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HOSPITAL MANAGEMENT OF DIABETES (GE UMPIERREZ, SECTION EDITOR)

Transitioning Safely from Intravenous to Subcutaneous Insulin

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Abstract The transition from intravenous (IV) to subcutaneous (SQ) insulin in the hospitalized patient with diabetes or hyperglycemia is a key step in patient care. This review article suggests a stepwise approach to the transition in order to promote safety and euglycemia. Important components of the transition include evaluating the patient and clinical situation for appropriateness, recognizing factors that influence a safe transition, calculation of proper SQ insulin doses, and deciding the appropriate type of SQ insulin. This article addresses other clinical situations including the management of patients previously on insulin pumps and recommendations for patients requiring glucocorticoids and enteral tube feedings. The use of institutional and computerized protocols is discussed. Further research is needed regarding the transition management of subgroups of patients such as those with type 1 diabetes and end-stage renal disease.

Keywords Inpatient diabetes management · Intravenous (IV) insulin transition · Subcutaneous (SQ) · Insulin · Insulin infusion

Introduction

Intravenous (IV) insulin is used in the hospitalized patient to control blood sugars for patients with and without diabetes who may exhibit uncontrolled hyperglycemia or for those who need close glycemic attention. Common hospital uses for IV insulin include the peri-operative setting, during the use of high-risk medications (such as corticosteroids), or during crises such as diabetic ketoacidosis (DKA) [1, 2]. Other conditions such as hyperglycemic hyperosmolar state (HHS) and trauma frequently require IV insulin, as well as specific hospital units such as the cardiothoracic intensive care unit [3, 4]. The correlation between hyperglycemia and poor inpatient outcomes has been well described in the literature [5, 6]. The treatment of hyperglycemia using an IV insulin infusion is established and promotes clinical stability [7–9]. IV insulin allows a safe dose of insulin to be administered on a continuous basis, is easily adjusted, and can provide a natural transition to subcutaneous (SQ) dosing.

The transition from IV to SQ insulin is an important step in the care of a patient, usually occurring when the patient has clinically improved significantly. In many situations, despite best efforts, the discontinuation of an IV insulin drip may be associated with a loss of glycemic control—specifically, rebound hyperglycemia can occur after discontinuation of the drip [10]. Therefore, the decision to progress the patient from IV to SQ insulin should be made carefully, minimizing risk, and with the patient exhibiting signs of stable glycemic control. There are numerous available options when transferring patients to SQ insulin injections. The various insulin options, along with recommendations for transitioning the routine and complicated patient from the IV to SQ route, will be presented below.

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Section 1: Before the Transition

Proper Management of IV Insulin and Assessing if the Patient Is Ready for Transition to SQ

IV insulin is typically administered as regular insulin (Humulin R or Novolin R), which has a half-life of several

minutes when given this route [3]. IV insulin can be infused through a peripheral or central line. The initial dosing of IV insulin is recommended at 0.1 units/kg/h for patients presenting with DKA [11] and 0.025 units/kg/h in patients who are not in DKA but have hyperglycemic crisis, or for those who have renal insufficiency [3]. IV insulin requires significant attention and time from the nursing staff to monitor drip rates and point of care (POC) testing. Based on the rapid half-life of IV insulin, consensus recommendation is for blood glucose (BG) to be monitored at the POC on an hourly basis, and the frequency may be liberalized only if the patient condition, drip rates, and BG are stable [12••]. There is limited evidence to suggest what the ideal monitoring interval should be, though many published protocols start monitoring hourly and then increasing the length of monitoring intervals, depending on overall patient presentation [3, 13, 14]. It is the opinion of the authors that the safest interval for IV insulin is hourly monitoring, with an interval increase to no more than 2 h between glucose checks for safety.

Indications that It Is Safe to Transition from IV to SQ Insulin

Due to the complexity of IV insulin administration and the need for frequent BG monitoring, it is understandable that providers plan to transition the patient to SQ insulin dosing as soon as possible. The management of IV insulin can be labor intensive, including hourly BG monitoring, titration of drip rates, maintenance of associated fluids, and care of an active IV access point. While these are understandable motivations, it is important to ensure that a transition should be made only when clinically and logistically appropriate. Consequences of premature transitions include failure of the transition (a return from SQ back to IV insulin), significant hyperglycemia, or, in select cases, a return of the patient into active DKA. Ideally, the patients should have stable blood sugars within the goal range (generally 140–180) [15] for several hours on the insulin drip prior to transition; some authors suggest a period as long as 24 h [16, 17].

