In-hospital blood glucose regulation

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Abbreviations

ADA:	American Diabetes Association
CGM:	Continuous Glucose Monitoring
FPG:	Fasting Plasma Glucose
GFR:	Glomerular Filtration Rate
ICU:	Intensive Care Unit
NHDS:	National Hospital Discharge Survey
NPO:	Nil Per Os
POC:	Point of Care
SC:	Subcutaneous
SSRI:	Sliding-Scale Regular Insulin
WHO:	World Health Organization

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Abstract

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This paper is a narrative review of the literature regarding in-hospital glucose regulation. Due to the increasing prevalence of diabetes in modern day medicine, proper management has never been more important. Acutely ill patients are at increased risk for developing hyperglycemia regardless of whether or not they have a pre-admission diagnosis of diabetes. The practice of maintaining tight glycemic control has been debated in the literature as it can be associated with an iatrogenic risk of hypoglycemia. However, there is a body of evidence that good glycemic control is associated with better outcomes. Currently, there is a consensus that blood glucose in hospitalized patients should be maintained below 10 mmol/L - an aim which might be individualized according to specific patient's variables and concurrent treatment plans. Insulin is recognized by most institutions as the treatment of choice in critically and non-critically ill patients in the hospital setting and is associated with better health outcomes compared to other modalities which are currently not recommended. However, in non-critically ill patients and those admitted for minor surgery their former treatment might be continued if blood glucose control is good. Stress hyperglycemia is fairly common in acutely ill patients and is associated with later development of new-onset diabetes thus reinforcing the value of effective communication and proper follow up in such patients.

Keywords: Glucose, BG Regulation, In-Hospital, Stress Hyperglycemia, Insulin

Sažetak

Regulacija glikemije u hospitaliziranih bolesnika
Michael Anthony La Delfa

Ovaj rad je narativni pregled literature o regulaciji glikemije u hospitaliziranih bolesnika. Zbog povećanja broja oboljelih od šećerne bolesti pravilno liječenje je od izuzetne važnosti za modernu medicinu. Oboljeli od akutnih bolesti isu imaju riziku natanka hiperglikemije bez obzira imaju li šećernu bolest od ranije ili ne. Striktna glukoregulacija u hospitaliziranih bolesnika je zadnjih godina dovedena u pitanje zbog velikog rizika jatrogene hipoglikemije i posljedično lošijih ishoda. S druge strane, jasni su dokazi da je dobra kontrola glikemije povezana s boljim ishodima liječenja. Aktualno je usuglašeno mišljenje da glikemiju u hospitaliziranih bolesnika treba držati nižom d 10 mmol/L. Taj cilj može biti individualiziran ovisno o karakteristikama bolesnika i pratećem liječenju. Inzulin se u većini institucija smatra terapijom izbora za kritične i nekritične hospitalizirane bolesnike i povezan je s boljim ishodima u usporedbi s drugim modalitetima koji se stoga ne preporučuju. Međutim, ako je glukoregulacija dobra u nekritičnih stabilnih bolesnika ili onih koji su primljeni radi manjih kirurških zahvata ranije se liječenje može nastaviti. Stres hiperglikemija je razmjerno česta u akutno oboljelih. Povezana je s rizikom kasnijeg razvoja šećerne bolesti. Stoga je važna edukacija tih bolesnika i kasnije adekvatno praćenje.

Ključne riječi: Glukoza, Regulacija glikemije, Hospitalizacija, Stres hiperglikemija, Inzulin

Introduction

Glucose irregularities are a commonly encountered problem in hospitalized patients and continue to be a costly yet seemingly preventable cause of prolonged hospital care in modern day medicine. Inpatient regulation of glucose levels in hospitalized patients not only applies to those with a pre-admission diagnosis of diabetes, but also patients without comorbidities who may be hospitalized in the general medicine ward, surgical ward or palliative care ward. Glucose regulation is a complicated matter that requires a good understanding of the underlying pathophysiology in different age groups and amongst different comorbidities, the variety of available treatments options and how these treatments must be modified under certain conditions with variables constantly changing in the hospital setting. Vigilant glycemic control is undoubtedly required in patients with a pre-admission diagnosis of diabetes, especially if the course of their disease has been poorly controlled as this can lead to high complication rates and longer length of hospitalization. Managing hyperglycemia in the hospital is particularly challenging due to the fact that patients experience many changes in medication regimens and nutritional intake with resultant fluctuations of glucose levels during the course of their care. The principle proportion of patients requiring proper attention to glycemic control are those who are admitted with pre-existing diabetes during their in-hospital treatment. Due to the expected increase in the incidence of diabetes on top of an already substantial number of affected patients, glucose management in the hospital has never been more important and efforts made to properly treat the risk of hyperglycemia and avoid its complications are of significant interest. Hospital complications and mortality can be significantly reduced with improvement in glycemic control (1).

