Insulin in Special Situations: Surgery

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In the 1960s surgery in diabetics was associated with 4 to 13% mortality.1,2 Due to better pre-operative assessment and judicious use of insulin per-operatively things have changed since then.

It has been seen that about 9% of all hospital beds at any given point is occupied by diabetics, and that about 11.3% of all surgeries were performed in patients who were diabetic. In fact diabetics have a 50% chance of undergoing surgery during their lifetime. Patients with diabetes undergo surgical procedures at a higher rate than do non-diabetic people.3

Diabetics are especially at higher risks of undergoing certain surgical procedures. Ophthalmological procedures are 1.5 times more commonly done in diabetics as compared to non-diabetics. Peripheral vascular disease, terminal renal failure, diabetic foot disease and coronary artery disease often require surgical intervention.

Diabetics need greater attention perioperatively, as they are prone to have more problems unless cared for. The patients are prone to develop acute hyperglycaemic complications. These are more common in patients of type1 diabetes, type 2 diabetics who are insulinopenic and in those in whom pre-operative glycaemic control is poor.

Hypoglycaemia is again more common perioperatively. In the perioperative state hypoglycaemia may be undetected as symptoms are difficult to identify in an ill, drowsy, sedated or anaesthetized patient leading to fatal outcome.

The treatment of diabetes perioperatively should ideally be done by a specialized “diabetes care team”. But unfortunately it is not possible to have such a team for every surgical set up. Usually the responsibility of treating diabetes is entrusted on the junior most doctor with the hope that he/she would know the latest management of diabetes. Unfortunately he/she is often unaccustomed with the practical aspects of management of diabetes in a surgical patient. This often leads to additional iatrogenic complications due to use of irrational insulin regimens.

Metabolic Response to Surgery

Surgery causes a prototypical stress response in a diabetic. There is a combination of anti-insulin effects of surgical stress and direct catabolic effects of stress hormones.

Anti-insulin effect of surgical stress: In addition to insulin resistance induced by circulating stress hormones, namely catecholamines and cortisol, surgical stress has a deleterious effect on pancreatic beta cell function. Plasma insulin levels fall and insulin secretory responses to glucose become impaired during surgery. The mechanism of impaired beta cell responsiveness during surgical stress is commonly ascribed to catecholamines; however, the defect poorly correlates with ambient intraoperative catecholamine levels. Post operatively, however, there is close inverse correlation between plasma epinephrine and insulin level.

These anti-insulin effects of the metabolic stress response essentially reverse the physiological anabolic and anti-catabolic actions of insulin. The important anabolic actions of insulin that may be reversed or attenuated during stress of surgery include, 1) stimulation of glucose uptake and glycogen storage 2) stimulation of amino acids uptake and protein synthesis by skeletal muscles 3) stimulation of fatty acid synthesis in the liver and storage in adipocyte and 4) renal sodium reabsorption and intravascular volume preservation. The anticytotic effects of insulin include 1) inhibition of gluconeogenesis 2) inhibition of lipolysis 3) inhibition of fatty acid oxidation and ketone body formation and 4) inhibition of proteolysis and amino acid oxidation. Thus inhibition of insulin secretion and action shifts the perioperative milieu towards hypercatabolism through variety of mechanisms. This can be overcome only by giving insulin perioperatively in dosages enough to overcome the relatively increased insulin resistance.4-6

Direct catabolic effects of stress hormones: The catecholamines stimulate gluconeogenesis and glycogenolysis and inhibit glucose utilization by peripheral tissues.

In addition glucagons levels are augmented by catecholamines, which also exerts effects similar to those of catecholamines.

Thus, the combination of relative hypoinsulinemia, insulin resistance and excessive catabolism due to the counter-regulatory hormones is a threat to glucose homeostasis in all patients with diabetes undergoing surgery, particularly in those whose preoperative metabolic control is less perfect. The degree of metabolic disturbance is, obviously, related to the amount of trauma associated with surgery. The logical conclusion is that insulin therapy will be needed perioperatively in the majority of patients with diabetes undergoing major surgery.

