross-sectional studies have reported an estimated prevalence of diabetes in older adults aged 65–75 and >80 years of 20% and 40%, respectively (12,13). Compared with individuals <65 years of age, hospital discharge rates related to diabetes are 1.5- and 2.4-fold higher among subjects aged 65–74 and >75 years, respectively (14). The Atherosclerosis Risk in Communities (ARIC) Study, with a follow-up period longer than 20 years, recently reported higher rates of hospitalization with increasing age in subjects with and without diabetes, with rates of hospitalization 3.1 times higher in individuals with diagnosed diabetes compared with those without a history of diabetes (15) (Fig. 1). In the hospital, the prevalence of hyperglycemia (defined as blood glucose >140 mg/dL [7.8 mmol/L]) in patients over the age of 65 years is reported in more than 70% of critically ill and cardiac surgery patients (16,17) and in about one-third of general medicine and surgery patients (7,18).

ECONOMIC BURDEN

Adults over 65 years of age account for more than one-third of all U.S. community hospital stays (19). In 2012, estimates from national surveys, medical standard analytical files, and claims databases for the commercially insured population in the U.S indicated that the total cost of diabetes was approximately $245 billion (20). Approximately 59% of health care expenditures attributed to diabetes are related to health resources used by the population older than 65 years of age, much of which is paid by the Medicare programs. The estimated average annual excess expenditure for patients with diabetes aged 65 years and above was $11,825 per year, which is twice the expenditure for patients younger than 65 years of age. In addition, elderly patients with hyperglycemia and diabetes are less likely to be discharged to home, frequently requiring transfer to a transitional care unit or nursing home facility, increasing medical costs (7). Similarly, elderly residents with diabetes in long-term care facilities have significantly higher number of comorbidities, cardiovascular disease, kidney disease, visual impairment, and foot problems (including amputations) and have higher odds of having emergency room visits compared with residents without diabetes (21,22).

PATHOPHYSIOLOGY

Hyperglycemia is commonly present in patients with acute medical or surgical conditions, resulting from the metabolic and hormonal changes associated with increased circulating counterregulatory hormones (cortisol, catecholamines, growth hormone, and glucagon) and proinflammatory cytokines that interfere with carbohydrate metabolism, leading to excessive hepatic glucose production and reduced glucose uptake in peripheral tissues (Fig. 2) (10,23). In addition, physiological changes in older adults contribute to the increased prevalence of hyperglycemia and diabetes (24,25). Aging is associated with reduced glucose-induced insulin release and increased insulin resistance in peripheral tissues, primarily in muscle and adipose tissue (26). Increasing age also tends to be associated with abdominal obesity and increased circulating levels of free fatty acids and inflammatory markers, specifically tumor necrosis factor α and interleukin 6, which are associated with increased insulin resistance in the elderly (27,28). Further contributors to the development of hyperglycemia in the elderly are the use of medications with adverse effects on carbohydrate metabolism such as diuretics, β-blockers, and glucocorticoids.

Several mechanisms explain the detrimental effects of hyperglycemia (Fig. 2). Hyperglycemia causes osmotic diuresis that leads to hypovolemia, decreased glomerular filtration rate, and prerenal azotemia. Hyperglycemia is associated with impaired leukocyte function, including decreased phagocytosis, impaired bacterial killing, and chemotaxis, leading to hospital infections and poor wound healing. In addition, acute hyperglycemia results in the activation of nuclear factor κB (NF-κB), the production of proinflammatory

