32 In-Hospital Treatment and Surgery in Patients with Diabetes

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Keypoints

- The diabetes epidemic is not sparing hospital practice. Approximately 12–24% of all hospital inpatients have diabetes.
- A significant proportion of hospital inpatients with hyperglycemia have undiagnosed diabetes and stress hyperglycemia.
- Hospitalization frequently presents a missed opportunity to diagnose diabetes and to identify those at risk for diabetes.
- In-hospital hyperglycemia and hypoglycemia are associated with poor outcomes in a broad range of specialties.
- There are few randomized controlled trials demonstrating benefit from interventions in the inpatient care setting.
- Hospital inpatients with diabetes frequently have multiple co-morbidities and complex medical and nursing requirements.
- Ward-based staff are frequently poorly trained and therefore ill-equipped to manage diabetes care safely and effectively.
- Care of the critically ill patient with diabetes and hyperglycemia requires highly skilled and appropriately trained staff.
- Insulin and diabetes management errors continue to compromise patient safety.
- Structured diabetes care delivered by appropriately trained staff and supported by a dedicated specialist inpatient team in partnership with the patient improves the patient experience, reduces diabetes prescribing and management errors and length of stay in many clinical settings in hospital.
- Patients with diabetes are more likely to undergo in-hospital procedures and should be individually managed by agreed and audited protocols.
- Patients undergoing surgery should have a preoperative assessment, a robust risk assessment and an individualized care plan including a safe and effective discharge plan.
- Standards of care for hospital inpatients have been defined by professional organizations but are not globally implemented.
- Audit of inpatient care reveals poor standards of care and patient experience and demonstrates the inadequacy of present systems and processes.

Introduction

Known diabetes in hospital

The global burden of diagnosed diabetes has reached epidemic proportions. The International Diabetes Federation predicts that by the year 2030 prevalence rates of type 2 diabetes will have increased by approximately 20% in Europe and by 65–98% in less economically developed countries [1]. Disproportionate numbers of people admitted to hospital have diabetes. The prevalence of diabetes in the inpatient population is almost certainly underestimated because of poor coding of diabetes as a co-morbidity. This applies equally to both planned and emergency care. Conservative estimates of diagnosed diabetes are between 12% and 24% of all inpatients in the USA [2]. Every year people with diabetes spend approximately 1.34 million days in hospital and it is estimated that in the UK there are 80 000 excess bed days per year. The cost of caring for inpatients with diabetes is around £485 million per year [3].

Undiagnosed diabetes and stress hyperglycemia in hospital

The number of hospital inpatients with diabetes has increased and is rising inexorably. This only represents the tip of the iceberg, however, as it takes no account of those patients with a raised plasma glucose level without a diagnosis of diabetes. In addition to those with diagnosed diabetes, there are two other groups of patients with hyperglycemia in hospital. First, there are those with unrecognized diabetes occurring during hospitalization and subsequently confirmed after discharge and, secondly, those with so-called "hospital-related" hyperglycemia (fasting plasma glucose >126 mg/dL (7 mmol/L) or random >198 mg/dL (11 mmol/L), occurring during hospitalization, which reverts to normal after discharge (also known as "stress hyperglycemia"). Recent studies suggest that these two groups may add a further 30% to the total numbers with raised plasma glucose levels [4].

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So when the burden of "in-hospital hyperglycemia" is considered to include all three groups, then the prevalence is approximately 40% of all hospital inpatients.

Evidence of harm from in-hospital hyperglycemia and benefit of glucose lowering

There is compelling evidence that poorly controlled blood glucose levels are associated with a higher in-hospital morbidity and mortality, prolonged length of stay, unfavorable post-discharge outcomes and significant excess health care costs [5–9]. Umpierrez *et al.* [4] showed that patients with new hyperglycemia had an 18-fold increased in-hospital mortality and patients with known diabetes had a 2.7-fold increased in-hospital mortality when compared with normoglycemic patients [4]. In 2004, a joint position statement from the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE) on inpatient diabetes and metabolic control concluded that hyperglycemia in hospitalized patients is a common, serious and costly health care problem [10]. There was a strong recommendation for early detection of hyperglycemia and an aggressive management approach to improve outcomes.

Randomized trials have demonstrated improved outcomes resulting from more aggressive management of hyperglycemia in the following areas.

Acute coronary syndromes

It is not clear whether high glucose is a marker or mediator of poor outcomes in acute coronary syndromes (ACS). In the management of myocardial infarction a meta-analysis of 15 studies showed that blood glucose (BG) >120 mg/dL (6.1 mmol/L), with or without a prior diagnosis of diabetes, was associated with an increased in-hospital mortality and subsequent heart failure [11]. Current evidence supports the use of intravenous insulin in the first 24 hours and intensified subcutaneous insulin for 3 months in the setting of ST-segment elevation myocardial infarction (STEMI) where the DIGAMI 1 study showed a 29% reduction in mortality at 1 year [12]. Other randomized controlled trials such as DIGAMI-2 and CREATE-ECLAT have failed to reproduce these findings [13,14].

Observational data from the UK Myocardial Infarction National Audit Programme (MINAP) of patients with troponin-positive ACS demonstrated poorer outcomes in those with an elevated BG on admission, with 30-day mortality of 20.2% in those with BG >170 mg/dL (9.4 mmol/L) compared with 3.3% in those with BG <170 mg/dL (9.4 mmol/L). Of 38 864 patients recorded on the MINAP database, around 10% (of those with no prior diagnosis of diabetes) had an admission BG >250 mg/dL (14 mmol/L). Patients who did not receive treatment with intravenous insulin had a relative increased risk of death of 56% at 7 days and 51% at 30 days [15].

Cardiac surgery

Most of the outcome data for patients undergoing cardiac surgery relates to the Portland Diabetic Project, which was a non-randomized observational study of 5510 patients undergoing cardiac surgery during 1987–2005. This has shown that patients with hyperglycemia managed with an intravenous infusion titrated to normoglycemia for 3 days postoperatively had improved mortality, reduction in deep sternal wound infections and reduction in length of stay [16].

Critical care setting

The landmark study by Van den Berge *et al.* [17] showed that postoperative intensive insulin therapy (IIT) reduced mortality and morbidity in patients in the surgical intensive treatment unit (ITU). In a later study by the same group in medical ITU patients, IIT reduced morbidity but not mortality [18]. Randomized trials of IIT have shown inconsistent effects on mortality and increased rates of severe hypoglycemia. A recent meta-analysis of 26 trials involving 13 567 patients including the recent NICE-SUGAR trial, the pooled relative risk of death with IIT compared with conventional therapy was 0.93 (95% CI 0.83–1.04). Fourteen trials reported hypoglycemic events and showed a significant increase in severe hypoglycemia with a relative rate (RR) of 6.0 (95% CI 4.5–8.0). The different targets of IIT did not influence either mortality or risk of hypoglycemia [19].

