Management of Diabetes and Hyperglycemia in Hospitalized Patients

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ABSTRACT

Diabetes is the most prevalent metabolic disorder and it is estimated to affect more than 460 million people globally. In the United States, 34.2 million Americans, or 10.5% of the population, have diabetes. Patients with diabetes have a 3-fold greater chance of hospitalization compared to those without diabetes. In 2016 in the U.S., there were over 7.8 million hospital stays for patients with diabetes. Hyperglycemia, defined as a blood glucose greater than 140 mg/dl (7.8 mmol/l), is reported in 22-46% of non- critically ill hospitalized patients. Extensive data indicates that inpatient hyperglycemia, in patients with or without prior diagnosis of diabetes, is associated with an increased risk of complications and mortality. Recently the American Diabetes Association recommended a target glucose between 140 mg/dl (7.8 mmol/l) and 180 mg/dl (10.0 mmol/l) for critically ill patients in the ICU as well as for most patients admitted to general medicine and surgery in the non-ICU setting. Insulin remains the best way to control hyperglycemia in the inpatient setting especially in the critically ill patient. Intravenously administered insulin is the preferred method to achieve the recommended glycemic target in the ICU. The use of oral antidiabetic agents was not recommended in previous guidelines because the lack of safety and efficacy studies in the inpatient setting. However, increasing evidence indicates that treatment with oral agents such as DPP4 inhibitors, alone or in combination with basal insulin, is safe and effective in general medicine and surgery patients with mild to moderate hyperglycemia. For complete coverage of all related areas of Endocrinology, please visit our on-line FREE web-text, WWW.ENDOTEXT.ORG.

INTRODUCTION

Diabetes is a prevalent metabolic disorder that affects more than 460 million people globally, and is projected to rise to 700 million (10.9% of the adult population) by 2045 (1). In the United States, data from the National Diabetes Statistics Report in 2020 estimated that a total of 34.2 million Americans, or 10.5% of the population, had diabetes (2). The percentage of the population with diagnosed diabetes is expected to rise, with one study projecting that as many as one in three U.S. adults will have diabetes by 2050 (3). People with diabetes have a 35% greater chance of referral for elective operations and an up to 4-fold greater chance of hospitalization compared to those without diabetes (4-7). Data from the US and Scotland estimate that of those individuals with a discharge diagnosis of diabetes, 30% will require 2 or more hospitalizations in any given year (5,6,8). In 2016 in the U.S., there were over 7.8 million hospital stays for people with diabetes (i.e., diabetes as either a principal diagnosis for hospitalization or as a secondary diagnosis, coexisting condition) (2), and in the UK the annual National Diabetes Inpatient Audit suggested that the prevalence of diabetes amongst inpatients had risen from 15% in 2010 to almost 20% in 2019 (9). In addition, those hospitalized with a diagnosis of diabetes stay in the hospital for longer than those without a diagnosis of diabetes admitted for the same condition (10,11).

Diabetes was the 7th leading cause of death in the United States in 2017, with 83,564 death certificates listing diabetes as the underlying cause of death, accounting for 25.7 deaths per 100,000 of the population (12). The care of people with diabetes imposes a substantial burden on the economy, with a total estimated cost of treating people diagnosed with diabetes in the United States in 2017 was $414 billion – or 24% or all health care spending in the US (11). This included $237 billion in direct medical costs. It is estimated that a further cost of $690 billion is incurred due to reduced productivity (11). Globally, diabetes care costs have been estimated at $1.3 trillion, rising to an estimated $2.1-2.5 trillion by 2030 (13,14). This represents a rise in spending on diabetes as a proportion of global gross domestic product from 1.8% in 2015 to 2.2% in 2030 (14). Other than the costs of diabetes medications, the largest component of this medical expenditure is hospital inpatient care, accounting for $69.7 billion of the total medical cost (11).

Hyperglycemia is defined as a blood glucose concentration of greater than 140 mg/dl (7.8 mmol/l) (15,16). It is reported in 22% to 46% of non-critically ill hospitalized patients (8,15). Extensive observational and trial data indicate that inpatient hyperglycemia, in patients with or without a prior diagnosis of diabetes, is associated with an increased risk of complications and mortality, a longer hospital stay, a higher admission rate to the intensive care unit (ICU), and a higher need for transitional or nursing home care after hospital discharge (8,17,18).

