

# Endocrine Press Books

## Emergent Perioperative Hyperglycemia Management

--Manuscript Draft--

|                                     |  |
|-------------------------------------|--|
| <b>Manuscript Number:</b>           |  |
| <b>Article Type:</b>                | Article  |
| <b>Section/Category:</b>            | Diabetes and Insulin   |
| <b>Corresponding Author:</b>        | Ketan Dhatariya, MBBS MSc MD MS FRCP<br>Norfolk and Norwich University Hospitals NHS Foundation Trust<br>Norwich, UNITED KINGDOM   |
| <b>First Author:</b>                | Ketan Dhatariya, MBBS MSc MD MS FRCP   |
| <b>Order of Authors:</b>            | Ketan Dhatariya, MBBS MSc MD MS FRCP<br>Glenn Matfin, MD   |
| <b>Manuscript Region of Origin:</b> | UNITED KINGDOM   |
| <b>Abstract:</b>                    | Persons with diabetes require surgical procedures at a higher rate and have longer hospital stays than those without diabetes. 1. In particular, diabetes patients admitted for general and orthopedic surgery have some of the longest overall lengths of hospital stay 2. The presence of diabetes and/or hyperglycemia in surgical patients also leads to increased morbidity and mortality, with perioperative mortality rates up to 50% higher than the non-diabetes population 3. The reasons for these adverse outcomes are multi-factorial, but includes failure to identify patients with diabetes and/or hyperglycemia <sup>4</sup> ; 5multiple co-morbidities including microvascular and macrovascular complications 6-12 complex polypharmacy and insulin prescribing errors 13; increased perioperative and postoperative infections 3;14;15; associated hypoglycemia and hyperglycaemia 3; lack or inadequate institutional guidelines for management of inpatient diabetes and/or hyperglycemia 3;16; and inadequate knowledge of diabetes and hyperglycemia management amongst staff delivering care. |

## **Emergent Perioperative Hyperglycemia Management**

Dr Ketan Dhatariya  
Consultant in diabetes, endocrinology and general medicine  
Elsie Bertram Diabetes Centre  
Norfolk and Norwich University Hospitals NHS Foundation Trust  
Colney Lane  
Norwich, NR4 7UY, UK  
+44(0) 1603 288170  
[ketan.dhatariya@nnuh.nhs.uk](mailto:ketan.dhatariya@nnuh.nhs.uk)

Glenn Matfin,  
Medical Director,  
International Diabetes Center  
3800 Park Nicollet Blvd  
Minneapolis, MN 55416, USA  
Phone: 952 993 3048  
Fax: 952 993 1302  
[Glenn.matfin@parknicollet.com](mailto:Glenn.matfin@parknicollet.com)

## Introduction

Persons with diabetes require surgical procedures at a higher rate and have longer hospital stays than those without diabetes <sup>1</sup>. In particular, diabetes patients admitted for general and orthopedic surgery have some of the longest overall lengths of hospital stay <sup>2</sup>. The presence of diabetes and/or hyperglycemia in surgical patients also leads to increased morbidity and mortality, with perioperative mortality rates up to 50% higher than the non-diabetes population <sup>3</sup>. The reasons for these adverse outcomes are multifactorial, but includes failure to identify patients with diabetes and/or hyperglycemia<sup>4;5</sup>; multiple co-morbidities including microvascular and macrovascular complications <sup>6-12</sup> complex polypharmacy and insulin prescribing errors <sup>13</sup>; increased perioperative and postoperative infections <sup>3;14;15</sup>; associated hypoglycemia and hyperglycaemia <sup>3</sup>; lack or inadequate institutional guidelines for management of inpatient diabetes and/or hyperglycemia <sup>3;16</sup>; and inadequate knowledge of diabetes and hyperglycemia management amongst staff delivering care.