The World Health Organization (WHO) estimated that 422 million adults were living with diabetes in 2014, a number which is expected to rise reflecting the global increase of overweight and obese individuals (2). Individuals who have diabetes are more likely to be hospitalized than those without diabetes (3). This number increases in the elderly with a three times higher rate for those aged 65 years and older compared to those younger than 45 years as determined by the National Hospital Discharge Survey (NHDS) (4). The importance of proper glucose control cannot be overstated as there is a strong association between inpatient hyperglycemia and

overall adverse outcomes such as mortality, morbidity, infections, and length of hospital stay (5,6). Observational studies indicated a prevalence rate of in-hospital hyperglycemia around 31.7% for non-critical care patients and 46% for ICU patients (6,7). These numbers not only include diabetics but also patients without a pre-admission diagnosis of diabetes and those who developed stress hyperglycemia in the hospital. Roughly 60% of patients who developed stress hyperglycemia in the hospital were found to have confirmed diabetes at one year post-hospitalization, despite the fact that their glucose values returned to normal before discharge (8). An important differentiator in determining patients with undiagnosed diabetes from those who developed stress hyperglycemia in the hospital is the measurement of an HbA1c value (9,10). According to The Endocrine Society, an elevated blood glucose HbA1c of greater than 6.5% can identify patients as having diabetes prior to admission (5). The American Diabetes Association (ADA) defines hyperglycemia as a blood glucose level in hospitalized patients >140mg/dL (7.8mmol/L) and hypoglycemia as glucose values <54mg/dL (3.0mmol/L) (11). Severe hypoglycemia is that characterized by substantial cognitive impairment irrespective of blood glucose values (11). Of clinical value however is a blood glucose of <70mg/dL which can be considered as a cautionary value of which titrations of insulin regimens may be based on (12).

Mechanisms and Consequences of Stress Hyperglycemia

Hyperglycemia is not only limited to patients with diabetes but also occurs during acute illness in patients who previously had normal glucose levels, in which case it is termed “stress hyperglycemia” (13,14). It is important to understand the pathophysiology and consequences of stress hyperglycemia as it is a commonly encountered reason for increased glucose levels in diabetic and non-diabetic hospitalized patients and a preventable source of adverse patient outcomes. Essentially the issue lies within an imbalance of hepatic glucose production and impaired peripheral glucose utilization, leaning towards an increase in production and decrease in utilization with subsequent increased blood glucose values. An interaction of glucoregulatory hormones, mainly insulin and the counter-regulatory hormones cortisol, glucagon, growth hormone and catecholamines, are responsible

for maintenance of blood glucose values. During acute stress, the counter-regulatory hormones predominate and alter carbohydrate metabolism by decreasing inducing insulin resistance, increasing hepatic glucose production and diminishing peripheral utilization of glucose (15). Furthermore, epinephrine which is released in the acute stress response stimulates glucagon secretion and inhibits pancreatic insulin release, all further contributing to increase blood glucose levels (16).

The clinical sequelae of prolonged levels of hyperglycemia are well documented in the literature, however hospitalized patients can be subjected to further detrimental effects due to their comorbidities. An estimated 33% increase in mortality has been associated with each 1mmol/L (18mg/dL) rise in FPG (17). Studies following coronary artery bypass surgery patients irrespective of their pre-admission diabetes status had higher mortality rates, increased wound infections and longer hospital stays if their hospital blood glucose levels were elevated >200mg/dL compared to those with lower levels (18–20). A retrospective cohort study by Falciglia et al. found inconsistent findings when comparing hyperglycemia in hospitalized ICU patients and whether each patient is equally susceptible to the consequences of hyperglycemia and whether they will benefit from subsequent treatments (21). The researchers did find marked differences, specifically an increase in mortality amongst patients admitted for similar organ diseases if glucose levels were elevated in these patients (21). Every 2.2 mmol/L increase in glucose levels was associated with a 30% increase in post-operative infection rate in one study (22).