Several studies and meta-analyses have shown that attempting 'tight' glycemic control using intensive insulin therapy is associated with increased risk of hypoglycemia (19-23). This has been associated with increased morbidity and mortality in hospitalized patients (15,24-28). Thus, while insulin therapy is recommended for the management of hyperglycemia in hospitalized patients, the concern about hypoglycemia have led to revised glucose target recommendations from leading professional organizations around the world (16,22,29-32).

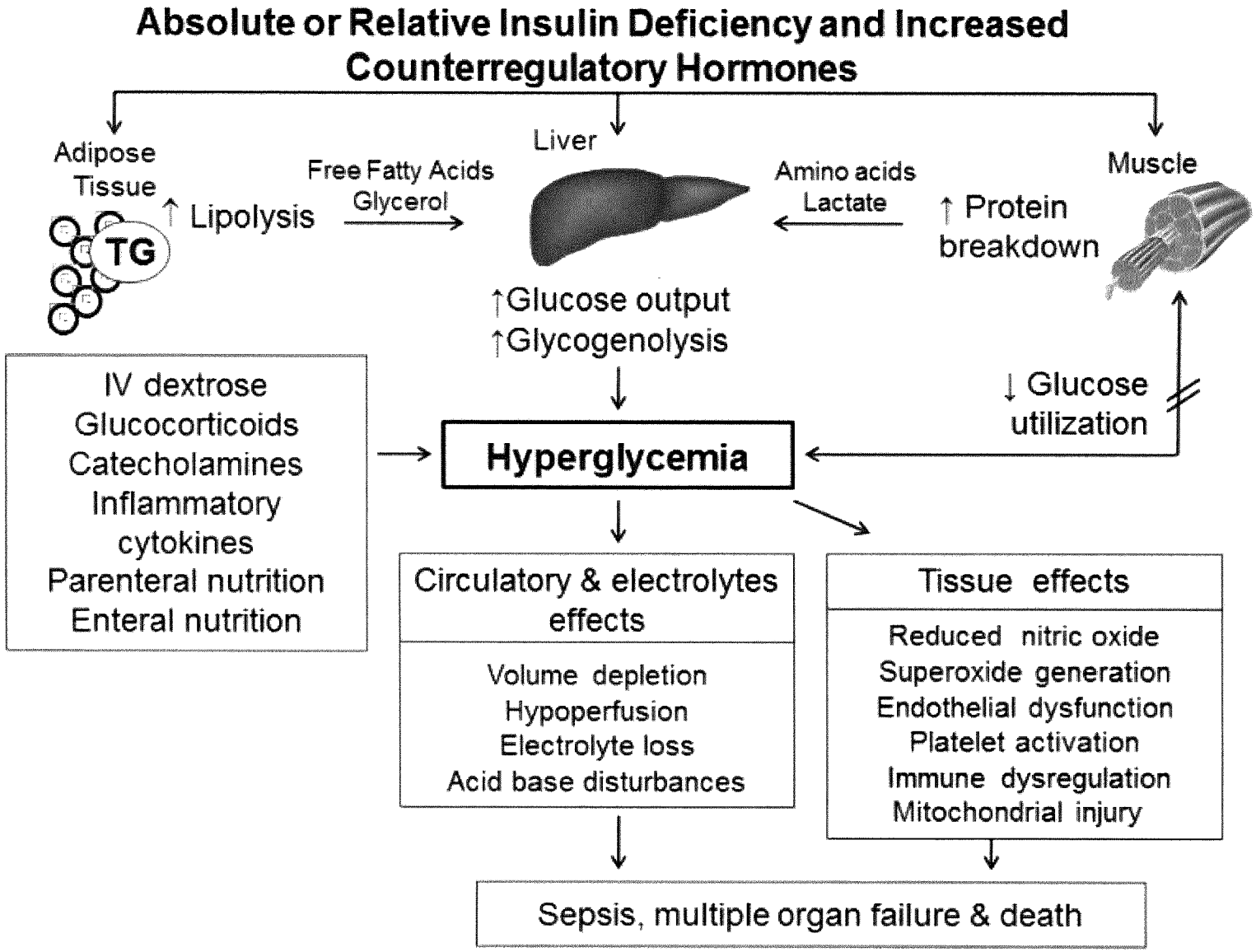

Figure 1.

