



Diabetes update: new medications and therapeutic updates

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Disclosures

SPEAKER BUREAU

- Abbott
- Dexcom



Hospital issues



- Patients are often attached to their outpatient diabetes regimen
- Patients are often attached to the provider providing their diabetes care (be careful what you say!)
- Patients might have excellent control or poor control at home
- Many medications the patient takes at home are not on the hospital formulary
- Medications the patients take at home might not be most optimal academically, but might be used at home based on costs, simplicity, formulary, etc.

Hospital issues



- Many medications might be contraindicated in acute illnesses or renal insufficiency (Ex: metformin, SGLT-2 inhibitors).
- Many medications might not be appropriate or needed for short-term hospital use (Ex: sulfonylureas, glinides, GLP-1 RA, SGLT-2 inhibitors)
- Many medications might not be optimal in a patient that might not be eating well or might be NPO (Ex: sulfonylureas, glinides)
- Patients with a poor support system at home might not be good at changing regimens (without lots of help)
- Explain to the patient why their meds are being withheld.

What is the goal of inpatient DM management



- Provide safe use of diabetes medications
- Avoid significant hypoglycemia
- Attempt to keep BG near target range
- For well trained patients, give them an experience that is nearly equal to their own ability to care for the DM at home; for less well trained patients: train them and acknowledge that the diabetes is a major concern for them
- Can this be accomplished in a short hospital stay? Does it make a difference? Does it have to be done with insulin or intensive insulin therapy?

Hospital issues



- Discharge planning should begin on admission (Shepperd, et al)
- Discharge patients with medications and supplies (meters, strips, etc.)
 that are on their formulary (such as what they were on at home) that
 they can afford, and that they can actually use effectively (the best
 insulin regimens often fail if a patient cannot use them effectively,
 and/or does not have a good support network).
- Train patients how to use these medications and supplies.
- Involve home care.
- Involve diabetes education department in the hospital and possibly as outpatient.

Hospital issues



- TYPE 1 DM
- Type 2 DM
- Other types(?): MODY, secondary causes, etc.
- Can have type 1 DM whether they are older or younger, heavy or thin, etc.
- Can have type 2 DM whether they are older or younger; most are overweight, but not all.

Insulin pumps



- Use only rapid-acting insulin in the pump
- Do not use long-acting insulin when the pump is being used
- Need long-acting insulin SC generally when the pump is removed

Hospital issues: insulin pumps



- Insulin pumps: some patients are more savvy with pump use than others. This might give the hospital staff some concern. Record keeping with pump patients: BG, dose, time, etc.
- Pump patients should bring extra supplies to change the infusion site every 3 days or so. Some diabetes education departments keep supplies
- Pump patients with mental status changes, surgery and anesthesia, etc.: when can they resume the pump and control of their diabetic care?
- Don't expose to x-rays, electrocautery, etc.

Hospital BG target



• BG goal: generally 140-180.

Target BG in hospital



 We do not have the perfect insulin and there are so many variables that perfection and consistency sometimes cannot be achieved at home or in hospital

(illness, variable absorption of meds and food, other meds, endogenous glucose production, etc.)



- A1c if not done in past 3 months.
- Rapid-acting insulin use based on algorithms based on glycemic fluctuations (and food).
- Consider giving rapid-acting insulin immediately after eating if not certain what or how much the patient will be eating. Adjustments based on pre-meal blood sugar level and actual food intake.
- Initial orders/note should state the type of diabetes (1, 2, gestational, etc.) Remember: this is not necessarily based on age or weight.



- Assess patient's diabetes knowledgebase.
 Diabetes education as needed. Nutrition training.
- Structured computerized order sets/insulin order templates.
- Consider consult DM education team and/or endocrine
- Insulin therapy used for persistent hyperglycemia >=180 mg/dl.
- Target range: 140-180 mg/dl for the majority of critically ill and noncritically ill patients (NICE-SUGAR Study)
- Some patient's goal might be 110-140 mg/dl (if can achieve without hypoglycemia).



