Perioperative Diabetes management

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Objectives

- To discuss the evidence for perioperative glycemic control
- To outline the principles of pre- and post-operative management of patients with Type 1 and Type 2 Diabetes
PHYSIOLOGY OF STRESS HYPERGLYCEMIA

STRESS HYPERGLYCEMIA

ENHANCED HEPATIC GLUCOSE PRODUCTION

DECREASED PERIPHERAL GLUCOSE UTILIZATION

COUNTER-REGULATORY HORMONE & TNF-α, IL-1 SECRETION

PERIPHERAL INSULIN RESISTANCE
Hypothesis

- Hyperglycemia or relative insulin deficiency (or both) directly or indirectly results in an increased predisposition to complications: infections, polyneuropathy, multiple organ failure, and death.
INTENSIVE INSULIN THERAPY
Van den Berghe et al 2001

- Does normalization of blood glucose levels with intensive insulin therapy reduce mortality and morbidity among critically ill patients (particularly post cardiac surgery patients)?
INTENSIVE INSULIN THERAPY
Van den Berghe et al 2001

PROSPECTIVE RANDOMIZED CONTROL TRIAL
(n = 1548)

Intensive insulin therapy (n=765)
Maintain BG: 80-110 mg/dL (4.44 - 6.1 mmol/L)

Conventional treatment (n=783)
Insulin only if BG > 215mg/dL (11.9 mmol/L)
INTENSIVE INSULIN THERAPY
Van den Berghe et al 2001

- Study population
  - 59% - coronary bypass surgery
  - 27% - valve replacement
  - 14% - combined procedure
  - 13% - history of diabetes
    - n = 103 in conventional group
    - n = 101 in intensive group
  - 5% - treated with insulin
    - n = 33 in conventional group
    - n = 39 in intensive group
- Blood sugar on admission (in both groups)
  - 75% - FBG > 6.1 mmol/L
  - 12% - NFBG >11.1 mmol/L
INTENSIVE INSULIN THERAPY
Van den Berghe et al 2001

**Results**
- Intensive insulin therapy reduced ICU mortality from 8.0% (w/ conventional therapy) to 4.6% (with intensive therapy)
  - Relative risk reduction of 42% (95% CI 22-62%)
  - P<0.04

- Benefit was attributed to effect on pts in ICU for > 5 days
  - Mortality 20.2% with conventional tx versus 10.6% with intensive tx
INTENSIVE INSULIN THERAPY
Van den Berghe et al 2001

- Intensive insulin therapy group
  - ↓ sepsis by 46%
  - ↓ prolonged inflammation
  - ↓ acute renal failure by 41%
  - ↓ critical illness polyneuropathy
  - Less likely to require prolonged mechanical ventilation
  - ↓ in duration of ICU stay but not overall length of stay in hospital
Conclusion:

“Intensive insulin therapy to maintain blood glucose at or below 110 mg/dL (6.1mmoL/L) reduces morbidity and mortality among critically ill patients in the surgical intensive care unit.”
Medical ICU patients

Van den Berghe et al 2006  NEJM

Note that despite these results, applicable mainly to post-cardiac surgery patients, the study of medical ICU patients failed to show any significant reduction in mortality with intensive insulin therapy, although it did show a reduction in morbidity particularly in pts with >3d length of stay.
Intra-operative insulin therapy

- No good quality data exists regarding perioperative glycemic control for non-cardiac surgical procedures

- One study of *intra-operative* tight glycemic control during cardiac surgery did not show a reduction in mortality or morbidity
Intraoperative glycemic control

- Randomized, controlled, open label, blinded outcome assessment
- 400 pts undergoing on-pump cardiac surgery at a single tertiary care centre
- Goal was to maintain BG in the range of 4.4-6.1 in the intervention group using iv insulin
- Glucose levels at the end of surgery were 6.3 vs. 8.7 in the intervention vs. control group
Results

- The primary outcome – composite of death, sternal infections, prolonged ventilation, arrhythmias, stroke and renal failure at 30 days was similar in both groups.

- Length of stay (ICU and hospital) did not differ (secondary outcome).

