Hyperglycaemia management in hospital and postdischarge care

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Hyperglycaemia in hospital inpatients is common and detrimental, often occurring in those without a prior diagnosis of diabetes, and is usually associated with poorer outcomes. Postdischarge GP screening for diabetes and treatment adjustments for patients with chronically poor glucose control is as crucial to patient outcomes as in-hospital treatments for hyperglycaemia.

Hyperglycaemia is common in hospitalised patients, with 7% of all inpatients who are admitted through the emergency department to a tertiary teaching hospital having blood glucose levels above 11.1 mmol/L (in the diabetes range) during the first 24 hours of their admission.[1] One-third of these patients have no previous history of diabetes. Inpatient hyperglycaemia is associated with higher mortality, more illness complications, higher risk of infection, longer hospital stay and more frequent intensive care unit admissions.[1-3] This has been reported for patients admitted with many different conditions, including myocardial infarction, stroke, pneumonia and trauma.[4-7]

Key points

- **Hyperglycaemia in hospital inpatients is associated with poorer outcomes.**
- **At least 7% of hospital inpatients have a glucose level of 11.1 mmol/L or more, and one-third of these patients have no prior diagnosis of diabetes.**
- **In-hospital use of intravenous or basal-bolus insulin is the recommended treatment for hyperglycaemia, and use of sliding scale insulin as sole therapy should be avoided. Short-acting 'supplemental' insulin may also be prescribed; however, if required then the dose of the patients' usual diabetes medications should be increased.**
- **Although in-hospital glucose targets and mechanisms for improvement remain controversial, there is no controversy over the need for continuing diabetes care or investigation of hyperglycaemia following discharge from hospital.**
- **Patients who experience hyperglycaemia in hospital without a prior diagnosis of diabetes represent an opportunity for diabetes to be diagnosed or treatment initiated to prevent progression to frank diabetes. A 75 g oral glucose tolerance test should be performed at six weeks' postdischarge because about 75% of these patients will have diabetes or impaired glucose tolerance.**
- **Good community diabetes management by GPs and community diabetes teams may help to prevent readmission.**
- **Excessively tight glycaemic control, which leads to hypoglycaemia, should be avoided both acutely and long term.**
- **HbA_{1c} treatment targets need to be individualised, with higher HbA_{1c} targets for patients at risk of hypoglycaemia, including those with type 1 diabetes, aged over 70 years or with a history of coronary artery disease.**

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Hospital inpatients with hyperglycaemia and without a prior diagnosis of diabetes have poorer outcomes than those with known diabetes.[2,8] Every 1 mmol/L increase in fasting plasma glucose levels above 5.6 mmol/L in hospital inpatients is associated with a 33% increase in mortality.[9] Although different cutoffs for hyperglycaemia are reported, there is a suggested linear or exponential increase in adverse outcomes with increasing glucose levels above normal.

Areas of uncertainty in hyperglycaemia management in hospital inpatients

There are many areas of uncertainty in the management of hyperglycaemia in hospital inpatients, including the direction of association between hyperglycaemia and poor outcomes, whether improvements after insulin treatment are due to normalisation of glucose levels or the presence of insulin itself,[10] and what the ideal target blood glucose level range should be.

Improved glycaemic control can reduce the rate of hospital complications (e.g. reduced postoperative wound infection rates) and mortality in critically ill and noncritically ill patients. However, treatment in hospital is associated with an increased rate of hypoglycaemia and mortality.[11] The direction of association between hypoglycaemia and mortality is another area of uncertainty.

In-hospital treatment with insulin to lower blood glucose levels has been shown to reduce morbidity and mortality in patients with myocardial infarction (the Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction [DIGAMI] trial[12]) and those in surgical intensive care.[13] Studies to determine if even lower blood glucose levels (tighter glycaemic control) would yield increased benefit were disappointing, with the occurrence of higher rates of severe hypoglycaemia and higher mortality. The DIGAMI2 trial failed to demonstrate a reduction in secondary cardiovascular events with more intensive glucose management compared with standard management.[14] Because of this, tight glucose control after acute coronary events was abandoned, although the findings may have been explained by inadequate separation in fasting glucose and HbA_{1c} between the treatment arms (presumably because standard management had improved since publication of the original DIGAMI study 10 years earlier). The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study sought to replicate the results of improved glycaemic control in intensive care patients seen above,[13] but ended early because of an increase in adverse events in the intensively treated group compared with standard treatment group.[15] Intensively treated patients experienced higher rates of severe hypoglycaemia.