Pathogenesis of hyperglycemia. Hyperglycemia results from increased hepatic glucose production and impaired glucose utilization in peripheral tissues. Reduced insulin and excess counter-regulatory hormones (glucagon, cortisol, catecholamines and growth hormone) increase lipolysis and protein breakdown (proteolysis), and impair glucose utilization by peripheral tissues. Hyperglycemia causes osmotic diuresis that leads to hypovolemia, decreased glomerular filtration rate, and worsening hyperglycemia. At the cellular level, increased blood glucose levels result in mitochondrial injury by

However, there was no difference in outcomes for those with diabetes, unless they had experienced severe hypoglycemia, in which case mortality rose (OR 2.95 95%CI 1.19-7.32) (72). Thus, despite a large amount of work having been done, the optimal blood glucose concentration for people on ICU has yet to be determined (73).

The association of hyperglycemia and poor outcomes also applies to those not in the ICU, but admitted to general medicine and surgery services. In such individuals, hyperglycemia is associated with poor hospital outcomes including prolonged hospital stay, infections, disability after hospital discharge, and death (5,8,56,57,66,74). In a retrospective study of 1,886 patients admitted to a community hospital, mortality in the general floors was significantly higher in patients with newly (stress) diagnosed hyperglycemia and with known diabetes compared to subjects with normal glucose values (10% vs. 1.7% vs. 0.8%, respectively; $p < 0.01$) (8). In a prospective cohort multicenter study of 2,471 patients with community-acquired pneumonia, those with an admission glucose levels >198 mg/dl (>11.0 mmol/l) had a greater risk of mortality and complications than those with glucose levels <198 mg/dl (<11.0 mmol/l) (68). The risk of complications increased 3% for each 18 mg/dl (1.0 mmol/l) increase in admission glucose (68). In a retrospective study of 348 patients with chronic obstructive pulmonary disease and respiratory tract infection, the relative risk of death was 2.1 in those with a blood glucose of 126-160 mg/dl (7.0-8.9 mmol/l), and 3.4 for those with a blood glucose of >162 mg/dl (9.0 mmol/l) compared to patients with a blood glucose of 108 mg/dl (6.0 mmol/l) (74).

General surgery patients with hyperglycemia during the perioperative period are also at increased risk for adverse outcomes. A systematic review of diabetes and the risk of surgical site infection across a variety of surgical specialties showed that high peri-operative glucose levels were associated with an increased risk of infection (75). In a case-control study, elevated preoperative glucose levels increased the risk of postoperative mortality in patients undergoing elective non-cardiac non-vascular surgery (76). Patients with glucose levels of 110-200 mg/dl (5.6-11.1 mmol/l) and those with glucose levels of >200 mg/dl (>11.1 mmol/l) had, respectively, 1.7-fold and 2.1-fold increased mortality compared to those with glucose levels <5.6 mmol/l (<110 mg/dl) (76). In another study, patients with glucose levels >220 mg/dl (>12.2 mmol/l) on the first postoperative day had a rate of infection 2.7 times higher than those who had serum glucose levels <220 mg/dl (<12.2 mmol/l) (77). A more recent study showed an increase of postoperative infection rate by 30% for every 40mg/dl (2.2 mmol/l) rise in postoperative glucose level above 110 mg/dl (6.1 mmol/l) (78) [67]. Furthermore, a study looking at perioperative glycemic control and the effect on surgical site infections in diabetic patients undergoing foot and ankle surgery showed that 11.9% of those with a serum glucose ≥200 mg/dl (11.1 mmol/l) during the admission developed a surgical site infection versus only 5.2% of those with a serum glucose <200 mg/dl (11.1 mmol/l) (odds ratio = 2.45; 95% CI 1.09-5.52, P = 0.03) (79). Lastly, a prospective randomized study looking at the impact of glycemic control at 1-year post liver transplant showed that in those randomized to a glycemic control of blood glucose below 140 mg/dl (7.8 mmol/l) any infection within 1 year occurred in 35 of the 82 patients (42.7%) versus 54 of 82 (65.9%) in those randomized to a glycemic control of 180 mg/dl (10.0 mmol/l) (P = 0.0046) (80). There is now emerging evidence to suggest that early intervention and the use of technology allowing pro-active identification of people at risk, helps to reduce hospital acquired infection rates, episodes of hyper- and hypoglycemia, as well as, in some cases, reduced length of stay (81-84). A meta-analysis also shows that improving peri-operative glycemic control reduced postoperative infection rates (85).