- There were 8 vs. 1 strokes ($p=0.02$) and 4 vs. 0 deaths ($p=0.06$) in the intensive group.
Pre-operative assessment

- Type of Diabetes
- Treatment regimen – Lifestyle/OHAs/Insulin – QHS, BID or MDI
- Glycemic control
- Type and duration of surgery
- Co-morbidities and Diabetes complications e.g. HTN, Renal insufficiency, CAD (for risk assessment and post-op monitoring)
Preoperative assessment

- Tests to order:
  - HbA1C
  - Creatinine
  - Electrolytes
  - Random BG
  - EKG
Background on insulin therapy

Different regimens available:

- Oral agents with bedtime basal insulin: NPH (intermediate acting) or Glargine/Levemir (long acting analogs)
- Pre-mixed insulin BID: 30/70, Humalog mix 25 or Novomix 30
- MDI: Basal insulin (NPH, Glargine or Levemir) with Bolus (Humalog, Novorapid)
Profiles of Human Insulins and Analogues

- Aspart, lispro (4 to 6 hours)
- Regular (6 to 10 hours)
- NPH (12 to 20 hours)
- Ultralente (18 to 24 hours)
- Glargine (20 to 26 hours)
### Table: Insulin Types and Characteristics

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Onset</th>
<th>Peak Effect</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid acting: insulin lispro (Humalog)</td>
<td>0 to 15 minutes</td>
<td>30 to 90 minutes</td>
<td>Less than 5 hours</td>
</tr>
<tr>
<td>Short acting: regular human insulin (Humulin R, Novolin R)</td>
<td>30 to 45 minutes</td>
<td>2 to 4 hours</td>
<td>6 to 8 hours</td>
</tr>
</tbody>
</table>

**Figure 2.** Mean glucose infusion rate response: regular insulin response (dotted line) and lispro response (solid line).
Peri-operative management

- Given the lack of substantial evidence, the goal is to avoid hypoglycemia and marked hyperglycemia (given concerns of possible poor wound healing, dehydration and decompensation during stress).

- In patients with T1DM, given absolute insulin deficiency, need insulin to suppress ketosis and avoid DKA.
Glycemic targets

- Not clearly defined – considerable variability amongst clinicians – acceptable glucose ranges:
  - 5-10 vs. 5-12 vs. 6-13 mmol/L

- It is also important to consider whether the patient will be able to eat after surgery or is likely to remain NPO
Type 2 Diabetes on OHAs

- If well controlled, hold OHAs on morning of surgery

- Patients who are poorly controlled with high dose OHAs or are undergoing major surgery may need i.v. insulin
Type 1 Diabetes or Type 2 Diabetes on insulin

- If undergoing a short procedure, less than 2 hours:
  - Can give \( \frac{1}{2} \) total AM dose of insulin or \( \frac{2}{3} \) of morning intermediate acting insulin dose subcutaneously prior to surgery
  - In addition, may need a subcutaneous insulin – R sliding scale for BG>10-12
Example 1

- Patient on 30/70 BID insulin 42 units QAM and 32 units QPM

- Undergoing short gyne procedure booked for 60-90 minutes

- Patient should take usual dose the evening before surgery

- Check CBG on am of surgery
Example 1 (cont’d)

- NPH component of 30/70 dose – 42 units = 28 units
- 2/3 of this ~ 18 units
- ½ AM dose = 21 units
- Therefore, can give 18-20 units of NPH on am of surgery s.c. and monitor CBG q2h with i.v. D5W @ 75cc/hour (required whenever pt is receiving insulin)
Example 2: surgery < 2 hours

- **Patient on MDI** – Humalog 12 units s.c. AC meals and Levemir or NPH 8 units QAM and 16 units QHS

- Take usual dose of insulin night before surgery (unless pattern of am hypoglycemia)

- Morning of surgery: give 2/3 of basal dose to be safe ~ 6 units s.c.
Example 2: surgery < 2 hours

- Consider adding on a sliding scale for BG greater than 10-12

- Question: How much will 1 unit of insulin lower this person’s blood glucose by?
Insulin sensitivity/correction factor

- For analog insulins, divide 90 by the total daily dose (TDD) of insulin:
  - TDD = 12x3 + 8 + 16 = 60 units
  - 90/60 = 1.5

- Therefore, in this patient, 1 unit of insulin will lower the BG by roughly 1.5 mmol/L

- This can be useful in designing the sliding scale/extra dose of insulin required for BG>10
Basal insulin: Glargine (Lantus)

- Given that Glargine has 24 hour coverage, for short procedures, may take usual dose night before surgery and hold bolus insulin on am of surgery (assuming surgery in am)

- Monitor CBG q 1-2 hours, more closely in T1DM patients

- If CBG>12, should give bolus of R or Humalog to lower BG, esp if TIDM given risk of DKA
Example 3

- Patient with type 1 DM, on Glargine 16 units QHS and Humalog 6 units TID

- Planned to have cataract extraction

- Should take usual dose of Glargine night before surgery

- Post-op CBG 14 – how much insulin would you give?
Example 3 (cont’d)

- Determine whether the patient is able to eat

- Even if not eating, need to correct hyperglycemia with a small amount of Humalog/short acting insulin