The key is ensuring that several key characteristics are met whenever an IV to SQ transition is planned. The patient may be ready for the transition if the following are in place [3]:

- Stable blood glucoses which are less than 180 mg/dL (7.7–10 mmol/L) for at least 4–6 h consecutively (see Table 1 for an example)
- Normal anion gap and resolution of acidosis in DKA
- Stable clinical status; hemodynamic stability
- Not on vasopressors
- Stable nutrition plan or patient is eating
- Stable IV drip rates (low variability)

Additionally, the transition is more likely to be successful if the insulin drip rates are <2 units/h and the concurrent BG's are <130 mg/dL [18]. For patients that did not have previously known diabetes, it is recommended that scheduled subcutaneous insulin be used if the insulin drip utilization is at least 20 units in a 24-h period [19].

Indications that It Is Not Safe to Transition from IV to SQ Insulin

Problems that can be encountered in an IV to SQ transition fall into two major categories including discontinuing the infusion when it is not yet safe to occur or discontinuing at a safe time but making logistical errors that allow the transition to fail. Specific indications that a safe transition cannot yet be made are as follows:

- High variability of drip rates
- High variability of glucose levels
- Drip rates still too high (greater than 2 units/h)
- Fewer than 6 h of IV drip administration (because a shorter time period may not provide enough data to accurately assess the patient's current insulin requirements)

(See Table 1 for an example.)

Some authors suggest that other predictors of a poor transition include advanced age of the patient, wide variations in BG in the 24 h leading up to the IV discontinuation [16], poor admission hemoglobin a1c (A1c) [20•], complex surgical procedure, intensive care unit (ICU) status, or receiving corticosteroids [6] .

A key logistical error that can be made, even when the timing is safe, is discontinuing the infusion without administering any SQ insulin [21]. The most common reason that this occurs is that the patient has become temporarily hypoglycemic on the IV infusion (i.e., BG<70 mg/dL), and the IV infusion is stopped for safety. Some providers elect to not turn the drip back on, regardless of whether the patient had steady infusion rates or BG monitoring data prior to the drip being stopped. The simplest solution to this problem is to restart the drip once the patient's BG reaches a certain threshold. In our institution, the drip is restarted to have the prior rate once the BG is >120 mg/dL. This method has been confirmed by other authors [22]. Some authors suggest editing the insulin order if the drip needs to be stopped for any reason to ensure nursing adherence and continued monitoring of the patient [23].

Certain patients who did not have a diagnosis of diabetes prior to hospitalization may have a new insulin requirement during hospitalization, often post-operatively. This is especially common in cardiothoracic surgery patients [24•]. Patients who are requiring a significant amount of IV insulin should be evaluated for transition to a scheduled subcutaneous regimen.

Table 1 Examples of insulin transitions

Patient data	Time (h)								
	0000	0100	0200	0300	0400	0500	0600	0700	0800
Example of ideal time to transition patient off of intravenous (IV) insulin									
• Drip rates are stable; blood glucoses are stable and within goal range									
IV Insulin drip rate (units/h)	0.60	0.60	0.55	0.55	0.55	0.60	0.55	0.60	0.60
Blood glucose (mg/dL)	140	138	135	141	133	142	139	135	140
Example of less than ideal time to transition patient off of IV insulin									
• Drip rates are variable; blood glucoses are variable and outside of goal range									
IV Insulin drip rate (units/h)	1.6	2.0	2.4	1.6	1.0	1.5	1.0	0.5	1.1
Blood glucose (mg/dL)	225	250	220	120	80	195	100	70	185

Care of the Patient Who Requires IV Insulin, but Is Also Eating

In general, most providers think of IV insulin for use while a patient is acutely ill and nil per os (NPO), whereas a patient who is able to consume PO intake is typically managed with SQ insulin. While some authors recommend transitioning the patient completely off IV insulin once they are prepared to eat [25], there are increasingly common situations in the hospital in which a patient needs to continue intravenous insulin as the safest method of glycemic control in conjunction with an oral diet. Other authors have also supported the idea of dosing prandial insulin in addition to the insulin drip as an effective method of glycemic management [18, 26•]. Examples of these situations include the following:

- The patient on several days of high-dose steroids. Common examples of this include the management of transplant rejection (bursts of high-dose solumedrol), managing CNS lesions and neurologic surgery (high-dose decadron), and managing oncologic patients whose chemotherapy regimen includes steroids. Because of the high corticosteroid doses associated, as well as frequent adjustments in dosing, these cases are often safely managed with IV insulin for a limited period of time (1–3 days). In some of these cases, especially with transplant recipients, the patient may feel well enough to be consuming three meals daily.
- A patient in DKA with slowly resolving acidosis. Insulin drips are typically recommended for DKA patients until the anion gap (AG) is closed and BG are stabilized. Many patients are kept NPO until this occurs, though some patients may be allowed to eat small meals if the process of gap closure is prolonged.
- Highly insulin-resistant patients. A patient with profound insulin resistance, seen now more commonly given the growing obesity and type 2 diabetes epidemic, may undergo an episode of HHS and require very high rates of IV insulin to re-attain glycemic control. Significant insulin resistance is also frequently seen with acute episodes such as myocardial infarction or pancreatitis [27]. The patient may be able to consume PO intake even when rates of IV insulin are still so high that a direct IV to SQ transition could be considered dangerous (i.e., if the daily requirement is several hundred units).

