



Perioperative Management of Diabetes Mellitus Patient

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ABSTRACT

Diabetes mellitus (DM) is the most common metabolic disorder, affecting presently 62.1 million (as per 2011) in India. By 2030, India's diabetes numbers are expected to cross the 100 million mark. Since, the incidence of diabetes is rising exponentially; the number of patients with diabetes is also rising. Diabetes related co morbidities increase the need for surgery and other operative procedures; it is not surprising that at least 10%-12% of the patients undergoing surgeries have diabetes and this percentage is also likely to rise.

People with diabetes undergoing surgery have an almost 50% greater chance of post operative mortality than those with normal glucose tolerance and there is also a threat of post operative morbidity. Mortality rates in diabetics following surgery are estimated to be 5 times greater than in non diabetic counter parts, often due to end organ damage and infections. Stress of surgery stimulates catabolic hormone secretion. Further, for people with pre operative hyperglycemia, unaware of their diabetes have up to 12 times higher risk of perioperative deaths than non diabetic counter parts; which may accelerate to 40 times, if the hyperglycaemia persists post operatively. Optimal glycemic control in the perioperative period decreases infection rate and other complications.

Some diabetic patients need optimization and improve blood glycemic control before surgery. Tight glycemic control with intensive insulin therapy (IIT) has shown to reduce morbidity and mortality and improve survival after cardiac surgery. However, recent evidence of severe hypoglycaemia and adverse outcomes with tight glycemic control brings its safety and efficacy into question. Hence, avoidance of hyperglycemia is clearly beneficial in the perioperative patients, although IIT continues to be standard of care, current consensus guidelines recommend less stringent glycemic goals, typically between 80-150mg/dl.

KEY WORDS: Diabetes mellitus, Glycemic control, Peri-operative, Hyperglycemia, Hypoglycaemia, Intensive insulin therapy.

Introduction

Diabetes mellitus is a major metabolic disorder; diabetic patients constitute 12%-25% of the

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hospitalized patients [1]. Besides, surgery is associated with high morbidity and mortality rates in diabetic patients [2-3]. Anaesthesia and surgery resulting in metabolic stress lead to metabolic derangements, resulting in Hyperglycemia [4]. Hyperglycemia is associated with increased risk of adverse outcomes in hospitalized patients, irrespective of whether patient is known to have diabetes or not [5-8]. For the surgical patient, there is a strong correlation between hyperglycemia and increased complications following surgery, especially nosocomial infection [6].

Pre operative glycemic control also influences the risk of post operative wound infection, with the recent study suggesting HbA1c $\geq 7\%$ doubles this risk. In this context tight glycemic control is a benefit in hospitalized patients. However, recent evidence of severe hypoglycaemia and adverse outcomes with tight glycemic control brings its safety and efficacy into question; hence, hypoglycemia should be avoided in perioperative patients. Treatment of post operative hyperglycemia reduces the risk of postoperative complications of cardiac surgery as well as morbidity and mortality in ICU [9]. Diabetic ketoacidosis though avoidable, still remains a possible cause of post operative deaths. The impact of surgery, fasting and interruptions to routine therapy contribute to poor glycemic control, which intern is a significant factor leading to the increased morbidity, mortality and length of hospital stay in patients with diabetes undergoing surgery.

Targets for therapy

1. Elective surgery should be postponed if glycemic control is poor (HbA1c $\geq 9\%$).
2. BGL should be kept between 90-180 mg/dl during perioperative period.
3. Hypoglycemia should be avoided.
4. For critically ill patients, who require admission to ICU, post-operatively, a “tighter” BGL target (e.g 80-110 mg/dl) may not exhibit any benefit.