- Correction factor:
  - TDD = 16 + 6x3 = 34 units
  - 90/34 ~ 3 i.e. 1 unit will lower his BG by 3mmol/L

- Therefore, if target BG = 8, will need 2 units of insulin to lower BG from 14 to 8
Example 3 (cont’d)

- If eating, will need extra insulin to cover carbohydrates in meal – useful to know pt’s insulin to carbohydrate ratio for this e.g. 1 unit for 10g or 15g of CHO

- Depending on what pt is eating, may need a total of 4-6 units

- If blood glucose above 16 in pt with TIDM, check electrolytes and serum ketones to r/o DKA
Longer duration of surgery

- For surgery >2 hours in patients with TIDM or T2DM on insulin, usually require an insulin infusion, to be started on the morning of surgery

- Also need i.v. D5W @ 75-100cc/hour

- To calculate starting hourly rate: divide TDD by 2 and then by 24 hours
Example 4

- 65 y.o. man with T2DM undergoing AAA repair

- Suboptimal glycemic control (A1C = 8.6%)

- On NPH 14 units QAM and 30 units QHS with Novorapid AC meals – approximately 16 units TID

- What will you order for him?
Hold usual am dose of insulin

CBG at 0700h on am of surgery

Mix 50 units of insulin R in 500cc D5W such that 1 unit = 10cc
- TDD = 14 + 30 + 16x3 = 92 units
- Hourly infusion rate: 92/2 = 46, divide by 24 hours ~ 2 units/hour

CBG q2h, call MD if BG<4 or >12
Example 4 (cont’d)

- Also start iv D5W @ 75cc/hour: this iv line is used to rapidly correct hypoglycemia if it develops

- How much would you give if hypoglycemia occurs?

- If elevated BG>10-12, can increase iv rate by 0.5 units/hour and recheck in 2 hours
Example 5

- Patient with T1DM on an insulin pump, undergoing surgery

- Usual recommendation is to continue basal rate on pump without any bolus insulin unless BG is high – then use correction factor

- If complex or major surgery and not comfortable with pump use, may discontinue pump and switch to iv insulin using same calculation – TDD/2/24hours ~ TDD/50!
Post-op management

- When the patient is able to eat, can restart oral agents including sulfonylureas such as Glyburide, Gliclazide and Metformin (as long as renal function is stable)
  - May need lower dose if not eating well e.g. start at half their usual dose and titrate up over 48-72h

- If pt is not eating but blood sugars are elevated, will need insulin
  - Infusion vs. sliding scale?
Post-op management

- Insulin infusions are required for all pts with Type 1 Diabetes given the risk of DKA
  - TDD/50 units /hour, titrate based on blood sugars
  - Should have capillary glucose monitoring at least q3-4h
  - Do not hold iv insulin more than 15-20minutes, if low, treat and restart at a lower rate
  - Always run i.v. D5W in a second line (75cc/hour)
Post-op management

- Patients with T2DM on insulin may be treated with a sliding scale of regular insulin R based on blood sugars if not eating
  - If not eating but fasting blood sugars consistently elevated (due to stress response, high cortisol levels) – use NPH at bedtime (0.1u/kg) and correct high blood sugars during the day with R sliding scale starting at BG above 10

- If on feeds, recommend using NPH q12h
Post-op management

- If pt is eating but insulin requirements are not clear
  - Recommend using some basal insulin e.g. NPH at bedtime with a sliding scale of Humalog or Novorapid with meals (not at hs)
  - Key is to give some short acting insulin with meals even at relatively normal blood sugars to avoid hyperglycemia
  - If previously on pre-mixed insulin, can restart at lower doses e.g. half their usual home dose and titrate up over the next 48-72h based on CBG
Summary

- No clear evidence exists to guide peri-operative management of Diabetes or glycemic targets
  - Hypoglycemia and marked hyperglycemia should be avoided

- There is good RCT data to suggest that post-cardiac surgery patients have decreased morbidity and mortality with tight glycemic control through intensive insulin therapy
Summary

- For patients with T2DM who are well controlled on OHAs, holding meds on the am of surgery is usually sufficient

- Patients with T2DM on insulin or TIDM undergoing short procedures < 2 hours can be treated with basal insulin s.c. on the morning of surgery with a reasonable sliding scale for BG > 10-12
Summary

- Patients with T2DM on insulin or T1DM undergoing major surgery should be maintained peri-operatively on an insulin infusion, with a starting dose of ~ TDD/50 units/hour, along with D5W @ 75-100cc/h.

- Patients with T1DM should be monitored more closely, and treated more aggressively if BG>12-14 given the risk of DKA.