Diabetics are more prone than non-diabetics to develop complications perioperatively. There are increased chances of developing cardiac complications in the form of acute coronary syndromes and acute myocardial infarction.8 The patients are also more prone to develop both fatal and non-fatal arrhythmias. Autonomic disturbances may lead to increased incidence of problems like vomiting, abdominal distension, bladder atony and altered regulation of breathing.

Insulin is necessary in the early stages of inflammatory response, but it does not affect collagen formation after the first ten days. Healing epithelial wounds unlike deep

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wounds have minimal leucocyte infiltration and hence their healing is not impaired in diabetics. However, deeper wounds need good glycaemic control for proper healing. Alteration in leucocyte function, decreased chemotaxis and impaired phagocytic activity of granulocyte and reduced intracellular killing of pneumococci and staphylococci are noted during hyperglycemia in experimental animal studies. High serum ketones also provide a permissive milieu for the development of infectious complications.9

In a Danish study 224 diabetic and 224 matched non-diabetic subjects reported wound infections rates of 5.8% and 5.4% respectively in these groups. It thus appears that with proper perioperative glycaemic control wound infection rates can be drastically reduced.10

Principles of Management

The management of the case would depend on the severity, nature of surgical trauma, the duration of perioperative fasting, whether the patient is insulin dependent, the pre-existing diabetic therapy and the pre-existing level of metabolic control.

The management protocol should be “safe” and yet be “simple” so that it can be followed and monitored by someone who is not a diabetologist. The treatment goals should be in achieving a glycaemic level between 110mg/dl and 200 mg/dl. In a study perioperative morbidity was shown to be higher if levels were lowered below 110mg/dl. On the other hand postoperative infections and perioperative metabolic complications were more at levels higher than 200 mg/dl.11

Thus with a safe protocol achieving the above level of glycaemic control the major outcome measures of surgery - duration of hospital stay, morbidity and rates of wound infections and other operative complications are generally comparable in diabetic and non-diabetic patients.

Pre-operative Assessment

Proper liaison between surgeon, anaesthetist and diabetes care team is essential. Pre-operatively glycaemic control should be optimized. All associated co-morbidities should be detected, assessed and treated properly. A holistic approach is important. Diabetics often have numerous chronic complications, which need to be borne in mind before contemplating surgery.

Pre-operative evaluation should include the following:

• Fasting and post-prandial blood glucose levels
• Blood urea, serum creatinine and electrolytes
• Urinary albumin/creatinine ratios
• Electrocardiography and echocardiography
• Assessment of retinopathy
• Assessment of autonomic neuropathy
• Atlanto-axial joint mobility and exclusion of stiff neck syndrome, which might lead to difficult airway management.

For Those on Non-pharmacological Therapy Only

Usually do not require any special pre-operative intervention. Blood glucose should be monitored intra-operatively in case of major surgery (i.e. any surgery where patient requires general anaesthesia for at least one hour).

If at any point of time blood glucose is above 200mg/dl intravenous infusion of insulin and dextrose should be considered and more frequent monitoring of blood glucose is recommended.

For those on Oral Agents

Ideally patients should have good control (fasting blood glucose less than 126 mg/dl and other values less than 200 mg/dl).

Long acting sulphfonylureas should ideally be stopped about 5 days before surgery. Shorter acting sulphonylureas can be used up to one day before the procedure, provided glycaemic control is good.

Although metformin has a short half life ~ 6 hours, it is prudent to temporarily withhold metformin 48 hours before the surgery, especially in sick patients and those undergoing procedures that increase the risks for renal hypoperfusion, tissue hypoxia and lactate accumulation and may only be restarted 72 hours post-operatively after proper re-evaluation of renal functioning.

Glitazones may be discontinued on the day of surgery. Similarly, alpha glucosidase inhibitors are of no use in the peri-operative patient until he resumes eating.

Patients with good metabolic control can be admitted on the day before surgery

Those who are poorly controlled and awaiting major surgery should be admitted 2-3 days before surgery and should be switched over to short acting insulin therapy and stabilized metabolically before venturing surgery.