Pathophysiology of hyperglycemia in acute illness

A key goal of inpatient diabetes management is minimizing the metabolic decompensation from the stress of illness and surgery. Stress-induced hyperglycemia is caused by the combined effects of integrated endogenous hormonal, cytokines and counter-regulatory nervous system signals on glucose metabolic pathways [20]. Inflammatory and counter-regulatory responses to critical illness alter the effect of insulin on hepatic glucose production and skeletal muscle. Stress leads to the increased secretion of counter-regulatory hormones (glucagon, epinephrine, norepinephrine, cortisol and growth hormone), which stimulates hepatic glycogenolysis and gluconeogenesis. Peripheral uptake of glucose is inhibited. A major consequence of severe hyperglycemia is osmotic diuresis accompanied by dehydration and electrolyte disturbances (sodium, potassium, magnesium and phosphate). This increased osmotic state is procoagulant.

The stress hormones also accelerate fat and protein breakdown leading to a generalized catabolic state. In the surgical setting, starvation preoperatively and postoperatively can be a large contributor to this process. In people without diabetes, a compensatory increase in insulin secretion helps to mediate against these catabolic effects. Patients with an absolute insulin deficiency are prone to unopposed lipolysis and ketone body formation that can ultimately result in diabetic ketoacidosis.

Stress increases the release of inflammatory mediators, leading to insulin resistance and hyperglycemia [21]. Inflammatory cytokines interleukin-1, interleukin-6 and tumor necrosis factor α (TNF-α) may directly or indirectly enhance both hepatic gluconeogenesis and glycogenolysis. TNF-α alters the signaling properties of insulin receptor substrate, leading to enhanced target organ insulin resistance.

Wound healing and the susceptibility to infection are also affected by hyperglycemia and insulin deficiency, as demonstrated by *in vitro* studies looking at white blood cell functioning [22]. Hyperglycemia-induced abnormalities in the phagocytic and bactericidal actions of neutrophils are reversed with improved glucose control.

There are other causes of hyperglycemia, which may be more specifically related to the hospital admission [23]. These include co-administered medications such as corticosteroids and immunosuppressants (e.g. cyclosporine, tacrolimus). Immobility secondary to surgery, trauma or acute illness can accelerate both hyperglycemic and procoagulant states.

Effects of glucose lowering and intravenous insulin therapy

The mechanisms behind the improved outcomes from intravenous insulin are numerous. The vasodilatory, anti-inflammatory and anti-atherogenic effects of insulin have been studied. *In vitro*, insulin induces a dose-dependent increase in nitrous oxide synthase production in the endothelium. Ultimately, insulin treatment may improve endothelial function in patients with diabetes [24].

Current recommended standards of care for hospital inpatients with diabetes

Several professional organizations from different countries have published suggested standards of care for hospital inpatients. The International Diabetes Federation (IDF) is an umbrella organization of over 200 national diabetes associations in over 160 countries which has also published a standards document about inpatient care in type 2 diabetes. The content of the major publications are reviewed below. There are a number of recurring themes which include equitable access to specialist services, empowerment of patients, delivery of care by agreed guidelines, setting of glycemic targets and embedding effective and audited hyperglycemic management protocols.

International Diabetes Federation 2005

Within the guideline produced by the IDF on the care of patients with type 2 diabetes, a number of recommendations were made concerning inpatient care [25]. The standard recommendation of the IDF group fell broadly into four categories:

1 *Inpatient care organization.* This should be undertaken by a trained diabetes care health care professional with focus on individual plans including discharge and follow-up, access to the multidisciplinary team and appropriate laboratory and investigative procedures, increasing staff awareness of the needs of people with diabetes and implementing strategies to prevent patient disempowerment by promotion of self-management of diabetes.

2 *General ward care.* Patients should be empowered to self-manage where appropriate with regard to glucose monitoring, food choices and insulin administration.

3 *Care of patients undergoing inpatient procedures.* There should be provision for assessment of glycemic control and of metabolic and vascular risk for those undergoing planned procedures and agreed protocols should be in place. Staff should be made aware of the special risks associated with diabetes such as development of new ulceration, cardiac risk and renal failure.

4 *Care of the critically ill.* Patients should be managed according to a strict glycemic protocol with glucose levels kept <110 mg/dL (6.1 mmol/L) and an active avoidance of hypoglycemia.

American Diabetes Association and American Association of Clinical Endocrinologists 2006

The American Diabetes Association (ADA) *Technical Review on the Management of Diabetes and Hyperglycemia in Hospital* was published as an in-depth review of the literature on this topic and outlined practical management strategies [26]. The implementation of these policies and recommendations had remained an elusive goal in everyday clinical practice. Therefore, in 2006, the ADA and the American Association of Clinical Endocrinologists (AACE) produced a further consensus statement entitled *Inpatient Diabetes and Glycemic Control: A call to action* in an attempt to identify and overcome barriers to change in practice to facilitate improvement in inpatient diabetes care [27]. This was updated in 2009 with new glycemic targets based on recent publications that have demonstrated concern about the harmful effect of in-hospital hypoglycemia in some clinical settings [28].

Canadian Diabetes Association

The Canadian guidelines include separate sections on peri-operative and peri-acute coronary syndrome glycemic control, recommending glucose levels of 6.1 mmol/L in post surgical ITU patients and 128–180 mg/dL (7.1–10 mmol/L) in peri-myocardial infarction patients [29].

UK Diabetes Services

National Service Framework for Diabetes 2004

The Diabetes National Service Framework set out the first set of national standards for the treatment of diabetes [30]. Two standards were set for hospital care.

1 *Standard 7.* The NHS will develop, implement and monitor agreed protocols for rapid and effective treatment of diabetic emergencies by appropriately trained health care professionals. Protocols will include the management of acute complications and procedures to minimize the risk of recurrence.

2 *Standard 8.* All children, young people and adults with diabetes admitted to hospital, for whatever reason, will receive effective care of their diabetes. Wherever possible, they will continue to be involved in decisions concerning the management of their diabetes.

National Diabetes Support Group (NHS Diabetes) 2008
In 2008, the National Diabetes Support Group produced a document focusing on improvement of diabetes inpatient services and the commissioning of these services [31]. NHS Diabetes has now updated the commissioning toolkit to include the commissioning of emergency and inpatient care [31].

Diabetes UK 2009
Diabetes UK has produced a document for patients entitled "What care to expect in hospital", available from Diabetes UK [32]. It is hoped that this empowerment of patients will help to drive up in-hospital standards of care. Diabetes UK in partnership with NHS Diabetes and a number of other professional bodies through the "Putting Feet First' campaign have recently promoted the dissemination of a national guideline for the management of patients with acute diabetic foot problems in hospital.