The optimal blood glucose range in the post-operative period may be dependent on the clinical context. In the ICU where close supervision is possible, maintaining blood glucose levels between 80-110 mg/dl has been shown to significantly reduce the mortality [9] in some studies(van den Berghe et al 2001,2006),while increase in mortality in others [10] (the NICE-SUGER

study investigators,2009). In critically ill patient, intravenous (IV) insulin therapy, BG targets of 140-180 mg/dl effectively maintains glycaemia control avoiding hypoglycemia. However, tight glycemic control; BG 80-110 mg/dl, are no longer recommended due to adverse outcomes associated with severe hypoglycaemia[11,12].

Perioperative response to surgery and anaesthesia

Surgery and anaesthesia invoke neuroendocrine stress response with catabolic hormone secretion, perioperative starvation, anaesthetic techniques, drugs, altered consciousness during general anesthesia, circulatory disturbances with altered absorption of subcutaneous insulin and immobilization [13-15]. Hyperglycemia promotes reactions of non-enzyme glycosylation leading to abnormal protein formation, deposition of glycation end products, lowering wound's tensile strength and stability. Leukocyte function is also deranged with reduced capability of phagocytosis and chemo-taxis, thereby making diabetic patients more vulnerable to infection and inflammation. Administration of insulin is crucial for early development of granulation tissue and collagen synthesis.

Preoperative Evaluation of patients with diabetic mellitus

For elective surgery, the potential problems should be identified, corrected and stabilized before surgical procedures. Preoperative evaluation of diabetic patients has to be very comprehensive, includes assessment of metabolic control and any diabetic associated complications, including macro vascular (coronary artery disease, cerebrovascular disease, peripheral vascular disease) and micro vascular (retinopathy, nephropathy and autonomic neuropathy), which could affect the surgical outcome.

Asymptomatic cardiac ischemia is relatively common in patients with diabetes. The presence of cardiovascular risk factors should prompt evaluation; at minimum by resting electrocardiography and echocardiography, however, computerized stress test (CST) is justified in suspected cardiovascular disease. Cardiac autonomic neuropathy may expose diabetic patients to perioperative hypotension, so the presence of orthostatic hypotension, resting tachycardia, loss of normal respiratory heart rate variability and peripheral neuropathy should be sought.

Diabetic nephropathy is common in diabetic patients leading to renal dysfunction. Presence of albuminuria in 24hour urine is diagnostic for severe diagnostic nephropathy. Hence, renal function should be evaluated by urine albumin, serum creatinine level and BUN in all diabetic patients.

Diabetic autonomic neuropathy (DAN) is one of the common micro vascular complications of DM. It can be accompanied by diarrhoea; sweating or postural hypotension. DAN results in gastro paresis and there by delay in gastric emptying, enhancing the risk of regurgitation and acid aspiration during the induction of general anaesthesia. DAN may lead to unexpected perioperative bradycardia, hypotension, ventricular arrhythmias and sudden death.

Peripheral neuropathy is especially important for anesthesiologists since it can have impact on outcome, especially when regional anesthesia is planned. Current investigations have shown higher susceptibility of peripheral nerves to trauma and toxic effects of local anesthetics in diabetic patients [12]

Airway evaluation

Restricted mobility of upper cervical spines may result in difficult tracheal intubation in DM. All diabetic patients require thorough

airway evaluation; patients with type I DM can develop Stiff joint syndrome (SJS), disabling neck extension and resulting in poor or impossible visualisation of glottis opening during direct laryngoscopy. SJS must be assessed preoperatively by performing the “prayer’s sign”. The patient is asked to put his hands in the position for prayer, and if stiffed interphalangeal joints prevent palmar sides of fists to touch, the test is positive, it predicts difficult intubation.

Glycemic control

Preoperative metabolic control in diabetes is usually obtained by the level of glycosylated haemoglobin (HbA1c). Normal HbA1c is in the range of 4%-6%, while levels $>7\%$ indicate that current therapy is inadequate. These patients will have increased risk of perioperative complications they need higher doses of perioperative insulin supplementation, While, HbA1c $>8\%$ indicates bad metabolic control with expected worst outcome of surgery. Elective surgery should be postponed if HbA1c is $>9\%$.