For those on Insulin

Ideally admit such patients 2-3 days prior to surgery and preferably stop long-acting insulins and switch the patient to short-acting insulins. NPH may be used at bedtime. Some advise dosage reduction (30% reduction) of NPH dosage prior to surgery.12,13

On the Day of Surgery

The surgery should be preferably be performed early in the morning. Breakfast is omitted and the morning dose of insulin or sulphonylurea is withheld. Blood glucose is perioperatively monitored 2 hourly. Start i.v. insulin and glucose (GKI or separate lines) in those who were on insulin or those on oral agents undergoing major surgery. Blood glucose is monitored hourly per-operatively (or more frequently if need be).

Peri-operative Use of Insulin

Previously various workers have tried various insulin regimens. Initially, people had tried to omit insulin use altogether perioperatively with the idea that it would reduce the incidence of hypoglycaemic episodes. But it worsened catabolism and was associated with serious metabolic complications and increased perioperative mortality.14

Thereafter some workers tried giving half to two-thirds of the morning dosage subcutaneously followed by glucose infusion. But due to variable absorption this regimen fell into disrepute.15

Thereafter i.v. boluses of soluble insulin were tried either empirically or according to sliding scale but the effects were very unpredictable with wide fluctuations in blood glucose levels.16
Workers next used low dose (0.5 to 1 U/hour) i.v. insulin with glucose but such low dose insulin often failed to prevent metabolic decompensations.27

Finally what has emerged is high rate of insulin delivery (2-4 U/hour) along with glucose infusion (5-10 gms/hour).

Such a regimen has wider safety margin and greater flexibility. It decreases the catabolic response to surgery and normalizes insulin sensitivity and proper substrate utilization in the postoperative period.18,19

Delivery Systems

Separate Line System

In this system, one infusion line is used to deliver 10% dextrose solution at 100ml/hr preferably using a high precision pump while the soluble insulin infusion can be given either through a separate vein or ‘piggy-backed’ (preferable) into the glucose line and the rate is titrated to maintain blood glucose in target range.20

This system is especially helpful in those who are metabolically unstable and are requiring variable dosages of insulin. It is also very helpful in those requiring higher insulin dosages, like those undergoing cardiac surgery and caesarean section.

This system needs more dosage adjustments than the GKI regimen and hence more medical attention. Overall outcome with regards to glycaemic control, hypoglycaemic events, post-operative infection rates and duration of stay in hospital was similar to GKI regimen.

Glucose-potassium-insulin or GKI Regimen

Also known as the Alberti regimen, it involves starting an i.v. infusion of a pre-mixed cocktail of 10% glucose solution and 10 mmol of potassium chloride and 15 units of soluble insulin, which is to be infused at the rate of 100ml/hour.21

This regimen can only be given to a patient who is metabolically stable with reasonable pre-operative blood glucose levels. After the start of the infusion the blood glucose levels are monitored hourly. Separate infusion bags are prepared using 500 ml of 10% dextrose with either 10, 15 or 20 units of soluble insulin added. To this potassium chloride is added. The potassium content can be varied according to serum potassium levels. Special caution needs to be taken in patients with compromised renal function or those on ACE inhibitors.

When blood glucose levels fall below 110mg/dl the bag containing 10 units of insulin is run and when blood glucose level is above 200mg/dl then the bag containing 20 units of insulin is run. At all times the rate of infusion is 100 ml/hour.

This regimen has additional risk of causing dilutional hyponatraemia, if i.v. fluids need to be continued beyond 24 hr; in such situations additional fluid and electrolytes may need to be infused through a separate i.v. channel.

The GKI regimen is considerably simpler and because insulin is given in balanced proportion the infusion rate is not so critical.

Post-operative Management

After surgery the patients tend to be less carefully monitored by the surgical team. It is during this period that patient often develops hypoglycaemia, which might go undetected.

As soon as the patient is able to eat, we can restart subcutaneous injections of insulin. The i.v. insulin should be discontinued after about one hour of resumption of subcutaneous insulin injection.

