



Peri-operative Management of the Patient with Diabetes

Magnitude of the Problem.....

30%-50% of patients with diabetes will require some surgery within their lifetime.

12% of the general population without diabetes

Regulatory Hormones a Background



Hypoglycaemic

Insulin

Glucagon-Like Peptide-1

Proglycaemic

Glucagon

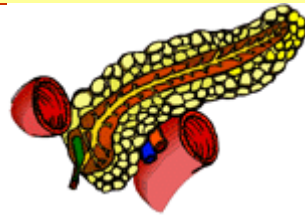
Catecholamines

Growth Hormone

Glucocorticoids

Somatostatin

Regulatory Hormones a Background



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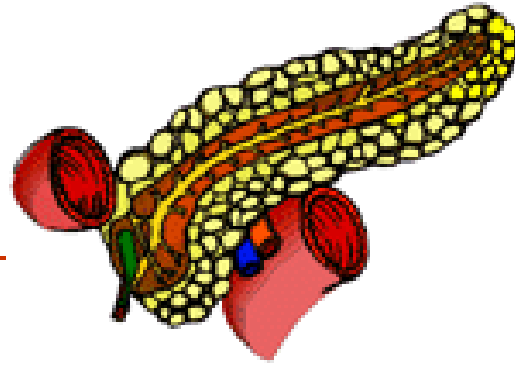
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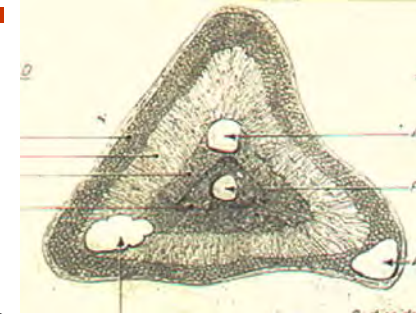
Glucocorticoids

Somatostatin



Cortisol +ve

Catecholamines +ve



Liver

Growth

Hormone

Pituitary



Proglycaemic hormones...

Glucagon.....Ketogenic

Catecholamines...Ketogenic...

Glucocorticoids....Ketogenic

Increase in stress

Pre op evaluation

Type and duration of diabetes

Complications- CAD, CKD, Autonomic neuropathy

Medications

Control of diabetes- HbA1c, Hypos

Associated disorders- Hypertension, Dyslipidemia

Preoperative Considerations, The threatening Trio.....

- 1. Silent Myocardial Ischemia**
- 2. Renal Dysfunction (Elevated Creatinine)**
- 3. Peripheral/Autonomic neuropathy**

Preoperative Considerations, The threatening Trio.....

1. Silent Myocardial Ischemia:

ECG: may not show anomaly

Autonomic neuropathy blunts angina

>5-years of diabetes mellitus: do preoperative TMT.

Empirical Beta-adrenergic blockade preoperatively

Preoperative Considerations, The threatening trio...(contd.)

2. Renal Dysfunction (Elevated Creatinine)

**70% reduction in a GFR with a creatinine of
>1.5mg/dl**

**Intravenous fluid sensitivity is high: propensity
for volume overload.**

**Increased half-life of insulin and increased risk of
hypoglycemia.**

Increase the frequency of glycemic monitoring.

Preoperative Considerations, The threatening trio...(contd.)

3. Peripheral/Autonomic neuropathy:

Impotence

**Postural drop in Blood pressure
($>20\text{mmHg}$ /or $>10\text{mmHg}$)**

3. Peripheral/Autonomic neuropathy (contd...):

Increased vascular damage and poor post-op healing

Increased decubitus ulceration

Intra-operative hypotension/ hypertension

Perioperative cardiac arrhythmias

Gastroparesis: increased aspiration

Hypoglycaemia unawareness

Does hyperglycemia have a detrimental impact?

Chronic Hyperglycemia:

**200-250mg/dl related to complications-
4 fold increase in death.**

Target: 140-180mg/dl

Preoperative preparation.....

Ideal control.....

HbA1c < 7% (fructosamine < 310uU/ml).

Ideal: admit for 24-48hours prior to surgery.

Not practical.

Not Cost effective.

Preoperative preparation.....

The Continuation of Oral Hypoglycaemic agents...

Spectrum of Oral Hypoglycaemic Agents

Biguanides

Metformin (Biguanides)

Sulphonylureas

Glibenclemide, Gliclazide

Glipizide, Glimepiride

α -Glucosidase inhibitors

Acarbose

Meglitinides

Repaglinide, Nateglinide

Thiazolidinediones

Rosiglitazone , Pioglitazone

Gliptins (DPP4 inhibitors)

Sitagliptin, Vildagliptin

Oral Hypoglycemic Agents the need to continue.....