Measuring Glucose Values

Adequate control of blood glucose levels requires accurate and effective monitoring by the health care team. Patients with pre-existing diabetes and those who developed hyperglycemia in the hospital require close continuous monitoring. Because there are many variables that can alter the schedule for monitoring blood glucose in different patients, care must be taken in order to determine the special arrangements and set up a proper schedule in these patients. These variables include the patient's nutritional intake, their individual medical treatment, and the schedule of their insulin administration (15). Proper alignment of these variables with

an appropriate monitoring and treatment schedule will ensure the most satisfactory control over blood glucose levels. For example, patients who are NPO receiving continuous intravenous insulin infusions in the ICU should have blood glucose levels measured every hour until stable levels are reached, in which a 2 hour schedule may be implemented (1). Patients receiving SC regular insulin every 6 hours or long acting basal insulin alone should have blood glucose measurements done every 6 hours (15). For patients eating three meals per day using a basal long acting insulin plus rapid acting insulin with meals, blood glucose levels should be monitored 4 times per day before meals and at bedtime regardless of the size of the meals and whether the patient is on high dose corticosteroids (15). Higher frequency of blood glucose monitoring not only allows treatment of elevated glucose levels but also prevents occurrences of hypoglycemia which can occur with over diligent use of insulin treatment (23). In patients without a history of diabetes, glucose values <7.8mmol/L without insulin therapy are a sufficient indication to end blood glucose testing (1).