GLYCEMIC TARGETS IN THE ICU AND NON-ICU SETTINGS

The American Diabetes Association (ADA) and American Association of Clinical Endocrinologist (AACE) task force on inpatient glycemic control and other groups recommended different glycemic targets in the ICU setting (16) (Table 1). These guidelines suggest targeting a glucose level between 140 and 180 mg/dl (7.8 and 10.0 mmol/l) for the majority of ICU patients and lower glucose targets between 110 and 140 mg/dl (6.1 and 7.8 mmol/l) in selected ICU patients (i.e., centers with extensive experience and appropriate nursing support, cardiac surgical patients, patients with stable glycemic control without hypoglycemia). Glucose targets >180 mg/dl (>10.0 mmol/l) or <110 mg/dl (<6.1 mmol/l) are not recommended in ICU patients. There is an argument to say that lowering glucose thresholds for those in hospital is likely to be associated with harm (27,86) and an equally persuasive argument to suggest that the implementation of the thresholds as advocated by national and organizational guidelines have led to safer care (87).

The most recent guidelines from the Society of Critical Care Medicine (SCCM) for the management of hyperglycemia in critically ill (ICU) patients recommended that a blood glucose ≥150 mg/dl (≥8.3 mmol/l) should trigger interventions to maintain blood glucose below that level and absolutely <180 mg/dl (<10.0 mmol/l) (30). They also suggest that the insulin regimen and monitoring system be designed to avoid and detect hypoglycemia (blood glucose <70 mg/dl [<3.9 mmol/l]) and to minimize glycemic variability (30). The technology to allow this to occur is being development and may enter routine clinical use relatively soon (88-92).

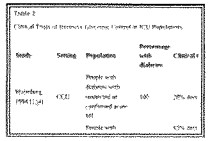

Table 2.

Clinical Trials of Intensive Glycemic Control in ICU Populations

The GLUCO-CABG trial was a randomized open-label clinical study that included those with and without diabetes undergoing CABG who experienced perioperative hyperglycemia, defined as a glucose >140 mg/dl (>7.8 mmol/l) (60). A total of 302 people between 18 and 80 years of age were randomized to the intensive glycemic control group (target glucose 100 – 140 mg/dl [5.6 – 7.8 mmol/l]) or to conservative – or conventional – control (glucose 141 – 180 mg/dl [7.9 – 10.0 mmol/l]) in the ICU. After transition from ICU to the telemetry floor, patients were managed with a single treatment protocol aimed to maintain a glucose target <140 mg/dl (<7.8 mmol/l) before meals during the hospital stay. The primary outcome included differences between intensive and conservative glucose control on a composite of perioperative complications including sternal wound infection, bacteremia, respiratory failure, pneumonia, acute kidney injury, and major adverse cardiovascular events including acute coronary syndrome, stroke, heart failure and cardiac arrhythmias (60). The mean glucose during the ICU stay was 132±47 mg/dl (7.3±2.6 mmol/l) in the intensive and 152±17 mg/dl (8.4±1.0 mmol/l) in the conservative group. Intensive glucose treatment resulted in a 20% reduction in perioperative complications compared to the conservative group (42% vs. 52%; p=0.08). Of interest, there were no differences in the rate of complications among patients with diabetes treated with intensive or conservative regimens (49.3% vs. 45.8%, p=0.68); however, in patients without diabetes intensive treatment was associated with significantly lower rate of complications compared to the conservative group (35% vs. 58%, p=0.006) (60). Hospitalization costs were lower in the intensive group (median [IQR] $36,681 [28,488 – 46,074] vs. $40,913 [31,464 – 56,629], p=0.04), with an average total cost savings of $3,654 per case compared to conservative glucose control (113).

To date, no large studies have been conducted to determine if improved control in those not in an ICU may result in reduced morbidity and mortality in general medical and surgical patients. For most people in the hospital with diabetes while there are observational data to show that dysglycemia is harmful, there were little data to show that improving glycemic control helps (114). A randomized controlled trial and a meta-analysis reported that improved glucose control may reduce hospital complications in general surgery patients (61). Improving glucose control with a basal bolus regimen resulted in a significant reduction in the frequency of composite complications including postoperative wound infection, pneumonia, bacteremia, and acute renal and respiratory failure (61). In that study, treatment with basal bolus insulin reduced average total inpatient costs per day by 14% or $751 compared to treatment with sliding scale alone (115).