In these cases, the patient may benefit from having SQ insulin on board simultaneously with the IV insulin before the transition occurs to control the BG and drip rates. This will also inform the provider of how much basal and bolus insulin may be ultimately needed. In the above scenarios, it is important to understand how to manage the potential use of IV and SQ insulin simultaneously and in a physiologic manner. A key concept is that an IV insulin infusion is ideally utilized to cover basal insulin requirements. If a patient is allowed to eat and only IV insulin is continued, it will generally not be effective for controlling the patient's prandial requirements, and the drip rates will vary dramatically–with markedly increased rates in the post-prandial hours.

To better manage these situations, providers in our institution will order the continued titration of the IV insulin on an hourly basis but will also order a low dose of rapid-acting insulin subcutaneously at each meal to cover the effects of food intake [3]. The dose of the rapid-acting insulin can be adjusted according to patient weight or given as a low dose, perhaps 2–4 units per meal [6]. Examples of subcutaneous orders in addition to IV insulin for a patient who is eating include the following:

- Infuse IV regular (Novolin or Humulin) insulin. Titrate according to usual nomogram/protocol, using data from hourly blood glucose monitoring.
- Give 4 units of lispro (Humalog) [or aspart (Novolog), or glulisine (Apidra)] insulin subcutaneously three times/day before meals only. Hold if patient is NPO (nothing by mouth) [3].

If there is uncertainty about whether the patient will actually eat, the rapid-acting insulin can be dosed immediately after the meal and the dose can be held for a BG< 100 mg/dL [18].

Section 2: The Process of Transition

Once it has been decided that it is indeed safe and appropriate to transition the patient from IV to SQ insulin, the actual process of transition must be planned and carried out systematically. It is important to recall that, as noted above, the half-life of IV insulin is less than 10 min [3]. Thus, a properly planned transition requires that the first dose of SQ insulin is administered at least 1 h (for short-acting SQ insulins; ideally 2–3 h for long-acting SQ insulins) prior to discontinuation of the infusion [28, 29]. Failing to follow this rule allows the rapid development of rebound hyperglycemia in a patient who does not have sufficient endogenous secretory capacity [10]. This can include not only patients with type 1 diabetes but also patients with long-standing type 2 diabetes [21]. A recent article suggested that administration of SQ basal insulin as early (at least several hours) as possible prior to drip discontinuation is an effective method of preventing future rebound hyperglycemia, without increased risk of hypoglycemia [49••].

Proper Calculation of the Total Daily Insulin Requirement

A safe transition requires careful analysis of the clinical situation of the patient in addition to a numerical assessment of IV insulin requirements. Post-operative stress, pain, variable PO intake, infection, and underlying insulin resistance are all complicating factors that affect the insulin requirement. Patients require close monitoring to match the amount of insulin to changing needs [2].

Indeed, the amount of insulin infused by the drip in 24 h (i.e., "24-h insulin utilization") cannot always be assumed to reflect the actual 24-h daily SQ insulin requirement of the patient for transition. The following circumstances need to be considered:

- Potential instability of the IV insulin infusion rates. In other words, if there has been considerable variability in the rates—then simply adding up the rates over 24 h will grossly misrepresent the patient's needs at the time of transition. For example, many patients who present with DKA or HHS will have extremely high rates in the first few hours on IV insulin, and then the rates will become variable, before finally settling down to a more stable pattern. Using the variable rates, especially the initial extremely high rates, in the 24-h insulin calculation will yield a result that potentially overestimates the patient's requirement. This is why it is recommended that a weight-based dose calculation be used in both of these clinical scenarios to optimize safety [11].
- If a full 24 h of data is not available, a cautious evaluation of the patient and insulin use must be considered. If one chooses to use less than 24 h of data, it is recommended that only basal requirements from the IV drip be used for transitioning. For example, overnight rates when the patient is not eating may be used to infer basal requirements as long as the patient's clinical condition is stable (reflected by overall clinical picture in addition to stable drip rates). It is generally not recommended to transition the patient when too few data are available; at least 6 h of data is seen as a minimum requirement [6, 30, 31].
- If 24 h of insulin drip data are available and the drip rates are stable, it is clinically pertinent to evaluate the patient's glycemic control while on the drip. If the blood sugars are not within goal range (140–180 mg/dL), the provider should evaluate the factors involved to determine the next steps. Options may include adding prandial insulin to the IV drip for patients eating, considering extenuating factors (such as corticosteroid dosing), and evaluating nursing adherence to the insulin drip protocol or mechanical problems with IV insulin infusion delivery.

