

Assessing the prevalence of dexamethasone use in patients undergoing surgery, and subsequent glucose measurements: a retrospective cohort study

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Received: 6 February 2017

Accepted in revised form: 15 March 2017

Abstract

A single dose of glucocorticoid can cause hyperglycaemia. Hyperglycaemia is associated with poor outcomes in all surgical specialties. Dexamethasone is widely used to prevent postoperative nausea and vomiting. We aimed to assess how many individuals were given dexamethasone as part of their general anaesthetic regimen, and how many had a subsequent capillary blood glucose concentration measured during the next 24 hours.

We undertook a retrospective case-note analysis, set in a single centre teaching hospital, of all patients undergoing surgery during one week in August 2013. In terms of interventions and measurements, we assessed how many patients were given dexamethasone perioperatively and the number of patients who had a capillary blood glucose concentration measured during the subsequent 24 hours.

It was found that 373 patients had had a general anaesthetic; 18 sets of case notes were unavailable. A total of 234 patients (66%) had dexamethasone. Twenty of the 355 (5.7%) had a blood glucose measured prior to surgery, 14 of whom had diabetes. Only 16/355 (4.5%) people had a blood glucose level measured during the first 24 hours after surgery. All of these had diabetes.

Despite evidence that postoperative hyperglycaemia is associated with harm, and that glucocorticoids are associated with hyperglycaemia, glucose levels are not commonly measured after dexamethasone administration. Copyright © 2017 John Wiley & Sons.

Practical Diabetes 2017; 34(4): 117–121

Key words

anaesthesia; pharmacology; surgery; dexamethasone

Introduction

Dexamethasone is a commonly-used anaesthetic drug, used in pain and fatigue, as well as to induce improvements in appetite and mood. However, its main use is for the prevention of postoperative nausea and vomiting (PONV). It is widely advocated as one of the drugs of choice for the prevention of this distressing side effect of general anaesthesia.^{1,2}

A Cochrane review of drugs used to prevent PONV showed that dexamethasone use reduced PONV by almost 50% compared with placebo, and was superior to more commonly-used drugs such as metoclopramide.¹ Until recently, dexamethasone was cheaper than 5-HT₃ receptor antagonists such as ondansetron, but because those drugs have become generic, they are now cheaper and more widely used than dexamethasone.³

Hyperglycaemia (a fasting plasma glucose of >7.0mmol/L [126mg/dl], or random plasma glucose of >11.1mmol/L [200mg/dl]) in surgical patients can be found in people

who are either previously known to have diabetes or who develop transient hyperglycaemia due to a combination of acute illness and the physiological trespass of surgery – so-called ‘stress hyperglycaemia’.^{4,5} It can also be found in people who had previously undiagnosed diabetes. The use of medication that may induce insulin resistance and subsequent hyperglycaemia is also a factor in the development of postoperative hyperglycaemia in any of these groups. Glucocorticoids are well known to induce insulin resistance and hyperglycaemia by a variety of mechanisms.⁶

There have recently been data to show that perioperative hyperglycaemia is associated with harm, worse with postoperative hyperglycaemia.^{7,8} In particular, it is those individuals who are not previously known to have diabetes who experience the worst outcomes. However, there are no data on what proportion of patients undergoing surgery are given dexamethasone, and how many of those individuals have their

blood glucose measured in the immediate postoperative period.

The present study was carried out to try to answer this question – to see how many people having surgery in a single, large institution during a single week were given dexamethasone, and then how many had their blood glucose levels measured.

Materials and methods

This was a retrospective cohort analysis from a single, large tertiary referral centre. Data from the operating theatre databases were collected for all patients who had any form of surgery during a one-week period in August 2013 from any surgical specialty. Four of the authors (AS, HMO'C, VN and LS) analysed the paper anaesthetic charts, observation charts, inpatient notes and electronic discharge summaries.

We gathered information on the following: demographic data; medical comorbidities; the operation performed; whether dexamethasone was given and in what dosage; if blood glucose monitoring was performed; and 28-day readmission and complication data.

The STROBE criteria were adhered to during the conduct and presentation of these data.⁹

Results

In total, 848 individuals entered the operating theatres for a procedure in our hospital during the week of 12–18 August 2013. Of these, 475 patients were excluded from the analysis because their procedures were not performed under general anaesthetic (i.e. under local anaesthetic, e.g. ophthalmological, epidural, or spinal). A further 18 were excluded because their anaesthetic charts were not available. Of the remaining 355 patients whose data were analysable, the median age was 49.1 years (range three months old to 97 years), and 168 (47.3%) were male. Twenty-four (6.7%) had type 2 diabetes, with no-one that week having type 1 diabetes. Of these, three were treated with diet alone, 19 were on oral hypoglycaemic agents, and two were insulin treated.