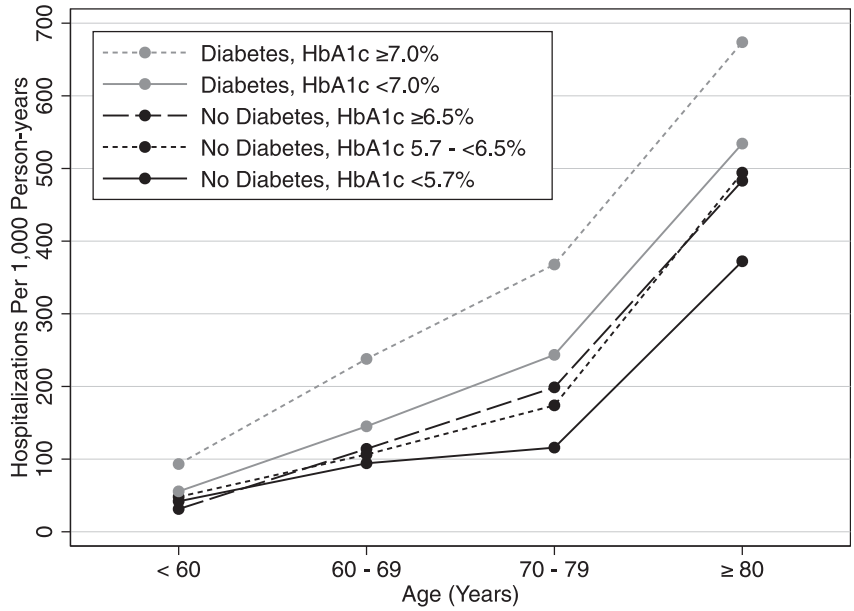

Figure 1—Longitudinal data on all-cause hospitalizations in the ARIC Study (15). Data are presented according to diabetes and HbA_{1c} categories.