The safest method is to find a several-hour period of time during which the BG values are at goal, IV insulin rates are not particularly elevated, and IV insulin rates are not particularly variable—in other words, the rate is reasonable and stable. One can then look at the infusion rates during this stable period of time, ideally 6–8 h in length [6], and extrapolate these data to a 24-h time period; this allows a reasonable calculation of the patient's 24-h IV insulin utilization.

For the reasons listed above, many authors would suggest making a distinction between the "24-h insulin utilization" of IV insulin versus the actual "24-h insulin requirement" of SQ insulin. Specifically, many experts feel that only a fraction should actually be used. There is no universal consensus on what this fraction should be: some suggest using the full dose—100 % of the IV insulin utilization—for optimum glycemic control [16]; others even suggest the option of weight-based dosing. A recent study explored the use of total body weight at 0.5 units/kg, and the results suggested no increase in hypoglycemia with slightly improved glycemic control [32•]. Other authors suggest using 80 % of the total insulin utilization for patients with diabetes and only 60 % for patients with stress hyperglycemia and no previous diagnosis of diabetes [31].

Despite the lack of consensus, most have suggested that using 80 % of the total 24-h IV insulin utilization to calculate the 24-h SQ insulin requirement is an effective percentage to allow glycemic control without precipitating hypoglycemia; [6, 14, 15, 26•, 33, 34], and the authors agree with this recommendation (Table 2).

Table 2 Calculating the total daily dose in the NPO patient: example of transitioning patient off IV insulin (overnight requirements; patient not eating)

Patient data	Time (h)								
	0000	0100	0200	0300	0400	0500	0600	0700	0800
IV Insulin drip rate (units/h)	2.2	2.0	2.2	2.0	2.0	2.0	2.0	2.0	2.1
Blood glucose (mg/dL)	155	132	145	125	121	130	132	122	136

Calculations:

From the above data, it is clear that the patient has both good glycemic control and stable IV insulin rates. Therefore:

- The average rate during this time is 2.0 units/h
- To complete the calculation, multiply 2.0 units/h×24 h=48 units
- Therefore, the 24-h IV insulin utilization is 48 units daily

As in the main text, many providers would use 80 % of the 24-h IV insulin utilization as the actual 24-h SQ insulin requirement

- 80 % of 48 units=38 units is the final 24-h SQ total daily dose

Because the patient is not eating (no prandial requirements), the entire total daily dose equals the patient's basal dose

- Final order: detemir/glargine 38 units SQ once daily

Deciding What Type of Insulin to Use

Deciding which insulin(s) to use after discontinuation of the IV insulin drip can have significant implications for patients, particularly those who previously did not use insulin as outpatients. Providers must understand the dynamics of each type of insulin prior to prescribing a regimen. The use of "sliding scale" insulin (intermittent quick-acting insulin to correct sugars) without scheduled dosing is not recommended [18, 25, 35–38].

In addition to the lack of evidence to support sliding scale only as a preferred treatment modality, there are also data to show that sliding scale only can contribute to poor glycemic control [39]. Studies have explored the use or basal or bolus insulin in direct comparison to sliding scale insulin only. The RABBIT-2 trial suggested that a basal-bolus regimen was superior to sliding scale insulin (SSI) in obtaining goal BG levels with no increase in hypoglycemia [39]. Datta et al. [40] suggested that a once daily glargine dose was more effective in the post-operative control of bariatric patients with diabetes than sliding scale alone. The RABBIT-2-Surgery trial suggested that a glargine and glulisine treatment improved glycemic control and reduced hospital complications compared to SSI alone in a general surgical population [25].

There are very few studies comparing basal-bolus regimens with Regular/neutral protamine hagedorn (NPH) regimens in the inpatient setting. A 2009 study of nonsurgical patients suggested equivalent glycemic control and no differences in hypoglycemia between a group treated with determir and aspart and one with a Regular/NPH split mix [41]. Several outpatient studies have demonstrated superiority of glucose control in patients treated with basal-bolus insulin versus regular and NPH in both type 1 and type 2 diabetes patients. Multiple studies have suggested improved a1c levels [42, 43], decreased glucose variability [42, 43], and decreased episodes of hypoglycemia [42–45] with long-acting insulins (such as glargine or detemir) compared to NPH insulin.