Several studies have shown that high preoperative and perioperative glucose and glycosylated haemoglobin (HbA1c) levels lead to poor surgical outcomes. These findings occur in both elective or emergency surgery, and include various types of surgery including spinal <sup>17</sup>, vascular <sup>18</sup>, colorectal <sup>19</sup>, cardiac <sup>20;21</sup>, trauma-related <sup>22</sup>, mastectomy <sup>23</sup>, foot and ankle <sup>24</sup>, neurosurgery, and hepatobiliary surgery <sup>25;26</sup>. Adverse outcomes related to increased morbidity and mortality includes increased wound infection rates, urinary tract infections, admission and time in intensive care, development of acute kidney

injury (AKI), or acute coronary syndromes (ACS). However, there are data to show that the outcomes of persons with diabetes may not be different – or may indeed be better – than those without diabetes if the diagnosis is known prior to surgery<sup>27;28</sup>. The reasons for this are unknown, and may be due to increased vigilance surrounding glucose control given to those with a diagnosis of diabetes.

In view of these findings, elective surgery with acceptable glycemic control (e.g. HbA1c <8.5% and ambient glycemic levels within acceptable range) and no evidence of diabetes-related acute decompensation (e.g. diabetic ketoacidosis [DKA], hyperglycemic hyperosmolar state [HHS], or electrolyte disturbance) would be the preferred option for diabetes patients requiring surgery (Figure 1). However, approximately 5% of persons with diabetes will require emergency surgery over their lifetime<sup>29</sup>. Emergency surgery is performed on patients who have an acute condition that threatens life, limb or the integrity of a body structure. Some emergency operations are time critical and need to be performed immediately (day or night). Emergency surgical care comprises 40–50% of the workload of most surgical specialties, and can result in additional complications, higher mortality (25%), increased costs, and is disruptive to elective surgery planning and implementation. By definition, the time of occurrence of these emergencies cannot be predicted, and appropriate surgical care must not be unduly delayed. Nonetheless, particular care must be taken in persons with diabetes who are being considered for emergency surgery to exclude DKA and other conditions (e.g. vomiting related to undiagnosed or poorly controlled gastroparesis or glucagon-like

peptide-1 [GLP-1] agonist adverse effect) that may be mistaken for surgical emergencies. Many patients with DKA and prominent abdominal symptoms have undergone needless surgical exploration for a nonexistent acute abdominal emergency.

### **Approaches to Management**

The actual treatment recommendations for a given patient should be individualized based on factors such as current glycemic control, type of diabetes, nature and extent of surgical procedure, and antecedent diabetes therapy<sup>30</sup>. Unfortunately, many patients who require emergency surgery will have suboptimal glycemic control. However, this is not necessarily a contraindication to the timely performance of potentially life-saving surgery. An intravenous (IV) access should be secured and immediate blood specimens should be sent for glucose, electrolyte, and acid-base assessment. Gross derangements of volume and electrolytes (e.g. hypokalemia, hypernatremia) should be corrected. Surgery should be delayed, whenever feasible, in patients with DKA, so that the underlying acid-base disorder can be corrected or, at least, ameliorated. Patients with HHS are markedly dehydrated and should be restored to good volume and improved metabolic status before surgery. For those having emergency surgery, aiming for a pragmatic blood glucose of between 110-180 mg/dl (6-10 mmol/L) should be the target. Blood glucose should be monitored at least hourly during the procedure and in the immediate postoperative period using an appropriate point-of-care measure to allow early detection of any alterations in metabolic

control. All patients receiving insulin before admission require insulin during the perioperative period. In the emergency setting, this is best achieved using continuous intravenous insulin infusion (CII, also known as variable rate intravenous insulin infusion [VRIII]). Other patients not previously on insulin therapy should be reviewed on an individualized basis to determine appropriate therapy. Patients not expected to miss more than one meal (i.e. short starvation period) might be candidates for alternative glucose-lowering therapies without the need for CII (VRIII). In comparison, patients expected to miss more than one meal should generally have a CII (VRIII). However, if blood glucose concentration rises above 180 mg/dl (10 mmol/L), a CII (VRIII) should be commenced and continued until the patient is eating and drinking. CII (VRIII) are often poorly managed in the perioperative setting and thus require explicit guidelines including how to transition from IV to subcutaneous insulin or noninsulin therapies. Other important factors includes optimizing and maintaining volume status, electrolyte balance, avoidance of pressure damage to the feet during surgery, and prevention and optimal treatment of hypoglycaemia. Early involvement of the critical care and diabetes specialist teams is recommended in the management of any high-risk surgical patient with diabetes and/or hyperglycemia.