**Metformin.....traditional phobia of lactic acidosis:
some stop 48 hours before any surgery.**

Definitely: septic state, hypotension,

Renal or any major organ failure.

No increased risk if hypoglycemia when used alone.

Sulphonylureas/ Meglitinides

Thiazolidinediones.....May be continued.

Oral Hypoglycemic Agents

Acarbose: Avoid due to GI side effects

DPP4 inhibitors: Avoid on the day of surgery because of delayed gastric emptying

Anaesthetic Considerations.....

Epidural Anaesthesia:

No significant increase in catecholamines, counter-regulatory hormones and precursors of gluconeogenesis.

General Anaesthesia:

Isoflurane- increase in growth hormone and glucose levels

Enflurane- no significant impact on insulin, cortisol or glucose levels.

Halothane- mild increase in hyperglycaemia.

Peri-operative insulin and glucose dosing....

The Standard:

**When on:- Intermediate acting + Regular insulin
[Mixtard(30/70) or Humusulin(30/70)
or Bovine Mixact(30/70)]**

Give 2/3rds of the PM dose (previous night)

Give Half of the AM dose or only ½ NPH dose.

**Start on IV D5W at 100ml/hour and titrate
according to the IV glucose algorithm**

Peri-operative insulin and glucose dosing....(contd).

Glucose-Potassium-Insulin

- IV 5%Dextrose/ saline 100-150ml/hour**
- + 1.5g KCL to each litre.**
- + Regular Insulin: 12 Units/litre**

Glucose infusion 3.75-5 gm/hr + Insulin infusion 0.02u/kg/hour

Severe infection: 0.04u/kg/hour

Steroid-Dependent State: 0.04u/kg/hour

CABG or on Vasopressors:0.06u/kg/hour

Blood glucose/ 100= insulin units/ hr infusion

Hourly GRBS- insulin dose adjustment

NO ROOM FOR URINE SUGAR MONITORING

Peri-operative insulin and glucose dosing....(contd).

Changing over to regular dosing:

Overlap the IV infusion for at least two more hours with the subcutaneous insulin prior to discontinuing the IV insulin, maybe for longer if the infusion rates are high.

Twice daily Mixtard with top up Actrapid with lunch if the midmorning sugars are $>300\text{mg/dl}$

Morning dose depends on the midmorning sugar

(So change the dose the next morning)

Night dose depends on the fasting sugar

(So change the dose the same evening)

Hyperglycemia in the critically ill- what is the evidence?

- ❑ Hyperglycemia –Fasting blood glucose level \geq 100 mg/dl is common during critical illness.
- ❑ Illness-induced hyperglycemia was considered a beneficial, adaptive response
- ❑ Provides brain and the red blood cells with additional energy.
- ❑ However, hyperglycemia in response to critical illness is also associated with adverse outcome.

Intensive Insulin therapy in SICU

Van Den Berge et al, NEJM 2001

- ❑ Single center study in adult surgical ICU patients (n-1548; cardiac surgery and high risk or complicated non-cardiac surgery)
- ❑ 2 Groups
 - Intensive control arm (80–110 mg/dl)
 - Conventional treatment arm (180-200 mg/dl; started when bl. Glu > 215 mg/dl)
- ❑ Arterial blood glucose measurements- 1 to 4 hrly
- ❑ Central venous continuous insulin infusion
- ❑ Dextrose 20% was administered on the first day and thereafter, enteral nutrition was started.

Intensive Insulin therapy in SICU - Results

- Intensive insulin therapy
 - Lowered ICU mortality from 8.0 to 4.6% (↓ 3.4%)
 - Lowered in-hospital mortality from 10.9 to 7.2% (↓ 3.7%).

- Intensive insulin therapy reduced morbidity by preventing organ failure as evidenced by
 - reduction of duration of mechanical ventilation
 - decrease in the incidence of acute kidney failure and of polyneuropathy
 - preventing severe infections.

Intensive Insulin therapy in MICU

Van Den Berge et al, NEJM 2006

- ❑ 1200 Patients
- ❑ In-hospital mortality was 40.0% in the control group and 37.3% in the intervention group (not statistically significant)
- ❑ Similar organ-protective effects were documented, but not as strikingly as in the surgical study.
- ❑ A larger proportion of patients in medical ICU who were admitted with established organ damage, possibly reducing the opportunity of prevention by glucose lowering.