A detailed history of type of diabetes and diabetic therapy is crucial during preoperative evaluation. Type I DM may be treated with various types of insulin whereas patients with type II might have been treated with diet, oral hypoglycemic agents (OH), and combination of OH and insulin. The physician providing services should be familiar with the type of insulin and type of OH (with regard to their duration of action, their adverse effects and drug interaction).

In type I DM patients, good perioperative outcome is anticipated if TDD of Insulin is within 30 units. However, risk of perioperative complications increases with TDD > 80 units due to Insulin resistance.

Therapeutic regimen in patients with type II DM can affect anesthetic management; hence,

details with regard to drug, its dose and mode of administration should be obtained and documented during preoperative evaluation. Drug interaction, duration of action and mechanism of action play a crucial role in the perioperative period and may lead to severe hypoglycemia and adverse outcome of surgery.

Preoperative management of patients with DM

Given that patients with DM are treated with variety of regimens and are scheduled for surgical procedures at varying times of the day, there is no established consensus for optimum perioperative management. The goal is to avoid: hypoglycaemia ($<70\text{ mg/dl}$) as well as excessive hyperglycemia ($>200\text{ mg/dl}$), loss of electrolytes (potassium, magnesium, phosphate), prevent lipolysis, proteolysis and ketogenesis [16-19].

Severe hypoglycemia during general anaesthesia represents the major risk for postoperative outcome in diabetic patients, which was responsible for the concept of “permissive hyperglycemia” in the past. High BG levels of 210 mg/dl and even 250 mg/dl in patients with bad metabolic control were tolerated[20-21].

Hence, in order to prevent and minimise adverse effects of both, hyperglycemia and hypoglycaemia, it is crucial to establish the target BG levels in the perioperative period. At present considerable controversy exists over the safety of different BG levels; tight glycaemia control ($80\text{-}110\text{ mg/dl}$) vs. liberal BG level ($110\text{-}200\text{ mg/dl}$)[22-23].

American College of Endocrinology (ACE) has recommended that BG should be in the range of $110\text{-}180\text{ mg/dl}$ in order to prevent effects of hypo-and hyperglycemia. ACE also states that significant variations in BG levels resulting attempts to achieve tight glycemia

control ($<110\text{mg/dl}$) cause more damage than BG itself [24-26]. The scheduled surgery need not be postponed if BG level on the morning of surgery is even 200 mg/dl . BG level $>360\text{ mg/dl}$ necessitates the postponement of scheduled surgery till BG control gets optimized.

Perioperative diabetes therapy

Perioperative management of the diabetic patient undergoing surgery is influenced by the type of diabetes, antecedent diabetic therapy (insulin, OH, combination of insulin and OH, diet), level of metabolic control, treatment of co-morbidities and length of surgical procedures [27-30].

Patients treated with diet alone, generally do not require any therapy during the perioperative period. According to the BG levels, small amounts of short acting insulin may be given with frequent BG monitoring (every 2-4 hrs) [31-34].

Perioperative management of the diabetic patient treated with OH depends on the type of preoperative OH, type and length of surgical procedure and expected resuming of oral intake. In the case of minor surgery, short acting OH should be continued till the morning of surgery (including the morning of surgery). Long acting OH should be held two days prior to surgery and should be replaced with short acting OH or short acting insulin. This resume should continue until patient resumes to eating. If for some reason, oral intake is discontinued for a longer period, some basal insulin should be provided. At present it is not that clear how to manage type II diabetics undergoing any surgery with moderate surgical stress. Insulin infusion alone can cause significant metabolic derangements. Hence, they can be managed better with administration of insulin and glucose by frequent monitoring of plasma blood glucose [35-38].