National Health Institute of Innovation and Implementation 2009
The National Health Institute of Innovation and Implementation recently launched a package of recommendations to improve standards of care in hospital inpatients. This was branded the "Think Glucose" campaign and has been cascaded to all UK hospitals. Each acute hospital in the UK has been provided with a set of recommendations and a toolkit to drive improvement in standards [33].

Aims of diabetes inpatient care

Diabetes care in hospital inpatients poses a real challenge as most patients are admitted to a hospital bed with a condition unrelated to their diabetes, be that electively or as an emergency. Non-diabetes specialists are often in charge of their care, and they may often have little understanding of diabetes management and its importance on patient outcomes. As a result, there can be an increased risk of harm from issues such as lack of insulin dose adjustment or prescribing errors.

Achieving a good outcome
Patients should come to no harm because of their diabetes management. Hypoglycemia and excessive hyperglycemia are both are associated with poorer clinical outcomes and should be managed according to local protocols. Clinical guidelines supported by the use of integrated care pathways should be in place to drive up standards of care. Management by a specialist team with agreed protocols against agreed standards improves care for those admitted to hospital [34].

Supporting a rapid recovery
Patients with diabetes are twice as likely to be admitted to hospital and stay twice as long in a hospital bed [35]. Minimizing excess length of stay should be one of the principal aims of good inpatient care. Prolonged length of stay occurs for a multiplicity of reasons but is often because of diabetes mismanagement secondary to poor staff knowledge and lack of education. There is evidence that involvement of the specialist diabetes team, and in particular diabetes inpatient specialist nurses (DISNs), significantly reduces length of stay and insulin errors and improves the patient experience [36–38]. This requires a culture that invests in excellent communication between the person with diabetes, diabetes specialists and non-specialist teams to activate timely intervention by avoiding glycemic deterioration during hospital stay.

Facilitating a good patient experience and patients expressed concerns about inpatient care
Patients are accustomed to managing their own diabetes. Traditionally, patients are disempowered in the management of their diabetes as soon as they are admitted to a hospital bed. For those people with diabetes accustomed to self-management by insulin adjustment this is a negative experience [35]. The ADA [28] and Diabetes UK [32], while acknowledging the importance of diabetes self-management, highlighted the need to educate people with diabetes to deliver safe self-care in the hospital setting. Individuals suitable for self-management in hospital must be competent adults with a stable level of consciousness who successfully manage their diabetes at home. In addition, while in hospital it is advised that these patients have the physical skills appropriate to self-administer insulin; be accustomed to performing self-monitoring of blood glucose; and have adequate oral intake. In the event that self-care is deemed unsafe or impossible (e.g. critically ill, post surgery or unwilling), then there must be a governance arrangement to assess patient competency and if necessary supersede patients' right to self-care.

Encouraging and supporting patients to have as much responsibility for their diabetes management as they wish for, and their clinical status allows, is likely to enhance the patient experience during a hospital stay. The Diabetes UK position statement on what care adults with diabetes should expect in hospital clearly focuses on the importance of patient self-management, while reminding health care professionals of the importance of policies and strategies being in place to support this concept in the ward setting (Table 32.1).

Barriers to safe and effective diabetes care delivery in hospital

Systems failures
It is essential that the patient with diabetes is identified and flagged at an early stage of the admission process. The ADA recommends that all patients admitted to hospital should be identified in the medical record as having diabetes. The UK NHS

Table 32.1 Patients' experiences of in-hospital diabetes care [60].

1	Experiences of disempowerment and distress. Patients felt that they were not engaged as partners in their care during their admissions, and in some cases patronized by staff members
2	Food/food timings and their coordination with medication. This often reflected a lack of understanding amongst staff of the relationship between food and good diabetes management
3	Medicines mismanagement in hospital. People were given the wrong medication or dose
4	Lack of communication between different multidisciplinary team members and with the person with diabetes. This led to basic failures in communication such as notification of both changes in timings of procedures and dosages of medications to the patient
5	Lack of hospital staff knowledge of diabetes management both in terms of basic care and respecting patient autonomy
6	Importance of people with diabetes being allowed to self-manage and thereby respecting the role of the person with diabetes in usually self-managing their condition on a daily basis
7	Positive experiences of good diabetes management and proactively allowing patients to self-manage

Institute for Innovation and Improvement also recommends a diabetes identifier as a prerequisite for ensuring quality of care [33]. Yet this has not been achievable in the UK in secondary care because of systems failure as a result of poor coding and inadequate information systems technology. In addition, if we are to identify those patients with undiagnosed diabetes and stress hyperglycemia and make an impact on their poor outcomes there needs to be a policy of routine blood glucose screening for all hospital inpatients. This is not standard practice in the UK.

Ward environment factors

Basic diabetes care is often not well delivered in hospital. An analysis of 44 US hospitals revealed persistent shortcomings in diabetes management, including persistent excessive hyperglycemia [39]. The hospital environment is one that is characterized by instability and unpredictability for the patient. It is a major contributor to the difficulty of managing inpatient diabetes well. Intercurrent illness, in-hospital changes to a patient's usual outpatient regimen, and the scheduling and unpredictability of tests and procedures contribute to glycemic instability [40]. A patient's dietary intake may also be erratic, because of poor appetite, palatability of food or timeliness of delivery.

Staff training challenges

In the UK, qualified staff numbers have been reduced to a minimum and ward staff have little or no protected time for education and training other than mandatory training (fire, manual handling, back care, infection control) defined by the employing organization. Despite the large numbers of patients with diabetes in hospital, the only mandatory training in diabetes is in blood glucose monitoring. People with diabetes, who generally have a high level of knowledge about their condition, are therefore often being managed by nursing and medical staff with only a rudimentary training in diabetes care [41].

Box 32.1 Defining adverse events and medical errors

Adverse events are described as: An unintentional injury caused by medical management rather than the underlying disease or condition of the patient. This can include physical or emotional harm [61]

Medical errors are described as: The failure to complete a planned action as intended or the use of a wrong plan to achieve an aim [61]

Insulin prescribing and delivery errors

Insulin treatment in hospital can be life-saving. It also has the potential to be life-threatening given its narrow therapeutic index. The prescribing of insulin is a minefield of ignorance and error. Insulin has been identified as one of the top five high-risk medications in the inpatient environment [42,43]. There is a wealth of material, predominantly from the USA and the UK, describing both medical errors and adverse events in the general inpatient population (Box 32.1). Medical errors, including those related to insulin treatment, are described as common in hospitals worldwide [44,45]. Insulin medication errors can occur at any stage in the process of prescribing, preparing and delivering the medication to the patient [46]. The potential consequences of error can be catastrophic. One-third of all inpatient medical errors that cause death within 48 hours of the error involve insulin administration [47].

