

Sunday Fun Day 2 - DKA

DRIP 4

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Insulin Therapy

- Helps to:
 - Inhibit lipolysis
 - Encourages fat synthesis
 - Suppresses gluconeogenesis
- Goal: reduce and maintain BG 100-250 mg/dL (5.5-14 mmol/L)
- Options
 - Regular insulin IV CRI
 - Regular insulin IM injections
 - Glargine IM +/- SC
 - Insulin aspart IM & SC?
 - Lispro insulin IV CRI



We've got to give them insulin, why? We need to stop the lipolysis, we need to stop the lipid metabolism that's going out of control in these patients. We want to go from a state of fat breakdown to a state of fat synthesis and we need to suppress gluconeogenesis. We're going to stop these ketones from being formed.

So we're going to try to get our glucose down to somewhere between 150 and 250 mg per deciliter and here's the really cool thing about insulin therapy guys, we have a lot of options, we have a lot of options from regular insulin CRIs to intermittent injection protocols.

Insulin Therapy



When to start insulin?

- Traditionally initiated 4-6 hours after IVF
- Early initiation associated with more rapid resolution of DKA in cats & dogs
- Humans: initiated after 1st hour of IVF as long as $K^+ > 3.3$ mmol/L

Omit initial IV bolus of regular insulin prior to starting CRI

- No benefit; may precipitate/aggravate development of hypokalemia

When do we start the insulin? Usually four to six hours after intravenous fluid therapy is started. Why? Well, we're trying to maximize perfusion before starting insulin therapy. But we are seeing that the sooner we start, our insulin therapy seems to be directly associated with a more rapid resolution of diabetic ketoacidosis, so we're trying not to wait 12 to 24 hours to start insulin therapy. Again, about four to six hours.

In our human colleagues, they start it within an hour, right around the first hour as long as our potassium is up. And so I am hopeful that the diabetic gurus out there, the Jackie Rands in Australasia and the patty Latham and Mississippi State, have somebody looking at, should we be initiating even sooner than four to six hours? I think it's a cool question that needs to be answered.

We don't need to give them that initial bolus of regular insulin CRI. When I was trained, if I was going to start a kiddo on a regular insulin CRI, to give an initial bolus of that regular insulin CRI and then start to CRI. There is no benefit to doing that, we know that now and we know that doing so could actually worsen a state of hypoxemia that we're always going to be watching for.

BG	[Dextrose] per L	Insulin On/Off
<4.44 mmol/L <80 mg/dL	2.5%	OFF
4.44-9.99 mmol/L 80-180 mg/dL	0%	ON
>9.99 mmol/L >180 mg/dL	0%	ON



- My regular insulin IV CRI protocol:
 - Regular insulin @ 2.0 U/kg/day IV CRI
 - If BG >180 mg/dL (9.99 mmol/L) >2 hours, increase insulin rate by 25%
 - If BG <60 mg/dL (<3.33 mmol/L), turn off insulin until >80 mg/dL (>4.44 mmol/L); then reduce insulin rate by 10-25%

Now, there are many, many protocols out there for regular insulin CRIs. I hate all of them, I think they're very esoteric, very complicated five and seven tiered systems, can't stand it. It's very complicated, I like things simple.

So this is my approach and I will fully claim that this is not one that I made up, it's the one that was taught to me too long ago to remember by Dr. Susan Hochner who is a fellow critic and internal medicine specialist. And this is the protocol in which I was reared and I always love to share it with you so you have it for your reference.

Now with that being said, do I think this works well? Dang skippy, I think it works wonderfully. I have no hesitations using this. However, we have some new data that is emerging that says, maybe we don't have to do CRIs and I know that's important because not everybody works in a tertiary facility with 24/7, 365 care.

Insulin Therapy – Glargine IM +/- SC



- 2U glargine/CAT SC on initiation of fluid and electrolyte replacement
- Begin 1U glargine/CAT IM, 1–2 h later (up to 4 h if persistent hypokalemia)
- Repeat IM glargine 4 or more hours later if glucose is >14 mmol/L (250 mg/dL)
- Continue SQ glargine every 12 hr
- Provide IV dextrose to maintain blood glucose levels 12–14 mmol/L (216–255 mg/dL) in the first 24 hr

So we've looked at insulin therapy in terms of glargine intramuscular and subcutaneous injections. And this was initially a protocol that was suggested by Jackie Rand and her team. And most recently they compared this protocol to the regular insulin CRI. This is recently published information, just within the past three or four months.