Prior to the operation, 14 of the 24 patients known to have diabetes had a preoperative glucose level

Surgical specialty	Total no. of cases	No. (%) given dexamethasone	Mean dose (mg) of dexamethasone given (\pm SD)
General	91	66 (73)	7.1 (1.5)
Gynaecology	54	27 (50)	7.4 (1.0)
ENT	11	8 (73)	8.0 (0)
Vascular	20	9 (45)	7.1 (1.3)
Orthopaedic	95	60 (63)	7.3 (1.4)
Dental	7	7 (100)	6.2 (2.3)
Urology	36	24 (67)	6.8 (1.8)
Thoracic	6	5 (83)	7.2 (0.8)
Paediatric	20	18 (90)	3.0 (1.5)
Plastics	11	10 (91)	6.9 (1.7)
Cardio	4	0 (0)	0 (0)
Totals	355	234 (66)	

Table 1. Breakdown of numbers of patients operated on according to surgical specialty

measured. Six people without diabetes also had blood glucose levels measured. Nineteen of those known to have diabetes had a preoperative HbA_{1c} available, but, in four of those, the value was more than three months old. However, further analysis showed that five had been emergency admissions, of whom two required urgent cancer surgery. Thus, there was only one purely elective case without an HbA_{1c}. Eleven patients were already on long-term glucocorticoid therapy.

Of the 355 patients available for review, the breakdown of surgical specialties is shown in Table 1. A total of 234 (66%) were given a single dose of dexamethasone in the immediate perioperative period. The median dose of dexamethasone given was 6.7mg, with a breakdown per specialty shown in Table 1. It can be seen that the lowest doses were given to paediatric patients in view of their smaller size, while there was no difference in the mean doses given to adults. No patients had more than a single dose. Eight of the patients given dexamethasone had pre-existing diabetes. Only 16 people (4.5%) had their blood glucose levels checked during the 24 hours postoperatively. All of these patients had diabetes. However, two

patients who had diabetes and who were given dexamethasone did not have a glucose level measured, and, overall, eight patients with diabetes did not have a postoperative glucose level measured.

Complications did occur in three patients who had high by-bedside capillary blood glucose (CBG) concentration measurements within 24 hours. They all had a previous diagnosis of diabetes. One patient developed a wound infection and pneumonia. This patient was admitted to the intensive care unit but eventually died. The patient's bedside CBG concentration at 24 hours was 12.1mmol/L. They had been given 8mg of dexamethasone postoperatively. The second patient required a further wound debridement and subsequent below-knee amputation. Their bedside CBG concentration at 24 hours was 27mmol/L; they had been given 6.6mg dexamethasone postoperatively. Patient three developed acute kidney injury and a wound infection; the patient's bedside CBG concentration at 24 hours was 24mmol/L, but they had not been given dexamethasone.

Twenty-eight day postoperative outcomes for the whole cohort of 355 patients were as follows: wound infection occurred in four patients;

pneumonia in two patients; acute kidney injury in two patients; urinary tract infection in two patients; five patients went to the intensive care unit; and four patients died.

Discussion

This observational study has shown that in an unselected cohort of 848 patients undergoing surgery, most people who required a general anaesthetic were given dexamethasone in the perioperative period. Despite the data showing that glucocorticoids are associated with hyperglycaemia, and that hyperglycaemia is associated with harm in the postoperative period, 95.5% of patients given dexamethasone had no evidence of postoperative blood glucose level measurements.

While we did not set out to look for differences in outcomes between those who were given dexamethasone and those who were not, previous work has shown that glucocorticoid administration is associated with hyperglycaemia.^{10–12} Further, there have been several studies showing that hyperglycaemia in the postoperative period is associated with harm. These include (but are not limited to) general surgery, cardiac surgery, vascular surgery,¹³ neurosurgery, orthopaedic surgery,¹⁴ colorectal surgery, trauma, breast surgery, liver transplantation, hepatobiliary and pancreatic surgery, cholecystectomy, and foot and ankle surgery.¹⁵

These studies showed that postoperative hyperglycaemia was associated with poor outcomes, such as: increased length of hospital stay; increased blood loss; increased length of surgery; anastomotic leaks; the development of acute kidney injury; acute myocardial infarction; wound infection; time spent on a ventilator or on the intensive care unit; and death.¹⁶