Medical prescribing

A common recommendation emerging in both diabetes management and prescribing errors has been the need for appropriate medical staff education in diabetes and insulin treatment. Hellman [47] suggests that endocrinologists take on this role and maintain that junior doctors should be taught the principles of drug dosage and prescription writing before starting their ward placements. A report from the National Patient Safety Agency 2007 [49] devotes one entire page to insulin errors and advocates changes to pre-registration training to incorporate the principles and therapeutics of safe prescribing. The curriculum for junior doctors has been revised in recent years and new models of education have been implemented yet this has not reduced insulin prescribing errors in junior hospital doctors and therefore the process merits review.

Non-medical prescribing

In the UK, legislation for nurse prescribing, now known as non-medical prescribing, was implemented in 2003. The editorial by Aronson *et al.* [50] compared medical student training (approximately 61 hours) to that of nurse prescribers (162 hours of theory

and 90 hours in practice). The authors called for the adoption of the British Pharmacological Society's prescribing and assessment processes to be applied for doctors in training in the teaching of diabetes and insulin treatment. Aronson also called for the formation of an independent systematic review of medical prescribing and teaching by a multi-organizational body in order to inform practice. This process has yet to be implemented but if introduced could form the basis for training in diabetes medicines management.

Delivering effective diabetes care: the role of diabetes inpatient team

Diabetes inpatient teams are multidisciplinary; the health care professionals involved individually contribute specialist skills and together provide a holistic approach to patient care. As well as operating as a discreet unit, the team works closely with other medical specialities including the specialist diabetic foot team. The defined roles forming the diabetes specialist inpatient team include the following.

The Patient

Central to the diabetes team is the patient. The majority of people living with diabetes have developed highly competent and individualized management skills, therefore it is essential, where possible, that the patient is encouraged to participate in the formulation and conduct of their own care plan while in the ward setting.

Consultant physician

The primary role of the consultant physician is as leader of the multidisciplinary team. The consultant physician has ultimate responsibility for the clinical care of diabetes inpatients. They work closely to provide clinical support to diabetes specialist nurses (DSNs) and certified diabetes educators (CDEs), while being heavily involved in the training and education of other diabetes and non-diabetes health care professionals. With the need to maintain standards of care and update clinical guidelines, physicians are also frequently involved in audit and research work in order to ensure the highest quality of diabetes care for inpatients with diabetes.

Certified Diabetes Educator

In 2009, the Association of Diabetes Educators published a position statement, which emphasized the key role of CDEs in patient and staff education, the promotion and implementation of glycemic control strategies and appropriate nutritional therapies. In close partnership with social work, case managers and home care coordinators, they are able to facilitate a smooth patient pathway from hospital to home at discharge.

Diabetes specialist nurse

The work of DSNs is exclusively in diabetes care. In 2009, there were 1361 DSNs in the UK working in primary and/or secondary care settings. DSNs deliver patient-centered care wherever required and influence care delivery at every stage of the patient journey, including inpatient care. The role of the DISN has evolved in recent times and specifically focuses on supporting inpatients and the ward staff caring for them. Aside from clinical care, DISNs are frequently involved in medical and nursing education and also in guideline production and update. Not only can DISNs significantly reduce inpatient length of stay [36,37], but if they also obtain non-medical prescribing skills, have also been seen to reduce insulin and diabetes management errors significantly [38].

Diabetes specialist dietitian

Diabetes specialist dietitians have a pivotal role in the care of diabetic inpatients with complex nutritional needs, in particular those patients who are unable to swallow or those required to adhere to a complex dietary regimen as in renal failure, cystic fibrosis and the elderly.

Other team members may include ward-based diabetes link nurses and diabetes specialist pharmacists.

Which type of patient needs to be seen by the diabetes specialist team?

The correct answer to this question is that all patients with diabetes should have access to specialist diabetes services; however, given that up to 20% of all inpatients now have diabetes then in real world it is going to be almost impossible for specialist team members to see every patient. Specialist teams therefore, driven by need, have drawn up a priority list for which patients should be referred for assessment. An example of one of these referral criteria documents from Leicester, UK, is seen in Table 32.2.

Management of in-hospital hyperglycemia

All hospitals should have a policy for glycemic management and or blood glucose monitoring in place according to the ADA [28] or the National Institute for Health, Innovation and Improvement (NHSIII) standards of care. The newly introduced UK "Think Glucose" campaign from the NHSIII has as its mantra, "It is as unacceptable for hospitals not to have a glycemic management policy as it is for them not to have an infection control policy" [33].

Hyperglycemia in hospital is a common problem and occurs in around 25% of all hospital inpatients. The majority of patients with diabetes are not admitted to hospital to address and treat complications associated with the disease. Control of blood glucose often becomes secondary to the care of the primary diagnosis requiring admission. In patients without diabetes who develop hyperglycemia during an acute illness, high glucose levels are often ignored or treated inappropriately. Poor glycemic control is common among inpatients with diabetes, particularly

Table 32.2 Indications for referral to diabetes inpatient specialist nurses (DISN). Adapted from University of Leicester Hospitals, UK.

Always refer	Hyperglycemic emergencies (e.g. DKA, HHS) Acute coronary syndromes Severe or repeated hypoglycemia New diagnosis of diabetes Problems with intravenous insulin infusion or duration >48 hours Active foot ulceration Reduced consciousness Enteral or parenteral nutrition Vomiting and sepsis Patient request Persisitent hyperglycemia Pregnancy
Consider refer	Educational needs Stress hyperglycemia NBM >24 hours Poor wound healing
Rarely refer	Minor hypoglycemia Routine dietetic advice Simple educational needs Well-controlled and managed diabetes

DKA, diabetic ketoacidosis; HSS, hyperosmolar hyperglycemic syndrome; NBM, nil by mouth.

in those treated with insulin, for many reasons. Poorly defined management plans, poor coordination of care, overly high or absent glycemic targets, lack of therapeutic adjustment, over utilization of "sliding scales" which are often not adjusted to optimize control and under-utilization of insulin infusions represent some of the reasons for poor control of blood glucose. A further important contributing factor has been the fear of provoking hypoglycemia.

Intravenous insulin to treat in-hospital hyperglycemia

Insulin provides the greatest flexibility in the hospital setting to achieve optimal blood glucose control. As protocols for tight glucose control are introduced in a variety of hospital settings it will be essential to implement safeguards to minimize the risk of hypoglycemia and ensure patient safety. The systemic problems that create obstacles to appropriate and safe care of patients receiving insulin in hospital are well recognized [45]. Insulin administration errors could be minimized and clinical outcomes improved by thorough analysis of the setting, additional training for ward staff, setting of goals focused on patient safety, double checking of insulin prescription and administration and regular audit of adverse incidents.