Although more inpatient comparison studies are needed to determine the ideal insulin regimen for the inpatient setting, the basal-bolus analogues have a more reliable pharmacokinetic and pharmacodynamic profile than the older insulins such as regular and NPH, and many authors suggest that the use of these insulins is preferred [1, 33, 41–45].

Of note, there are some specific situations in which NPH insulin may be especially useful, particularly in patients who are on glucocorticoid therapy. The pharmacokinetics of NPH more closely mimics the effects of steroids on glucose control and may be administered at the same time as steroid therapy to counter the glycemic effects. Depending on the dosing of steroids, the patient may require only one dose of NPH in the morning to coincide with morning steroid administration [46] or NPH BID, with a higher dose given in the morning [30].

Understanding the pharmacokinetics and pharmacodynamics of each type of insulin is imperative before selecting one to match individual patient needs. The onset of regular insulin occurs in approximately 30 min, with a peak effect between 2 and 4 h and a duration of action between 5 and 8 h. NPH insulin has an onset of 2–4 h, a peak between 4 and 10 h, and a duration between 10 and 18 h [47, 48]. Rapid-acting insulins such as aspart, lispro, and glulisine have an onset of 5–15 min, a peak of 30 min-2 h, and a duration of action of 3–5 h [47, 48]. Long-acting insulin such as glargine has an onset of 2–4 h, no peak, and a duration of action up to 24 h. Detemir insulin has a slightly quicker onset, a small peak at 6–8 h, and a shorter duration of action around 16 h [47, 48].

In choosing insulin regimens, the needs of the patient and clinical circumstances must be considered carefully.

Therefore, in the examples below, we will give recommendations on how to transition to basal-bolus analogue regimens as well as Regular/NPH generic regimens.

How to Transition from IV to SQ Insulin in the Patient Who Is Still NPO

Many hospitalized patients are still not eating by mouth (NPO) during the period of transition from IV to SQ insulin. The process for transitioning the NPO patient is simplified by that fact that the provider need only calculate basal requirement without regard to prandial coverage. There are several options for transitioning a patient who is not eating to a regimen of SQ basal insulin only.

Scenario A: Convert from IV Insulin to SQ Long-Acting Basal Insulin in the Patient Still NPO (Table 3)

Transition with Glargine or Determir Insulin. In general, both of these long-acting insulins are appropriate for transition for the patient who is NPO after discontinuation of an insulin drip. The long-acting insulin should be administered at least 2 h and preferably 2–4 h before discontinuation of the IV insulin drip to prevent rebound hyperglycemia (due to the short half-life of IV insulin) [6, 18]. Starting basal insulin even earlier may provide additional benefit. For example, Hsia et al. [49••] found that starting patients on a glargine regimen within 12 h of IV insulin initiation (as close to the initiation of IV as possible) at a dose of 0.25 units/kg prevented rebound hyperglycemia compared to those who received glargine immediately prior to SQ transition. Considering an earlier administration of basal insulin may provide increased glycemic stability if clinically relevant and feasible.

As noted previously, many authors recommend prescribing only 80 % of the total 24-h IV insulin utilization as the actual 24-h SQ insulin requirement, in order to allow glycemic control without precipitating hypoglycemia [6, 14, 15, 26•, 33], and the authors agree with this recommendation (Table 2).

Table 3 Examples of IV to SQ transition in NPO patient using regular or NPH insulin

Transition to NPH BID

From Table 2, the final 24-h SQ insulin requirement was determined to be 38 units

- As described above, if the patient is not eating, twice daily dosing of NPH can be calculated by splitting the total basal dose (38 units) in half, with 50 % administered in the morning and the other 50 % given 12 h later. Therefore:
- Final order: 19 units of NPH insulin administered twice daily, once in the morning and once at bedtime

Transition to Regular q 6 h

From Table 2, the final 24-h SQ insulin requirement was determined to be 38 units

- This can then be split up into 4 equal doses of SQ Regular insulin to cover the basal requirements (Furnary and Braithwaite [6]; Clement [53])
- 38 divided by 4 equals approximately 10 units with rounding. Therefore:
- Final order: 10 units of SQ regular insulin administered every 6 h

Scenario B: Convert from IV Insulin to SQ Regular/NPH in the Patient Still NPO (Table 3)

There are certain circumstances, often including financial/affordability concerns, which require a patient to rely on older Regular-NPH regimens instead of the newer, more physiologic agents.

Several authors have suggested that using NPH twice daily can be an effective regimen when the patient is not eating [20•, 50]. Twice daily dosing of NPH can be calculated by splitting the total basal dose in half, with 50 % administered in the morning and the other 50 % given 12 h later. Due to the longer duration of action, NPH should be administered with caution, similar to long-acting glargine, as a higher rate of hypoglycemia has been noted with its administration [44, 51]. Alternatively, Yeldandi et al. [52] suggested that transitioning a patient off an insulin drip to Regular/NPH regimen yielded similar glucose control to the group that was randomized to glargine, but these authors also reported a higher incidence of hypoglycemia in the Regular/NPH cohort. An example of transitioning a patient to NPH insulin is given in Table 3.

