Curr Diab Rep (2014) 14:458
DOI 10.1007/s11892-013-0458-9

HOSPITAL MANAGEMENT OF DIABETES (G UMPIERREZ, SECTION EDITOR)

Management of Patients with Type 1 Diabetes in the Hospital

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Published online: 8 January 2014

Abstract Managing a patient with type 1 diabetes mellitus can be challenging to the inpatient medical team. These patients require a continuous supply of exogenous insulin, and the omission of even a single dose can result in severe hyperglycemia and diabetic ketoacidosis. This article aims to equip the inpatient medical team with the knowledge and expertise required to care for these patients in the hospital, including transitioning from home to hospital, transitioning from the intravenous insulin infusion to the subcutaneous route, subcutaneous insulin dosing including the insulin pump, and transitioning back to home.

Keywords Type 1 diabetes · Inpatient management of type 1 diabetes in the hospital

Introduction

Type 1 diabetes mellitus (T1DM) accounts for 5–10 % of all the cases of diabetes. Traditionally thought to be a disease of childhood, it can also manifest during adulthood, albeit at a lower frequency [1]. The worldwide incidence of T1DM is increasing by a rate of 3 % per year [2]. The pathogenesis of T1DM involves pancreatic beta cell destruction that is immune-mediated in the vast majority of cases [3, 4].

The lack of functioning pancreatic beta cells results in an absolute insulin deficiency necessitating a continuous exogenous supply of insulin to prevent hyperglycemia, catabolism, and the serious, life-threatening complication of diabetic ketoacidosis (DKA). The constant need for insulin presents unique management challenges to the physician when these patients are admitted to the hospital as any interruption in insulin administration might result in the aforementioned consequences.

It is well known that hyperglycemia in the hospital is associated with longer length of hospital stay and increased risk of infections, morbidity, and mortality [5–10]. Glucose control is of utmost importance in hospitalized patients, as studies have shown that managing hyperglycemia leads to significant reductions in the rate of infections and mortality in a variety of patient populations [11–14]. However, achieving optimal glucose levels is often at the expense of increasing the risk of hypoglycemia [15, 16]. This poses a clinical dilemma and a delicate balance must be struck between the need to prevent both hyperglycemia and hypoglycemia in these hospitalized patients.

This review endeavors to provide the clinician with a practical guide for managing patients with T1DM in the hospital setting.

Identification of T1DM in the Hospital

It is important to try to determine what type of diabetes a patient has on admission to the hospital. Many times, medical records may not accurately reflect the type of diabetes a patient has. Sometimes, verifying the early onset of diabetes in a lean patient who has been only on insulin since the time of diagnosis may suffice. However, some patients with T1DM may have been placed on metformin or thiazolidinediones for insulin resistance and may be misclassified as type 2 diabetes (T2DM) based on the home regimen. It is a critical responsibility of the physician to make this determination to distinguish between patients with T1DM and those with T2DM. Patients with T2DM may not suffer immediate consequences if there is a delay in insulin administration in the hospital, but patients with T1DM require insulin administration to prevent hyperglycemia and diabetic ketoacidosis (DKA). The omission of even a single dose of basal insulin may be the stimulus to precipitate DKA in a patient with T1DM.

This article is part of the Topical Collection on *Hospital Management of Diabetes*

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In certain situations, it may be unclear what type of diabetes the patient has— type 1 or type 2. Though prudent to manage the patient as if having type 1 diabetes, certain tests may be done in the hospital in anticipation of discharge disposition, or at outpatient follow-up, depending on the circumstances. To help determine if the patient has T1DM vs T2DM, one can measure serum C-peptide levels and autoimmune markers including antibodies to glutamic acid decarboxylase, insulin, tyrosine phosphatase, and islet cells [17]. These autoimmune markers are present in 95 % of patients with T1DM, and their presence combined with an absolute insulin deficiency is virtually diagnostic of T1DM. Serum C-peptide levels, when measured after an acute episode of glucotoxicity has resolved, gives an indication of exogenous glucose production. This is often low in T1DM and high in T2DM.

