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Transoperative Management in Diabetics

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Abstract

Background: *There is an association between transoperative hyperglycemia in diabetic surgical patients and adverse clinical outcomes. There is a 'diabetes of injury' and immunosuppression following any surgery to a varying extent. Cytokines are responsible for the host response but potentially hazardous if uncontrollable or in excess.*

This paper discusses the understanding and management of hyperglycemia and diabetes in hospitalized surgical patients outside the critical care setting. We here outline the management of transoperative hyperglycemia and prevention of hazardous complications before, during and after surgery (i.e. in transoperative period).

Objectives: *To reiterate method for the transoperative management of blood glucose levels in known diabetic non-cardiac surgery, non-ICU patients.*

Material & Methods: *The present article is based on observations on management and outcome of a study conducted on 55 diabetic patients undergoing elective surgeries at Anugrah Narayan Magadh Medical College Hospital, Gaya, Bihar, India during a two year period. No ICU cases were included in the study. Outcomes were comparable with the contemporary practice.*

Conclusion: *Surgery is a stressor that affects homeostasis. Excess cytokines cause insulin resistance and thus type-2 diabetes like state through a complex immuno-physiological response to surgery. A precise understanding of the cytokine response to surgical trauma may bring in interventions that would optimize the transoperative care of the patient, decrease morbidity and enhance recovery.*

Outcomes of our study were comparable with the contemporary practice.

Keywords: *Transoperative hyperglycemia, Cytokines, Metabolism, Surgical stress, Insulin resistance, Diabetes of injury.*

Introduction

Diabetes needs a serious consideration during any kind of operation. The stress response to surgery and the resultant hyperglycemia, osmotic diuresis, and hypoinsulinemia can lead to postoperative ketoacidosis or hyperosmolar syndrome. Hyperglycemia impairs leukocyte function and wound healing.

Transoperative hyperglycemia is reported in 20-40% of patients undergoing general surgery[1,2,3] and approximately 80% of patients after cardiac surgery.[4,5] Most patients with hyperglycemia have a known diagnosis of diabetes.

The pathophysiology of these adverse clinical outcomes in transoperative period is not completely understood. Free radical injury, vascular and immune dysfunction, cytokine activation, direct cellular damage, overproduction of inflammatory mediators and impaired neutrophil function probably underlie the whole scenario.

Any wound, including a surgical one, in a diabetic patient has a potential for delayed healing and getting severely infected with a variety of bacteria. The wound may gap, suppurate and even gangrene may follow leading to a life threatening condition.

The management goal is to optimize metabolic control through close monitoring, adequate fluid and caloric repletion, and judicious use of insulin.[6]

Historicals:"Diabetes offers a serious bar to any kind of operation, and injuries involving open wounds, hemorrhage, or damage to the blood vessels are exceedingly grave in subjects of this disease. A wound in the diabetic patient will probably not heal while the tissues appear to offer the most favorable soil for the development of putrefaction and pyogenic bacteria. The wound gapes, suppurates, and sloughs. Gangrene readily follows an injury in diabetics, and such patients show terrible proneness to the low form of erysipelas, and cellulitis." (Treves,1896.)

It has been estimated that a diabetic has only a 50% chance of avoiding surgery during his Lifetime (Root, 1966).Diabetes often presents *de novo* on surgical wards as a result of the stress either of the surgical condition or of admission to hospital.

Beaser (1970) states that 25% of the diabetic patients on a surgical ward may be newly discovered cases. It is thus of paramount importance that surgical cases be screened adequately, as failure to make the diagnosis before operation may lead to a stormy postoperative course. Even in good centers surgery among diabetics carries a significant mortality and morbidity.

Aims & Objectives

In surgical patients, careful glucose control has associated with decreased mortality and morbidity. There is substantial evidence linking hyperglycemia in hospitalized patients (with or without diabetes) to poor outcomes. The objectives of this paper are:1. To discuss mechanisms of blood glucose regulation in transoperative period and 2.To demonstrate optimal management of transoperative dysglycemia to improve transoperative outcomes.