HYPOGLYCEMIA

Hypoglycemia is the commonest side effect of treatment of all types of diabetes and stress hyperglycemia in the hospital setting. It presents a major barrier to satisfactory long-term glycemic control. Hypoglycemia results from an imbalance between glucose supply, glucose utilization and current insulin levels. Hypoglycemia is defined as a lower-than-normal level of blood glucose. For the purposes of hospital inpatients, hypoglycemia is defined as any glucose level <70 mg/dl (<3.9 mmol/l) (31,116). Severe hypoglycemia has been defined by many as <40 mg/dl (<2.2 mmol/l) (117). The incidence of severe hypoglycemia among the different trials ranged between 5% and 28% depending on the intensity of glycemic control in the ICU (118). Rates from trials using subcutaneous insulin in non-critically ill patients range from less than 1% to 33% (61,119,120). In 2017, the UK National Diabetes Inpatient Audit (NaDIA) data showed 18% of people with diabetes in hospital experienced one or more hypoglycemic episodes with a blood glucose <72mg/dl (<4.0 mmol/l) – down from 26% in 2011, with 7% (1 in 14) experiencing episodes requiring third party assistance to administer rescue therapy (121). The NaDIA data also showed that those with type 1 diabetes had the highest prevalence, with 25% experiencing a severe hypoglycemic episode (121). Furthermore 1.3% (1 in 80) of those in hospital with diabetes required some form of injectable rescue treatment (i.e. IV glucose or IM glucagon), down from 2.1% in 2011 (121). The same data showed that the highest proportion of episodes took place overnight (28%) between 05:00 and 09.00am when snack availability was likely to have been lowest (121).

The key predictors of hypoglycemic events in those hospitalized include older age, greater illness severity, diabetes, and the use of oral glucose lowering medications and/or insulin (122-124). In-hospital processes of care that contribute to risk for hypoglycemia include unexpected changes in nutritional intake that are not accompanied by associated changes in the glycemic management regimen (e.g., cessation of nutrition for procedures, adjustment in the amount of nutritional support), interruption of the established routine for glucose monitoring, deviations from the established glucose control protocols, and failure to adjust therapy when glucose is trending down or steroid therapy is being tapered (124-126). A common cause of inpatient hypoglycemia is insulin prescription errors including misreading poorly written prescriptions – when 'U' is used for units (i.e. 4U becoming 40 units) or confusing the insulin name with the dose (e.g. Humalog Mix25 becoming Humalog 25 units) (127).

The burden on inpatient diabetes falls most frequently to junior medical staff who often have little or no specialist diabetes training. As such, it is perhaps not surprising that errors occur. In the UK, a survey of junior doctors showed that unlike other commonly encountered medical conditions, such as acute asthma or angina, their knowledge about and confidence in managing diabetes was significantly lower (149). In 2019, this was also shown in a multicenter study from the US – with the major difference being that the while most staff felt confident and comfortable managing diabetes, when challenged on how to manage certain situations, and in particular identifying glucose targets for those who were critically ill or the threshold for defining hypoglycemia, their confidence was far higher than their knowledge – a potentially devastating combination (150). Given the high prevalence of diabetes amongst hospital inpatients, basic diabetes management should be part of mandatory training.

Management of Inpatient Hyperglycemia in the ICU

Insulin is the best way to control hyperglycemia in the inpatient setting especially in the critically ill patient. A variable rate, intravenous insulin infusion is the preferred method to achieve the recommended glycemic target. The short half-life of intravenous insulin makes it ideal in this setting because of flexibility in the event of unpredicted changes in an individual's health, medications, and nutrition.

When someone is identified as having hyperglycemia (blood glucose ≥180 mg/dl [≥10.0 mmol/l]), a variable rate intravenous insulin infusion should be started to maintain blood glucose levels <180 mg/dl (<10.0 mmol/l). A variety of intravenous infusion protocols have been shown to be effective in achieving glycemic control with a low-rate of hypoglycemic events, and in improving hospital outcomes (63,70,96,104,151-156). A proper protocol should allow flexible blood glucose targets modified based on the individuals' clinical situation. Further, it should have clear instructions about the blood glucose threshold for initiating insulin infusion and the initial rate. The appropriate fluids should also be prescribed. It should be validated in order to avoid hyperglycemia if adjusted too slowly and hypoglycemia if adjusted too fast. Accurate insulin administration requires a reliable infusion pump that can deliver the insulin dose in increments of 0.1 unit per hour (118,154).