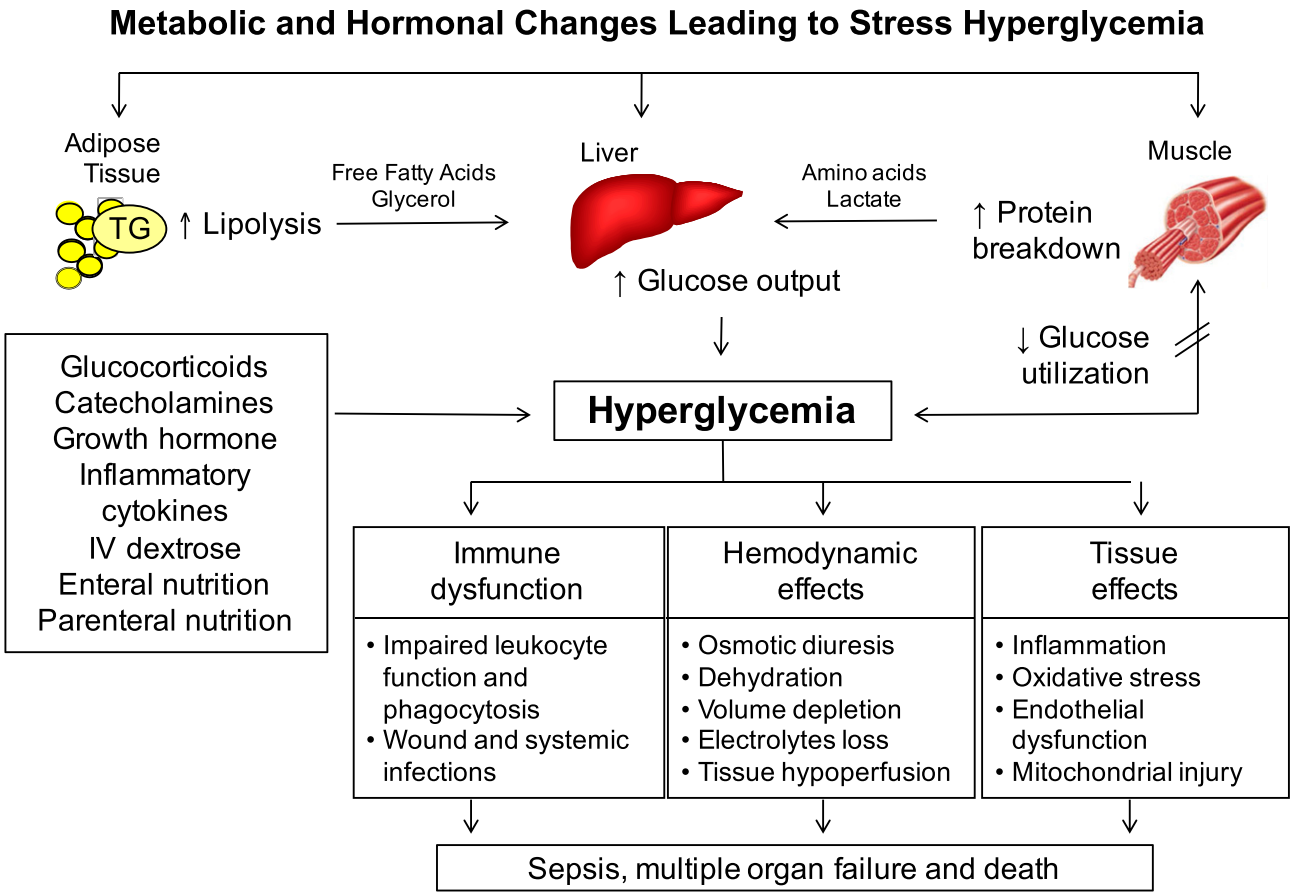

Figure 2—Pathophysiology of hyperglycemia and its complications in older adults. TG, triglycerides.

cytokines, and oxidative stress, leading to increased vascular permeability and mitochondrial dysfunction (29,30). Furthermore, hyperglycemia impairs endothelial function by suppressing formation of nitric oxide and impairing endothelium-dependent, flow-mediated dilation (30).

CLINICAL PRESENTATION

Elderly patients are less likely to experience typical symptoms of hyperglycemia, such as polyuria and polydipsia, because the renal threshold for glycosuria increases with age and the thirst mechanisms are more likely to be impaired. Elderly patients often present with weight loss and fatigue; however, these symptoms frequently go unnoticed or are attributed to old age, failure to thrive, or confusion (21).

Elderly patients differ according to the time of diabetes onset. Patients with longer duration of diabetes have a much greater burden of microvascular disease and worse glycemic control than patients with shorter duration of disease (31). Also, the interaction of age and duration of diabetes (age × duration) has been associated with end-stage renal disease, eye disease, lower-limb amputation, stroke, heart failure, and mortality (32), suggesting that older patients with longer duration of diabetes admitted to the hospital are a particularly vulnerable population.

The two leading causes of hospital admissions in older adults with diabetes are cardiovascular disorders (coronary artery disease, angina, heart failure, and stroke) and respiratory diseases (pneumonia and chronic obstructive pulmonary disease (33,34). They are followed by diseases of the digestive and genitourinary systems, with diabetes as the primary diagnosis (34).

Of great interest is the increasing number of admissions due to adverse drug reactions in the elderly (aged 65 years or older) adults accounting for more than 700,000 emergency department visits and 120,000 hospitalizations in the U.S. each year (34). Older adults (aged 65 years or older) are twice as likely as others to come to emergency departments for adverse drug events (over 177,000 emergency visits each year) and nearly seven times more likely to be hospitalized after an emergency visit. Data from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project (NEISS-CADES) (2007 through 2009) estimated that about half of the hospital admissions for adverse drug reactions were for adults older than 65 years of age and half of these hospitalizations were for people over the age of 80 years (35). Four medications or medication classes were implicated (alone or in combination) in 67.0% (95% confidence interval [CI], 60.0–74.1) of hospitalizations: warfarin (33.3%), insulin (13.9%), oral antiplatelet agents (13.3%), and oral hypoglycemic agents (10.7%). Among older Medicare beneficiaries with diabetes, hospital admissions for hypoglycemia now outpace those for hyperglycemia (36), which is likely the result of increased efforts to intensify glycemic control over the past decade.

GLYCEMIC CONTROL TRIALS IN ELDERLY POPULATIONS

The results of observational and randomized trials in hospitalized patients with and without a history of diabetes have reported a strong association between hyperglycemia and poor clinical outcome in all patients including the elderly. Few studies, however, have reported on the impact of hyperglycemia and its treatment on hospital outcomes in elderly patients, and most randomized clinical trials that examined the effect of inpatient glycemic control on outcomes excluded frail older persons (11,37–39). A large observational cohort study that included 250,040 admissions from 173 medical, surgical, and cardiac intensive care units, of whom 66% of patients were older than 60 years of age, reported that hyperglycemia was significantly associated with increased mortality in critically ill individuals, independent of severity of illness (40). Compared with normoglycemic individuals, adjusted odds of mortality [odds ratio (95% CI)] for mean glucose 146–199, 200–300, and >300 mg/dL were 1.82 (1.74–1.90), 2.13 (2.03–2.25), and 2.85 (2.58–3.14), respectively.