### **Summary**

There is a wealth of evidence to show that poor preoperative, perioperative and postoperative glycemic control is associated with poor surgical outcomes. Despite the lack of robust data to confirm this, most clinicians agree that controlling glucose levels to an acceptable range is likely to reduce the risk of developing complications. The management goal is to optimize metabolic

control through close monitoring, adequate fluid and caloric repletion, and judicious use of insulin. The management of perioperative glucose control in the emergency setting usually requires the use of a CII (VRIII). However, where opportunities arise to optimise glycaemic control preoperatively (especially to allow stabilization of patients with diabetes-related crises), then these should be undertaken.

## Reference List

1. Daultrey H, Gooday C, Dhatariya K. Increased length of inpatient stay and poor clinical coding: audit of patients with diabetes. *J R Soc Med Sh Rep* 2011; 2(11):83.
2. Sampson MJ, Dozio N, Ferguson B, Dhatariya K. Total and excess bed occupancy by age, speciality and insulin use for nearly one million diabetes patients discharged from all English Acute Hospitals. *Diabetes Res Clin Pract* 2007; 77(1):92-98.
3. Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010; 33(8):1783-1788.
4. Rayman G. Inpatient audit. Diabetes Update. [http://www.diabetes.org.uk/upload/Professionals/publications/Comment\\_inpatient%20audit\\_new.pdf](http://www.diabetes.org.uk/upload/Professionals/publications/Comment_inpatient%20audit_new.pdf). 2010.
5. Hamblin PS, Topliss DJ, Chosich N, Lording DW, Stockigt JR. Deaths associated with diabetic ketoacidosis and hyperosmolar coma. 1973-1988. *Med J Aust* 1989; 151(8):441-442.
6. Cullinane M, Gray AJ, Hargraves CM, Lansdown M, Martin IC, Schubert M. Who Operates When? II The 2003 report of the national confidential enquiry into perioperative deaths. <http://www.ncepod.org.uk/pdf/2003/03full.pdf>. 2003.
7. Cuthbertson BH, Amiri AR, Croal BL, Rajagopalan S, Brittenden J, Hillis GS. Utility of B-type natriuretic peptide in predicting medium-term mortality in patients undergoing major non-cardiac surgery. *Am J Cardiol* 2007; 100(8):1310-1313.
8. O'Brien MM, Gonzales R, Shroyer AL, Grunwald GK, Daley J, Henderson WG et al. Modest serum creatinine elevation affects adverse outcome after general surgery. *Kidney Int* 2010; 62(2):585-592.
9. Lee TH, Marcantonio ER, Mangione EJ, Polanczyk CA, Cook EF, Sugarbaker DJ et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; 100(10):1043-1049.
10. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16(2):434-444.
11. Veglio M, Chinaglia A, Cavallo-Perin P. QT interval, cardiovascular risk factors and risk of death in diabetes. *J Endocrinol Invest* 2004; 27(2):175-181.