The principles of perioperative management of insulin treated diabetics (both type I and some of type II) are same. Long acting insulin should be discontinued 1-2 days before surgery. It should be replaced with intermediate-acting mixed with short acting insulin twice daily or with short acting insulin before every meal. If the procedure is short and simple, subcutaneous insulin can be continued. Long and complex procedures require intravenous insulin infusions. Complex procedures are long surgeries characterized with significant hemodynamic fluctuations, or associated with variable tissue perfusion and disabling predictable absorption of subcutaneously administered insulin [32].

Insulin for intravenous administration are either rapid acting or short acting, they can be administered in two ways: as small IV boluses (4-6-8 U) or IV infusions. Infusion can be prepared as GIK, glucose, insulin and potassium in the same bottle or variable rate infusion, where insulin and glucose are administered from separate bags in the same vein ("piggyback technique"). Variable rate infusions are preferred method of IV insulin administration, since it allows easy administration of both infusions. They are usually prepared to contain 1U of insulin/ml, by mixing 100 U of short acting insulin in 100ml of normal saline [35].

Insulin infusions are safe and readily titrated because the half life of short acting insulin is 5 minutes and biological duration of action is less than 20 minutes. They are usually started at 0.5-1 U /hr with concomitant administration of 5% dextrose (100 ml /hr). Insulin infusion rate (insulin dosage) is adjusted to the observed BG level. Well controlled diabetics will require smaller doses of insulin, while patients undergoing extensive surgery, those treated with steroids and diabetics treated with TDD of insulin $>$ 80 U require higher doses

of insulin for achieving targeted BG levels. Insulin infusions are started on the morning of surgery (or the evening before surgery) and should be continued up to 2 hours after the first meal [35].

Insulin infusion administration can be associated with the occurrence of hypoglycaemia (BG level $<$ 60 mg/ dl), which has to be treated promptly, because of potentially deleterious effects on organs using glucose as main metabolic substrate resulting in adverse outcomes of surgery. Management of hypoglycaemia during insulin infusion should be based on the following strategy [35].

1. Stop insulin.
2. Give 50% dextrose IV (25ml if the patient is awake or 50ml if the patient is under general anaesthesia).
3. Recheck BG every 20 minutes.
4. Give 50% dextrose IV again in 25 minutes if BG is still $<$ 60mg/ dl.
5. Continue insulin infusion once BG is $>$ 70mg/ dl.

When diabetic patients resume eating, their therapy should involve insulin divided into basal, prandial and correction insulin. Basal insulin (0.2- 0.3 U/KG/d) should be provided in the form of long acting insulin once daily or twice daily intermediate insulin. Prandial insulin (0.05-0.1 U/ kg) is usually given in the form of short- acting or rapid acting insulin before meal, serving to prevent post-prandial spikes of BG. Correction insulin, in the form of short- acting insulin should be administered if BG $>$ 144 mg/ dl (1-4U for each increments of 54mg/ dl based on suspected insulin sensitivity [32,35,38].

Insulin requirement may be increased or decreased in the perioperative period, frequent BG level monitoring is therefore essential.

Major surgery and poorly controlled diabetes require BG measurement every hour. Once BG achieves target range, BG monitoring can be continued every 2hours, and then every 4hours. More reliable results are obtained from venous samples (plasma blood glucose) than from capillary blood. It should be emphasized that results of BG measurements are influenced by variety of factors, such as: hypo-perfusion, anaemia, hyperbilirubinemia, and manitol administration as well as treatment with dopamine and paracetamol [39].

Summary

Perioperative glycemia control can reduce morbidity, particularly the incidence of infectious complications, in surgical patients even in those without established diabetes. Optimum management of glycemia in perioperative period involves applying principles of physiological insulin replacement. The important goals in diabetic patients should be minimizing hyperglycemia and avoiding hypoglycemia during hospitalization. Attempts to keep BG in tight, physiological range might be inappropriate for diabetic patients during perioperative period. Diabetic patients will require close blood glucose monitoring during perioperative period.

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