Factors that Precipitate Admission to Hospital

Patients with T1DM may be admitted for acute issues related to their glucose control. These include severe hyperglycemia and DKA, which may be precipitated by infections, trauma, acute illness, or non-compliance with their insulin regimen. It is important to review these precipitating factors so that education on their avoidance or prevention can be reinforced in the hospital. More often, however, patients are admitted for medical conditions or surgical procedures not related to hyperglycemia itself, and the hospital physician may be called upon to assist in the peri-procedural management of their insulin regimens.

Review of Home Medication Regimen for T1DM

It is important to ascertain the home medication regimen of a patient with T1DM at admission to better facilitate treatment in hospital and a smooth transition back to home regimen on discharge. The mainstay of the home regimen for patients with T1DM consists of exogenous insulin, although some may also be on oral agents such as metformin or thiazolidinediones given for concomitant insulin resistance.

The term basal-bolus insulin has been used in recent years to describe several insulin regimens. To give perspective, a healthy patient without diabetes who has a functioning pancreas produces insulin throughout the day, even when fasting, and this is referred to as the basal insulin as it is present regardless of nutritional intake. After consumption of food the pancreas produces a surge or "bolus" of insulin in response to the glucose content of the ingested food. For patients on exogenous insulin, basal insulin is the insulin required to control cellular glucose uptake and hepatic glucose production during the day regardless of nutritional intake. The basal insulin requirement is usually provided by long-acting insulin such as glargine and detemir, or by an intermediate-acting insulin such as neutral protamine Hagedorn (NPH). Bolus insulin, on the other hand, comprises a mealtime or prandial insulin (given to cover the carbohydrate content of a meal), with or without a correctional or supplemental insulin (to adjust for hyperglycemia). This is usually provided by rapid-acting insulin such as aspart, lispro or glulisine, although some patients may use short-acting insulin (regular insulin), to cover their prandial intake.

For many years prior to the advent of insulin analogues, multiple doses of insulin injection (MDII) regimens consisted of NPH insulin as the basal component and regular insulin as the prandial component of this regimen. With this regimen, NPH is often given at breakfast and at bedtime and regular insulin at breakfast and dinner. NPH has a peak, and so the morning dose also provides some insulin coverage for the noontime meal. Many patients with T1DM, especially some older patients who have been on this regimen since diagnosis, remain on these human insulins. For some, this regimen may be effective. For others, this may be due to habit, reluctance to change their routine of care or due to economic concerns as the cost of insulin analogues can be prohibitive. More and more frequently, however, MDII regimens tend to consist of a long-acting basal insulin plus mealtime rapid-acting insulin.

In contrast to using MDII, some patients might be on an insulin pump that provides a continuous subcutaneous insulin infusion (CSII). With this device, basal insulin is provided by a constant infusion, while bursts of higher doses of insulin (boluses) are given to cover the carbohydrate content at mealtimes and to correct for hyperglycemia.

Though insulin is the cornerstone of therapy, some patients with T1DM may also be receiving oral DM medications, which may lead to an erroneous medical history entry of T2DM in the charts or electronic medical records if one were to go by medication prescription for diagnosis. Although not endorsed by any endocrinology society, metformin is sometimes used in patients with T1DM who also have evidence of insulin resistance, and has been shown to be effective in lowering total insulin doses, weight, and total cholesterol [18]. It is important to keep in mind that patients with T1DM may theoretically be prone to lactic acidosis—a rare but serious adverse effect seen with metformin. The mechanism by which this occurs is related to their complete deficiency of insulin [19]. Therefore, metformin should be used with caution in this population.

Another class of oral agents that have been used in T1DM with evidence of insulin resistance is the thiazolidinediones (TZDs). An additional benefit of TZDs in T1DM that has been suggested from animal studies is their ability to reduce the autoimmune response to islet cells within the pancreas [20, 21].