We conducted this study to reiterate method for the transoperative management of blood glucose levels in known diabetic non-cardiac surgery, non-ICU patients.

Materials and Methods

The study was conducted at the department of Surgery, A.N. Magadha Medical College Hospital, Gaya, Bihar, India.

Case Selection

Adult patients (aged ≥20 years) with a diagnosis of NIDDM (n=30) and IDDM (n=25) who underwent an elective surgical operation between August 1, 2015, and July 31, 2017, were included in this study. Electronic records of the patients were used to identify them. Patients who were in ICU were not included. No cardiac cases were included. Patients on outpatient insulin pump therapy for the management of diabetes were excluded from this study. Our hospital ethics committee approved this study.

Table 1: Characteristics of 55 Patients with Diabetes under study.

Characteristic	**Number (n) (%)**
Age, mean (SD), years	62 (31)
Male sex	32 (58)
BMI, mean (SD)	32.4 (15)
NIDDM, type 2, mean (SD)	30(54.5)
IDDM, type 1, mean (SD)	25(45.5)
Preoperative medical evaluations	38 (69)
Hemoglobin A1c, mean (SD)	7.3 (1.3)
Home DM medication	
Oral and insulin	4 (7)
Diet	9 (15)
Insulin	13 (25)
Oral	29 (53)
Duration of DM, mean (SD), years	12 (12)
ASA level 3	29 (53)

NIDDM=Non Insulin Dependent Diabetes Mellitus , IDDM= Insulin Dependent Diabetes Mellitus, ASA= American Society of Anesthesiology; BMI= body massindex [weight in kg/height in m^2]

Data Analysis

The electronic medical record for each patient was reviewed, and relevant data were abstracted. Type of diabetes, duration of diabetes, type of home diabetes therapy (e.g., diet, oral agents, insulin) prior to surgery, BMI, HbA1c, blood glucose levels, ASA classification and type of surgery done were taken into account. Age and sex were recorded. The transoperative period was taken as the time from admission to the discharge from the surgical care unit. The transoperative period was further divided into preoperative, intraoperative, and postoperative phases. Preoperative, intraoperative, and postoperative records were reviewed for each patient. The following variables were recorded for each patient: duration of specific transoperative phases; preoperative, intraoperative, and postoperative blood glucose levels; type of blood glucose monitoring; and transoperative treatment of blood glucose. Data are reported as mean (standard deviation (SD)) or as number (percentage),as applicable. If multiple glucose values were obtained within a perioperative segment, they were averaged prior to making statistical comparisons. The protocol has been outlined in table 2. Diabetics undergoing surgery tend to be a high-risk group.

Table 2. Blood-glucose concentration (mmol/litre) in normal subjects, NIDDM and IDDM subjects during and after surgery. NIDDM subjects were given either (a) an insulin infusion until the next first meal or (b) no insulin until after the operation. Both groups received regular insulin (40IU/ml) t.i.d. after operation based on glucometer readings. Glucose was given as 5% glucose-saline infusion until oral feeding regularized. Insulin dependent subjects were treated by following one of four regimens. Groups (c) received glucose-potassium-insulin(GKI) from 30 min before operation until normal feeding reinstituted. Group (d) comprised five subjects from group (c) where the glucose-potassium-insulin (GKI) infusion was continued for 72 h. Group (e) patients received no insulin or glucose before or during operation. Groups (f) received half the usual morning dose of insulin s.c. together with 25gm glucose given i.v. over 5 minutes.