Although patients in subacute care units may not necessarily represent acutely ill patients in the hospital, the demographic characteristics are comparable to elderly hospitalized patients. We recently reported the results of a prospective randomized controlled trial evaluating the efficacy and safety of diabetes treatment in elderly patients with type 2 diabetes admitted to long-term care facilities, with >90% of them admitted to subacute care units (41). A total of 150 patients (aged 79 ± 8 years, duration of diabetes 8.2 ± 5.1 years) with a randomization glucose of 194 ± 97 mg/dL were treated with low-dose basal insulin (glargine, starting dose 0.1 units/kg/day) or oral antidiabetic drug (OAD) therapy as per primary care provider discretion for 26 weeks. Both groups received supplemental rapid-acting insulin before meals for blood glucose >200 mg/dL. There were no differences in the mean fasting glucose, hospital complications, or mortality between treatment groups. A major finding in our study is that treatment with a low dose of basal insulin and OAD resulted in a similar frequency of hypoglycemia, with ~30% of patients experiencing glucose <70 mg/dL. These results suggest that starting with a low daily dose of basal insulin of ~0.1 units/kg is sufficient to maintain blood glucose levels in a reasonable range in elderly patients. Unfortunately, no prospective studies have been conducted in hospitalized elderly patients with diabetes, and these results cannot necessarily be extrapolated to the inpatient setting.

INPATIENT HYPOGLYCEMIA

Hypoglycemia is common in hospitalized elderly patients and is associated with poor outcomes. In general medicine and surgical patients with diabetes, hypoglycemia occurs in 12–38% of patients with type 2 diabetes receiving insulin therapy (11,24,38,39,42,43). In critically ill patients enrolled in clinical trials, the prevalence of severe hypoglycemia (glucose ≤40 mg/dL) ranged between 5 and 18.7% with intensive glycemic control (17,44–46). The Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial reported that among 6,026 patients, a total of 2,714 (45.0%) patients had hypoglycemia (45). During follow-up, mortality was 23.5% in patients without hypoglycemia, 28.5% in subjects with moderate hypoglycemia (41 to 70 mg/dL [2.3 to 3.9 mmol/L]) and 35.4% in those with severe hypoglycemia (<40 mg/dL [2.2 mmol/L]). The hazard ratio for death with adjustment for treatment assignment, as compared with those without hypoglycemia, was 1.81 (95% CI 1.59–2.07) for moderate hypoglycemia and 3.21 (95% CI 2.49–4.15) for patients with severe hypoglycemia (46).

Hospitalized patients who are elderly are especially vulnerable to the adverse effects of inpatient hypoglycemia (47). Several observational and randomized clinical trials have reported that hypoglycemia in elderly patients is associated with longer length of stay and increased hospital mortality (48–50). In a study exclusively involving hospitalized patients aged 70 years or older, Kagansky et al. (48) reported that hypoglycemia is common and associated with twofold increased mortality during hospitalization and during 3-month follow-up. Similarly, Shilo et al. (49) reported that in patients aged 65 years and older admitted to acute medical and geriatric wards, hypoglycemia (mean glucose 39 ± 7 mg/dL) was a predictor of mortality [odds ratio 3.67 (95% CI 1.2–11.2)] even after the adjustment for other risk factors.

Many risk factors contribute to development of inpatient hypoglycemia (Table 1). Treatment with insulin is the most common risk factor for inpatient hypoglycemia (47,51). Other risk factors include use of sulfonylurea therapy, failure to adjust insulin to nutritional intake, and changes to hospital routine (51,52). Interruptions in usual nutritional intake and changes in medications frequently occur during hospitalization and can precipitate hypoglycemia when hypoglycemic agents are used. Elderly people are more prone to hypoglycemia during hospitalization because of the higher rate of comorbidities such as renal failure, malnutrition, malignancies, dementia, and frailty (48,53). In addition, older hospitalized patients often experience failure of regulatory mechanisms, especially in stress situations, such as reduced release of glucagon and epinephrine in response to hypoglycemia (54). In addition, despite a comparable prolongation of reaction time induced by hypoglycemia, elderly patients fail to perceive neuroglycopenic and autonomic hypoglycemic symptoms (55), which can delay the response to correct a hypoglycemic episode by the hospital staff.