In the hospital, however, it is recommended that noninsulin medications be discontinued [22–24]. The following sections will focus on insulin management in the hospital.

Management in the Hospital

Transition from Home to Hospital Regimen

When a patient is admitted, the most physiologic insulin regimen would be a basal-bolus regimen using long-acting insulin for basal needs and rapid-acting insulin for bolus (prandial and correctional) needs. If patients are already on this kind of regimen at home, then the home doses may be used as a starting point for determining the doses needed during admission in the hospital. A review of the patient's glucose control on their home insulin doses will give the physician an idea of whether this starting dose is adequate, bearing in mind that the patient may report hyperglycemias at home brought about by the stress of acute illness (such as infections, acute myocardial infarction, etc), necessitating an increase in the insulin doses. On the other hand, if the patient reports hypoglycemias at home related to poor appetite, then the insulin doses must be reduced. If a hemoglobin A1c level had not been drawn in the previous 2–3 months, obtaining this during the hospital admission might also provide information as to the adequacy of the home regimen, and assist the hospital physician in deciding whether the home regimen can be used as initial insulin doses in the hospital.

If the home doses cannot be obtained, then a starting dose of 0.2–0.3 units/kg body weight/d can be used, using the lower end of the range for elderly patients with decreased renal function, and the higher range if patients have infections or other conditions that would exacerbate hyperglycemia. Other authors recommend 0.5–0.7 units/kg/d with the presumption that the patient will have adequate nutritional intake, with dose reduction by 50 % if nutrition is compromised [24]. Our approach is to take the lower dose; therefore an initial dose 0.2–0.3 units/kg/d, with insulin dose increases within the same day or the following day as the patient's food intake improves and stabilizes. Half of the daily total requirement can be given as the basal long acting insulin and the other half divided into 3 doses given as rapid-acting insulin for meals. The mealtime doses should be omitted if the patient is not eating. However, the correction insulin can still be given.

For patients on any regimen of subcutaneous injections other than long-acting plus mealtime rapid-acting insulin (such as those on NPH and regular insulin combinations, or premixed insulins), it is often advisable to change their regimen while in the hospital to a long-acting and rapid-acting basal-bolus regimen, since NPH has a peak that makes it difficult to use as a true basal insulin. A quick conversion is to add up all insulin doses in a day, giving half of this total daily dose as long-acting basal and give the other half as rapid-acting insulin divided between 3 meals, adjusting for previous history of hypo- or hyperglycemias.

Patients who were using an insulin pump at home and are awake and alert may continue using their pump. If a patient was well controlled at home on an insulin pump, the pump can be continued at the same settings. If blood glucose control was poor, then the pump settings may need to be adjusted. Management of the insulin pump will be discussed in further detail below.

Insulin Management in Clinically Stable Hospitalized T1DM Patients

All patients with T1DM, when admitted to the hospital, require a continuous supply of exogenous insulin regardless of nutritional intake in order to prevent hyperglycemia and to suppress hepatic ketone production. In the clinically stable patient, insulin can be given as MDII. Depending on their clinical and their nutritional status, the insulin doses should be adjusted to achieve a balance that prevents both hyperglycemia and hypoglycemia. In general, the fasting and pre-meal target blood glucose in hospital is <140 mg/dL [22, 25] (Table 1). If random blood glucoses are checked, the goal is <180 mg/dL. The best mode of achieving this in the hospital is via a scheduled subcutaneous regimen of long-acting basal insulin plus rapid-acting bolus insulin. Bolus insulin consists of prandial with or without correctional insulin at mealtimes, and often of lower correctional insulin doses at bedtime to adjust for the hyperglycemia yet factoring in the lesser insulin requirements during sleep. Correctional insulin may be helpful in estimating the dose changes needed for the subsequent day's basal and prandial doses, but should not be used as the only form of insulin during hospitalization as it is merely a reactive means to correct hyperglycemia. If used alone it may cause fluctuating blood glucoses and DKA. DKA has been classified by the National Quality Forum as a Hospital Acquired Condition that is not reimbursable at the higher-weighted Medicare Severity diagnosis related group level. Therefore, increased vigilance is warranted to prevent its occurrence [26].