Transition with SQ Regular Insulin Given Every 6 h (Table 3). For patients who are not consuming food, regular insulin administered every 6 h in a scheduled dosing (not sliding scale) is another option for basal requirements. Instead of administering one injection of glargine daily, the q 6 h dosing may provide flexibility in the face of changing health status—for example, after major surgery or in patients with some degree of clinical instability [21, 53]. This particular therapy is also a good option for patients who are receiving continuous enteral feeds, those who are on high-dose steroids, or patients who may have a rapid change in status necessitating a change in insulin therapy. Due to the shorter half-life of regular insulin, this allows for more flexibility with dosing, as well as less risk of prolonged hypoglycemia if the nutrition source is lost [53, 54]. Due to the onset and peak of SQ regular insulin, it is recommended that the dose of SQ regular be administered at least 1 h before completely discontinuing the IV insulin drip [55].

How to Transition from IV to SQ Insulin in the Patient Who Is Already Eating

Scenario A: Convert from IV Insulin to SQ Long-Acting Basal and Rapid-Acting Bolus Insulins in the Patient Already Eating (Table 4)

As described above for patients who are NPO, it is recommended that the subcutaneous long-acting insulin be given at least 1 h (but preferably 2–4 h) before stopping the IV insulin [6, 18]. If the patient will be eating, an order for rapid-acting insulin may be added to cover prandial requirements. Similar to administration while on an IV insulin drip, the bolus dose may be a small amount, such as 2–4 units with meals, or may be weight based [6, 35].

Rapid-acting insulins are typically given three times daily immediately before meals. For patients who may have poor PO intake, the dose can be given immediately after finishing the meal in order to prevent hypoglycemia. To ensure the transition is safe, ensure that the IV insulin rates truly reflect the patient's basal needs. If there is evidence (variation in drip rates around meal times) that the IV insulin may actually be also covering prandial needs, then the first step should be to up-titrate the prandial SQ insulin dose accordingly so that the IV rates are stable and only reflecting basal needs before proceeding with a transition.

Scenario B: Convert from IV Insulin to SQ Regular and NPH Insulins in the Patient Already Eating (Table 4)

Regular and NPH are typically used together in patients who are eating, with the regular insulin given before meals and the NPH given at bedtime to cover the overnight basal requirement. Because of the longer duration of action of regular

Table 4 Transition from IV to SQ in the patient who is already eating

Patient data	Time (h)								
	0000	0100	0200	0300	0400	0500	0600	0700	0800
Transition to basal-bolus regimen									
• Patient weighs 80 kg, type 2 DM; data from overnight period of time when patient is not eating									
IV Insulin drip rate (units/h)	1.2	1.0	1.0	1.1	0.8	0.9	1.0	1.1	0.9
Blood glucose (mg/dL)	140	138	125	130	128	137	127	125	130
Calculations:									
From the example above (average 1 unit/h),									
• The calculated 24-h IV insulin requirement=1 unit/h×24 h=24 units									
• Therefore, the 24-h IV insulin utilization is 24 units daily									
As in the main text, many providers would use 80 % of the 24-h IV insulin utilization as the actual 24-h SQ insulin requirement									
• 80 % of 24 units=19 units is the final 24-h SQ total daily dose									
• Since this was calculated from an overnight period of time when the patient is not eating, this can then be administered as 19 units of basal insulin once daily.									
Next, to determine the prandial requirement, use a weight-based calculation									
• Given the possibility of decreased appetite, a conservative estimate in this patient with DM-2 is 0.2 units/kg for total prandial dose									
• 0.2×80 kg=16 units, and 16 units/3 meals=approximately 5 units/meal.									
• Final prandial dose in this patient: 5 units with each meal									
Final orders:									
• 19 units SQ daily (detemir/glargine) and									
• 5 units SQ TID CC (lispro/aspart/glulisine)									
Assuming the calculations above,									
• 19 units basal and 5 units bolus with each of 3 meals=TDD of 34 units									
• 25 % (¼) of the total daily dose is given at each meal (Regular Insulin before breakfast, before lunch, and before dinner), for a total of 75 % of the TDD									
• 25 % (¼) of the total daily dose is given as NPH Insulin before bedtime (Lien et.al. [21])									
• Thus, ¼ of 34=approximately 9 units									
Final orders:									
• 9 units SQ Regular insulin given 3 times daily before meals and									
• 9 units SQ NPH insulin given once daily before bedtime									

insulin, it will typically cover some portion of basal requirements during the day in addition to prandial intake.