There is no ideal protocol for the management of hyperglycemia in the critically ill patient. In addition, there is no clear evidence demonstrating the benefit of one protocol/algorithm versus any other. The implementation of any of these algorithms requires close follow up by the nursing staff and is prone to human errors. Some institutions have developed computerized protocols that can be implemented in order to avoid errors in dosing (157-161). Essential elements that increase protocol success of continuous insulin infusion are: 1) rate adjustment that considers the current and previous glucose value and the current rate of insulin infusion, 2) rate adjustment that considers the rate of change (or lack of change) from the previous reading, and 3) frequent glucose monitoring (hourly until stable glycemia is established, and then every 2 – 3 hours) (118,152,162-164).

Several computer-based algorithms aiming to direct the nursing staff adjusting the insulin infusion rate have become commercially available (158-160,165). Retrospective cohorts have been reported, as well as controlled trials have reported a more rapid and tighter glycemic control with computer-guided algorithms than standard paper form protocols in ICU patients (157,159), as well as lower glycemic variability than patients treated with the standard insulin infusion regimens. Despite differences in glycemic control between insulin algorithms, another study showed no difference between computerized protocols versus conventional glucose control (110). Thus, most insulin algorithms appear to be appropriate alternatives for the management of hyperglycemia in critically ill patients, and the choice depends upon the physician's preferences and cost considerations.

Managing Hyperglycemia in the Non-ICU Setting

Subcutaneous insulin is the preferred therapeutic agent for glucose control in those admitted to non-ICU settings (general medicine and surgery). Several studies have shown that the commonly used subcutaneous sliding scale insulin (SSI) is not acceptable as the single regimen in people with diabetes, because it results in undesirable levels of hypoglycemia and hyperglycemia (166-168). It has become evident in recent years that the use of scheduled subcutaneous insulin therapy with basal (e.g., glargine, detemir or degludec) once daily or with intermediate acting insulin (NPH) given twice daily alone or in combination with short (regular) or rapid acting insulin (lispro, aspart, glulisine) prior to meals is effective and safe for the management of most patients with hyperglycemia and diabetes (16,169).

The basal-bolus (prandial) insulin regimen is considered the physiologic approach as it addresses the three components of insulin requirement: basal (what is required in the fasting state), nutritional (what is required for peripheral glucose disposal following a meal), and supplemental (what is required for unexpected glucose elevations, or to dispose of glucose in hyperglycemia (169).

A prospective, randomized multi-center trial compared the efficacy and safety of a basal/bolus insulin regimen with sliding scale insulin in people with type 2 diabetes admitted to a general medicine service (119). The use of basal-bolus insulin regimen had greater improvement in blood glucose control than subcutaneous sliding scale alone. A blood glucose target <140 mg/dl (<7.8 mmol/l) was achieved in 66% of those in the glargine plus glulisine group and 38% in the sliding scale group (119). The incidence of hypoglycemia, defined as a glucose <60 mg/dl (<3.3 mmol/l), was less than 5% in those treated with basal bolus or SSI. A different study in general surgery inpatients also compared efficacy and safety of a basal bolus regimen to SSI in those with type 2 diabetes (61). The basal bolus regimen resulted in a

Glucose Monitoring in the Hospital

All patients admitted to the hospital with a diagnosis of diabetes and those with newly discovered hyperglycemia should be monitored closely (38). The frequency of monitoring and the schedule of the blood glucose checks will depend on the nutritional intake, patient treatment, and schedule of insulin. There is some controversy regarding the best method to monitor blood glucose. However, considering the convenience and wide availability of the capillary point of care (POC) testing we suggest this as the best approach as long as it is done with a monitoring device that has demonstrated accuracy (184,185). It is important that when using POC blood glucose meters, that several things be kept in mind, in particular overall clinical conditions that might affect the POC value such as hemoglobin level, perfusion, and medications. Table 4 summarizes potential schedules for blood glucose monitoring based on the patient's nutritional intake and medical regimen.