Condition	Before op.	30 min after induction	After operation				
			1 h	4 h	24 h	48 h	72 h
NIDDM(30)							
(a)Insulin infusion (20)	10.5+/-1.2	11.4+/-1.1	9.6+/-1.2	9.9+/-1.1	11.5+/-1.3	11.1+/-1.3	10.6+/-1.1
(b)No therapy (10)	9+/-1	8.9+/-0.9	9.5+/-1.1	13.3+/-1.5	12.5+/-1.1	12.2+/-1.1	11.2+/-1.5
IDDM(25)							
(c)Insulin-infusion;for 4days) (10)	9.2+/-1.8	9.4+/-1.9	9.2+/-1.1	10.5+/-1.2	12.1+/-1.3	11.8+/-0.9	9.1+/-0.5
(d)Insulin-infusion (for 72 h) (5)	13.1+/-2.3	12.3+/-1.2	12.5+/-0.5	13.5+/-2.1	11.2+/-2.3	10.3+/-1.4	11.6+/-1.8
(e) No insulin or glucose (5)	9.1+/-1.2	8.8+/-1.1	11.9+/-1.5	13.9+/-1.1	12.1+/-1.2	13.8+/-0.6	13.9+/-0.2
(f) S .c. insulin +i.v. glucose(5)	9.5+/-1.1	8.5+/-1.2	11.5+/-1.3	13.8+/-1.2	13.2+/-1.1	13.1+/-1.3	14.3+/-1.1
Non-diabetic (20)	6.2+/-0.4	6.8+/-0.6	7.5+/-0.3	7.9+/-0.5	7.6+/-0.7	7.2+/-0.3	6.8+/-0.2

Table 3: 5As (Aims) of transoperative management.

1. Avoid hypoglycemia
2. Avoid excess hyperglycemia
3. Avoid large swings in blood glucose; keep blood glucose in the range of 7-10mmol/l.
4. Avoid ketoacidosis
5. Avoid electrolyte disturbances e.g. hypokalemia

Pathogenesis of Surgical Stress

Claude Bernard in 1877 first reported hyperglycemia due to stress from hemorrhage.[7] He told that this was due to the glycogenic function of the liver. Acute hemorrhage causes insulin resistance which mobilizes glucose from liver which energizes fluid movements and plasma refill. Literature termed this hyperglycemia due to traumatic stress as 'diabetes of injury' which is analogous to type 2(non-insulin dependent) diabetes.[8] Now it is known that insulin resistance is a hallmark of surgical stress and is basically a result of cytokine activation.[9]

Factors that would mitigate the surgical stress include have been given in table 5.

Table 4: Factors that potentiate the surgical stress response.
• Nature of injury. • Severity of injury. • Anaesthesia and drugs. • Complications (infections, DVT, PE).

Table 5: Factors that mitigate the surgical stress response.
• Epidural anesthesia. • Minimally-invasive surgery. • Meticulous and gentle tissue handling. • Prompt and adequate fluid replacement. • Preoperative and early postoperative feeding.

Transoperative Glycemic Targets

Glycemic targets recommended by different organizations are as follows:

- SAMBA (The Society for Ambulatory Anesthesia) recommends intraoperative blood glucose levels <180 mg/dL (10 mmol/l).
- AACE (The American Association of Clinical Endocrinologists) Task Force and ADA (the American Diabetes Association) recommend target glucose levels between 140 and 180 mg/dL (7.7-10 mmol/l) in critically ill patients.
- SCCM (The Society of Critical Care Medicine): recommends treatment should be started at blood glucose levels ≥ 150 mg/dl (8.3 mmol/l0 with a goal to maintain blood glucose below that level, and absolutely <180 mg/dL (10 mmol/l).
- STSPG (The Society of Thoracic Surgeons Practice Guidelines) proposes maintaining serum glucose levels ≤ 180 mg/dL (10mmol/l) for at least 24 hours after cardiac surgery.
- ADA/AACE Practice Guidelines recommended a target pre-meal glucose of <140 mg/dL (7.7 mmol/l) and a random BG of <180 mg/dL (10 mmol/l) for patients treated with insulin for patients in non-ICU settings.
- JBDS (Joint British Diabetes Societies) guideline, for the perioperative management of adult patients, recommends to start insulin treatment when glucose levels are >10 mmol / l (180 mg/dL). It target a glucose range between 6 -10 mmol/l (108–180 mg/dL) but with acceptable values 4-12 mmol/l (72–216 mg/dL).