If the patient had been previously eating (and already begun on subcutaneous prandial injections) while being treated with an IV infusion, ensure that the calculated dose requirement includes the prandial insulin. The general rule in proper distribution of Regular and NPH insulin is as follows:

- A 25 % (¼) of the total daily dose is given at each meal (Regular Insulin before breakfast, before lunch, and before dinner), for a total of 75 % of the TDD
- A 25 % (¼) of the total daily dose is given as NPH Insulin before bedtime [21, 35]

Transition to Pump Therapy

A small percentage of inpatients are those who use insulin pump therapy, also known as continuous subcutaneous insulin infusion (CSII), as outpatients. Most patients using insulin pump therapy are sophisticated and desire independence and control over their glucose management, even in the inpatient setting.

Unfortunately, many hospitals require pump patients to discontinue use of the pump and transition to SQ injections while in-house due to lack of provider/RN understanding or lack of hospital guidelines and procedures regarding insulin pump management [56], and most often, lack of supplies.

When the resources are available to allow pump use in the inpatient setting, many diabetes educators and endocrinologists will actually encourage a rapid return to CSII use as soon as medically appropriate to promote self-management and independence [2, 57].

Several institutional studies have documented safe results with patients using pump therapy in-house, including good evidence of compliance with institutional documentation regarding the pump settings and compliance with blood glucose monitoring [58–60]. Many institutions will require that patients sign a waiver, acknowledging the benefits and risks of operating an insulin pump in the inpatient setting. It is essential that there are hospital personnel available to assist with inpatient pump troubleshooting, should an issue arise [15].

Basic knowledge required for inpatient self-management should include the following: ability to manually manipulate the pump and required settings, ability to correctly count carbohydrates and bolus accordingly, retain responsibility for all pump supplies, and be willing to adjust pump settings according to provider recommendations [29, 56].

In situations where the care team would like to transition the patient directly from IV to CSII therapy, it is recommended that the provider assess the pre-admission basal settings and compare those to the patient's current IV basal requirement. When these values are similar, the pump may be simply reattached, with insulin infused at pre-admission settings. If the rates are dissimilar, a safe option may be to utilize the temporary basal rate function on the pump, to try to account for the difference in rates. If this option is used, it must be done with close monitoring and good communication between the patient and provider.

The authors recommend careful selection of patients who are allowed to transition back to insulin pump therapy. Many patients may simply not have an inpatient clinical status which allows return to insulin pump therapy. Those situations include critically ill patients, altered mental status, suicide risk, patient unwilling to self-manage pump, those still in active DKA, operating room procedure greater than 2 h, or certain radiology procedures [2, 57, 61].

For patients who are ready for transition off IV insulin but not directly ready for CSII, the provider should proceed with a normal IV to SQ insulin injection transition first. In some situations, the patient may need to be discharged still on SQ insulin injections. In this case, the patient should be referred to their outpatient endocrinologist or primary care provider for follow-up to determine if they can eventually restart CSII later.

Blood Glucose Monitoring After Transition to SQ Therapy

The first 24 h after a transition is an important time to assess the patient's insulin requirements as they may continue to change with clinical improvement. Even with a successful transition, it is still likely that stress, infection, medications, or a change in oral intake may drastically affect a patient's insulin requirements. The only way to safely determine this is to closely monitor the glucose levels in conjunction with the amount of SQ insulin given. Many authors recommend monitoring BG's at least five times daily for patients who are on multiple daily injections (MDI) [18]. The ideal times for monitoring would include before each meal, before bedtime, and at 0300, though many patients are monitored only pre-meal and at bedtime to minimize sleep interruption [62]. If blood glucoses are not at goal after the transition, consider increasing the relevant insulin dosing by 10–20 % to achieve glycemic targets [16]. In any case, the key is recognizing that proper glucose management requires daily close follow-up of glucose data along with appropriate daily adjustment of the SQ insulin doses in order to keep the patient safe.

Assistance with the Transition Process—Institution-Specific and Computer Protocols

Given the complexity of IV insulin and the transition to SQ insulin as described above, there is growing interest in tools that can help the practitioner complete the process safely and effectively. This is especially important in centers without endocrinology consultants and in teaching hospitals with

non-specialist trainees who are responsible for writing the transition orders and evaluating the results.