Several studies have reported on the efficacy of continuous glucose monitoring (CGM) in insulin treated patients in the hospital (88-92). The CGM devices provide estimated glucose values every 5-15 minutes resulting in a better assessment of glycemic control than capillary POC testing (186-188). Recent observational studies have shown increased detection of hypoglycemic events using CGM in the hospital in insulin treated patients (139,189). Additionally, a recent randomized trial by Singh et al. showed the ability of CGM to prevent and reduce hypoglycemia in high-risk hospitalized patients with diabetes through the use of remote CGM alarms (190). There are some concerns including the accuracy of CGM data when acute physiologic disturbances are present (i.e., hypoxemia, vasoconstriction, and rapidly changing glucose levels in diabetic ketoacidosis) or interference with glucose readings (such as salicylic acid, acetaminophen). They should also be removed for certain procedures – with each company having their own list –such as MRIs, CT scans, and diathermy. The use of CGM in the hospital has not been approved by regulatory agencies and remains investigational. Ongoing studies (NCT03832907) with factory-calibrated CGM are testing its accuracy in diverse inpatient populations and the use of a Glucose Telemetry System (GTS) with which glucose values can be wirelessly transmitted from the patient's bedside (CGMS) to a monitor device at the nursing station (NCT03508934, NCT03877068).

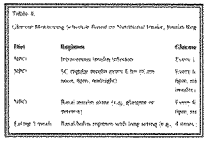

Table 4.

Glucose Monitoring Schedule Based on Nutritional Intake, Insulin Regimen, and Special Patient Situations

Medical Nutrition Therapy (MNT) in Hospitalized Patients with Diabetes

Medical nutrition therapy is a key component of the comprehensive management of diabetes and hyperglycemia in the inpatient setting. Maintaining adequate nutrition is important for glycemic control and to meet adequate caloric demands. Caloric demand in acute illness will differ from that in the outpatient setting. Achieving the proper nutritional balance in the inpatient setting is challenging. Anyone admitted to the hospital with diabetes or hyperglycemia should be assessed to determine the need for a modified diet in order to meet caloric demand.

The general approach to address MNT in the inpatient setting is usually based on expert opinions and patient need. There is limited data regarding what is the best approach or method to achieve the ideal caloric supply. To determine the best approach, method, and caloric needs of their patients, providers should work closely with a nutrition professional.

All patients with diabetes or hyperglycemia should receive an individualized assessment. In general, most patients will receive adequate caloric needs with 3 discrete meals per day. Further, the metabolic need for patients with diabetes is usually provided by 25 to 35 calories/kg where some critically ill patients might require less than 15 to 25 calories/kg per day (191). A consistent carbohydrate meal-planning system might help to facilitate glycemic control and insulin dosing in the inpatient setting. Most patients will require 1,500-2000 calories per day with 12-15 grams of carbohydrates per meal (15). Ideally, the carbohydrates should come from low glycemic index foods such as whole grains and vegetables.

Those individuals not able to achieve these goals should be evaluated in order to determine the need for enteral or parenteral nutrition. Enteral nutrition is the second-best option after oral nutrition and should be preferred over parenteral nutrition in hospitalized individuals (192,193). There are several advantages of enteral feeding versus parenteral feeding including: low cost, low risk of complications, physiologic route, less risk for gastric mucosa atrophy, and lower risk of infectious and thrombotic complications compared with the latter form of therapy (192,194). The benefit of parental nutrition has been documented in the critically ill patient. However, some research has shown a detrimental effect on patients with diabetes and hyperglycemia. Parental nutrition should be considered only in patients that are not able to receive enteral nutrition and should be coordinated with the institution parenteral nutrition team.

Closed-Loop Technology

Recent studies have reported that closed-loop systems, also referred to as artificial pancreas or automated insulin delivery systems have reported good efficacy with improved time in target and lower mean daily blood glucose without an increased rate of hypoglycemia in the ICU (201,202) and in non-ICU settings (203,204). In one non-ICU study, the time in target range between 100-180 mg/dl (5.6-10.0 mmol/l) was reported to be 59.8% in patients using the closed-loop technology compared to 38.1% with standard subcutaneous insulin regimen (204). Similarly, a closed-loop study in patients receiving nutritional support also reported higher time in target glucose range (68% vs 36.4%) and lower mean glucose values (153 vs 205 mg/dl [8.5-11.4 mmol/l]) compared to a standard insulin regimen (205). Same as the use of CGM in the hospital, treatment with artificial pancreas is experimental and larger studies are needed to prove safety and efficacy in ICU and non-ICU settings.