• Less intensive insulin regimen in terminally ill patients with limited life expectancy (minimize dehydration, electrolyte disturbances)

FINGERSTICK GLUCOSE



- Less accurate than laboratory glucose levels.
- If eating: glucose monitoring ac and HS at least (and sometimes overnight). Perhaps monitor about 2-3 am in select patients
- If not eating: glucose monitoring every 4-6 hours.
- More frequent monitoring with insulin drips and hypoglycemia.
- CAVEAT: patients with hypoperfusion or peripheral edema, fingerstick BG might be falsely low
- CAVEAT: some dialysis infusions or medications might falsely elevate BG (Rice, et al)



- Basal insulin (to address hepatic glucose production) or basal plus bolus regimen for non-critical hospitalized patients with poor intake or NPO. In some cases, home regimen might be appropriate, including non-insulin agents. If non-insulin agents are held, should have a protocol for resuming them 1-2 days before discharge if appropriate.
- For those eating: basal insulin, scheduled prandial rapid-acting insulin; correction rapid-acting insulin.
- Don't generally only use a sliding scale for high blood sugars.
- Critical care: intravenous insulin drips (my personal comment: if patient is eating, this might not be optimal).

ADA RECOMMENDATIONS



- Human insulin vs. insulin analogues can result in similar glycemic control in the hospital.
- Rapid-acting insulin before meals or every 4-6 hours based on hyperglycemia if no meals are given, or with continuous enteral/parenteral nutrition.

Pre-mixed insulin



- Pre-mixed insulin (70/30, 75/25, 50/50): generally not used in the hospital as could cause more hypoglycemia likely due to the fixed ratio of intermediate to rapid-acting insulin. We sometimes use this (70/30) every 8 hours in patients on continuous feeds.
- But can be a reasonable regimen also for select patients at home, especially
 patients who eat 3 meals daily and need, want, or are doing well with a simplistic
 insulin regimen.



- Type 1 DM: always use a basal-bolus regimen
- Bolus regimen consists of prandial scheduled insulin if eating and correction insulin for BG level
 - Personal note: if the basal insulin dose is correct, the BG should not increase or decrease significantly overnight (assuming not eating at night and not taking rapid-acting insulin at nighttime).
- If carb counting at home (and some hospitals provide the nutritional content of their food), carb counting should be used as feasible.

TYPE 1 DM



- Almost always need basal insulin, even if not eating, to cover the hepatic production of glucose, etc.
- Sliding scale rapid-acting insulin alone for correction of high BG is generally not effective, but can be used in situations when the patient is not eating or not predictably eating
- Scheduled rapid-acting insulin for carbs is generally necessary plus sliding scale correction



 Adjusting it just based on the fasting glucose alone, with the goal of getting the FBS in range (Treat to Target Algorithm) or adjusting based on the A1c alone: very dangerous but common mistake

 Expecting basal insulin alone to do everything such as to control the blood sugar all day including with meals, even in very insulin deficient patient. Many patients and all insulin deficient patients, will need basal-bolus insulin.



- Not using a pill or injection that specifically counteracts carbs, along with the basal insulin
- When the patient is intensified to multiple daily injections, not educating the patient to learn carb counting (or variable doses for variable sized meals) and a correction scale (or a simplistic version)
- Not giving any if insulin pump has to be removed
- Resuming an insulin pump before 20-24 hours following a shot of basal insulin (can do this if temporarily reduce the basal rate)



- Not further titrating the regimen after discharge.
- Assuming the hospital dose will be the outpatient dose and vice versa.
- Expecting basal insulin to be effective without prandial medication, especially in an insulin deficient patient.
- Expecting to have perfect sugars rapidly. These regimens take a while to titrate to effectiveness and the unpredictability of the hospital setting often precludes good control in the short-term with intensive insulin



 Not giving it when an insulin drip is stopped, along with rapid-acting insulin in a very insulin deficient patient or patient with type 1 DM

Errors with insulin in Type 1 DM



• Insulin requirements should be based on sensitivity to insulin (weight based often), not based just on their BG level (i.e.: very high BG's often do not very need high doses of sliding scale coverage, etc.)

SGLT-2 inhibitors



- For people with type 2 DM
- Can cause euglycemic DKA rarely
- Can cause increased risk of UTI's, vaginal/penile yeast infections
- Can acutely worsen the creatinine due to dehydration, although have beneficial effects on renal function in the long run
- CV benefits; weight benefits; BP lowering benefits; No significant hypoglycemia
- Avoid in severe illness and with surgical procedures or if fasting (risk of euglycemic DKA, dehydration, etc.). Stop 3-4 days before scheduled surgeries.