These later studies led to the revision of international guidelines for in-hospital diabetes management from tight to more moderate glycaemic targets,[16] with the Australian Diabetes Society guidelines suggesting a level of 5 to 10 mmol/L for most clinical situations.[17]

Optimal treatment type also remains open to interpretation. Intravenous insulin infusion has been shown to be safe for patients in intensive care, but guidelines suggest that treatment should be based on local expertise and experience.[16] In terms of subcutaneous glucose delivery, regular dosing using long-acting insulin with prandial insulin (and supplemental short-acting insulin to cover unexpected hyperglycaemia), with or without oral medication to proactively prevent hyperglycaemia, is preferred to intermittent dosing (i.e. sliding scale insulin). A multicentre randomised controlled trial showed that basal-bolus insulin was superior to sliding scale insulin (intermittent short-acting insulin administered only in reaction to a high glucose level) for achieving glycaemic targets.[18] This is because when sliding scale insulin is used as sole therapy it is, at best, ineffectual and, at worst, results in poor control with large glucose excursions.[19] These greater glycaemic excursions are linked to poor outcomes.[20] Doses administered via sliding scale should be incorporated into usual diabetes medications (e.g. by increasing regularly prescribed insulin doses), and sliding scale insulin should not be used as sole therapy.

In-hospital hyperglycaemia reflects undiagnosed diabetes or poor chronic glycaemic control

Despite the above uncertainties, it cannot be disputed that patients who experience hyperglycaemia in hospital are at high risk of having and/or developing diabetes if they do not already have the diagnosis. This is in contrast to suggestions that acute hyperglycaemia represents a normal part of a temporary 'stress response', related to acute cortisol and adrenaline release during acute illness. The presence of stress hyperglycaemia indicates the patient is at risk of diabetes, and it is usually not temporary.[21] It occurs in patients susceptible to insulin deficiency and usually reflects chronic dysglycaemia.[22,23] It is associated with even poorer outcomes than in people previously diagnosed with diabetes, and should therefore be treated.[24,25]

In one Australian study, three-quarters of hospital inpatients with a blood glucose level of 10 mmol/L or more had either diabetes or impaired glucose metabolism after discharge.[21] Despite this, only 2 to 9% of patients are diagnosed in hospital.[1,26,27] A diagnosis of diabetes was self-reported by 4.2% of Australians in 2011-12, with almost 1.2 million Australians registered with the National Diabetes Services Scheme as of June 2015.[28,29] For every diagnosed case there is another undiagnosed case.[30] It is therefore unsurprising that some of these people will present in hospital with hyperglycaemia.

Acute hyperglycaemia in hospital is not only associated with disease severity, but also with chronic hyperglycaemia, as measured by HbA_{1c}.[31] In patients with hyperglycaemia, a higher HbA_{1c} (≥6.0%) compared with a normal HbA_{1c} was associated with higher mortality (11.3% *vs* 4.4%). Even so, in-hospital treatment and having a discharge plan were associated with a trend to lower rates of readmission (18% *vs* 30% if untreated; p = 0.09), despite patients who were treated having higher HbA_{1c} compared with untreated individuals (9.0% *vs* 7.3%, respectively).[32]

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Table. HbA_{1c} targets for people with type 1 or type 2 diabetes*

HbA_{1c} target	Type 2 diabetes patient population	Type 1 diabetes patient population
<6.0%	Lifestyle management Metformin alone Planning pregnancy	Nil
<7.0%	General target for all patients with type 2 diabetes Insulin treated Longer duration Clinical cardiovascular disease	General target for all patients with type 1 diabetes Planning pregnancy
<8.0%	Recurrent severe hypoglycaemia Hypoglycaemia unawareness	Recurrent severe hypoglycaemia Hypoglycaemia unawareness
Symptomatic treatment alone	Comorbidities limiting life expectancy	Comorbidities limiting life expectancy

* HbA_{1c} targets for different patient population groups as recommended by the Australian Diabetes Society.[40]

In-hospital hyperglycaemia is frequently missed

Despite evidence for improved patient outcomes when treated, and high short-term progression to frank diabetes, inpatient hyperglycaemia remains frequently missed.[1] Of patients with a glucose level of 11.1 mmol/L or more during hospitalisation, 50% will have the diagnosis missed[1] and no further action taken.

