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Optimal Perioperative Blood Glucose Management and its Effect on Patient Outcomes

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Abstract

This literature review was performed based on Objective Structured Clinical Examination (OSCE) completion. The case presented was a preoperative evaluation of a patient with comorbidities including uncontrolled diabetes mellitus type two. Upon evaluation of the case, the topic chosen was examining optimal perioperative blood glucose management and its effect on patient outcomes. Databases including PubMed, CINAHL, and Scopus were utilized for this research. Search terms utilized include “perioperative blood glucose” and “patient outcomes”. The search was limited to sources published within the last five years and focuses on meta-analysis and systemic reviews. To ensure all available relevant information was analyzed the literature search included utilizing the National Guidelines Clearinghouse and Trip Database.

Research revealed a variety of recommendations related to exact goals for blood glucose management perioperatively, all reporting specific correlation of hyperglycemia and increased perioperative complications. A general summary of all sources reveals endorsement of maintaining perioperative blood glucose levels under 180 mg/dL while avoiding hypoglycemia although specific suggestions were diverse. Recommended treatment modalities also were inconsistent. Insulin with basal bolus timing was found highly effective in several scenarios. The lack of a single recommendation for perioperative blood glucose management reveals the need for further research in this area to increase consistency.

Optimal Perioperative Blood Glucose Management and its Effect on Patient Outcomes

Background

Blood glucose imbalances can have a marked impact on the overall health of a person. Normal fasting blood glucose is 80 - 130 mg/dL (American Diabetes Association, 2020). Acutely, hyperglycemia presents with symptoms of frequent urination, increased thirst, fatigue, headache, and blurred vision (Mayo Clinic, 2020). Such symptoms can be a reversible short-term inconvenience for patients, but if left untreated, hyperglycemia can progress in severity causing irreversible complications. Blindness, nerve damage, kidney failure, and cardiovascular disease are a few of the serious complications of long-term hyperglycemia (Mayo Clinic, 2020). Hyperglycemia can result in emergency situations including diabetic ketoacidosis or a hyperglycemic hyperosmolar state. Hypoglycemia can present with early symptoms including fatigue, anxiety, sweating, hunger, irritability, and shakiness progressing to later symptoms of confusion, seizures, and loss of consciousness (Dunphy, Winland-Brown, Porter, & Thomas, 2019, p. 935). It is important to note that everyone may experience symptoms of hyper or hypo glycemia at different blood glucose levels.

Blood glucose imbalances are more common for individuals who are diabetic but, any person can experience them. “In 2017, the International Diabetes Federation estimated that 425 million people worldwide age 18-99 years have diabetes mellitus with this number projected to increase” (Kuzulugil et al., 2019). According to the Centers for Disease Control (2017) “as of 2015 30.3 million Americans have diabetes. Another 84.1 million have prediabetes.” When considering rates of diabetes, it is important to note that “up to half of people with diabetes are undiagnosed” (Kuzulugil et al., 2019).

It has been found that the rate of adverse events in the perioperative period are higher in diabetic patients versus those without diabetes (Kotagal et al., 2015). For patients without diabetes, there is a direct correlation between increased blood glucose levels and increased rates of adverse perioperative events. The Centers for Disease Control (2020) report that for all people, regardless of diabetic status, “surgical site infection is the most costly health care associated infection type with an estimated annual cost of $3.3 billion, and is associated with nearly 1 million additional inpatient-days annually.” Because of these factors, it is important to address perioperative blood glucose management.

The report included in this paper discusses a patient who presented for a preoperative evaluation for right total knee arthroplasty. The main purpose of a perioperative evaluation is to assess the patient’s risk for and implement strategies to mitigate complications related to undergoing surgery. Upon complete evaluation of history and physical examination of this patient, risk factors were revealed. One significant risk factor is uncontrolled diabetes mellitus type two. Even under normal circumstances, blood glucose imbalance can demonstrate a pronounced impact on the body. The risk for glucose imbalance increases when the body is under acute stress (Mayo Clinic, 2020). Examples of such stress include illness, injury, or surgery. The effects of glucose imbalance along with management becomes increasingly complex in such stressed states (Mayo Clinic, 2020). There are no specific guidelines available related to how blood glucose should be managed perioperatively. This paper evaluates appropriate blood glucose levels during the perioperative period and the best interventions to accomplish this goal. The purpose of this report is to analyze the literature for the best practice options for optimal perioperative blood glucose management and its effects on patient outcomes.