Adjusting Subcutaneous Insulin Doses in the Hospital

In addition to keeping pre-meal glucose levels <140 mg/dL, it is recommended that the insulin regimen be re-evaluated if the premeal glucose levels go below 100 mg/dL and modified when the pre-meal values reach <70 mg/dL unless there is an obvious reason such as missing a meal (Table 1). If the fasting

Table 1 Target blood glucose in the hospital [22, 25]

Pre-meal glucose	<140 mg/dL	No change in regimen
Random glucose	<180 mg/dL	No change in regimen
Pre-meal glucose	<100 mg/dL	Re-assess regimen
Pre-meal glucose is	<70 mg/dL	Modify regimen unless there is an obvious cause such as a missed meal

glucoses are elevated but the pre-lunch, pre-dinner, and bedtime glucoses are at goal, then the basal insulin should be increased. If both the fasting glucoses and the previous night's bedtime glucose levels are high, then either a decrease in carbohydrate intake at dinner or a higher dose of rapid-acting insulin at dinner may lower both the bedtime and the subsequent day's fasting glucose values. If the fasting blood glucose is low, the basal insulin should be decreased. If the fasting blood glucose is at goal but the rest of the glucose levels are high, then the prandial doses of insulin should be increased. Fast-acting prandial insulin doses are usually adjusted by 1–2 unit increments. Long-acting basal insulin is often adjusted by 1–2 units at a time if the total daily basal dose is 20 units or less and by 10–20 % if total daily basal dose is greater than 20 units.

Patients who are nothing-by-mouth (NPO) for procedures present a special challenge. It is essential that patients with T1DM continue to receive a basal dose of insulin even while NPO to prevent catabolism and ketogenesis. Many providers may erroneously discontinue the patient's insulin because they may think that no insulin is required in the absence of caloric or carbohydrate intake. This is a critical error that must be avoided since DKA will likely ensue. Basal insulin and an IV fluid containing dextrose must be supplied to the patient who is NPO. The long acting basal insulins, glargine, and detemir are relatively peakless and are associated with less hypoglycemia than NPH. Their full doses can usually be given especially if a patient was on a ratio of basal: bolus insulin of 50:50 and was not experiencing hypoglycemic episodes. If the relative proportion of basal insulin is higher than prandial insulin or the patient was having hypoglycemic episodes, then it is judicious to reduce the basal dose of insulin by 10–20 % [27•]. The intermediate-acting insulin NPH does have a peak in its pharmacodynamic profile. If for some reason the patient remains on an NPH-based regimen in the hospital, it is recommended to reduce the dose prior to the omitted meal/s by 25–50 %. Regardless of the ratio of basal to bolus insulin or the type of basal insulin a patient is taking at home, it is imperative that the patient receive some basal insulin to prevent DKA in the hospital.

Insulin Management in the ICU or in Critically Ill Patients

Sometimes in the peri-operative period, a patient's glucose control may be erratic and insulin may have to be given intravenously in a continuous fashion. An insulin infusion may also be utilized during critical medical situations such as myocardial ischemia and stroke to attain uniform blood glucose control. Insulin infusion rates may be initiated at 0.02 unit/kg/h or lower for patients with lower body weight or renal or hepatic failure [24], and monitored and titrated hourly.