Previous studies have looked at the impact of dexamethasone and glucose in postoperative patients,^{17–20} but none have observed an association between dexamethasone-induced hyperglycaemia and adverse outcomes. However, for those people who do develop steroid-induced hyperglycaemia, there are no data to show whether the outcomes for those individuals are any different. This is

likely to be because the vast majority of studies are under-powered to demonstrate any effects of this postoperative hyperglycaemia.²¹ This is also likely to be the case for studies involving 'medical' patients which have failed to show differences in outcomes despite a significant difference in plasma glucose concentrations in those given glucocorticoids.²²

The hyperglycaemia associated with dexamethasone use is likely to be transient. However, with the data to show that with each mmol/L increase in blood glucose levels *even within the reference range* there is a rise in mortality of 19%, it is important to measure blood glucose levels to ensure no harm is potentially being done to patients.²³ Therefore, it is likely that the previous work looking at any potential harm associated with dexamethasone use is flawed because the wrong questions were being asked and/or the wrong analysis was being done.²¹

There are no data to show what proportion of patients develop hyperglycaemia when given dexamethasone, even if they do not previously have diabetes. While educated guesses can be made, it is not clear what makes a particular person more susceptible to developing dexamethasone-induced hyperglycaemia after surgery. As mentioned, the vast majority of papers looking at the question of whether dexamethasone induces hyperglycaemia, or if the hyperglycaemia is associated with harm are methodologically flawed. Very large data sets will be required to answer these questions, because the number of people likely to develop hyperglycaemia is small; achieving sufficient numbers where outcomes of dexamethasone-induced hyperglycaemia can be analysed, and reach statistical significance, will entail coordination between centres and between diabetes and surgical teams.

The National Institute for Health and Care Excellence does not currently recommend routine blood glucose screening preoperatively for elective surgery; it is perhaps, therefore, unsurprising that so few patients had this measured.²⁴ In addition, there are currently no standards for postoperative blood glucose measurements, despite the

evidence that postoperative hyperglycaemia is associated with harm.

There are some limitations to our study in that this was a single-site, retrospective study. We only had 28-day follow-up data and we had insufficient numbers of patients having their blood glucose levels measured to be able to make any meaningful analysis of the impact of hyperglycaemia postoperatively. Our institution does not offer neurosurgery or cardiac surgery and is not a trauma centre; however, all other forms of surgery are carried out here. Another limitation is that it is not known what happened to patients when they were discharged home – e.g. if they consulted their primary care team for postoperative complications that did not necessitate hospital contact. A further limitation is that no information was recorded in the hospital notes as to the reason for dexamethasone being given, or not given – i.e. if any of the patients had any predictors of PONV, or whether dexamethasone was being used as an analgesic.²⁵ In addition, we did not know what proportion of patients were given intravenous dextrose as part of their fluid regimens. However, if dextrose is given as a maintenance fluid it is usually 5% dextrose which rarely has an impact on overall glucose levels. Finally, because this was a retrospective case-notes analysis, we did not collect patients' body mass index which is known to be an additional risk factor for the development of insulin resistance and hyperglycaemia.²⁶

We omitted patients undergoing regional anaesthesia. We acknowledge that many of these patients would have received glucocorticoid therapy as part of their anaesthetic regimen, but, in the first instance, we wanted to limit analysis to those people who were most likely to be given dexamethasone as an antiemetic for PONV – i.e. those who had a general anaesthetic.

The strengths of our data are that we are a large unit, we had a full data set collected from every surgical specialty, and we had data from a large number of anaesthetists; therefore this information is likely to be extremely generalisable to other units.

Our data are also in contrast to previous work that suggested that the rates of hospital admission are double those of the background population without diabetes for any particular condition.²⁷ In our cohort, 6.7% of patients had diabetes which is just over the reported prevalence of diabetes in the UK.²⁸

While there remains no evidence to show that treating postoperative hyperglycaemia makes a difference to outcome, it does seem right to try to maintain normal blood glucose levels.²⁹ The NICE 2016 guideline did not advocate routine preoperative glycaemic assessment.²⁴ However, since then, the impact of poor glycaemic control on surgical outcomes has become apparent. Thus, optimisation of perioperative glycaemic control in people with diabetes has been strongly advocated in the UK by the Joint British Diabetes Societies Inpatient Care Group and the Royal College of Anaesthetists who have produced national guidelines on the perioperative management of adult patients undergoing surgery or other procedures.^{30,31} In April 2016, NICE updated its preoperative testing recommendations to say: 'Offer HbA_{1c} testing to people with diabetes having surgery if they have not been tested in the last 3 months.'²⁴ However, somewhat disappointingly given the rapid increase in obesity reported by the World Health Organization and a recent report on the global rise in the numbers of people with diabetes, it makes no such recommendations for people who are at risk of diabetes.^{32,33}

Further work, involving large enough numbers to be able to discern differences in outcomes, needs to be done to answer the question about whether or not dexamethasone causes harm.³⁴ However, the numbers involved will need to be very large, given that the number of complications is likely to remain small, and to be able to negate the multiple confounders involved in postoperative recovery.