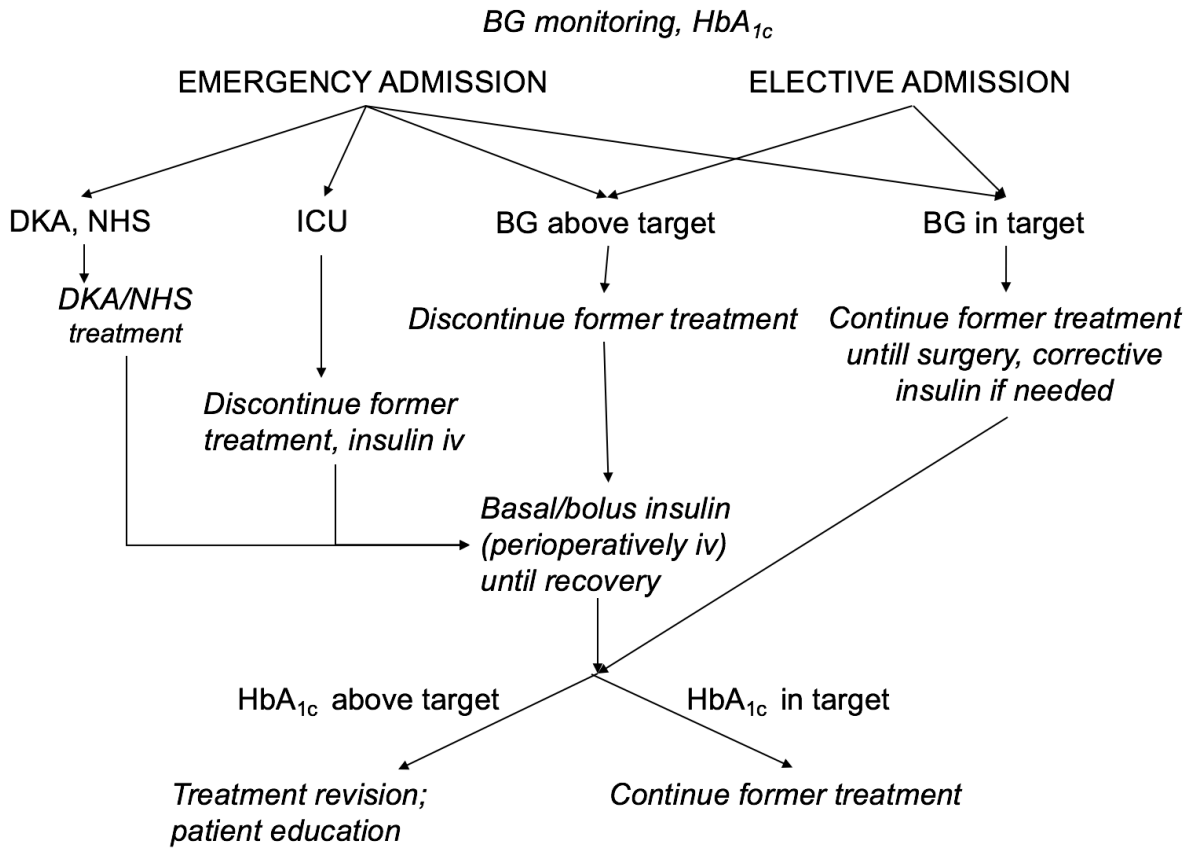

Figure 1. Blood Glucose Monitoring Algorithm (24).

Methods for obtaining blood glucose levels are fairly uniform throughout the literature. The most accurate method would be obtaining an arterial glucose level by using blood gas analyzers (25). This method is appropriate for use in critical care patients in the ICU as other accurate methods such as venous blood sampling are too time consuming (26). Handheld meters for POC testing are standard in hospital care for determining glucose values however their accuracy has been questioned as up to 20% in one study showed an inaccurate reading compared to plasma glucose levels (27). Inaccuracies can be a result of suboptimal hemoglobin levels in anemic patients, decreased tissue perfusion, hypotension and interactions with other medications (15). The ADA recommends that conventional laboratory tests with greater accuracy should be used to confirm glucose levels in patients whose clinical status does not correlate with the measured POC result due the possible discrepancies between samples of capillary, venous and arterial samples of blood (12). Continuous glucose monitoring (GCM) is another method employed by some hospitals which provides frequent measurements, helping protect against the dangers of hypoglycemia with treatment, however the literature does not fully support its use as it does not significantly improve glucose control and has subsequently not been recommended by a recent review (12,28).

Proper monitoring of glucose values is still not optimal, and serves as an area of glucose management that should be given appropriate research in order to develop an appropriate standard which can correctly and quickly identify patients at risk while keeping nursing hours and cost efficiency in mind. For example, nurses consume approximately 4.7 minutes of patient hours and up to 2 hours of nursing time per day on certain patients, with the longer times attributable to finding blood glucose monitors, troubleshooting the devices and taking extra precautions when drawing blood from patients in isolation (29). Some nurses also believe that hourly glucose measurements are simply too much and prefer to keep monitoring to a minimum to avoid obtrusiveness and direct their time to other matters (29). This dilemma has been noticed by many companies worldwide as efforts are underway to create a continuous glucose monitoring tool using fibre optics, infrared technology and transdermal methods that are unobtrusive, accurate and reliable after previous attempts to create such technologies have had limited success (30).

Glycemic Targets

The literature is fairly consistent in recommendation values for optimal glycemic control however debates arise over how strict the recommended glucose range should be set and whether there is any discernable advantage of adopting tight glycemic control versus having a more conservative approach. Due to variations in hospitalized patients' nutritional status and other factors contributing to their comorbidities, higher than normal glucose targets can be advised for these patients opposed to those who are in outpatient care (31). Therapy should be initiated in the majority of critically ill and non-critically ill patients who have consistent levels of hyperglycemia once they have crossed a threshold of >180 mg/dL (10.0 mmol/L) and maintained in a target glucose range of 140-180 mg/dL (7.8-10.0 mmol/L) (31). These glucose ranges are maneuverable however and are not a set standard for all hospitalized patients. Certain patients may be given more aggressive goals of < 140 mg/dL (<7.8 mmol/L) though glucose levels must be monitored appropriately to prevent hypoglycemia (12). On the other hand, if patients are in a position where strict glucose monitoring is simply not possible or glucose control is perhaps second to other more significant issues in their medical care such as palliation or severe comorbidities, then a higher target glucose range may be explored (12). Because of these outliers, an individualized approach to target glucose values may be worth the extra effort as treatment can be tailored to each individual patient to decrease hyperglycemia risk and avoid hypoglycemia due to overaggressive therapy.