Management of Patients with Diabetic Ketoacidosis (DKA)

Intravenous insulin is also a major component in the treatment of diabetic ketoacidosis (DKA). DKA is most commonly precipitated by infection. The mainstay of management of DKA is intravenous fluid therapy to correct the dehydration, intravenous insulin to correct the hyperglycemia and close the anion gap, correct the electrolyte abnormalities and treat the underlying cause of the DKA. The initial insulin is usually 0.1 to 0.14 units/kg/h. The initial choice of fluid is normal saline. Intravenous fluids are changed to dextrose-containing half-normal saline when the plasma glucose reaches 200 mg/dL to allow for continued insulin infusion, as it takes longer to clear the ketonemia than it is to achieve euglycemia. There are many published algorithms to determine the subsequent choice and rate of fluids based on serum sodium and glucose measurements. It is beyond the scope of this article to discuss DKA evaluation and management in-depth, and readers are encouraged to peruse the article referenced [28•].

Transitioning From Intravenous Insulin Infusion to Subcutaneous Insulin

Regardless of the reason for using an insulin infusion, the question then arises as to when is the appropriate time to transition a patient off intravenous insulin and how should this transition be done. During the transition, the long-acting basal subcutaneous insulin should be given first while the insulin infusion is continued for another 2 hours. After this 2-hour period, the insulin infusion can be discontinued.

Patients transitioning off the insulin infusion but that had good glucose control at home, or during the hospital day preceding the insulin infusion (for example, patients who were admitted to the hospital, placed on subcutaneous basal-bolus insulin, then placed on an insulin infusion for a surgical procedure) can be resumed on the previous doses of subcutaneous insulin, adjusting for any hypo- or hyperglycemia as already discussed above. Prandial insulin can be resumed once the patient starts eating.

If home doses are not known, and the patient had not yet been given subcutaneous insulin injections in the hospital but needs to be transitioned off an intravenous insulin infusion to subcutaneous doses, then weight-based calculation as discussed above can be initiated (see section on transition from home to hospital). With a weight-based calculation, the initial total daily insulin dose is 0.2–0.3 units/kg body weight, possibly higher if the patient has ongoing stressors such as infection, with half as basal insulin and the other half as prandial insulin. Another method of calculation is to use the insulin doses from the intravenous insulin infusion. This is subject to more variation as patients may or may not have been eating (institution-dependent), may have been on

vasopressors or steroids that raise the glucose levels, or may otherwise have been clinically unstable (such as the first few hours of DKA) while on the insulin infusion, resulting in over estimation of insulin requirements when converting to subcutaneous insulin.

Insulin Pump Management

The use of insulin pumps is increasing, with 1 registry study in T1DM showing close to 50 % [29]. Patients often request to manage their insulin pumps in the hospital, having had T1DM for years and having a good understanding of their blood glucose patterns. They may be reluctant to discontinue their pump and relinquish control of their diabetes to a provider whom they are not accustomed to. The insulin pump remains the most physiologic commercially available means of administering insulin, similar to a functioning pancreas, so it is advisable to continue it if the patient can manage the pump.

It is important to select patients for self-management of an insulin pump appropriately. The patient should be awake, alert and physically be able to manage the pump. The hospital provider should obtain and record the kind of insulin (usually rapid-acting) and the pump settings on admission. The latter usually comprise the basal rate/rates, the carbohydrate ratio (grams of carbohydrate for 1 unit of insulin), and the correction or sensitivity factor (similar to the correctional or supplemental insulin for MDII). In addition, the pump settings also include a target glucose level, upon which the correction or sensitivity factor dose is based. If the outpatient physician managing the diabetes and the patient were aiming for tight control, it is not unusual for this target to be set at 80–100 mg/dL, which may be too low for the hospital setting. Since there is no proven benefit of tight control in the hospital setting and the risk of hypoglycemia is high, these targets should be relaxed accordingly. The hospital physician should discuss this with the patient so that changes to the pump setting can be made. Assessment of glucose control by reviewing the blood glucose log and measurement of hemoglobin A1c should be done to help ascertain if the current insulin dose settings are appropriate for the patient's clinical condition. If the patient has to undergo a surgical procedure that will last for hours and the pump has to be removed, it is crucial that the patient receive a subcutaneous injection of basal insulin to cover their basal requirements during the procedure. If the patient becomes clinically unstable, there is a change in mental status or there is poor blood glucose control, the physician must assess the appropriateness of self-management and institute an alternative means of blood glucose control when necessary. During an acute illness, blood glucose levels increase and require frequent changes in insulin dose. In this situation, patients may not be able or willing to manage their pump, and the medical team should start multiple daily insulin injections or intravenous insulin [30, 31].

