

EDITORIAL II

Does dexamethasone-induced hyperglycaemia contribute to postoperative morbidity and mortality?

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Why is a diabetologist writing in an anaesthetic journal? I hope that by the time you have finished reading this you will reflect on your own practice and consider whether you may be contributing—albeit unwittingly—to the postoperative morbidity and mortality at your institution.

Almost everyone reading this will have heard of the obesity epidemic, with a substantial proportion of the population being overweight or obese.¹ In addition, almost everyone reading this will know that being overweight or obese is associated with an increased risk of developing dysglycaemia or type 2 diabetes mellitus.² What may not be so familiar to specialties outside of diabetes is that recent data have shown that the mean prevalence of diabetes in all hospitalized inpatients in the UK, regardless of their reasons for admission, is 15%.³ Finally, almost everyone reading this will know that glucocorticoid use is associated with an increased risk of developing insulin resistance, and hyperglycaemia.^{4 5}

Consider the following situation: a 47-yr-old previously fit and well woman with no history of glucose intolerance who has just undergone an uncomplicated gall bladder removal. She has a body mass index of 32 kg m⁻². She is just about to be taken off the operating table to go to recovery and, in line with the principles of the Enhanced Recovery After Surgery Program, she is given a single dose of i.v. dexamethasone to minimize the risk of postoperative nausea and vomiting.⁶ The patient eventually goes back to the ward, and the anaesthetist moves on to the next case.

Given that glucocorticoids have a multitude of effects on glucose levels what is the potential impact of that single dose of dexamethasone? Does anyone routinely measure the glucose levels of someone without a history of diabetes, despite them being given a drug that is known to raise blood glucose levels? Does it, in fact, matter?

There are now plenty of data to show that perioperative glycaemic control is associated with postoperative outcomes.^{7–13} High glucose levels or raised levels of glycated haemoglobin (a measure of prevailing glucose control) are associated with poor outcomes. In particular, recent data suggest that poor postoperative glycaemic control is associated with an increase in the risk of postoperative

mortality,¹³ with the highest risk in those who were not previously known to have diabetes.

Dexamethasone is a very commonly used antiemetic and in the face of a limited number of drugs available to prevent postoperative nausea and vomiting has been shown to have many advantages.¹⁴ However, whilst there are data to show that dexamethasone use in the perioperative period raises blood glucose levels,^{15 16} there almost are no published data on the effects of these raised blood glucose levels of postoperative morbidity and mortality.

Thus, despite the evidence that even a single dose of glucocorticoids can raise blood glucose, and that postoperative glycaemic control is associated with increased risk of morbidity and mortality, how many anaesthetists ask for postoperative bedside blood glucose measurements—especially in people not previously known to have diabetes?

What is needed is a concerted effort to collect data, initially observational, and eventually interventional trial data to assess the effects of glucocorticoid use on postoperative outcomes. The problem is of course the numbers needed to see an effect. If blood glucose levels in people without diabetes only increase by a few millimoles per litre and the effect size is small, then the numbers needed to see a statistically significant difference will be large. Or do the benefits of administering corticosteroids outweigh the potential side-effects of short-lasting hyperglycaemia?¹⁷ Does this mean that this should not or cannot be done? Over the last few years, endocrinologists have been hit by a series of events that have questioned their use of drugs that were used for years before their use was shown to be harmful.^{18 19} Maybe the harm done by dexamethasone use should be subjected to the same degree of rigorous scrutiny that was applied to these drugs. Anaesthetists and diabetes teams need to collaborate to ensure that patients are not being harmed by the use of what has always been deemed to be another 'safe' drug.

Declaration of interest

K.D. was the lead author on the NHS Diabetes guideline on the management of patients with diabetes undergoing

surgery or procedures, available at http://www.diabetes.nhs.uk/areas_of_care/emergency_and_inpatient/perioperative_management/. K.D. is a full time employee of the National Health Service.

References

- 1 Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *J Am Med Assoc* 2012; **307**: 491–7
- 2 Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. *Ann Intern Med* 1995; **122**: 481–6
- 3 NHS Diabetes. 2011 National Diabetes Inpatient Audit (NaDIA) 2010. Available from http://www.diabetes.nhs.uk/information_and_data/diabetes_audits/national_diabetes_inpatient_audit/ (accessed 15th November 2012)
- 4 Gounarides JS, Korach-Andre M, Killary K, et al. Effect of dexamethasone on glucose tolerance and fat metabolism in a diet-induced obesity mouse model. *Endocrinology* 2008; **149**: 758–66
- 5 de Oliveira C, de Mattos AB, Biz C, et al. High-fat diet and glucocorticoid treatment cause hyperglycemia associated with adiponectin receptor alterations. *Lipids Health Disease* 2011; **10**: 5
- 6 National Health Service Institute for Innovation and Improvement. Enhanced Recovery Programme. Available from http://www.institute.nhs.uk/quality_and_service_improvement_tools/quality_and_service_improvement_tools/enhanced_recovery_programme.html (accessed 15 November 2012)
- 7 Walid MS, Newman BF, Yelverton JC, et al. 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**: E10–4
- 8 O'Sullivan CJ, Hynes N, Mahendran B, 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**: 188–97
- 9 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**: 1358–64
- 10 McConnell YJ, Johnson PM, Porter GA. Surgical site infections following colorectal surgery in patients with diabetes: association with postoperative hyperglycemia. *J Gastrointest Surg* 2009; **13**: 508–15
- 11 Halkos ME, Lattouf OM, Puskas JD, et al. Elevated preoperative hemoglobin A1c level is associated with reduced long-term survival after coronary artery bypass surgery. *Ann Thorac Surg* 2008; **86**: 1431–7
- 12 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**: 704–8
- 13 Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010; **33**: 1783–8
- 14 Murphy GS, Szokol J, Greenberg SB, et al. Preoperative dexamethasone enhances quality of recovery after laparoscopic cholecystectomy: effect on in-hospital and postdischarge recovery outcomes. *Anesthesiology* 2011; **114**: 882–90
- 15 Hans P, Vanthuyne A, Dewandre PY, Brichant JF, Bonhomme V. Blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing abdominal surgery. *Br J Anaesth* 2006; **97**: 164–70
- 16 Dieleman JM, Nierich AP, Rosseel PM, et al. Intraoperative high-dose dexamethasone for cardiac surgery: a randomized controlled trial. *J Am Med Assoc* 2012; **308**: 1761–7
- 17 Eberhart LH, Graf J, Morin AM, et al. Randomised controlled trial of the effect of oral premedication with dexamethasone on hyperglycaemic response to abdominal hysterectomy. *Eur J Anaesthesiol* 2011; **28**: 195–01
- 18 Loke YK, Kwok CS, Singh S. Comparative cardiovascular effects of thiazolidinediones: systematic review and meta-analysis of observational studies. *Br Med J* 2011; **342**: d1309
- 19 Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the women's health initiative randomized controlled trial. *J Am Med Assoc* 2002; **288**: 321–33

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EDITORIAL III

Aprotinin and cardiac surgery: a sorry tale of evidence misused

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Although evidence from clinical trials is crucial to the advancement of modern medicine, its quality varies

considerably. Counterintuitively, high-quality evidence can be ignored and low-quality evidence may lead to the