- Prospective randomized clinical trial comparing regular insulin IV CRI (n=10) vs. basal-bolus SC & IM glargine (n=10)

- Regular insulin IV CRI:

- 1.1 U/kg added to 0.9% NaCl starting 2 hours after initiating IVF (10 mL/hr; 0.05 U/kg/hr)
- Adjusted q2 hr to achieve decrease in glucose of 2-3 mmol/L/hr (36-54 mg/dL)

- Glargine:

- 2 U SC bolus irrespective of BW concurrently when starting rehydration
- Then 1 U/cat IM 2 hr later
- Then 1 U/cat IM q4 hr if glucose >13.9 mmol/L (250 mg/dL)
- Glargine 0.25 U/kg SC q12 hr (based on ideal BW) rounded to next whole unit



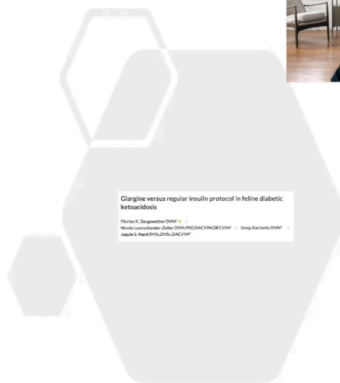
So they took that protocol, that glargine protocol and compared it to standard of care, a regular insulin CRI. So from the regular insulin CRI standpoint, it took 1.1 units per kilo mixed it in saline and started two hours after starting fluid therapy. So they were faster than the four to six hours.

And then they adjusted their rates every two hours trying to reach a scenario where the glucose basically went down by about 50 mix per deciliter within that period. Compared that to the experimental protocol which is using glargine. So every cat got-- and this is a cat study, every cat got two units regardless of body weight when starting fluid therapy. Got two units, boom, subcutaneous.

And then two hours later all the cats got one unit per cat, one unit intramuscularly. And then every four hours, each cat got another unit IM if their blood sugar was greater than 250.

They also got glargine Q12 hours sub Q, and was on a unit per kilo basis, a quarter unit per kilogram. So again, it's this combination of intramuscular and subcutaneous glargine in these cats, their primary endpoint was measuring beta hydroxybutyrate.

- Primary endpoint: β -OHB <2.55 mmol/L
- 85% survived to discharge (n=17) – no difference in survival between groups
- Glargine group had significantly shorter:
 - Times of primary endpoint (30 vs. 42 hr)
 - Time to 1st improvement of hyperglycemia (2 vs. 6 hr)
 - Time to hospital discharge (140 vs. 174 hr)



They had the ketone meter, they wanted to get to a point where the ketones, the beta hydroxybutyrate was less than 2.5 milliosmoles per liter. 85% survived to discharge and there's no difference in survival between the two groups, so that's good, both protocols are valid.

But what's really cool is that, in this small group, the glargine group took a shorter period of time to get to that beta hydroxybutyrate end point, shorter time to the first improvement in their glucose, and they didn't stay in the hospital as long.

So the point here again is to emphasize that we have an additional option, multiple options, but at least one with evidence based data, at least in our cats. That we don't have to admit them to the hospital for continuous rate infusions intravenously. We can have them hospitalized for injections, because I know doing CRIs can be very, very challenging for a lot of colleagues, especially in primary care. So this is just another weapon in our arsenal.

Potassium Supplementation



- Anticipated within 2-4 hours of initiating therapy
- Must be closely monitored & proactively supplemented
- Use IV CRI if <3.2 mmol/L
 - Total hourly administration should generally not exceed 0.5 mmol/kg BW (*but can with careful monitoring!*)
- Nutritional support important for maintaining K^+

Potassium supplementation is absolutely indicated. Normal, you should consider low. You're going to have to supplement them, you're going to have to monitor them closely. And I will tell you that when your potassium is less than 3.2, CRIs do tend to be superior in terms of rate of improvement, nutritional support is also of paramount importance for these guys during times when potassium chloride injectable is not available.

Sometimes oral supplementation with something like tumble k can be helpful.



Potassium Supplementation



	Typical Guidelines	DKA Guidelines
Serum K ⁺ (mmol/L)	K ⁺ mmol per L IVF	K ⁺ mmol per L IVF
>5	Wait	Wait
4.0-5.5	10	20-30
3.5-4.0	20	30-40
3.0-3.5	30	40-50
2.5-3.0	40	50-60
2.0-2.5	60	60-80
<2.0	80	80

If you can't do CRIs, then we're probably all familiar with this middle column, our typical guidelines for fluid supplementation with potassium chloride.

Just remember that our DKA patients need a heck of a lot more potassium because of that concurrent insulin therapy that's causing transcellular shifts. So our insulin therapy is driving potassium from the extracellular location to the intracellular location and that's why we need to be prepared to supplement.