DDP-4 inhibitor



No cardiovascular or weight benefit, but no significant hypoglycemia

GLP-1 receptor agonists



- ?Pancreatitis
- Nausea
- Diarrhea or constipation

?Pancreatic cancer

CV benefits; weight benefits; no significant hypoglycemia

Sulfonylureas/glinides



- Insulin secretagogues
- Hypoglycemia
- Generally avoid in the hospital

Metformin



 Lactic acidosis, rare, but more likely in patients with severe renal or hepatic insufficiency

(many patients in the hospital have elevated lactic acid levels, but not all of these have lactic acidosis)

Don't assume high lactic acid levels are due to metformin (most of the time they are not).

Renal dose adjustments. Also, stop if GFR <30.

Don't make it seem to the patient that the metformin caused their renal insufficiency.

Hold on day of surgery.

Thiazolidinediones



- Edema
- Weight gain
- CHF
- Likely have CV benefits
- Beneficial for fatty liver probably
- No significant hypoglycemia

Insulin



- Explain to the patient why on insulin if they weren't on it at home: it's rapid-acting is safer in the hospital than their oral/SC agents, since patient might not be eating predictably, etc.
- Explain why patient might be on different rapid-acting insulin than the one they use at home: formulary, but likely similarly in action to their home rapid-acting insulin.
- Explain why they aren't on their home pills/medications.
- Explain why on basal insulin if not on it at home.
- Explain why the basal insulin in the hospital might be different than their usual one at home: formulary but likely similar in action to their home basal insulin.

NPH insulin



- Often is better than basal insulin in patients on once daily prednisone, given about the same time as prednisone.
- Often is better than basal insulin in patients on nighttime peritoneal dialysis.
- Cheaper than basal insulins

R U-500 insulin



- Concentrated insulin to deliver large amounts of R insulin in less volume
- Has properties of rapid-acting insulin and intermediate acting insulin
- Should ideally use the insulin pen form
- If using the vials, should use U-500 syringes

ICU



IV insulin drip can be very effective.
 However, if the patient is eating, then IV insulin drips can allow marked fluctuations in BG after eating, leading to post-meal hyperglycemia and then significant hypoglycemia, leading to the insulin drip being stopped, which then can cause hyperglycemia.

TYPE 1 DM in the ER with DKA



- IV Insulin drip initiation: 0.05-0.10 units/kg/hour with Regular insulin.
- Start as soon as possible in the ER.
- Generally don't recommend an IV bolus of Regular insulin before the insulin drip.

DKA



- There is no significant difference in outcomes for intravenous regular insulin versus subcutaneous rapid-acting analogs when combined with aggressive fluid management for treating mild or moderate DKA. Patients with uncomplicated DKA may sometimes be treated with subcutaneous insulin in the emergency department or step-down units, an approach that may be safer and more cost-effective than treatment with intravenous insulin.
- Several studies have shown that the use of bicarbonate in patients with DKA made no difference in resolution of acidosis or time to discharge, and its use is generally not recommended.

TRANSITION OFF INSULIN DRIP



- A patient with type 1 DM being transitioned off an insulin drip should probably receive basal insulin, first dose 2-4 hours before stopping the insulin drip (I favor closer to four hours before stopping the drip).
- Alternatively or in addition, rapid-acting insulin can be given about 20-30 minutes before stopping the insulin drip.

DISCHARGE: ADA recommendations



- Rate of readmission is between 14-20% (twice that of people without diabetes).
- Factors associated with readmission: male sex, longer duration of hospitalization, number of prior hospitalizations, number and severity of comorbidities, older age, neurocognitive function, support, lower socioeconomic and/or educational status.
- Home visits and timely outpatient f/u reduce rates of readmission.
- Targeting ketosis prone people with diabetes.
- Targeting people with A1c>9%.

Discharge



- Discharge patient, if insulin is needed, on insulins covered by their insurance (or the same one's they were on at home).
- Decide which non-insulin meds to have them continue and discontinue at home.
- Meters, strips, lancets at home on their formulary
- Rx insulin pen needles or syringes.
- How often for them to check their BG levels at home?
- Glucagon at home (nasal, injectable)
- Hypoglycemia instructions, rule of 15's

Discharge



- Discharge planning should start at admission
- Discharged home? ECF? Help at home?
- Patient's capacities and preferences.
- Insurance formulary.
- Discharge algorithm (Algorithm: Umpierrez, 2014)
- F/u visit within 1 month if hyperglycemia, earlier if issues.
- If they came in on a simplistic insulin, such as pre-mixed (70/30; 50/50; 75/25): was there a reason they were on it such as simplicity and ease? Was it working for them? Can they handle change?