In addition, there is currently poor continuity in complex patient care, with a follow-up plan present in discharge notes in only 24% and 27% of patients without, and with, a prior diagnosis of diabetes, respectively.[1,32] The presence of a follow-up plan was more likely in patients for whom an endocrinology team had been consulted. Having a follow-up plan was associated with lower readmission rates.[32] The association of higher HbA_{1c} with higher readmission suggests that improved chronic diabetes treatment might reduce admission rates.

Postdischarge care: the crucial role of the GP

Identification of hyperglycaemia in hospital inpatients allows implementation of acute treatment for glycaemic control, as well as follow up to detect impaired glucose metabolism (for which treatment with lifestyle modification or oral therapies may reduce progression to frank diabetes) or reduce diabetes complications.[33,34] Testing to differentiate between temporary versus more chronic dysglycaemia is best achieved with a 75 g oral glucose tolerance test, delayed by at least six weeks' postdischarge to minimise the effect of acute illness on glucose levels. HbA_{1c} measurements may be unreliable in the setting of acute illness because of blood loss or illness states with altered red cell turnover.

The principle of avoiding hypoglycaemia that applies to the acute setting is carried over into data guiding HbA_{1c} targets for chronic (community) glycaemic control. That is, that lower HbA_{1c} is better if hypoglycaemia can be avoided. It is well established that improvements in HbA_{1c} are associated with reductions in microvascular complications in both type 1 and type 2 diabetes.[34,35] However, tight glycaemic control (HbA_{1c} <7.0% *vs* <8.0%) increases the incidence of hypoglycaemia in some populations, and there is increasing evidence that hypoglycaemia may be detrimental to health.[36] Excessively tight glycaemic control may not reduce (and may even increase) cardiovascular death and morbidity.[37-39]

In older patients (such as male war veterans) with a history of coronary artery disease, HbA_{1c} of less than 7.0% was associated with an increased rate of cardiovascular events, particularly if diabetes was of a longer duration.[39] One explanation is that in patients with at-risk myocardium, any fall in glucose levels might result in relative hypoglycaemia at sites beyond any coronary artery stenosis, predisposing to infarction. This has lead to the Australian Diabetes Society guidelines recommending higher HbA_{1c} targets for patients at risk of adverse events due to hypoglycaemia (Table).[40]

Summary

The identification of hyperglycaemia in hospital inpatients represents an opportunity to screen for abnormal glucose tolerance and implement diabetes prevention strategies after discharge. For patients who already have a diagnosis of diabetes it is the chance to improve chronic glycaemic control through good community diabetes management (see the flowchart). Screening for diabetes should ideally be carried out with a 75 g oral glucose tolerance test at least six weeks' postdischarge.

Treatment targets both in hospital and in the community should be to lower blood glucose levels and HbA_{1c} while avoiding hypoglycaemia. Targets should be individualised to the patient, depending on the presence of other comorbidities.[40]

A multidisciplinary approach, with good communication between care providers, is required to improve the care of hospital inpatients with hyperglycaemia. Hospital house officers with training to recognise the importance of hyperglycaemia and confidence to institute appropriate treatment need to be provided. Treatment should include regular diabetes medications, for example, basal,