12. Gordojs A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic peripheral neuropathy in the U.S. *Diabetes Care* 2003; 26(6):1790-1795.
13. National Patient Safety Agency. Insulin safety. Reducing harm associated with the unsafe use of insulin products. <http://www.patientsafetyfirst.nhs.uk/Content.aspx?path=/interventions/relatedprogrammes/medicationsafety/insulin/>. 2010.
14. Jhanji S, Thomas B, Ely A, Watson D, Hinds CJ, Pearce RM. Mortality and utilisation of critical care resources amongst high-risk surgical patients in a large NHS trust. *Anaesthesia* 2008; 63(7):695-700.
15. Pearce RM, Harrison DA, James P, Watson D, Hinds C, Rhodes A et al. Identification and characterisation of the high-risk surgical population in the United Kingdom. *Critical Care (London)* 2006; 10(3):R10.
16. Sampson MJ, Brennan C, Dhatariya K, Jones C, Walden E. A national survey of in-patient diabetes services in the United Kingdom. *Diabetic Med* 2007; 24(6):643-649.
17. Walid MS, Newman BF, Yelverton JC, Nutter JP, Ajjan M, Robinson JS. Prevalence of previously unknown elevation of glycosylated hemoglobin in spine surgery patients and impact on length of stay and total cost. *J Hosp Med* 2010; 5(1):E10-E14.
18. O'Sullivan CJ, Hynes N, Mahendran B, Andrews EJ, Avalos G, Tawfik S et al. Haemoglobin A1c (HbA1C) in non-diabetic and diabetic vascular patients. Is HbA1C an independent risk factor and predictor of adverse outcome? *Eur J Vasc Endovasc Surg* 2006; 32(2):188-197.
19. Gustafsson UO, Thorell A, Soop M, Ljungqvist O, Nygren J. Haemoglobin A1c as a predictor of postoperative hyperglycaemia and complications after major colorectal surgery. *Br J Surg* 2009; 96(11):1358-1364.
20. Halkos ME, Lattouf OM, Puskas JD, Kilgo P, Cooper WA, Morris CD et al. Elevated preoperative hemoglobin A1c level is associated with reduced long-term survival after coronary artery bypass surgery. *Ann Thorac Surg* 2008; 86(5):1431-1437.
21. Alserius T, Anderson RE, Hammar N, Nordqvist T, Ivert T. Elevated glycosylated haemoglobin (HbA1c) is a risk marker in coronary artery bypass surgery. *Scand Cardiovasc J* 2008; 42(6):392-398.
22. Kreutziger J, Schlaepfer J, Wenzel V, Constantinescu MA. The role of admission blood glucose in outcome prediction of surviving patients with multiple injuries. *J Trauma* 2010; 67(4):704-708.
23. Vilar-Compte D, Alvarez de Iturbe I, Martin-Onraet A, Perez-Amador M, Sanchez-Hernandez C, Volkow P. Hyperglycemia as a risk factor for

surgical site infections in patients undergoing mastectomy. *Am J Infect Control* 2008; 36(3):192-198.

24. Shibuya N, Humphers JM, Fluhman BL, Jupiter DC. Factors associated with nonunion, delayed union, and malunion in foot and ankle surgery in diabetic patients. *J Foot Ankle Surg* 2013; 52(2):207-211.
25. Chuang SC, Lee KT, Chang WT, Wang SN, Kuo KK, Chen JS et al. Risk factors for wound infection after cholecystectomy. *J Formos Med Assoc* 2004; 103(8):607-612.
26. Ambiru S, Kato A, Kimura F, Shimizu H, Yoshidome H, Otsuka M et al. Poor postoperative blood glucose control increases surgical site infections after surgery for hepato-biliary-pancreatic cancer: a prospective study in a high-volume institute in Japan. *J Hosp Infect* 2008; 68(3):230-233.
27. Kwon S, Thompson R, Dellinger P, Yanez D, Farrohi E, Flum D. Importance of perioperative glycemic control in general surgery: A report from the surgical care and outcomes assessment program. *Ann Surg* 2013; 257(1):8-14.
28. Fortington LV, Geertzen JH, van Netten JJ, Postema K, Rommers GM, Dijkstra PU. Short and long term mortality rates after a lower limb amputation. *Eur J Vasc Endovasc Surg* 2013; 46(1):124-131.
29. Dagogo-Jack S, Alberti K. Management of diabetes mellitus in surgical patients. *Diabetes Spectr* 2002; 15(1):44-48.
30. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97(1):16-38.

Legend to Figure 1.

An example of an algorithm to see if a patient with diabetes is suitable for day case surgery or not

Figure 1