REFERENCES

1. Federation ID. IDF atlas 9th edition. 2019; https://www.diabetesatlas.org/en/.
2. Prevention CfDCa. National diabetes statistics report 2020. Estimates of diabetes and its burden in the United States. 2020; https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf.
3. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Population Health Metrics. 2010;8:29. [PMC free article: PMC2984379] [PubMed: 20969750]
4. Pournaras DJ, Photi ES, Barnett N, Challand CP, Chatzizacharias NA, Dlamini NP, Doulias T, Foley A, Hernon J, Kumar B, Martin J, Nunney I, Panagiotopoulou I, Sengupta N, Shivakumar O, Sinclair P, Stather P, Than MM, Wells AC, Xanthis A, Dhatariya K. Assessing the quality of primary care referrals to surgery of patients with diabetes in the East of England: A multi-centre cross-sectional cohort study. International Journal of Clinical Practice. 2017;71:e12971. [PubMed: 28618177]
5. Jiang HJ, Stryer D, Friedman B, Andrews R. Multiple hospitalizations for patients with diabetes. Diabetes Care. 2003;26:1421–1426. [PubMed: 12716799]
6. Donnan PT, Leese GP, Morris AD. Hospitalizations for people with type 1 and type 2 diabetes compared with the nondiabetic population of Tayside, Scotland: a retrospective cohort study of resource use. Diabetes Care. 2000;23:1774–1779. [PubMed: 11128351]
7. Harding JL, Benoit SR, Gregg EW, Pavkov ME, Perreault L. Trends in rates of infections requiring hospitalization among adults with versus without diabetes in the U.S., 2000 - 2015. Diabetes Care. 2020;43:106–116. [PubMed: 31615853]
8. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: An independent marker of in-hospital mortality in patients with undiagnosed diabetes. Journal of Clinical Endocrinology Metabolism. 2002;87:978–982. [PubMed: 11889147]
9. Digital N. National Diabetes Inpatient Audit (NaDIA) - 2018. 2019; https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-inpatient-audit/2018.
10. Sampson MJ, Dozio N, Ferguson B, Dhatariya K. Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. Diabetes Research & Clinical Practice. 2007;77:92–98. [PubMed: 17097183]
11. Association AD. Economic costs of diabetes in the U.S. in 2017. Diabetes Care. 2018;41:917–928. [PMC free article: PMC5911784] [PubMed: 29567642]
12. Prevention CfDCa. National vital statistics report. Deaths: Final data for 2017. 2019; 9:https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_09-508.pdf, 68.
13. Bommer C, Heesemann E, Sagalova V, Manne-Goehler J, Atun R, Barnighausen T, Vollmer S. The global economic burden of diabetes in adults aged 20-79 years: a cost-of-illness study. Lancet Diabetes and Endocrinology. 2017;5:423–430. [PubMed: 28456416]
14. Bommer C, Sagalova V, Heesemann E, Manne-Goehler J, Atun R, Barnighausen T, Davies J, Vollmer S. Global economic burden of diabetes in adults: Projections from 2015 to 2030. Diabetes Care. 2018;41:963–970. [PubMed: 29475843]
15. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM, Seley JJ, Van den Berghe G. Management of hyperglycemia in hospitalized patients in non-critical care setting: An Endocrine Society clinical practice guideline. Journal of Clinical Endocrinology Metabolism. 2012;97:16–38. [PubMed: 22223765]
16. Moghissi ES, Korytkowski MT, Dinardo MM, Hellman R, Hirsch IB, Inzucchi S, Ismail-Beigi F, Kirkman MS, Umpierrez GE. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Diabetes Care. 2009;32:1119–1131. [PMC free article: PMC2681039] [PubMed: 19429873]
17. Dhatariya K, Mustafa OG, Rayman G. Safe care for people with diabetes in hospital. Clinical Medicine. 2020;20:21–27. [PMC free article: PMC6964176] [PubMed: 31941727]
18. Sampson M. A good inpatient diabetes service. https://abcd.care/sites/abcd.care/files/resources/A_good_Inpatient%20Service_FINAL_Aug_19.pdf 2019; https://abcd.care/sites/abcd.care/files/resources/A_good_Inpatient%20Service_FINAL_Aug_19.pdf.