The presence of renal failure, sepsis (49,53), and low albumin level (56) are predictive markers of hypoglycemia in elderly hospitalized patients. Under normal conditions, renal glucose release accounts for 20–40% of overall gluconeogenesis

Table 1—Factors contributing to inpatient hypoglycemia in older adults with diabetes

Medications: insulin, sulfonylureas, glinides, quinolones
Intensive glycemic control
Inappropriate insulin dosing and medication errors
Poor coordination of insulin administration and food delivery
Interruption of enteral nutrition or parenteral nutrition infusion
Hypoglycemia unawareness
Renal insufficiency
Liver failure
Severe illness, sepsis
Dementia
Frailty
Medical and surgical procedures

and, in conditions such as fasting and hypoglycemia, can increase two- to threefold. In patients with renal insufficiency, decreased renal gluconeogenesis, lack of gluconeogenic substrates with decreased food intake, decreased renal degradation and excretion of insulin, and impairment of counterregulatory hormonal responses can all lead to hypoglycemia.

Recent studies have reported that the increased mortality rates associated with inpatient hypoglycemia may not be caused directly by hypoglycemia per se but may instead be due to the association between hypoglycemia and more severe illness (47,57,58). These studies have shown that in patients with and without diabetes, mortality was higher only among those with spontaneous hypoglycemia and not in iatrogenic-induced hypoglycemia (i.e., insulin therapy). Thus, it is possible that antihyperglycemic therapy may unmask a propensity to develop hypoglycemia in the severely ill rather than directly cause death. As elderly patients are at increased risk of comorbidities and inpatient mortality, it has not been possible to determine if hypoglycemia is a marker of severity of illness or a direct cause of mortality.

GLYCEMIC TARGETS

In the absence of specific recommendations for the inpatient management of diabetes and hyperglycemia in older adults, we recommend to follow general clinical guidelines for adult patients but with emphasis in preventing hypoglycemia. For inpatient glycemic control, the American Diabetes Association's *Standards of Medical Care in Diabetes—2016* recommends target glucose levels between 140 and 180 mg/dL (7.8 and 10 mmol/L) for most intensive care unit (ICU) patients (59). More stringent goals, such as 110–140 mg/dL (6.1–7.8 mmol/L), may be appropriate for select patients, such as cardiac surgery patients and patients with acute ischemic cardiac or neurological events, provided the targets can be achieved without significant hypoglycemia. The Society of Thoracic Surgeons Blood Glucose Guideline Task Force recommended that patients with or without diabetes who have persistently elevated serum glucose >180 mg/dL (10 mmol/L) during the perioperative period should receive intravenous (IV) insulin infusions to maintain serum glucose <180 mg/dL (10 mmol/L) (60). In agreement with less aggressive targets, two recent randomized controlled trials in cardiac surgery patients failed to demonstrate that intensive insulin therapy targeting glucose between 100–140 mg/dL reduces hospital complications compared with a target of 140–180 mg/dL (61,62).

A glucose target between 140 and 180 mg/dL (between 7.8 and 10.0 mmol/L) was recommended for most patients in noncritical care units (59). Patients with a prior history of successful glycemic control in the outpatient setting in the absence of hypoglycemia may be maintained with a glucose target below 140 mg/dL (7.8 mmol/L). For avoidance of hypoglycemia, daily insulin dosage adjustment is usually necessary when glucose values fall below 100 mg/dL (5.6 mmol/L) (8). The admission HbA_{1c} concentration was recently shown to be a good predictor of inpatient glycemic control and risk of hypoglycemia <70 mg/dL (3.9 mmol/L) in insulin-treated patients with type 2 diabetes (64). In this study, patients admitted with HbA_{1c} levels <7% were at higher odds for hypoglycemia (63).

Higher glucose ranges may be acceptable in terminally ill patients, in patients with severe comorbidities, and in inpatient care settings where frequent glucose monitoring or close nursing supervision is not feasible. These recommendations, in agreement with Endocrine Society recommendations (8) for inpatient management of hyperglycemia and diabetes in non-ICU settings, suggest the need of individualization of glycemic targets based on the patient's clinical status, risk of hypoglycemia, and presence of comorbidities.