It is always preferable to continue using subcutaneous insulin even in those patients who were receiving oral agents pre-operatively for the initial post operative period (10 days or until stitches are off), as strict glycaemic control is required early on for proper wound healing and insulin usage during this period allows greater ease of achieving tight glycaemic control.

The insulin requirement increases over baseline requirements on the day of surgery and the first two post-operative days and usually comes down to normal levels on the third post-operative day in an otherwise uncomplicated surgery. The mean insulin requirement increases about 66% on the day of surgery and increases by about 23% and 15% over baseline requirements on the first two days following surgery.22

Sulphonylureas, alpha glucosidase inhibitors and glitazones can be restarted in those who were pre-operatively well controlled on these, once the patients started eating.

Metformin should be restarted after 72 hours only after re-evaluation of renal status and documentation of normal renal function post-operatively.23

Special Situations

Emergency Surgery

It is important to find out what medication the patient was receiving and when did the patient receive the last dose of oral agents or insulin.

If possible the surgical procedure should be delayed until the patient can be metabolically stabilized. Usually it is possible to stabilize a patient with “separate line” regimen within about 4 hours. Frequent monitoring of blood glucose is advisable and the case should preferably be managed under the guidance of a diabetes specialist care team.

Open Heart Surgery

Glucose containing fluids are used to prime the bypass pumps. There are unusual degrees of trauma to tissues during bypass surgeries and inotropes with catecholamine like action are often used. This, along with the hypothermia induced per-operatively increases insulin resistance. Thus, very high dosage of insulin may be required perioperatively in patients undergoing open-heart surgeries.24-25 However, with newer surgical techniques, like ‘beating heart surgery’ for CABG the surgical stress associated with cardiac surgery is coming down.

It is preferable to use “separate line” infusions in patients undergoing heart surgery.

In a study of 340 diabetic and 2522 non-diabetics undergoing CABG there was marginal increase in operative mortality in diabetics (1.8% vs. 0.6%).26

In another study, 291 diabetics (95% type 2 diabetics) underwent CABG (40% had pre-existing retinopathy, nephropathy or neuropathy at baseline). During hospitalization (median 7 days), 27% of the patients had
adverse outcomes (non-fatal strokes, acute myocardial infarctions, septic complications or died). Such complications occurred more frequently in those whose glycaemic levels were in the highest quartile on the first post-operative day. Adverse events were increased by 17% for each 1 mmol/L increase in blood glucose levels above 6 mmol/L.27

But if good glycaemic control is achieved then the overall mortality of cardiac surgery in diabetics is almost similar to non-diabetics.

Minimal Access Surgery

It has been found that the stress of surgery and the degrees of metabolic derangement in those undergoing minimal access surgery is similar to conventional approach surgery and hence they should be managed like those undergoing conventional approach surgeries.28 However, the i.v. insulin regimen is needed for a shorter duration.

Caesarean Section

Pregnancy itself is a state of relative insulin resistance and to make matters worse drugs like ritodrine used for labour and dexamethasone used for induction of foetal lung maturation worsens insulin resistance. Hence, very high doses of insulin are required. When using a GKI regimen it is advisable to start with a bag containing 20 units of insulin. Use of separate line infusion is preferable in this situation for smoother metabolic control.

After the delivery of placenta, insulin requirement drops drastically and at this point dose reduction of insulin (or, stopping insulin altogether in cases of gestational diabetes) and frequent monitoring is required.

Sub-cutaneous injections can be resumed (at lower than pre-operative dosage) once the patient is able to eat if the patient had pre-gestational diabetes.

Elderly

Special care is required in the elderly as they are more prone to develop macrovascular complications and they tend to have other co-morbidities that increase the incidence of post-operative complications. There is poor tolerance of hypoglycaemia in the elderly. Fluid overload has to be avoided as their renal function as well as cardiac functioning is often compromised.29

Thus in conclusion it can be said that surgery is a frequent requirement for diabetic patients and that in the past it has been associated with increased mortality and morbidity. It is likely that with recent advances in surgical science, anaesthesiology, intensive insulin therapy and above all close monitoring, the perioperative fate of diabetic patients has improved in recent times.

References
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