Management of Hyperglycemia in Non-Critically Ill Inpatients

There are many different strategies for approaching the hyperglycemic patient that should be taken into consideration however for simplicity and effectiveness the use of insulin has become the mainstay of hyperglycemia in the hospital setting. The traditional use of sliding scale insulin was once considered an essential treatment method of high blood glucose levels but has now been considered inappropriate for safe management in hospitalized patients. The risk of inadequately treated hyperglycemia and severe hypoglycemia in patients treated with the use of sliding scale insulin had become far too common and increased complication rates in the

hospital (3,32). In general medicine and surgery patients who are not in critical care, subcutaneous short-acting insulin before meals or every 4-6 hours if NPO has become the mainstay of treatment to adequately control hyperglycemia in diabetics and non-diabetics (12,15). When possible, specifically in patients who are being fed, an insulin regimen that simulates physiological secretion is preferred. The basal bolus (prandial) insulin regimen is effective because it follows the physiological response by covering the basal, nutritional and supplemental requirements of insulin production (33). Well controlled glucose levels, less hypoglycemia and elimination of frequent feeding to prevent hypoglycemia were all achieved by one study using this regimen (33). In patients receiving enteral nutrition therapy, a basal insulin dose with consequent postprandial insulin doses resulted in lower levels of hyperglycemia compared to sliding-scale regular insulin regimens and decreased the risk of adverse events (34). A study by Korytkowski et al. found increased baseline glucose levels, greater insulin requirements, increased adverse outcomes, and a greater incidence of hypoglycemia in patients treated with sliding-scale regular insulin versus a basal dose of insulin glargine with SSRI (34). In patients being treated solely with SSRI therapy, they had a three times greater chance of having blood glucose levels >300mg/dL compared to those given basal-bolus insulin (9). A prospective randomized multicenter trial found 14% of patients being treated with sliding-scale insulin therapy had a blood glucose > 240mg/dL despite administering higher insulin doses compared to patients treated with insulin glargine and glulisine, though no differences in length of hospital stay or incidence of hypoglycemia were noted (35). A sliding-scale regimen can be of use for initial therapy in non-diabetic patients with moderate hyperglycemia, however these patients should be transitioned to a scheduled insulin regimen once insulin requirement is determined (34). The issue with treating patients with SSRI therapy is that the underlying mechanism acts to correct hyperglycemia only when it occurs and has no beneficial effect of preventing or decreasing recurrences of hyperglycemia, something which a basal-bolus regimen can achieve.

The use of a constant intravenous insulin infusion has the benefit of a very rapid achievement of glycemic control however it is not recommended in non-critical care patients in many hospitals, especially when feeding protocols are subject to change, requiring insulin dosage to be adjusted accordingly (36). If patients are being

weaned off of intravenous insulin during their hospital care, a proper transition protocol to subcutaneous insulin can lower costs and prevent morbidity and is thus recommended (37). Consideration about the patient's age, comorbidities, renal function, and nutritional intake should all influence the clinician's decision about the amount of total daily insulin required for patients. Most patients should be started with a starting total daily dose of insulin between 0.3 and 0.5 units/kg as higher doses greater than 0.6 to 0.8 units/kg/day have been associated with hypoglycemia (13,29,36,38). The seemingly increased safety profile of basal bolus (prandial) insulin regimen as well as its success rate of achieving and maintaining appropriate glucose levels in treated patients should lead to its uniform implementation in hospitalized non-critical care patients.

Noninsulin antihyperglycemic treatments are currently not recommended in the treatment of hospitalized patients as evidence regarding safety and efficacy is lacking. Research is currently being conducted to determine if there is any benefit using oral hyperglycemic agents compared to the current insulin standard with some initial promising results (12). One study indicated that glycemic control using sitagliptin alone or in a combination with insulin showed improved blood glucose levels in all patient groups, with less dosing and injections of insulin required in the sitagliptin combination group versus the basal bolus group (39). When compared to using insulin treatment, oral agents undergo a different pathway for distribution in the body and different mechanisms of action with delayed onset of therapeutic goals, meaning its use would better be served for treatment of outpatient hyperglycemia rather than the inpatient setting that requires rapid correction. Many inpatients in the hospital have clear contraindications for the use of certain oral antihyperglycemic agents. Metformin is generally not prescribed for patients with renal insufficiency, hepatic and cardiovascular disease due to concerns over lactic acidosis though its use in the hospital is still common despite these concerns (39). Sulfonylureas act as long-acting insulin secretagogues and are very commonly used in patients with type 2 diabetes however their side effect profile includes a high risk of hypoglycemia, limiting its use for inpatients (40). A nested case-control study showed 19% of hospitalized patients taking a sulfonylurea developed hypoglycemia, with the majority of cases occurring in patients older than 65 years, those with decreased GFR of 30ml/minute/1.73m^2 and those who were receiving concurrent intermediate or long-