Recently, an alternative antiemetic, ondansetron, has become generic and the cost has substantially come down – indeed, the cost to NHS hospitals is less than the price quoted in the *British National Formulary*; it is now cheaper than

Key points

- Dexamethasone is commonly given in the perioperative environment, predominantly as an antiemetic
- Glucocorticoid use – even a single dose – can be associated with hyperglycaemia
- Postoperative hyperglycaemia is associated with harm
- We show that glucose testing is rare after dexamethasone use and ask whether its use is associated with harm

dexamethasone, and does not have an effect on glucose.³

One of the questions that arises from this work is: 'Who is responsible for any steroid-induced dysglycaemia?' The anaesthetist who gave the drug may feel that, once the patient has left the recovery area, they are no longer responsible for the patient, and the patient remains under the care of the consultant surgeon. However, the surgeon may feel that, given they did not administer the drug, any resultant effects are not their responsibility. This issue remains unresolved.

In summary, our data have shown that, in an unselected cohort of patients undergoing surgery of any sort in our institution, a large proportion of them were given dexamethasone; however, only 4.5% had their blood glucose levels measured postoperatively. From our small dataset it is difficult to infer anything about the effects of the dexamethasone on outcomes, because there are too many confounding factors – such as perioperative HbA_{1c}, different surgeries, the wide age range, and different therapies for type 2 diabetes. Until the potential harms associated with dexamethasone are more thoroughly evaluated we recommend that diabetes teams work with surgeons and anaesthetists to develop a protocol to ensure that patients given perioperative dexamethasone have their glucose concentrations regularly checked. It remains to be determined whether maintaining euglycaemia needs to be a standard part of postoperative care.

Declaration of interests

There are no conflicts of interest declared. Funding: none.

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POEMs



30-minute office BP monitor readings are 23/12mmHg lower than a single office reading

Clinical question

How well does monitoring blood pressure for 30 minutes in the clinic compare with a single clinic reading in patients suspected of having white-coat hypertension?

Reference

Bos MJ, Buis S. Thirty-minute office blood pressure monitoring in primary care. *Ann Fam Med* 2017;15:120–3.

Synopsis

This study took place over a six-month period in a single primary care practice in the Netherlands. The authors recruited every patient who underwent 30-minute office blood pressure monitoring (OBP30) for medical reasons. For the OBP30 the patient sits alone in a quiet area with an automated unit that measures and records blood pressure every 5 minutes. The final OBP30 reading is the simple average of the six readings. The authors

report that approximately 20% of the patients had diabetes and 20% had cardiovascular disease, but they don't report how many had hypertension. The most common reasons for ordering the OBP30 included suspected white-coat hypertension, newly-diagnosed hypertension, inconsistent office readings, and monitoring medication effectiveness. On average, the systolic OBP30 readings were 23mmHg lower than the office readings, and the diastolic OBP30 readings were 12mmHg lower than in the office. Approximately 80% of the clinicians would have intensified treatment based solely on the office blood pressure readings compared with only 25% who would have intensified treatment based on the OBP30. The existing data of treating hypertension are based on a diagnosis established after three elevated readings on separate occasions, and a few studies have suggested that white-coat hypertension is not an altogether benign condition.

POEMs



Type 2 diabetes: metformin first, other treatments second

Clinical question

What should we use as the primary treatment of type 2 diabetes mellitus?

Reference

Qaseem A, *et al.*, for the Clinical Guidelines Committee of the American College of Physicians. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med* 2017;166:279–90.

Synopsis

The recommendations of the Committee focus on improving patient-oriented outcomes and are based on graded evidence. The authors recommend prescribing

metformin 'when pharmacologic therapy is needed to improve glycemic control', implying that there should be a specific goal for glycaemic control but not stating what it should be. Metformin remains the cornerstone of treatment on the basis of its effectiveness in reducing cardiovascular mortality as compared with sulphonylurea treatment, its effectiveness in reducing glycaemic levels, its association with weight loss, low risk of hypoglycaemia, and cost. When additional glycaemic control is needed (again, no guidance regarding when that would be), the authors suggest using either a sulphonylurea, a thiazolidinedione, an SGLT2 inhibitor, or a DPP-4 inhibitor in addition to metformin. The authors focused only on oral therapy here and did not give recommendations regarding insulin.