Case Report

History of Present Illness

The patient is a 57-year-old female who presents for a pre-op evaluation prior to right total knee arthroplasty. History of present illness (HPI) reveals that the patient has been experiencing pain in her right knee for the past two months when her knee reportedly "went out". Patient was unable to walk at the time. Pain is reported to be 7-8 out of 10, constant, and local to the right knee. Treatments thus far includes physical therapy and diclofenac with minimal improvement or relief. No other alleviating factors reported. Aggravating factors include increased physical activity that requires weight bearing.

Current Medications

• Diclofenac Sodium (VOLTAREN) 75 mg delayed-release (enteric coated) tablet Take 1 tablet (75 mg) by mouth 2 times a day 60 tablet 0

• Liraglutide (VICTOZA) 18 mg/3 mL subcutaneous injection solution (pen) Inject 1.8 mg subcutaneously 1 time per day 9 mL 2

• Fluticasone (FLONASE) 50 mcg/spray nasal spray Spray 1 spray into each nostril 1 time per day 16 g 5

• Insulin Needle (BD PEN NEEDLE NANO U/F) 32G X 4 mm Use once daily as directed 100 each 3

• MetFORMIN (GLUCOPHAGE XR) 500 mg extended release tablet TAKE FOUR TABLETS BY MOUTH EVERY DAY 360 tablet 3

• Acetaminophen (TYLENOL) 500 mg tablet Take 1,000 mg by mouth Every 4 hours as needed (do NOT exceed 4000mg/ 24 hours including all sources)

• Vitamin C, ascorbic acid, 500 MG tablet Take 1,000 mg by mouth 1 time per day

• Milk Thistle-Tumeric (SILYMARIN) CAPS capsule Take 1 capsule by mouth 1 time per day

• GlipiZIDE ER (GLIPIZIDE XL) 10 mg extended release tablet (24 hr) Take 1 tablet (10 mg) by mouth 1 time per day 90 tablet 3

• Multiple Vitamins-Minerals (ZINC PO) Take 1 tablet by mouth 1 time per day

• Blood Glucose Test Strip (ONETOUCH VERIO) 1 Strip 1 time per day 2 box 3

• Lancets (ONETOUCH DELICA) 1 each 1 time per day 100 each 3

• Specialty Vitamins Products (ECHINACEA C COMPLETE PO) Take 1 tablet by mouth 1 time per day

• CINNAMON PO Take 1 capsule by mouth 1 time per day

Allergies

- Amlodipine Besylate (Amlodipine). Reaction: Rash
- Cats (Pet Dander). Reaction: Watery eyes, difficulty breathing, sneezing
- Environmental Allergens (Hay Fever). Reaction: Itchy eyes, watery eyes, sneezing

Past Medical History

Review of past medical history is significant for pertinent findings including osteoarthritis of both knees, type two diabetes, chronic kidney disease (CKD), sleep apnea, and obesity. Beginning with evaluation of diabetes management, assessment reveals poorly controlled diabetes mellites type two. Patient does not check her blood sugar at home. Hemoglobin A1C today is 7.9%. This value is despite treatment including Metformin ER 2000 mg po daily, Glipizide ER10 mg po daily, and Victoza 18 mcg/3mL sq. 1.8 mg daily. All three of these medications are at maximum dosages considering renal impairment. Chronic kidney disease is at stage III with a blood urea nitrogen of 21mg/dL, creatinine is also elevated at 1.57 mg/dL, estimated glomerular filtration rate is low at 46 mL/min/1.73m2. Patient has a CPAP for sleep apnea but does not use it.

Past Surgical History

Left total knee arthroplasty 5/8/19 with subsequent full recovery.

Social History

Social history reveals patient is married and lives with her husband in a private house. They have two adult children and patient reports no social or relationship issues. Patient's occupation is sedentary, working in tourism. General lifestyle is also reported to be sedentary. Patient reports she experiences fatigue and right knee pain when performing activities such as walking two city blocks or up a flight of twelve stairs. She has no tobacco or drug use. Alcohol use consists of two standard drinks of wine or beer per week. Caffeine intake amounts to 2-3 cups of coffee a day. She denies stress or any other concerns.