VISEP- Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008

Brunkhorst FM et al

- Multicenter trial (n = 537) was designed as a four-arm study to assess
 - the difference between two choices of fluid resuscitation (10% pentastarch *vs.* modified Ringer's lactate)
 - the efficacy and safety of intensive insulin therapy in patients with severe sepsis and septic shock
- Blood glucose targets
 - intervention (79–110 mg/dl)
 - control (180–200 mg/dl) groups.

WISEP- Results

- ❑ The insulin arm of the study was stopped early, because of increased hypoglycemia (12.1%) in the intensive insulin therapy group
- ❑ The fluid resuscitation arm of the study was also suspended because of increased risk of organ failure in the 10% pentastarch arm.
- ❑ The 90-d mortality was 39.7% in the intensive *vs.* 35.4% in the conventional treatment arm.

Impact of tight glucose control by intensive insulin therapy on ICU mortality and the rate of hypoglycaemia: final results of the glucontrol study

Devos P et al Intensive Care Med 2007

- ❑ Multicenter RCT (n = 1101)
- ❑ Tight glycemic control (80–110 mg/dl) vs. an intermediate glucose control (140–180 mg/dl)
- ❑ Impact on survival in a mixed population of critically ill patients
- ❑ Stopped early -increased incidence of hypoglycemia (9.8%).
- ❑ Hospital mortality did not differ between the intensive insulin therapy group (19.5%) and the control group (16.2%).

NICE-SUGAR (Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) multicenter study

NEJM, March 2009

- ❑ Multicenter study - 6100 patients
- ❑ Tight glucose control (81-108 mg/dl) vs. usual care (<180 mg/dl)
- ❑ Targeting tight glucose control increased 90-d mortality from 24.9 to 27.5% (↑2.6%)
- ❑ Excess deaths were attributed to cardiovascular causes (41.3 vs. 35.8%)
- ❑ No difference in organ failure or septicemia
- ❑ Severe hypoglycemia was more common in the tight control group (6.8%) as compared to usual care (0.5%)

Real-Time Continuous Glucose Monitoring in Critically Ill Patients

DIABETES CARE, VOLUME 33 (3), MARCH 2010

- A total 124 patients receiving mechanical ventilation were randomly assigned to 2 groups
- Intensive insulin therapy to maintain normoglycemia (80–110 mg/dl)

the real-time CGM group

$n = 63$

**glucose values
given every 5 min**

the control group

$n = 61$

**selective arterial
glucose measurements
according to an algorithm
(simultaneously
blinded CGM)
for 72 h**

Table 2—Primary and secondary end points

	Real-time CGM	Control	P
n	63	61	
Mean sensor glucose (mg/dl)	105.8 ± 18.1	110.6 ± 10.4	0.076
Mean blood glucose (mg/dl)	113.2 ± 14.3	114.0 ± 11.0	0.731
Time of glucose <110 mg/dl (%)	59.0 ± 20.4	55.0 ± 18.0	0.245
Time of glucose <150 mg/dl (%)	94.2 ± 7.9	92.9 ± 8.4	0.395
Time to reach 110 mg/dl (min)	150 (48–275)	118 (45–240)	0.557
Rate of hypoglycemia (% of patients)	1.6	11.5	0.031
Insulin (IU/72 h, study period)	104 ± 78	110 ± 52	0.320
Length of stay	17.4 ± 14.4	16.8 ± 12.2	0.785
ICU mortality (%)	22	26	0.677
Hospital mortality (%)	33	31	0.849

Data are means ± SD, median (interquartile range), or %.

In critically ill patients, real-time CGM reduces hypoglycemic events but does not improve glycemic control