Indications for an intravenous insulin infusion

Whether the patient has previously recognized diabetes or not, insulin provides the greatest flexibility to meet rapidly changing requirements in different hospital settings to achieve optimal blood glucose control. Intravenous infusion of insulin is the only insulin treatment strategy specifically developed for use in the hospital setting. The American College of Endocrinologists advised that intravenous insulin infusion should be used to control glycemia in certain indications (Box 32.2).

Box 32.2 Indications for an intravenous insulin infusion

- To treat critical care illness
- Acute coronary syndromes
- Postoperative periods following heart surgery
- Patients on "nil by mouth" status
- Type 1 diabetes
- General preoperative, intra-operative and postoperative care
- Organ transplantation
- Stroke
- Hyperglycemia during high-dose corticosteroid therapy
- Labor and delivery
- Other acute illness for which prompt glycemic control is judged important to recovery such as prevention or treatment of infection
- Diabetes emergencies such as diabetic ketoacidosis or hyperosmolar hyperglycemic syndrome

Insulin infusion protocols

The ideal insulin protocol should be safe, understandable, easily ordered and implemented. It should be effective in correcting hyperglycemia quickly and in maintaining glucose levels within a defined target range. The provision of an algorithm for making incremental changes to the infusion rate, which can be executed by nursing staff, is likely to improve the efficacy of the protocol. Hypoglycemia is a potential complication of intensified insulin therapy and is associated with poor outcomes. It is for this reason that intravenous insulin infusions should be supported by caloric input. In most patients this is in the form of a simultaneous infusion of dextrose but calories can be provided by other routes (e.g. enteral, parenteral or in a diasylate). If hypoglycemia develops despite adequate provision of calories then the patient should be treated promptly for hypoglycemia according to local protocol and the insulin infusion adjusted accordingly.

Successful implementation of an insulin infusion protocol is best achieved with the appointment of a champion to lead the multidisciplinary team. The protocol should be submitted to a medicines advisory or therapeutics committee and implemented with a widespread educational program to include medical, nursing and pharmacy staff. Adherence to a standard protocol is likely to reduce adverse events for patients and limit medical errors in insulin prescribing.

Table 32.3 Insulin infusion table adapted from Oxford Radcliffe NHS Trust, UK.

Blood glucose (mmol/L)	Insulin infusion rate (unit/hour)				
	Rate A	Rate B	Rate C	Rate D	Tailored rate
0–4.0	0 and treat hypo	0 and treat hypo	0 and treat hypo	0 and treat hypo	0 and treat hypo
4.1–6.0	1	1	2	3	
6.1–8.0	2	3	4	5	
8.1–10.0	3	4	6	8	
>10.1	4	6	8	10	
		>10 mmol/L			

If blood glucose remains >10.1 for 4 hours move to the next infusion rate (e.g. A to B)
Prescriptions should include the signature, bleep and date as well as the time and date infusion started

Box 32.3 AACE/ADA recommendations for in-hospital glycemic control

A target of 140–180 mg/dL (7.8–10.0 mmol/L) is preferable in *most* patients
A target of 110–140 mg/dL (6.1–7.8 mmol/L) may be appropriate in *selected* patients
A target of >180 mg/dL (10 mmol/L) or <110 mg/dL (6.1 mmol/L) is *not* recommended

Box 32.4 Converting patients to subcutaneous insulin

(a) *Estimation of insulin dose for a patient being converted from an intravenous insulin infusion*
- Calculate average hourly insulin dose by totaling the last 6 hours' doses on the chart and dividing by 6 (e.g. 15 units divide by 6 = 2.5 units/hour. Multiply by factor of 20 to get the total daily dose (TDD) insulin (e.g. 50 units)
- For a basal : bolus insulin regimen, divide 50 : 50 basal : bolus (e.g. 25 units as basal; 25 units as bolus. Give 25 units as a basal insulin (e.g. Lantus). Divide total bolus dose by three to get bolus for each meal (e.g. 8 units short-acting insulin, e.g. Novorapid)
- For a twice daily fixed mixture regime divide 60 : 40 morning : evening (e.g. Humalog Mix 25, Novomix 30). Give 36 units am; 14 units pm

(b) *Estimation of insulin dose when no insulin infusion has been used*
Calculate the total daily insulin dose insulin according to diabetes type
- Known type 2 diabetes 0.5–0.7 unit/kg
- Known type 1 diabetes 0.3–0.5 unit/kg
- Unsure 0.3–0.5 unit/kg
- Divide insulin 50 : 50 for basal bolus regime (see above)
- Divide 60 : 40 for twice daily mixed insulin (see above)

Preparation and delivery of an insulin infusion

The insulin infusion is prepared by adding 50 units of soluble insulin to 49.5 mL normal saline, which will provide 1 unit of insulin in 1 mL saline, which is delivered via an infusion pump. This insulin infusion can be piggy-backed into the infusion of dextrose using a three-way connector and a non-return valve. All patients should commence on algorithm A and uptitrate to achieve target glucose range (Table 32.3).

Targets for glycemic control

The AACE/ADA has recently set new targets for the management of hyperglycemia in hospital (Box 32.3) [62]. The recommendation is that once intravenous insulin has been commenced the blood glucose level should be maintained at 140–180 mg/dL (7.8–10 mmol/L) with greater benefit possibly realized at the lower end of the target. There is recognition that lower targets may be beneficial in specified groups but there is insufficient evidence to make firm recommendations. It is recommended that target glucose should not fall below a level of 110 mg/dL (6.1 mmol/L). Where lower targets are being used, patients should be treated in sites with extensive experience and appropriate support such as areas caring for coronary artery bypass graft patients, sites with low rates of hypoglycemia, patients on total parenteral nutrition and those in ITUs.

Transition from intravenous to subcutaneous insulin

Conversion to subcutaneous insulin should be delayed until patients are able to eat and drink normally without nausea or emesis. The most appropriate time to switch from IV to subcutaneous insulin is at the usual time of the patient's insulin administration, before a meal. Patients with known type 1 diabetes will become insulin deficient within minutes of the IV infusion being stopped because of the short half-life of IV insulin. It is therefore good practice to continue the infusion of insulin for 1 hour after the subcutaneous insulin has been administered to allow time for the insulin to be absorbed.

If the patient has been on an established insulin regimen, then this regimen should be restarted, but doses may have to be adjusted depending on the patient's clinical condition. If the patient is new to insulin therapy, then a rough estimation of the total daily dose (TDD) of insulin can be made from a simple calculation using the hourly rates delivered in the IV insulin infusion (Box 32.4a). Estimation of insulin doses can also be made

Table 32.4 Causes of in-hospital hypoglycemia.