MANAGEMENT OF HYPERGLYCEMIA IN THE ICU

Several strategies have been used to achieve glycemic control in critical care settings. The short half-life of IV insulin (<15 min) allows flexibility in adjusting the infusion rate in the event of unpredicted changes in nutrition or the patient's health. In most patients, the use of continuous insulin infusion (CII) lowers blood glucose levels to target range in less than 4–8 h and allows for rapid dose titration in accordance with changes in clinical status. The Society of Critical Care Medicine and The Society of Thoracic Surgeons recommend that a glucose level >180 mg/dL should trigger initiation of insulin therapy, titrated to maintain glucose values between 140 mg/dL and 180 mg/dL while avoiding hypoglycemia (60,64). A large number of CII protocols for the treatment of medical and surgical patients in the ICU are reported in the literature (65). Recently, computer-based algorithms aiming to direct the nursing staff in adjusting insulin infusion rates have become commercially available. Although the use of computer-based algorithms has been associated with lower rates of hypoglycemia, glycemic variability, and a higher percentage of glucose readings within target range, no studies have reported reduction in hospital complications or mortality compared with treating patients with the standard regimens (9,64). The use of subcutaneous insulin has not been formally studied in ICU patients and should be avoided in critical ill patients, in particular during hypotension or shock.

MANAGEMENT OF HYPERGLYCEMIA IN NONCRITICAL CARE SETTINGS

Subcutaneous insulin is the preferred agent for glycemic control in non-ICU settings. For most patients in non-ICU settings, subcutaneous insulin therapy with basal insulin once or twice daily, alone or in combination with prandial insulin, is effective and safe. The use of sliding scale insulin is not acceptable as the single regimen in patients with diabetes, as it results in undesirable hypoglycemia and hyperglycemia and increased risk of hospital complications. Selecting the treatment regimen in elderly patients is based on patient's nutritional status, body weight, and hypoglycemia risk.

Basal Prandial Regimen

Patients with adequate oral intake should receive a basal prandial regimen divided half as basal and half as prandial insulin starting at a total daily dose (TDD) of 0.3 units per kg (Fig. 3). Half of the TDD should be given as basal insulin once daily and half as rapid acting insulin before meals. Several studies have shown that basal-bolus regimen results in better glycemic control and in lower rates of perioperative complications compared with sliding scale insulin therapy alone (11,38).

Multiple doses of NPH and regular insulin were compared with basal-bolus regimen with insulin analogs in two controlled trials in medical patients with type 2 diabetes (37,43). Both studies reported that treatment with NPH and regular insulin resulted in similar improvements in glycemic

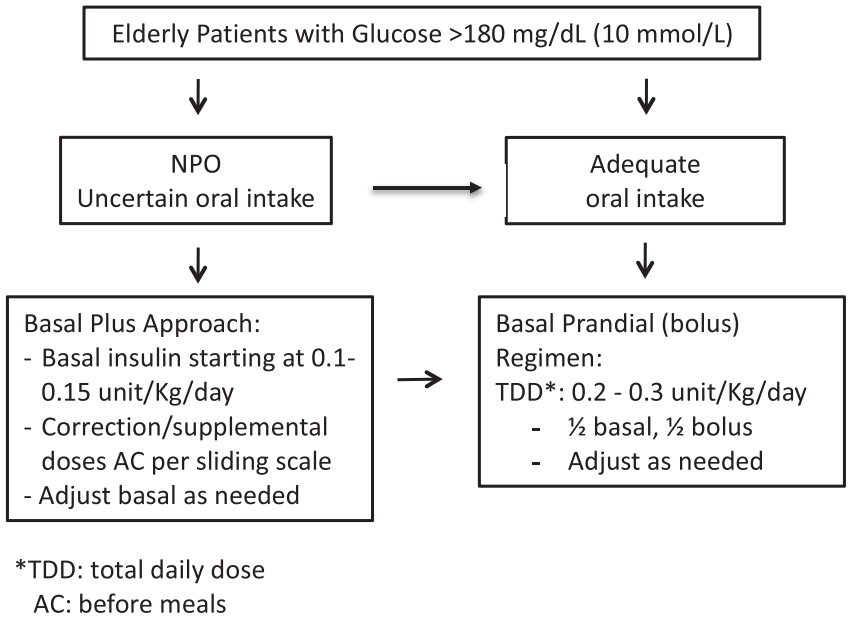

Figure 3—Insulin therapy in hospitalized elderly patients with diabetes.