Institution-Specific Protocols

One such protocol is described by Furnary and Braithwaite [6], with a particular focus on the care of cardiac and cardiothoracic surgery patients. Several key points of emphasis in this protocol include the following:

- The use of basal-bolus analogue insulins
- The importance of giving rapid-acting SQ analogue insulin in addition to the IV insulin infusion in patients who are eating
- The importance of finding a several ("6- to 8-h") interval during which rates are stable to assess the average insulin infusion rate and project out to a 24-h basal dose requirement estimate
- The suggestion to use only 80 % of the total 24-h IV insulin requirement
- The need to continue the IV infusion at least 2 h after the administration of long-acting SQ insulin

Another protocol is described by Stahnke et al. [24•], again focusing on cardiothoracic surgery patients. Key points of emphasis in this protocol include the following:

- The importance of attention to the actual rate of the IV insulin infusion—with different instructions for the care of patients on less than versus more than 1 unit/h
- The need to continue the IV infusion at least 2 h after the administration of long-acting SQ insulin
- The importance of blood glucose monitoring throughout the process

Finally, Dickerson et al. [20•] describe a protocol where the transition focuses on a regimen of twice daily SQ NPH. Of note, this paper also describes an atypical suggestion for corrective IV Regular insulin coverage. Most endocrinologists argue strongly against the use of IV insulin as one-time bolus administrations for coverage because the half-life of IV insulin is so short [3].

Computerized Protocols

Computerized protocols such as EndoTool© [63, 64] and Glucommander© [65] focus on glycemic management and adjustment of blood sugars while the patient is on an IV insulin infusion to achieve desired targets. These protocols have reported effective management of hyperglycemia with a higher percentage of values in the target range, less variability, and no increase in hypoglycemia [63–67]. Other articles have reviewed various institutional protocols that produce varying results. Variability between protocols includes initiation, dosing, methods of titration, calculations, and use of bolus dosing [68, 69].

Glytec© has recently developed a computerized module (eGlycemic Management System or eGMS© [70]), used with Glucommander© [65], which offers recommendations for transitioning patients from IV to SQ insulin. This module is the first known computerized tool offering recommendations based on patient metrics such as A1c and most recent glucose values. A pilot study evaluating this program suggested that patients transitioned using eGMS had more BG within the goal range, low incidence of hypoglycemia less than 60 mg/dL (0.56 %), and no incidence of extreme hypoglycemia (<40 mg/dL) than those who were transitioned using a paper protocol system [70].

As of the publication date of this article, no other copyrighted tools have been published which offer recommendations for both IV management and the transition to SQ, though these may be in development.

Review of the 2013–2014 Literature

There is significant opportunity for knowledge expansion in the area of transitioning from IV to SQ insulin. There is currently no standardized "one-size-fits all" protocol for the transition of patients from IV to SQ, as the variation between patients is significant. A recent study suggested that the cardiothoracic surgery population may benefit equally from using weight-based dosing of insulin (0.5 units/kg) compared to using a percentage of the total daily dose IV utilization [32•]. Stanke et al. [24•] described less hypoglycemia and fewer sternal wound infections in open heart surgery patients post protocol implementation, when patients were converted at 80 % of their total insulin utilization.

Dickerson et al. [20•] described how to transition patients from IV to SQ insulin in those requiring continuous enteral feedings. This population can be challenging due to changing status and potential interruptions of feedings which affect insulin requirement. This article suggests transitioning patients from IV infusion to SQ BID NPH dosing, initially based on 30–50 % of the previous day insulin utilization and with doses escalated daily to achieve glucose targets. The risk of hypoglycemia in this population was greater for patients >60 years of age, those who had more glucose lability pre-transition, and those with poorer glycemic control pre-admission.

Finally, a new mathematical model for insulin drip titrations has been proposed. This model includes a comprehensive approach that takes into account fluctuations of blood sugar and correction factors to achieve more specific glucose targets [23]. The goal of this model would be more precise representation of patient insulin requirements to allow safer IV to SQ transitions.

Conclusions and Areas for Future Research

With the expansion of computerized algorithms to direct clinical care, more research is needed into the development of computerized glucose control systems which can achieve more individualized patient transitions, i.e., by taking into account physiologic variables such as creatinine, comorbid conditions, and population specific target BG ranges. Of note, concerns have been raised that widespread use of protocols may detract from providers recognizing the importance of their own understanding of safe IV insulin use and effective transitions, and this will likely be an ongoing debate.

Further research should be done regarding which insulins are most effective (and cost efficient) for the IV to SQ transition in various populations. Specifically, more research is needed in how to perform IV to SQ transitions in unique patient situations (such as DM-1, enteral and parenteral tube feedings, labor, renal failure).

Compliance with Ethics Guidelines

Conflict of Interest Kathryn Evans Kreider declares that she has no conflict of interest.

Lillian F. Lien has been a consultant for Merck, Eli Lilly, Novo Nordisk, and Sanofi-Aventis; has received honoraria from the American College of Physicians; and has received royalties from Springer Inc. for a book she edited.

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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