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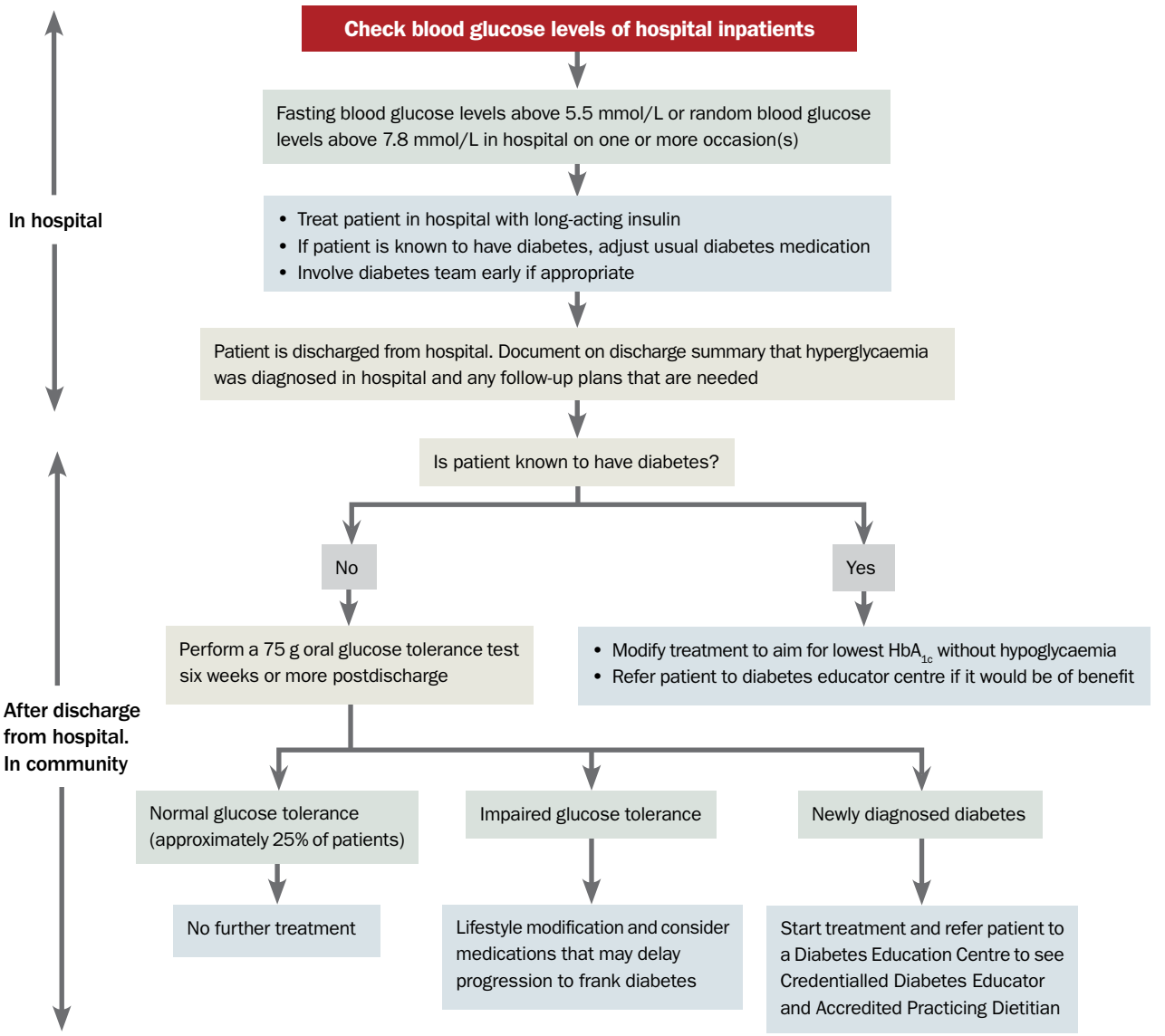
Suggested approach to the management of hyperglycaemia in hospital inpatients and postdischarge care



mixed or basal-bolus insulin or oral agents. Sliding scale insulin should not be used as sole therapy because of the likelihood of increasing glucose excursions. There needs to be clear communication to both the patient and community health team (GP, endocrinologist or other) regarding the occurrence of hyperglycaemia in hospital, and the treatment changes that occurred in hospital.

Once the patient returns to the community, it is important for GPs to recognise that inpatient hyperglycaemia is a signal to screen for diabetes or address chronic diabetes management. GPs should be supported in managing these patients in the long term, and multidisciplinary care is the gold standard. Ensuring access and interaction between GPs, local diabetes education centres (which provide multidisciplinary outpatient diabetes care) and endocrinologists is paramount. Better glycaemic control is achieved if there is good communication between GPs and diabetes teams to provide co-ordinated diabetes care.[41] **ET**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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