control and no difference in the rate of hypoglycemic events or in hospital length of stay, compared with basal-bolus regimen. However, because NPH has a peak of action ~8–12 h after injection, there is risk of hypoglycemia in patients with poor oral intake. In one of the studies, the number of severe hypoglycemic episodes was higher in patients receiving human insulin compared with insulin analogs (43). In a more recent study, the use of premixed human insulin in elderly patients (mean age ~70 years) in general medicine and surgery areas resulted in a threefold higher rate of hypoglycemia compared with the use of basal-bolus regimen with insulin analogs, indicating that premixed formulations should be avoided in the hospital setting (66).

Basal-Bolus Regimen

Most elderly patients have reduced oral intake due to lack of appetite, acute illness, medical procedures or surgical interventions. In such patients, the starting insulin total daily dose should be reduced to 0.1–0.15 units/kg/day, given mainly as basal insulin (39). If necessary, additional rapid-acting insulin analogs or short-acting insulin is administered as correctional insulin coverage for glucose levels >180 mg/dL (10 mmol/L) before meals and at bedtime. The recently reported Basal Plus trial (39) randomized patients with type 2 diabetes to receive a basal-bolus regimen with glargine once daily and glulisine before meals and to a basal plus regimen with glargine once daily and supplemental doses of glulisine for correction of hyperglycemia per sliding scale. This trial reported that the use of basal insulin at a starting dose of 0.25 or 0.15 units/kg/day in patients younger or older than age 70 years, respectively, resulted in similar improvement in glycemic control and in the frequency of hypoglycemia compared with a standard basal-bolus regimen. These results indicate that the basal plus correction regimen is preferred for patients with poor oral intake, whereas a basal-prandial (basal-bolus) insulin regimen may be preferred for patients with good nutritional intake.

SUPPLEMENTAL/CORRECTION DOSES OF REGULAR INSULIN ("SLIDING SCALE")

The use of sliding scale insulin (SSI) continues to be a common practice to correct hyperglycemia in hospitalized patients, including elderly patients. Potential advantages of SSI are convenience, simplicity, and promptness of treatment. It is possible that in some patients with good glycemic control treated with diet alone or with oral antidiabetes agents before admission, the use of SSI may be sufficient for glycemic control over the short term. The use of a SSI regimen alone is faced with several challenges that include inadequate coverage of glycemic excursions and increased risk of complications (11,38). Several randomized multicenter trials comparing the efficacy and safety of SSI and basal insulin analogs reported greater improvement in blood glucose control and reduction in hospital complications compared with the use of SSI. In patients with poor nutrition intake, the use of a daily dose of basal insulin in combination with SSI to correct hyperglycemia has been shown to be effective in improving glycemic control and in preventing complications (39).

NONINSULIN THERAPIES

The use of noninsulin antihyperglycemic agents are not recommended for the management of hyperglycemia in hospitalized patients. There are potential limitations to the use of most oral antidiabet agents, including the slow onset of action, which may not allow rapid dose adjustment to meet the changing needs of the acutely ill patient, and risk of hypoglycemia with insulin secretagogues (8). In addition, many patients have one or more contraindications to the use of metformin upon admission including acute heart failure or renal or liver failure, which may increase the risk of lactic acidosis (67). The use of thiazolidinediones may precipitate or worsen heart failure and peripheral edema.

There has been recent interest in using incretin-based therapies in the hospital because they have few side effects and are associated lower rates of hypoglycemia compared with insulin regimens (68). A recent randomized, open-label pilot trial determined differences in glycemic control between treatment with sitagliptin alone or in combination with basal insulin in noncardiac patients with type 2 diabetes (69). Patients in the sitagliptin group received a single daily dose of 50–100 mg based on kidney function. Sitagliptin was well tolerated, and, in combination with supplemental (correction doses) rapid-acting insulin or in combination with basal (glargine) insulin, resulted in no significant differences in mean daily blood glucose, frequency of hypoglycemia, or the number of treatment failures compared with a basal-bolus regimen. These results suggest that treatment with a dipeptidyl peptidase 4 inhibitor alone or in combination with basal insulin is safe, may represent an alternative for the management of hyperglycemia in the hospital, and may prove especially