Family History

Family history includes a mother with type two diabetes and a father who is a smoker with emphysema. She has three sisters and two brothers with no reported medical conditions.

Review of Systems

Review of systems (ROS) is negative for bleeding tendencies, prior complications with anesthesia, recent illness, rash, chest pain, or shortness of breath. Patient reports her mood is stable. She denies any shortness of breath or chest pain with activity. Pertinent positive findings found during ROS include the following. Musculoskeletal system is negative for any significantly changed arthralgias and myalgias. Right knee pain as reported in the HPI above. Denies any numbness or tingling to extremities. Patient denies any concerns today.

Physical Exam

Vitals: Temp: 98.9 degrees Fahrenheit, BP: 136/90 (manual cuff, left arm, sitting), Pulse: 88 per minute, Resp: 18 per minute, Pain: 7 of 10 in right knee constant, SpO2 98% room air, Height: 5 feet 10 inches, Weight: 168.3 kg (371 lb), Body mass index is 53.23 kg/m^2.

- Constitutional: Alert, calm, cooperative. No acute distress. Oriented to person, place, time, and situation. Appropriate affect, mood, and concentration.
- HEENT: PEERL, EOM’s intact. Conjunctivae/corneas clear. Face symmetrical with full strength. Bilateral external ear canals negative for erythema or edema. Bilateral TM intact with no erythema or bulging. Oropharynx has no edema, erythema, or exudate. Mucosa moist, intact, no oral lesions. No drainage or sinus tenderness. Teeth intact.
- Neck: Supple, symmetrical, trachea midline, no adenopathy, no carotid bruit, and no JVD. Full ROM front to back, side to side and ear to shoulder bilaterally. Full rotation.
- Lungs: Clear to auscultation bilaterally. No tachypnea, retractions, or cyanosis.
- Cardiovascular: Heart rate and rhythm regular. S1, S2, no murmur, click, rub or gallop.

- Abdomen: Obese. Active bowel sounds in all four quadrants. Soft, nontender. No organomegaly or masses.
- Musculoskeletal: Pain to right knee upon movement. Full ROM to bilateral knees without crepitus. No erythema or edema to bilateral lower extremities. Negative anterior and posterior draw, negative valgus and varus laxity of bilateral knees.
- Skin: Color, texture, turgor normal. No rashes or lesions.

Risk Evaluation

Surgery risk: this is an orthopedic high-risk surgery. Revised cardiac risk index (RCRI) score of class III. Ariscat scoring low risk for pulmonary complications. Mallampati score of class one.

Diagnostics

Labs and imaging include the following. Electrocardiogram on file from last year was reviewed revealing normal sinus rhythm. X-ray of right knee 01/23/2020 reveals moderately severe patellofemoral degenerative change, marked narrowing of joint space laterally, lateral deviation of the patella with no acute fracture or dislocation. Complete metabolic panel, complete blood count with differential, and hemoglobin A1C drawn today and were reviewed with patient. Pertinent abnormal laboratory findings are as listed above.

Assessment/Plan

1. Osteoarthritis of bilateral knees: discussed the risks of intraoperative complications. Patient verbalized understanding, and she does wish to proceed. Discussed stopping all NSAIDs including diclofenac 7 days prior to surgery. Patient requested to report any

illness or fever to surgeon. Patient educated on use of incentive spirometer, deep breathing, and coughing. NPO beginning at midnight before surgery. The patient may take discussed medications the morning prior to surgery with a sip of water.

2. Type 2 diabetes: discussed with patient that her blood sugar is uncontrolled despite maximum dosages of three medications. Education completed related to the need for strict medication adherence. Patient educated on risk of uncontrolled diabetes. Currently patient is refusing insulin therapy. Patient referred to diabetic educator. Patient is to provide us with fasting blood glucose readings for a week and may need medication adjustment at that time. Metformin should be held 48 hours prior to surgery. Patient educated that she may be on insulin perioperatively. Check blood glucose the night before surgery. If less than 100 mg/dL, eat a snack of one carbohydrate equivalent.
3. CKD stage III: comprehensive metabolic panel checked today and referral to nephrology placed. Education completed on proper dosage of NSAIDS.
4. Sleep apnea: patient educated on need for CPAP use and rational behind long term use.
5. Obesity: patient educated on lifestyle modification including diet and exercise. Will set up with weight management post op.