Pre-Operative Glycemic Management

Type of diabetes, nature and extent of the surgical procedure, length of pre and post-operative fasting, type and frequency of daily medication, and state of metabolic control before surgery determine the pre-operative medication use and dose.[10]

The use of most oral antidiabetic agents is recommended up to the day before surgery. Certain medications may be safely continued on the day of surgery. It has been recommended insulin secretogogues such as sulfonylureas and glinides be discontinued the day of surgery due to risk of lactic acidosis.

The SAMBA consensus statement on perioperative biguanide management in diabetic patients advices that metformin may be taken the day before surgery, and restarted when normal diet is resumed.

In patients with renal impairment (GFR < 45mL/min), those undergoing procedures with use of intravenous contrast dye or with long surgical procedures, metformin should be stopped when the preoperative fast begins, and restarted postoperatively when normal diet resumes. Metformin is discontinued until renal function normalizes.

The FDA released a safety statement in 2015 regarding occurance of diabetic ketoacidosis (DKA) in patients taking sodium glucose-cotransporter 2 (SGLT-2) inhibitor (e.g. empagliflozin, dapagliflozin, and canagliflozin) therapy. Guidelines then issued which advised stopping the drug in patients undergoing emergency surgery and holding the medication 24 hours before an elective surgery or invasive procedure.

Currently, trials are underway examining use of incretins (DPP-4s and GLP-1 agonists) e.g. sitagliptan for use in both cardiac and general surgery patients with type 2 diabetes. DPP-4 inhibitors have been proved to be safe in a recent randomized trial of non-cardiac surgery patients with type 2 diabetes .DPP-4 inhibitors (sitagliptin and vildagliptin) may be taken on the day of surgery and continued into the perioperative period.[11]

Patients with type 2 diabetes treated with insulin should continue their insulin therapy. The patient's basal insulin (Glargine or Detemir) dose be reduced by approximately 25% of normal dose the evening before or morning of surgery. NPH insulin is reduced by 20% the evening before surgery and by 50% the morning of surgery.

In addition, it is better holding the dose of NPH in the morning of surgery in patients with type 2 diabetes and fasting glucose < 120 mg/dl.

Patients with type 1 diabetes undergoing surgical procedures continue insulin during the perioperative period. These patients should take 80% of basal insulin dose on the evening before surgery and on the morning of surgery. Postprandial insulin is stopped when the fasting state begins.

Intraoperative Glycemic Management

The intraoperative blood glucose management depends upon the length of surgery, invasiveness of surgery, type of anesthesia, and expected time to resume oral intake and previous antidiabetic therapy. The Endocrine Society and SAMBA recommend that intraoperative blood glucose levels be maintained <180 mg/dL. Hyperglycemia (>180 mg/dL, 10 mmol/l) is treated with subcutaneous (SC) rapid-acting insulin analogs (insulin lispro/insulin aspart) or with an intravenous infusion of regular insulin. Rapid-acting insulins are used in insulin pumps, also known as continuous subcutaneous insulin infusion (CSII) devices.

Patients undergoing short procedures (< 4 hours operating time) are often good candidates for SC insulin treatment. When subcutaneous insulin is used BG testing should be done at least every two hours. Rapid-acting insulin should not be given more frequently than every two hours to minimize the risk of insulin stacking. The short duration of action of rapid-acting insulin analogues limits the risk of ‘insulin stacking’ with repeat dosing.

In patients with expected hemodynamic instability, significant fluid loss, hypothermia ,use of inotropes, or long operating times (>4 hours) an intravenous (IV) insulin infusion is recommended

The short half-life of IV insulin (less than 15 minutes) allows for rapid-adjustment in dose delivery and tight glycemic control. Blood glucose testing should occur hourly when using a variable rate insulin infusion.