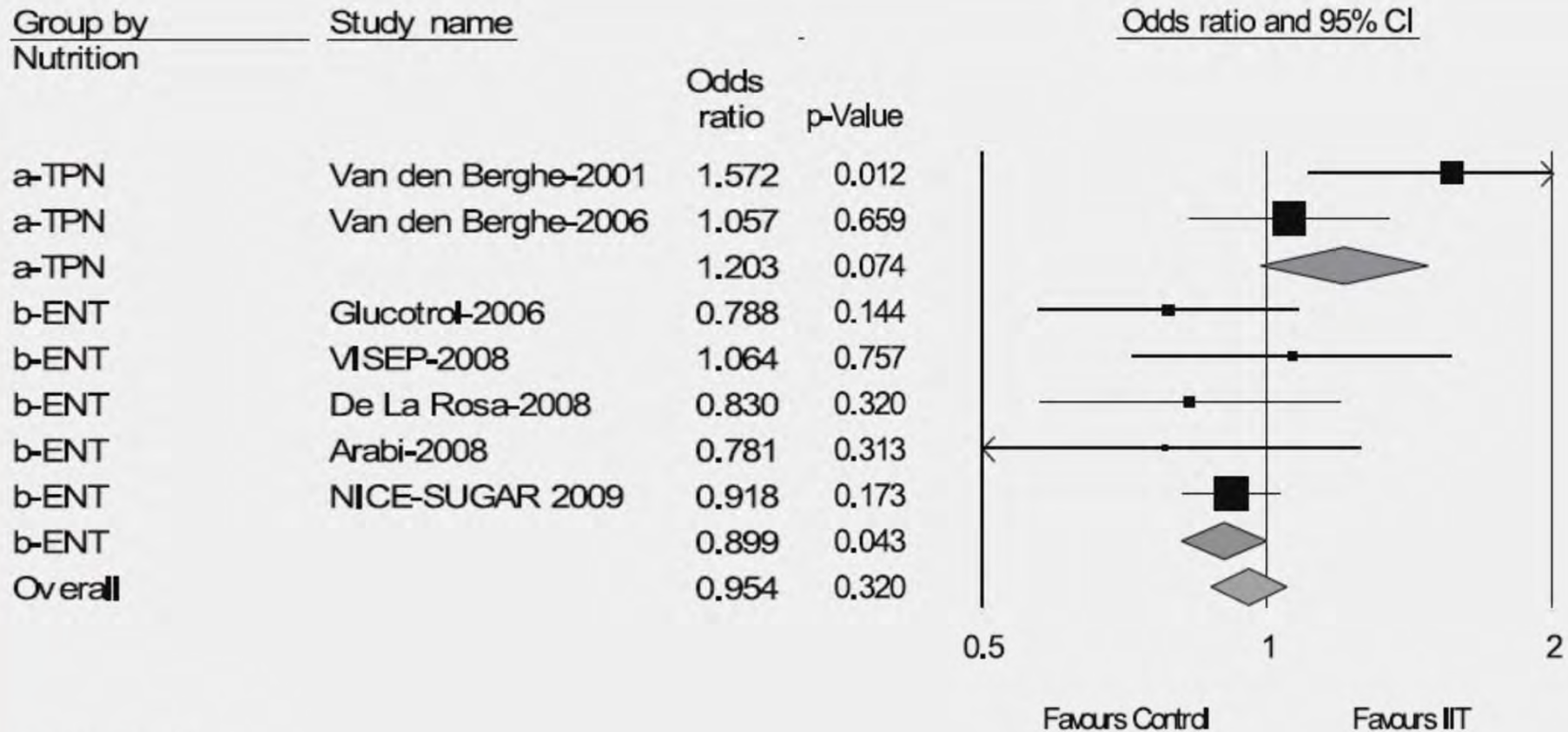
Toward Understanding Tight Glycemic Control in the ICU

A Systematic Review and Meta-analysis

CHEST 2010; 137(3):544–551


Study	ICU	No of pts	Insulin dose U/day		Mortality %	
			Control group	Intervention group	Control group	Intervention group
Vanden Berge 2001	SICU	1548	33	71	10.9	7.2
Vanden Berge 2006	MICU	1200	10	59	30.1	29.9
Glucontrol 2007	Mixed	1078	10	43	25.9	24.7
WISEP 2008	Mixed	537	5	32	15.3	18.7
De La Rosa	Mixed	504	12	52	32.4	36.6
Arabi 2008	Mixed	523	31	71	13.6	16.9
NICE SUGAR 2009	Mixed	6022	17	50	20.8	22.3

Effect of intensive insulin therapy (IIT) on 28-day mortality




Meta Analysis


FIGURE 2. Effect of intensive insulin therapy (IIT) on 28-day mortality. a-TPN = parenteral nutrition; b-ENT = enteral nutrition.

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- ❑ There is no evidence to support the use of intensive insulin therapy in general medical-surgical ICU patients who are fed according to current guidelines.
 - ❑ Tight glycemic control is associated with a high incidence of hypoglycemia and an increased risk of death in patients not receiving parenteral nutrition.

Joint statement by AACE and ADA

Beneficial effects on outcomes can be derived
from glucose in the target range
between 140 and 180 mg/dl
in critically ill patients

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- ❑ Glucose is not just an innocent bystander during critical illness because altering its circulating levels has been shown to affect outcome in both directions.
 - ❑ Lowering blood glucose has the potential to prevent secondary injury to threatened vital organ systems and thereby to improve outcome.
 - ❑ The optimum level as well as the optimal mode to reach that level should be defined.



□ Maintain blood glucose levels as close to normal as possible

without evoking

- unacceptable glucose fluctuations
- hypoglycemia
- hypokalemia.

THANK YOU