Literature Review

This work will examine perioperative blood glucose management focusing on three main areas. First, consideration will be given to how perioperative blood glucose management effects patient outcomes. Next, we will address optimal blood glucose control perioperatively. Finally, treatment modalities to regulate blood sugar will be analyzed.

Effect on Outcomes

Perioperative blood glucose management affects patient outcomes in a variety of ways. Examination of the literature reveals perioperative hyperglycemia has a greater overall impact on patient outcomes in comparison to hypoglycemia. Rates of surgical site infections increase with hyperglycemia (DeVries et al., 2016). Increased rates of surgical site infections result in increased length of stay and health care cost (Leininger, 2018). Kheir, Tan, Kheir, Maltenfort, and Chen, (2018) report “The rate of periprosthetic joint infection increased linearly from blood glucose levels of ≥ 115 mg/dL.” Both morbidity and mortality increase with perioperative hyperglycemia (Evans, Lee, & Ruhlman, 2015; Nair et al., 2016). Strict blood glucose control maintaining levels under 150mg/dL reduces surgical sight infections by 95% according to DeVries et al. (2016). Authors did note that while hypoglycemia was more common in this group, there was no increase in rates of death or stroke found as a result. Simha and Shah (2019) found perioperative hyperglycemia is related to increased rates of wound infection, pneumonia, sepsis, and cardiovascular events. Simha and Shah (2019) also report that preoperative blood glucose level has a greater impact on outcomes versus hemoglobin AIC, and that “intensive insulin therapy in the postoperative period has been associated with lesser risk of infection and overall morbidity and mortality.” This group defines the goal for random blood glucose levels to be 100 to 180 mg/dL.

When discussing diabetic patients specifically, it has been found that this population perioperatively is at increased risk for pneumonia, blood transfusions, delayed hospital discharge, surgical site infection, and in hospital mortality (Akiboye, & Rayman, 2017). Bacteremia, respiratory failure, and acute renal failure are also more common in this population. Diabetic patients experience delayed wound healing along with increased rates of periprosthetic infection, length of stay, and morbidity. In relation to hemoglobin A1C, preoperative levels greater than 7.0% increase the risk for surgical site infection in thoracic and lumbar spinal instrumentation surgery while hemoglobin A1C has not been found to be connected to periprosthetic infection of the hip or knee. Periprosthetic infection has been found to be three times more common when the patient's blood glucose the morning of surgery is greater than 140 mg/dL (7.8 mmol/L). The risk of poor recovery is four times greater if perioperative blood sugar is >6.9 mmol/L versus normally <6.1 mmol/L.

Optimal Blood Glucose

When determining the optimal range for blood glucose control during the perioperative period, there are many different recommendations from a variety of sources. Kuzulugil et al. (2019) report by optimizing glycemic control there is a potential to reduce perioperative complications. This group proposes target blood glucose for inpatients to be a range from 106 to180 mg/dL (Kuzulugil et al., 2019). Initiating treatment for hyperglycemia is called for when intraoperative blood glucose levels reach 140 mg/dL in order to lessen postoperative hyperglycemia according to Nair et al. (2016). This group does stress the importance that, although intraoperative hyperglycemia does increase postoperative rates of hyperglycemia, there is still great importance of controlling blood glucose without causing hypoglycemia. DeVries et al. (2016) along with Akiboye and Rayman (2017) both found that perioperative blood glucose should be maintained under 150 mg/dL (8.3 mmol/L). In doing so, blood glucose should be checked prior to surgery and also hourly for surgeries over two hours (Akiboye, & Rayman, 2017).

Blood glucose levels under 180 mg/dL are recommended perioperatively by the American Association of Clinical Endocrinologists (Leininger, 2018). Evans, Lee, and Ruhlman, (2015) report surgical goals for blood glucose should be between 140 and 180 mg/dL and these goals need to incorporate the individual patient's clinical status. Research by Kheir, Tan, Kheir, Maltenfort, and Chen (2018) report controlling blood glucose between the range of 80-110 mg/dL results in more hypoglycemia with no additive benefits. This group recommends optimal blood glucose control to be maintained under 137 mg/dL. Peak intraoperative blood glucose >360 mg/dL has been found to be an independent risk factor for complications regardless of diabetic status (Akiboye, & Rayman, 2017). Four or more consecutive blood glucose readings of at least 200 mg/dL or 11.1 mmol/L increases patient risk of complications.