Post-Operative Glycemic Management in non-ICU Patients

When the patient is shifted to the surgical ward, use of sliding scale insulin alone is not acceptable as the single regimen in patients with diabetes, as it results in unpredictable glycemic response. The administration of once or twice daily basal insulin (glargine, detemir, NPH) alone, or in combination with post-meal insulin is recommended approach. This is known as a “Basal Bolus” insulin regimen.[12]

In general surgery patients, basal-bolus regimens significantly reduce the number of postoperative complications, particularly wound infections.NPH ,regular insulin, or premixed (70/30) combinations are equally effective when compared to basal bolus regimens, but are associated with higher rates of hypoglycemia in fasting patients. The “Basal Plus” regimen includes a long-acting basal insulin once daily plus a rapid-acting insulin if blood glucose (BG) > 180mg/dL. Sliding scale insulin regimens do not supply basal insulin.

For patients who are NPO or with poor oral intake, the starting daily dose of basal (glargine, detemir) insulin is 0.2 to 0.25 units./kg/day. As patients are allowed orals and tolerate soft diet (regular, low carbohydrate or diabetic), a basal bolus regimen is started.

In elderly patients (age > 70) and those with impaired renal function (GRF < 45ml/min), the daily basal insulin dose is reduced by approximately half of the normal recommended dose (0.1 to 0.15 units/kg/day) to reduce the risk of hypoglycemia.

Insulin resistant patients are given higher doses of basal insulin (0.3units/kg/day) to limit hyperglycemia.

The home insulin regimen of a diabetic patient is used to calculate total daily dose (TDD). Reducing TDD by 20-25% gives the starting hospital dose of basal insulin in fasting patients. The reduction in basal insulin reduces the risk of hypoglycemia, particularly in those with poor or uncertain caloric intake. The dose of basal insulin is adjusted daily if the patient's blood glucose is not within target range over the previous 24 hours. If there is no hypoglycemia (BG<70mg/dL, 3.8mmol/L), the basal insulin dose is increased by 10 or 20% respectively for persistent BG > 180mg/dl (10mmol/L) or 240mg/dl (13mmol/L).

As orals are resumed, insulin therapy can be shifted to the patient's usual basal and home regimen.

The use of oral antidiabetic agents is generally not recommended in hospitalized patients. These patients frequently have contraindications to oral medications and the slow onset of action may preclude achieving timely glycemic control. But, recently, the use of DPP-4 inhibitors has been proposed for the management of transoprative hyperglycemia. A recent randomized study in patients with type 2 diabetes undergoing surgery reported that the use of sitagliptin alone, or in combination with a single basal insulin dose, resulted in similar mean daily glycemic control when compared to basal bolus insulin regimens.[10]

Results

1. Patients undergoing short procedures (< 4 hours operating time) responded well to SC insulin treatment.
2. In patients with expected hemodynamic instability, significant blood loss, hypothermia or long operating times (>4 hours) an intravenous (IV) insulin infusion resulted in good control of transoperative hyperglycemia.
3. In general surgery patients, basal-bolus regimens significantly reduce the number of postoperative complications
4. Glucometers showed 22% error and are not intended for monitoring IIT (intensive insulin therapy).

In this series, the mortality rate, among 55 diabetic patients who underwent either elective surgeries between 2015 and 2017 was 5-8%.The major causes of mortality and morbidity were infection and cardiovascular events.

Conclusion

Hyperglycemia is common in diabetic surgical patients. Surgery is a stressor that affects homeostasis. A precise understanding of the cytokine response to surgical trauma has led to optimise the transoperative care of the patient, decrease morbidity and enhance recovery.

The independent factors predicting infection rate, morbidity and length of hospital stay are (a) type of surgery, (b) perioperative blood loss and (c) postoperative insulin resistance.

The enhanced recovery after major elective surgery is facilitated by reducing the surgical stress using epidural anesthesia and minimally invasive (laparoscopic) surgery; avoiding stress-induced hyperglycemia by rapid resumption of pre-operative anabolic setting and avoiding fasting; treating hyperglycemia with insulin; postoperative pain control and early postoperative feeding .Epidural analgesia reduces postoperative insulin resistance by 45% .

Also the present day BG monitoring devices are not up to the mark and should be used with caution and wisdom.

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