Cause of in-hospital hypoglycemia	Example
Primary reason for hospital stay	Medical causes: hepatic failure, cardiogenic shock, severe sepsis Surgical causes: nil by mouth for operation or procedure
Inappropriate food administration	Change of meal times, missed meals, poor access to snacks
Errors of insulin prescription or administration	Poorly written medication charts (e.g. writing of "U" instead of units) so that 4 U becomes 40 units, poor injection technique
Inappropriate use of "stat" insulin doses	Corrective dosing of insulin prescribed by untrained staff
Inappropriate use of sulfonylureas or interactions with other prescribed medication	Long-acting hypoglycemic agents should be avoided in hospital
Inappropriately timed diabetes medication for meal/enteral feed	Food and insulin or oral hypoglycemic agents mismatch
Use of unopposed intravenous insulin therapy	Dextrose infusion should be prescribed concurrently
Mobilization after acute illness	Insulin requirements may decrease with exercise

according to body weight, which is useful in calculating TDD in patients who are new to insulin but have not required an insulin infusion (Box 32.4b).

Avoiding and treating in-hospital hypoglycemia

There is an increasing body of evidence supporting the widespread occurrence of hypoglycemia in hospitals and poor knowledge of how to detect and manage it. Acute hypoglycemia is associated with significant morbidity and more rarely mortality as it causes an intense hemodynamic response that can lead to potentially fatal cardiac arrhythmias, myocardial ischemia, cerebrovascular accidents, coma and death. In-hospital hypoglycemia is defined as a blood glucose level equal or below 72 mg/dL (4.0 mmol/L).

Causes of in-hospital hypoglycemia

There are many reasons why hypoglycemia is more likely to be to occur during hospitalization but most of these relate to insulin administration and prescribing errors and inappropriate food administration (Table 32.4).

Management of in-hospital hypoglycemia

In 2005, Tomky *et al.* [51] gave a clear overview of the topic in their article. 2006 saw the introduction of Hypoboxes™ for the management of hypoglycemia in the UK [52]. These boxes are often in a prominent place (e.g. on resuscitation trolleys) and are brightly colored for instant recognition. They contain all the equipment required to treat hypoglycemia, from cartons of fruit juice to intravenous 20% glucose. There are general guidelines for the treatment of in-hospital hypoglycemia and these should be available in each ward and outpatient setting; however, each patient developing in-hospital hypoglycemia should be assessed as an individual and diabetes teams should agree local guidance for self-management. Certain conditions such as renal impairment or heart failure may require tailored treatment to avoid fluid overload. Many people with diabetes carry their own treatment supplies for hypoglycemic events and should be supported to self-manage when capable and appropriate. This information regarding capacity to self-manage should be recorded in the patient notes at the time of the admission assessment.

If the patient is not capable and/or uncooperative but is able to swallow, give either 1.5–2 tubes GlucoGel™ squeezed into the mouth between the teeth and gums or, if this is ineffective, give 1 mg glucagon intramuscularly (Figure 32.1). Monitor the blood glucose levels after 15 minutes. If the blood glucose levels are still less than 4 mmol/L, GlucoGel treatment can be repeated up to three times. If the hypoglycemia does not resolve at this stage, IV 10% glucose infusion at 100 mL/hour should be considered. Once the blood glucose is above 4 mmol/L and patient has recovered, a long-acting carbohydrate snack should be offered.

In adults who are unconscious with or without seizure activity and/or very aggressive, the patient's airway, breathing and circulation should be assessed, any insulin infusion *in situ* should be discontinued and a medical practitioner summoned. At this stage any of the following treatments can be considered for use.

Treatments such as 15–20 g quick-acting carbohydrate (e.g. 50–60 mL of Ensure Plus juice or Fortijuice 25 mL original or 3–4 heaped teaspoons sugar dissolved in water) can be administered via a feed tube. The capillary blood glucose measurement should be repeated 5–10 minutes later. If blood glucose is still less than 4 mmol/L, repeat this step up to three times. If the hypoglycemia is still not resolved after 15 minutes or three cycles, IV 10% glucose infusion at 100 mL/hour can be considered as a treatment option. Once the blood glucose is above 4 mmol/L and patient has recovered, a long-acting carbohydrate such as 200 mL milk (not soya) can be given and the feed. Insulin should not be omitted and regular continued capillary blood glucose level monitoring should be recorded for 24–48 hours.

Prevention of recurrent in-hospital hypoglycemia

When hypoglycemia has been successfully treated it is important that the reason for hypoglycemia is ascertained and the treatment documented in the patient notes. If the hypoglycemic episode was severe or a recurrent event, or if patient has concerns regarding treatment of further recurrence of hypoglycemia and its treatment, then referral should be made to the CDE, DISN or specialist medical team. Measures such as medication adjustment or timing of meals should be introduced to prevent further episodes of hypoglycemia.