The work of Simha and Shah (2019) presents a variety of specific findings for reference. Preoperatively they found no evidence for the need to control hemoglobin A1C levels in relation to postponing surgery, but if results are found to be above 8%, an attempt should be made to reduce this value. On the other hand, if the blood glucose is found to be greater than 250 mg/dL, elective surgery should be postponed. When the patient presents for surgery, a report should be obtained from them containing their last blood glucose reading along with the time of that reading and the time and dose of the last glycemic altering medications. Blood glucose readings under 70 mg/dL preoperatively should be treated with glucose supplementation in the form of tablet or gel if the patient is on nothing by mouth status. It is desirable for blood glucose levels to be over 100 mg/dL prior to starting surgery. Treatment of hyperglycemia perioperatively should begin with a blood glucose level of >180 mg/dL. Blood glucose controlled within the range of 80-100 mg/dL intraoperatively was found to be of no additional benefit. Postoperative blood glucose recommendations are for pre-prandial levels of 100-140 mg/dL with random levels from 100-180 mg/dL. Although there is not one specific recommendation for optimal perioperative blood glucose levels, there is a substantial amount of evidence for providers to use when formulating goals of care.

Treatment

Insulin Therapy.

What treatment should be utilized to obtain optimal blood glucose control perioperatively? Insulin is the fastest acting treatment for hyperglycemia and allows for the most sensitive titration. Insulin can be used regardless of comorbidities (Akiboye, & Rayman, 2017). There are three main modalities of insulin administration in the acute setting which include: intravenous (IV) and subcutaneous with either basal-bolus or sliding scale timing. Basal bolus scheduling of insulin allows for the closest replication of endogenous insulin production (Cheisson et al., 2018). Basal bolus timing of insulin also has been found to be superior for reducing perioperative complications (Kuzulugil et al., 2019). Akiboye and Rayman (2017) report insulin infusion is indicated for surgeries lasting at least three hours, or when the patient misses more than one meal. Using insulin therapy for acute blood glucose management perioperatively is common. This is true both for patients already on insulin preoperatively and those who are not on insulin. If an insulin pump is to be used, it requires the patient to be independent (Akiboye, & Rayman, 2017). Akiboye and Rayman (2017) have found that insulin pumps can be safely used intraoperatively for up to three hours in a same day surgery setting.

Simha and Shah (2019) discuss measures that can be taken preoperatively that aide in perioperative blood sugar management. A complete evaluation of all medications a patient is currently taking is necessary, including written directions for the patient regarding medication use preoperatively. Long acting basal insulin is the only medication that consideration for adjustment the day prior to surgery may be indicated. Seventy five percent reduction in basal insulin dose the night before surgery has been found to be ideal for type two diabetics. For type one diabetics, if they are on a stable basal dose, no adjustment may be deeded. For those using an insulin pump, if the patient is well versed on using their pump and has favorable glycemic control, continuation of the device may be considered. Related factors include the surgery being under two hours with a quick recovery expected while early morning operative times are favorable. The patient should be hemodynamically stable, have a pump site that is not by the operative site, and reduce the basal rate of insulin infusion. When initiating insulin therapy perioperatively, Simha and Shah (2019) recommend starting with rapid acting insulin every two hours as needed, then insulin infusion when indicated making sure to check blood glucose levels every 1-2 hours.

Oral Therapy.

Traditionally, on the day of surgery it was the standard of practice that all oral blood glucose lowering medications are held at the discretion of the surgical team. New research reveals this needs to be individualized based on patient factors, their specific medications, and surgical parameters. Metformin should be held the day of surgery according to the American Diabetes Association (Kuzulugil et al., 2019). The rationale behind this recommendation is due to hypoglycemia risk although the Association of Anesthetists of Great Britain and Ireland have found this causation link between hypoglycemia and metformin invalid (Hulst et al. 2018). Sulfonylureas are found to cause more hypoglycemia without symptoms and should continue to be held the day of surgery (Kuzulugil et al., 2019). The class of sodium-glucose cotransporter-2 inhibitor (SGLT2i) medications have been found to be linked to higher rates of ketoacidosis.