useful in treating elderly patients with mild to moderate hyperglycemia. Similar results were found in a multicenter trial (n = 279) (70) comparing sitagliptin plus basal insulin with basal-bolus therapy in hospitalized patients and a study (NCT02182895, n = 70) enrolling patients with good glycemic control (HbA_{1c} <7.5%) comparing saxagliptin with insulin therapy. Both studies were presented at the 76th Scientific Sessions of the American Diabetes Association, New Orleans, LA, 10–14 June 2016. Caution is recommended with the use of saxagliptin and alogliptin in patients with established heart or kidney disease because of a potential increased risk of heart failure, according to a recent FDA safety communication.

The sodium–glucose cotransporter 2 (SGLT2) inhibitors, a class of oral antidiabetic agents that decrease concentrations of plasma glucose by inhibiting proximal tubular reabsorption in the kidney, have been shown to be effective in reducing HbA_{1c} by ~0.6–1.0% with a low risk of hypoglycemia. These agents, however, have been associated with increased risk of urinary and genital tract infections and dehydration and are contraindicated in patients with impaired renal function. In addition, an association has been reported between the use of SGLT2 inhibitors and the development of diabetic ketoacidosis among patients with type 1 and type 2 diabetes (71). These potential side effects make the use of SGLT2 inhibitors less attractive in acutely ill hospitalized patients with hyperglycemia.

HOSPITAL DISCHARGE PLANNING

The discharge period is often a further opportunity to improve the global care of the older patient with diabetes. Although insulin is used in the hospital for most patients with diabetes, many patients do not require insulin after discharge. At discharge, most elderly patients with type 2 diabetes who are clinically stable can, in the absence of contraindications, recommence oral medications. Admission HbA_{1c} has been shown to help in tailoring diabetes treatment after hospital discharge (72). Elderly patients with acceptable diabetes control (HbA_{1c} <7.5–8%) could be discharged on their prehospitalization treatment regimen (oral agents and/or insulin). Subjects with HbA_{1c} between 8.0 and 10% could be discharged on oral agents plus basal insulin at 50% of the hospital basal dose. Patients with HbA_{1c} >10% should be discharged on a basal-bolus regimen or on a combination of preadmission oral agents plus 80% of hospital basal insulin dose (72).

Patients who are either newly started on diabetes medications or those with diabetes who have treatment modifications during the hospital stay are at risk for medication errors and adverse effects following hospital discharge if clear information about glycemic management is not provided at time of discharge (73). To avoid confusion and reduce the likelihood of readmission, it is important to effectively communicate the discharge diabetes regimen to both the patient (and/or the caregiver) as well as the patient's primary care physician. Although glucose control may be beneficial in decreasing diabetes complications, the risk of hypoglycemic events can be detrimental in the elderly and may lead to increased morbidity and mortality. Physicians should keep in mind that no randomized controlled trials have shown benefits of tight glycemic control on clinical outcome and quality of life in ambulatory elderly patients and in residents admitted to long-term care facilities. Until those studies become available, we believe that safe and moderate glycemic control, minimizing the risk of hypoglycemic events, are indicated in elderly patients with diabetes.

CONCLUSIONS

Both diabetes and hyperglycemia are common and are associated with increased risk of complications among elderly hospitalized patients. Careful attention to goal-directed glycemic management can help avoid complications of uncontrolled hyperglycemia and hypoglycemia in these patients. Scheduled insulin therapy is recommended for the majority of patients with type 2 diabetes in the hospital. Patients treated with insulin prior to admission can continue to receive their usual home regimen modified according to severity of illness, risk of hypoglycemia, and level of glycemic control. For patients not previously treated with insulin, weight-based dosing algorithms can be used for calculation of basal and/or basal-bolus regimens as the preferred treatment alternative in the hospital. Increasing evidence indicates that the use of dipeptidyl peptidase 4 inhibitors alone or in combination with low-dose basal insulin may represent an effective and safe alternative to a basal-bolus insulin regimen. Providing patients and their caregivers with the skills and information necessary to manage their regimen as outpatients can contribute to improved glycemic control while lowering the risk for hypoglycemia and readmission.

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