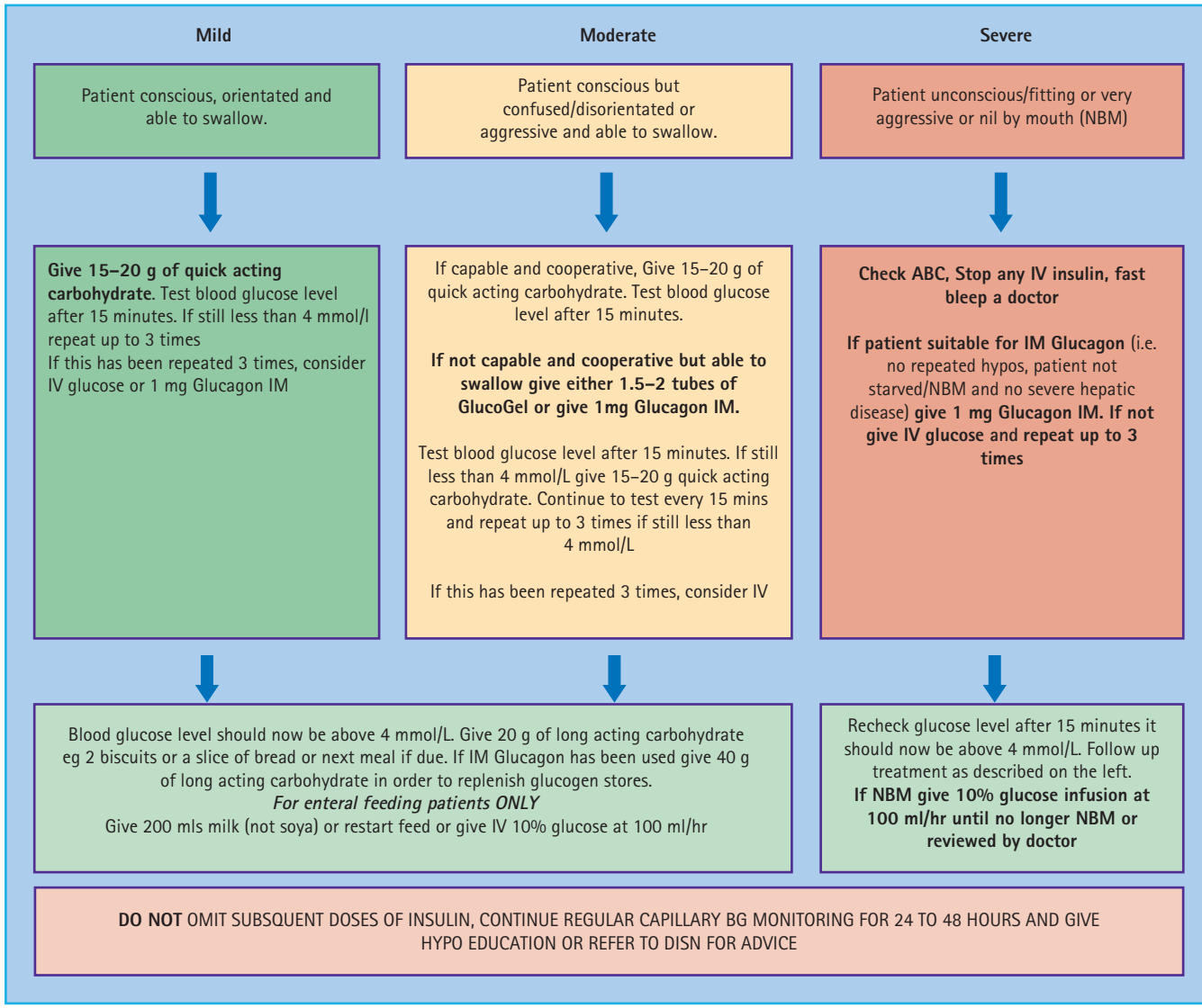

Figure 32.1 Algorithm for the treatment and management of hypoglycemia in adults with diabetes mellitus in hospital. Hypoglycemia is defined as blood glucose of <4 mmol/L (if not <4 mmol/L but symptomatic, give a small carbohydrate snack for symptom relief). ABC, Airway, Breathing and Circulation; DISN, diabetes inpatient specialist nurse; IM, intramuscularly; IV, intravenously; NBM, nil by mouth.

Surgery in patients with diabetes

Patients with diabetes have poorer health than those without diabetes so this means they are more likely to undergo surgery. It is estimated that 50% of those with diabetes will require surgery in their lifetime. Diabetes is associated with increased risk of perioperative infection and postoperative cardiovascular morbidity and mortality. The complex interplay of the operative procedure, anesthesia, fasting and additional postoperative factors such as artificial feeding and emesis all contribute to labile glycemic control in the perioperative period.

Metabolic response to surgery

Surgery and anesthesia causes a state of relative insulin hyposecretion and insulin resistance. It induces a complex series of hormonal and metabolic changes [53,54]. The secretion of the counter-regulatory or "stress" hormones, particularly cortisol and catecholamines, is greatly increased, and this can lead to an acute decrease in insulin sensitivity [54,55]. Enhanced sympathetic activity, together with raised circulating catecholamine concentrations, tends to inhibit insulin secretion. The net result of these changes is to push metabolism towards catabolism, leading to increased hepatic glucose production and hyperglycemia and enhanced breakdown of protein and fat. The magnitude of the counter-regulatory response varies in each individual and is greater with prolonged surgery and other factors such as postoperative sepsis.

Preoperative evaluation

Nowadays, most patients are admitted on the same day as scheduled surgery. Pre-assessment planning in diabetes can prevent

Table 32.5 Goldmann risk index [56].

Risk	Patient characteristics	Preoperative investigation
Low	<60 years old No history of cardiopulmonary disease Non-specific ECG changes	No further investigation necessary
Medium	All patients >60 years old Stable angina or previous MI Compensated heart failure	Determine functional capacity using ECG, exercise stress test (has a predictive value of 81% detection of multivessel disease)
High	Acute coronary syndromes Decompensated heart failure Supraventricular arrhythmias Known COPD	Consider preoperative coronary angiography

COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; MI, myocardial infarction.

Table 32.6 Surgery-specific risk.

	Procedure
Low	Peripheral and laparoscopic procedures
Medium	Orthopedic and prostatic operations
High	Major abdominal and thoracic operations, particularly major vascular surgery and ones where there are anticipated major fluid or blood loss

unnecessary cancellation of surgery, give opportunities for joint care planning with the person with diabetes and enables optimization of glycemic control prior to surgery which can reduce length of stay, medication errors and improve the patient experience.

Assessing cardiac risk

Careful assessment of patients with diabetes is required because of their complexity and high risk of coronary heart disease, which is sometimes asymptomatic. It is therefore vital that all patients with diabetes attending for surgery have a robust risk assessment with particular focus on cardiopulmonary risk. In the assessment of risk for elective procedures one must one must consider the risk associated with the procedure itself in addition to the individual patient risk associated with pre-existing co-morbidities. Those at highest risk are those in whom there is significant cardiorespiratory pathology. There are several cardiac risk stratification indexes in the literature but essentially all use clinical variables that allow patients to be classified as low, intermediate or high risk of a major cardiac event during or after surgery. The Goldmann cardiac risk index [56] is widely used in clinical practice (Table 32.5).

Assessing surgical risk

The American College of Cardiology/American Heart Association guidelines introduce the concept of "surgery-specific risk." Risk stratification is based on the degree of hemodynamic stress associated with specific procedures [57]. Table 32.6 summarizes the risk associated with various types of surgery.

Physical assessment

All patients require a careful history and physical examination. Key aspects of this should include assessment of glycemic control, long-term complications, occurrence of hypoglycemia and its frequency, and the patient's awareness and knowledge of all drug therapy. Patients should be given written information about changes in diabetes-specific and other medication in the days leading up to surgery.

Laboratory assessment

Basic investigations should include HbA_{1c} as there is a suggestion that elevated levels over 7% (>53 mmol/mol) are associated with higher risks of postoperative infections [58].

There is good evidence that effective pre-assessment of people with diabetes will enable a safe and effective discharge from hospital. In Bolton, UK, a DSN has implemented a patient pathway from pre-assessment to discharge. This pathway includes assessment, optimization of glycemic control, the writing up of an insulin infusion scale preoperatively and the implementation of planning for routine diabetes care postoperatively. This work has resulted in significant improvement in reduced length of stay, medication errors and positive patient experience [59].