acting insulin while being treated with a sulfonylurea (41). Patients being treated with a sulfonylurea have the increased risk of prolonged hypoglycemia due to the pharmacodynamics of the agent, and require further monitoring and strict management with glucose preparations (41). Other oral antihyperglycemic agents such as thiazolinediones, Sodium glucose co-transporter 2 inhibitors, α-glucosidase inhibitors and incretin based therapies generally have side effect profiles and contraindications in hospitalized patients that substantially limit their use for inpatient treatment.

Management of Hyperglycemia in Critically Ill Inpatients

Insulin is indisputably the gold standard for treating critically ill patients in the hospital setting, as agreed upon by the majority of the literature. Intravenously administered insulin is preferred due to its rapid delivery which allows for quick correction of deteriorating glucose levels with greater predictability and effectiveness compared to subcutaneously administered insulin (1). However, infusing insulin intravenously is quite labour intensive and in a majority of health centres requires ICU admission for proper administration and monitoring (1). In the critical care setting, predetermined written or computer protocols factoring glycemic fluctuations and insulin dose may be used for adjustments of the infusion rate when considering infusing patients with insulin (31). Obvious fluctuations in the patients' clinical status and glucose targets should be accounted for when adjusting insulin infusion rates. Traditionally a blood glucose target was achieved by using a drip which was mathematically calculated by the medical staff using an established algorithm (42). Unfortunately, errors in dosing can be common due to human errors which is why computer protocols have set the stage to replace simple predicting on the physicians part (15). Computer based algorithms proved to deliver tighter glycemic control with less risk of hypoglycemia when compared to the traditional paper protocol (42).

Hypoglycemia in Hospitalized Patients

Hypoglycemia can occur in hospitalized patients due to aberrations in feeding times, NPO orders, interactions with medications, problems with feeding mechanisms and

over judicious use of insulin or other antihyperglycemic agents. Hypoglycemia in patients being treated with intensive insulin therapy can occur frequently and has been shown to be a risk factor for death in hospitalized patients (18). There is a divide in the literature between the benefits and risks of using tight glycemic control with regards to subsequent hypoglycemia. A study by Furnary et al. discovered that tight glucose control with continuous insulin infusion in diabetic patients being treated with coronary artery bypass grafting was significantly better at controlling glucose levels and decreased the mortality that beset these patients in the past (43). On the contrary, a magnitude of studies have demonstrated significantly elevated risks of hypoglycemia with tight glycemic control. The Glucontrol study found an 8.7% increased risk in patients being treated with tight glycemic control (4.4-6.1 mmol/L) compared to the conventional group (7.8-10 mmol/L), with sicker patients having a greater risk of hypoglycemia and death (44). The NICE-SUGAR study found that while there was not a significant difference in the amount of days spent in the ICU or hospital between intensive-control groups and conventional-control groups, 6.8% of patients in the former group developed severe hypoglycemia (<2.2 mmol/L) compared to only 0.5% of patients in the later (45). The researchers concluded that a blood glucose target of ≤180 mg/dL resulted in a lower mortality than a tight glycemic target between 81-108 mg/dL (45).

The importance of preventing hypoglycemia is significant as its occurrence has been associated with many serious adverse outcomes in hospitalized patients. The ADVANCE study found severe hypoglycemia being a contributing factor in the development of major macrovascular and microvascular events, and all-cause mortality but also found hypoglycemia to be a marker of vulnerability to these events (46). The fact that a patient exhibits severe hypoglycemia during glucose-lowering intervention should prompt evaluation into their susceptibility for adverse outcomes and address the associated issues that may arise (46). Another study in acute myocardial infarction patients determined that iatrogenic hypoglycemia was not associated with a higher mortality risk compared to patients who developed spontaneous hypoglycemia, and that only spontaneous hypoglycemia was a risk factor for increased mortality (47). The evidence is debatable and more research should be conducted to determine the correlation between iatrogenic hypoglycemia and all cause morbidity and mortality, although the literature can agree that

hypoglycemia in hospitalized patient is at the very least marker for vulnerability to adverse events and should be avoided at all costs. The American Diabetes Association acknowledges that hypoglycemia may just be a marker of underlying disease and not a cause of mortality, however they do recommend that hypoglycemia be avoided until the link can be proven (12).