DISCHARGE SUMMARY: ADA recommendations



- Include information in the discharge summary about the reason for hyperglycemia or hypoglycemia
- Include the provider responsible for DM f/u.
- Level of understanding of the patient regarding diabetes; compliance; complications known; understanding of hyperglycemia and hypoglycemia; goals; when to call provider; self-monitoring; food knowledge
- Appropriate timing and method of taking DM meds; sick day management
- ?Need for DM education, nutrition therapy f/u

Continuous glucose monitor (CGM)



- Not yet FDA approved for inpatient use
- Measures interstitial glucose (not blood glucose)
- ?continue it in the hospital: they often are very dependent on it.
- If using an insulin pump, the pump might need the CGM readings for hybrid closed loop mode
- Have hospital protocols for these; currently fingerstick BG's are needed along with them.

Insulin pumps



- Have a hospital protocol: patient to record their data such as glucose reading, bolus given. Pump type and settings must be recorded. Patient should have a extra infusion sets and insulin cartridges as the sets need to be changed every 3 days, earlier if problems. Don't give basal insulin if on a pump.
- To continue or discontinue pumps: Patient alert and able to operate the pump?
- Don't expose pumps to x-rays, electrocautery, MRI's, etc.
- Have protocol for taking the pump off: basal insulin right away generally and rapid-acting insulin with meals for food and elevated glucose levels

Insulin pumps



- Look at the endocrinologist's notes: usually we mention the type of pump, the settings (basal rates, insulin to carb ratio, correction factor or sensitivity, target BG, insulin duration, etc.)
- We usually also mention how much basal insulin to give right away if the pump is removed.

Insulin pumps



- Remember, one of the most common causes of DKA in an insulin pump patient is infusion set problem, such as kinked cannula causing mal-delivery of insulin; possibly bad insulin in the pump or the vial
- It is often best to resume insulin pump therapy as soon as possible, especially once the patient is eating; or even once the patient is alert enough to use the pump even if not able to eat (since the basal rate can be used regardless of food, and since the pump can help calculate how much insulin to give for hyperglycemia). This might even be more useful if the patient has a hybrid closed loop system with a CGM (continuous Glucose Monitor).

Kinked infusion set cannula





Total Estimated daily insulin dose



- Remember that most people need a total daily dose of insulin of about 0.5-1 unit/kg per day.
- -Patients on insulin generally need about $\frac{1}{2}$ of their insulin as basal insulin and $\frac{1}{2}$ as rapid-acting insulin.
- -This, of course, can be affected by insulin resistance, DM medications they are taking, activity, food intake, etc.

Formulae for estimating rapid-acting insulin doses



- Total Daily Dose (units) of insulin (TDD): weight in pounds x 0.23 (or weight in kg x 0.5-1).
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- Carbohydrate ratio (Insulin to carb ratio; I:C ratio): 500/TDD
- For example: if TDD is 50 units, the carb ratio would be 10 (i.e.: 1 unit insulin for every 10 grams of carbs).

Formulae for estimating rapid-acting insulin doses



- Insulin Sensitivity Factor (ISF): 1,700/TDD
 - (How much 1 unit of insulin drops the BG over 1-2 hours)
- For example: if TDD is 50 units, the ISF would be 34 (i.e.: 1 units of insulin drops the blood sugar by 34 mg/dl).
- Then we calculate the correction dose of insulin as follows:
- (current blood sugar level target blood sugar level)/ISF

Formulae for estimating rapid-acting insulin doses



- These are good approximations and we also we have to keep in mind that many patients have different ISF and I:C ratios at different times in the day.
- Also, morbidly obese patients might be so insulin resistant and very thin type 1 patients, for example, might be very sensitive to insulin that we might have to make some initial adjustments in these formulae to be safe. Then if they don't work, we just change the formulae based on what seems to be needed.

Basal Insulin calculation



- For Basal Insulin:
- Rough daily Basal insulin requirement would be: TDD/2.
- Of course we generally start with the recommendations per the package insert for basal insulin of 0.1-0.2 units/kg /day; but this equation at least lets us estimate what the eventual basal dose might be. I generally titrate the basal insulin so that the HS BG roughly equals the FBS (assuming no food in between). If the HS BG is much higher than the FBS, then I add or adjust rapid-acting insulin before dinner (and possibly each meal), or possibly add an agent that particularly targets food intake (GLP-1 agonist, DPP-4 inhibitor, sulfonylurea, etc.)

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