During the course of the pre-assessment visit each patient should undergo an explanation of the procedure and the planned anesthesia. The diabetes management plan should be discussed, thus enabling the patient to make an informed decision around the diabetes care to be offered. Further appointments should be offered if optimization of glycemic control is required. All information should be supported with appropriate literature. All recommendations for treatment should be written in the patient's notes and in a handheld record kept by the patient.

Same-day admissions and specific preparations

High-risk patients are not suitable for same-day admission and should be admitted the day before surgery for assessment and optimization of glycemic control. There is evidence that elevated preoperative glucose levels >200 mg/dL (11 mmol/L) were associated with deep wound infections in a case–control study.

On the day of admission the patient's notes including the diabetes management plan should be available to all staff caring for that individual. All guidelines pertaining to the plan of care should be in place and accessible for staff. If the blood glucose is unacceptably high on the day of admission, plans should be in place for rapid optimization of glycemic control including the use of an intravenous infusion of insulin.

Table 32.7 Instructions for diabetes management on day of minor or intermediate surgery. Adapted from Nottingham University Trust, UK.

Morning list	Day before: normal food and medication. NBM from 02.00 Day of surgery: fast from 02.00 On tablets: omit diabetes tablets On insulin: omit any short-acting insulin, withhold insulin mixtures Give stat dose of isophane insulin, give 75% total daily dose if on once day insulin and 50% TDD if on twice daily insulin Continue long-acting analogs (Lantus, Levemir) at full dose Postoperative: lunch and normal insulin or tablets
Afternoon list	Day of surgery: light breakfast, fast from 08.00 On tablets: take diabetes tablets On insulin: take 50% normal insulin dose Continue long-acting analogs (Lantus, Levemir) at full dose Postoperative: late lunch and normal insulin or tablets

NBM, nil by mouth; TDD, total daily dose.

Individual intra-operative diabetes care treatment plan

Management of the individual patient is determined by the following:

- Severity and nature of surgery (major or minor surgery)
- Duration of perioperative fast
- Timing of surgery
- Pre-existing diabetes treatment

Major surgery (prolonged fast >6 hours)

All patients with diabetes undergoing major surgery should have a dextrose and insulin infusion.

Minor surgery (short fast <6 hours)

Table 32.7 shows an example of the various treatment options for patients being admitted for minor surgery.

Goals of glycemic management

The goals of perioperative diabetes care are avoidance of marked hyperglycemia and of hypoglycemia. Patients with type 1 diabetes have no endogenous insulin and will therefore require exogenous insulin to prevent the development of severe hyperglycemia and subsequent life-threatening complications such as diabetic ketoacidosis. Such patients will also need a continuous supply of glucose of 5–10 g/hour to prevent hypoglycemia.

It is not clear how "tight" glucose control needs to be during surgery. There are a paucity of clinical trials to inform clinical practice in the surgical arena with the exception of cardiac surgery where there is evidence that good control, defined as BG 80–110 mg/dL (4.4–6.1 mmol/L), may reduce mortality.

The lack of clear evidence on glycemic specific targets is reflected in the varying glucose targets recommended by national guidelines [24,27,28]. It would seem reasonable therefore to advise treatment regimens to aim for as near normal glycemia with avoidance of hypoglycemia (80 mg/dL, 4 mmol/L). This range seems to be a safe and practicable target during the perioperative period.

Intra-operative management of glycemia

Use of an IV insulin infusion to control glycemia has the advantage of easy titration to the glucose level because of the short half-life of IV insulin. Its safety has been demonstrated in many studies and is therefore the treatment of choice during surgery. The infusion requires close monitoring of blood glucose and potassium as well as appropriate interpretation by well-trained staff.

Types of intravenous insulin infusion

No type of insulin infusion used during surgery has been shown to be superior in either safety or effectiveness in achieving glucose control. The fixed rate insulin infusion and the intermittent bolus regimens have failed to gain popularity and are little used in clinical practice and are therefore not discussed further.

Variable rate separate insulin and glucose intravenous infusions

In this commonly used regimen, intravenous dextrose is infused at a rate of 5–10 g/hour and a separate insulin infusion is given. The rate varies depending on the procedure and the level of insulin resistance. Following coronary artery bypass graft operations, insulin requirements may increase 10-fold [38]. Glucose should be measured hourly and electrolytes every 4 hours.

Glucose insulin potassium infusion

The glucose, insulin and potassium infusion is a single solution infusion comprising 500 mL 5% dextrose, 10 mmol/L potassium chloride and 15 units of soluble insulin. This is infused at a rate of 100 mL/hour. Glucose is usually measured 2-hourly and the insulin content of the infusion can be changed if necessary. This method has the disadvantage of inflexibility and wastefulness as the entire infusion has to be discarded and replaced if insulin requirements change.

Postoperative care and discharge

For those undergoing minor surgery characterized by a short fast, generally the preoperative diabetes treatment can be reinstated at an early stage once the patient is eating well. For those undergoing major surgery, particularly abdominal surgery where there may be several days of fasting, then it is better to keep these patients on IV insulin infusion with appropriate fluid replacement. The IV fluid regimen should consist of replacement crystalloid, a minimum of 2 L/day (normal saline, Hartmann solution, Ringer lactate) and a supply of substrate (e.g. 100 mL/hour 5% dextrose) to prevent onset of catabolism. Conversion to normal therapy, whether insulin or oral hypoglycemic therapy, should occur when the patient is eating and drinking and free from nausea and emesis.

For patients with prolonged periods of nil by mouth or who are severely unwell or malnourished, hyperalimentation may be introduced. In these circumstances, insulin requirements may increase considerably and so these patients are better managed on high dose IV insulin with the support of the specialist diabetes

team. Hospitals should have protocols in place to support this practice.

Conclusions

Patients with diabetes are twice as likely to be admitted to hospital and stay twice as long as those without diabetes. They have worse outcomes and a poorer patient experience than those without diabetes. Diabetes inpatient care and training has become the Cinderella area of diabetes care delivery despite the setting of clinical standards by several professional bodies. Although there is now a wealth of evidence that specialist inpatient diabetes teams reduce length of stay, reduce errors in prescribing, improve the patient experience and clinical outcomes, many hospitals across the world still lack inpatient specialist teams.

Patients voices are being raised in anger against this imbalance in care delivery. Providers of care need to listen to patients and professionals and ensure the delivery of a high quality inpatient service to include appropriate medical and nursing staff training, an equitable access to specialist services across the board, and an active partnership with patients to deliver a comprehensive range of services. Systems need to be in place to enable patients to self-manage where it is clinically appropriate. If standards are to be improved there needs to be agreed national targets and key performance indicators for diabetes inpatient care for which health care providers should be held accountable.

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