Hyperglycemia in High Risk Patients

Certain subsets of patients are deemed high risk due to their underlying comorbidities, concurrent medications and procedures in the hospital which can contribute to hyperglycemia. Corticosteroids, which are commonly used in the hospital as a single therapy or in combination therapies, can contribute to hyperglycemia more commonly by late morning when it is prescribed, but can have a prolonged effect throughout the course of the day if daily doses are required (15). It is essential to monitor capillary blood glucose values in patients on high dose corticosteroids, especially during the period 4 to 8 hours after oral administration and sooner after intravenous administration (15). A basal dose of intermediate or long-acting insulin may be able to offset the increased glucose levels of early morning corticosteroid therapy, however care should be taken to avoid episodes of hypoglycemia when long acting insulin preparations are used in these cases (15). The COIITSS study hypothesized that patients being treated for septic shock in the ICU with corticosteroids may benefit with intensive insulin therapy versus a conservative therapy, even though general ICU patients may not (48). Prolonged bed rest for as little as seven days in hospitalized patients may also contribute to insulin resistance in skeletal muscle and decreased glucose uptake (49). Severe hyperglycemia (minimum 9.99 mmol/L) has been shown to increase the likelihood of developing graft versus host disease in nondiabetic patients after allogenic stem-cell transplantation, though the researchers' results were found in non-obese patients only (50). One study analyzing cardiac surgery patients found that while glucose concentrations were lower at the end of surgery with intensive insulin treatment, there was no decrease in perioperative death and mortality between this group and the conventional treatment group, in fact showing more deaths and strokes in the intensively treated group (51). Intensive glycemic control in the range of 80-180

mg/dL (4.4-10 mmol/L) was not shown to benefit perioperative patients with diabetes undergoing surgical procedures and showed a higher incidence of hypoglycemia in these patients, advising against practicing tight glycemic control in surgical patients (52). A multicenter randomized trial found improved glycemic control in general surgery patients with a basal plus regimen with glargine once daily and corrective glulisine before meals compared to a standard basal-bolus regimen (52).

Nutritional Therapy in Hospitalized Hyperglycemic Patients

Nutritional therapy is an essential component in the treatment plan of hospitalized patients and requires special attention in patients with new onset hyperglycemia or diabetes since their nutritional requirements differ from those in the outpatient setting. Ultimately nutritional therapy can serve as a useful tool if managed properly or can become a hindrance in patient care by causing more problems that require further treatment. Like all hospitalized patients, it is important that a specialized meal plan be tailored to their individual needs to provide adequate nutritional intake while avoiding hyperglycemia or hypoglycemia. A nutritional professional should work very closely with health care providers when treating patients with diabetes or new onset hyperglycemia in the hospital (15). When considering providing medical nutrition therapy to patients with elevated glucose levels, the first step should be to determine whether the patient requires more in depth assessment by implementing a screening and referral process (53). While an individualized nutritional program should be implemented in all patients with diabetes or hyperglycemia, three discrete meals should be adequate to achieve their caloric needs (15). The ADA does not advise a specific meal plan or percentage of macronutrients, however the patient's physiological parameters, treatment goals and current medications should all factor into a favourable nutritional plan (12). If possible, whole grains and vegetables should be the primary source of carbohydrates due to their low glycemic index (15). In patients who cannot tolerate oral feeds, the next best option is enteral nutrition and is preferred over parenteral nutrition in hospitalized patients (54). This is due to the lower cost, lower complication rate, less risk for atrophy of the gastric mucosa and lower risk of the complications associated with parenteral therapy such as infectious and thrombotic complications (55). Many hospitals prefer using a

consistent carbohydrate meal plan as intake carbohydrate intake can be matched with a prandial insulin dose to offset any increase in blood glucose levels that may occur by unregulated nutritional intake (56).