There is a range of recommendations on SGLT2i therapy based around stopping therapy 24 hours to over 72 hours before moderate to major procedures. Dipeptidyl peptidase 4 inhibitors (DPP4i's) have not been found to effect blood glucose levels in relation to hyperglycemia or hypoglycemia. It is justifiable to hold or continue glucagon-like peptide-1 receptor agonists (GLP 1 agonists) based on individual clinical scenarios. GLP 1 agonists have been found to improved glycemic control perioperatively, but an increase in gastrointestinal symptoms need to be considered.

Other Factors.

Kuzulugil et al. (2019) discuss some unique factors in relation to optimal perioperative blood glucose management not significantly analyzed elsewhere. This work does have a patient population focus of those who are diabetic. Such factors examined include aspects of care beyond the medication itself that have an impact on treatment results. The skill level of staff who are administering the insulin contribute to the overall outcome. This varies based on location and consistency reflecting individual clinical practices. In some cases, one institution has been found to have more than one guideline for perioperative blood glucose management. Quality assurance, process improvements, and standards of care are not to be overlooked or underestimated. Variation within these factors needs to be minimized. Kuzulugil et al. (2019) report utilizing multidisciplinary teams to their highest potential is instrumental to effecting patient outcomes in a positive manner. Further benefit to the patient can be obtained if they are seen by a diabetic specialist in the first 24 hours of their hospital stay (Kuzulugil et al., 2019). Along the same lines of looking at unique patient factors in relation to perioperative blood glucose management, it is important to address altered nutritional ingestion. Daniel, Vulluri, and Furlong (2017) examined the unique nutrition in neurosurgery patients utilizing enteral tube feeding or parenteral nutrition. Fasting promotes insulin resistance which in turn hinders wound healing (Akiboye, & Rayman, 2017). Leininger (2018) reveals that a team approach involving providers, surgeons, and nursing staff has been proven to result in superior blood glucose management.

Maintaining continuous glucose monitoring (CGM) perioperatively is a multidimensional issue. Continuing CGM use shows increased glycemic control for patients who utilize this therapy (Kuzulugil et al., 2019). The concern is that the patient needs to exhibit independence in order to maintain its use. Intraoperative hypoglycemia is treated with IV dextrose. Simha and Shah (2019) recommend CGM perioperative only for research currently. For obtaining the actual blood glucose measurement, rather than using a capillary blood glucose reading, Evans, Lee, and Ruhlman (2015) report the gold standard method is a venous plasma sample.

Conclusion

Perioperative blood glucose management has an impact on a variety of patient outcomes. The major complications that are a result of hyperglycemia perioperatively include increased risk for surgical site infections, length of stay, health care cost, morbidity, and mortality. Blood glucose should be kept at least under 180 mg/dL without hypoglycemia to minimize risk. Strategies to maintain this level of control begin preoperatively with patient education. Education includes checking blood glucose levels the night before and morning of surgery along with medication management, specifically if long acting insulin doses need to be decreased. For elective procedures, blood glucose must be between 70 to 250 mg/dL to proceed with surgery in order to obtain the lowest risk of complications. Blood glucose levels should be checked every 1-2 hours intraoperatively and as needed with venous plasma sampling being the gold standard method to obtain readings. Treatment of hyperglycemia perioperatively should begin with subcutaneous basal bolus insulin administration and should be converted to IV insulin infusion when there is an inability to maintain blood glucose levels under 180 mg/dL.

Learning Points

- Perioperative hyperglycemia of blood sugar greater than 130 mg/dL increases risk for surgical complications including surgical site infections, length of stay, health care cost, morbidity, and mortality.
- Optimal blood glucose levels during the perioperative period have not been determined, but they should be maintained at least below 180mg/dL while avoiding hypoglycemia.
- Treatment modalities to manage blood glucose levels in the acute perioperative period include insulin through intravenous infusion, subcutaneous basal bolus, or subcutaneous sliding scale timing; insulin via basal bolus timing should be implemented first.

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