Transitioning From Hospital to Home

The hospital physician's responsibility extends beyond the hospital walls. When a patient is being discharged, the hospital physician should determine whether the patient should go back on his or her home insulin regimen, or if changes should be made depending on what has transpired in the hospital, until the patient is able to get in contact with the outpatient managing physician. The most physiologic insulin regimen to go home with would be a basal-bolus regimen. If the patient was already on basal-bolus insulin comprising long-acting and fast-acting insulin at home and continued on this during hospitalization, then their glucose control in the days prior to discharge may be used to estimate their insulin doses upon discharge, bearing in mind that the patient, together with the outpatient managing physician may have to change the doses as he/she resumes the premorbid diet and activity.

Patients who were on other regimens such as NPH and regular insulin, or premixed insulin, may be discharged on this same regimen, with doses modified for previous reports of hypo- or hyperglycemia. On the other hand, the patient and hospital physician might find a compelling reason to change the regimen entirely to long-acting plus mealtime fast-acting insulin (for example, if with multiple hypoglycemias on the previous home regimen and virtually none while on long-acting and rapid-acting regimen in the hospital). In this situation, education on the new regimen should be initiated while in the hospital prior to discharge, this should be communicated to the outpatient managing physician, and education should

Table 2 Key points

Do not omit basal insulin as this may lead to DKA. Reduce the dose if necessary.
Determine initial doses by reviewing the patient's history or by using weight-based calculations (total daily dose of 0.2–0.3 units/kg body weight).
If the home insulin regimen is inappropriate for the clinical condition, give half of the total daily insulin dose as long-acting basal insulin and the other half as rapid-acting insulin divided further for the 3 meals is a good starting regimen.
Set target glucose levels and review glucose level patterns to facilitate dose adjustments in the hospital and transition to home.
The mainstays of management of DKA consist of treatment of the underlying cause, intravenous fluids to correct the dehydration, intravenous insulin to correct the hyperglycemia and the ketonemia, and correction of electrolyte abnormalities.
Patients for self-management of an insulin pump should be awake, alert, and physically be able to manage the pump.

DKA diabetic ketoacidosis

be reinforced in the outpatient setting. Factors that precipitated admission should be reviewed and modified to prevent recurrence of severe hyperglycemia or DKA, if this was the case

Patients who were well-controlled on the insulin pump, using it appropriately, accurately entering their blood glucoses and carbohydrate content of their meals can be resumed on the pump at the same settings. If blood glucose control was poor, then the basal insulin, the sensitivity factor or the carbohydrate ratio may need to be adjusted

Conclusions

Management of patients with T1DM in the hospital can be challenging and daunting to the inpatient medical team. However, remembering a few key points will help with this task: (1) basal insulin should always be given, (2) initial doses can be determined by reviewing the patient's history or by using weight-based calculations, and (3) target glucose levels should be set and glucose level patterns should be reviewed to facilitate dose adjustments in the hospital. These key points are highlighted in Table 2. By putting these into practice, a smooth transition from home to hospital, avoidance of diabetic ketoacidosis during hospitalization, and a speedy transition back to home and outpatient care will ensue.

Compliance with Ethics Guidelines

Conflict of Interest Divya Yogi-Morren declares that she has no conflict of interest. M. Cecilia Lansang serves on the advisory board and receives honoraria from Sanofi.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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