Communication and Discharge of Hyperglycemic Patients

The transition of a hospitalized diabetic or hyperglycemic patient to the outpatient setting can be difficult, thus requiring careful discharge orders and proper communication to prevent outpatient complications. Generally a patient with an HbA1C of less than 6.5% can be discharged with no antidiabetic treatment, and those with elevated HbA1C levels should be prescribed insulin, oral antihyperglycemic agents or combination therapies for the outpatient setting (1). Proper communication is imperative to ensure the patient administers their treatment correctly and at the appropriate times in order to prevent aberrations in their glucose levels. Due to the complexity of insulin treatment regimens, it is recommended that written orders be given to the patient as oral communication can lead to errors and complications in management (1). To prevent these types of errors, several organizations have implemented strategies that incorporate clear, formal discharge instructions about medications and follow up appointments, however evidence is still lacking regarding the ideal method of providing a safe transition to the outpatient setting (57). Part of the importance in proper outpatient management of these patients is that hyperglycemic patients may be at increased risk of future preventable morbidities. A systematic review found that patients who have been treated for stress hyperglycemia in the hospital are at increased risk for developing subsequent diabetes and should be followed up accordingly (58). Another study determined a prevalence of new-onset diabetes of 8% in stress hyperglycemia patients during follow up, and noted a positive correlation between the degree of in-hospital hyperglycemia and risk of subsequent diabetes development (59). Hospitalized in-patients with severe hyperglycemia showed a striking 28% increased risk of developed new-onset diabetes after discharge (59). This perceived link necessitates further research into the development of new-onset diabetes in stress-hyperglycemia patients and reiterates the importance of proper discharge orders and follow up appointments in such patients as research on the pathophysiology of such events is still lacking.

Discussion

The global burden of obesity and overweight individuals is contributing to an overwhelming increase in the prevalence of diabetes in the population. Unfortunately, these patients are susceptible to greater health risks which must be managed appropriately to prevent further morbidity and mortality. The hospital setting proves to complicate the treatment of these patients due to pathophysiological mechanisms under the stress state of acute or chronic illness, comorbidities altering treatment plans, newly prescribed medications and a different and sometimes unpredictable nutritional intake. Development of hyperglycemia not only applies to patients with a pre-admission diagnosis of diabetes but also develop sporadically as "stress" hyperglycemia in acutely ill patients. These patients seemingly are increased risk for the future development of new-onset diabetes. Hyperglycemia has many clinical complications that can increase morbidity, hospital stay and even mortality in some patients and should be avoided by proper monitoring of blood glucose levels and prompt treatment when required. Monitoring of glucose levels in the hospital is adequate however advancements should be made to develop a continuous, non-obtrusive means of obtaining measurements which can cut down on health care costs and decrease nursing time spent on constantly measuring these patients. Excessive or inappropriately timed treatment with insulin and antihyperglycemic agents may lead to dangerously low glucose levels so care must be taken when setting up a treatment plan for diabetic patients and patients with stress hyperglycemia. Nutritional intake and the route of administration can significantly change the treatment plans and must be factored in by the health care team, including a professional nutritionist. Glycemic targets can vary in individual patients depending on their clinical status and comorbid disease severity, therefore no gold standard glycemic target has been developed and relies somewhat on clinical experience and judgement. Insulin is recognized across the literature as the treatment of choice in treating hyperglycemic patients in the hospital setting as it has a rapid and predictable course of action. Antihyperglycemic agents are generally avoided in the hospital as evidence cannot recommend them in light of the fact that they are associated with harmful side effects with little benefit compared to insulin. Nutritional therapy is another important aspect of the treatment plan of hyperglycemic patients and should be approached with caution by a nutritional

professional and the health care team to factor in all patient and treatment variables. Parenteral nutrition should be avoided in patients who cannot tolerate oral feeding as enteral nutrition has been shown to be associated with less complications. Upon discharge of hospitalized diabetics or patients who developed hyperglycemia, proper communication is imperative to ensure these patients follow their treatment plans properly and understand the details and importance of their follow up appointments.

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Biography

Michael LaDelfa is currently a sixth-year medical student at the University of Zagreb who was born on August 29, 1988 in Brampton, Ontario, Canada. He obtained his B.Sc. in kinesiology at McMaster University with a minor in psychology. Passionate about the medical sciences, he moved to Zagreb to pursue his medical career with the hopes of one day practicing medicine back home in Canada. He enjoys playing sports and is a passionate musician, playing with and writing music for his Croatian tambura band “TS Frajeri” in Toronto.