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Glycaemic control during cataract surgery under loco-regional anaesthesia: a growing problem and we are none the wiser

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The presence of sight-impairing opacification in the natural lens of the eye is termed as cataract, an age-related condition and is the foremost cause of blindness in the world.[1] UN data[2] indicates that the proportion of older persons has increased substantially in recent years both in developed and developing countries, irrespective of whether it is in urban or rural areas. This trend is poised to accelerate in the coming decades; and will have an impact on the worldwide socioeconomic and healthcare landscape.

The patients with diabetes are also at a high risk of developing retinopathy and cataracts.[3] Diabetes is a progressive endocrine disease that results in end organ dysfunction if left untreated over prolonged periods. Diabetes is as a result of either the pancreas not producing enough insulin (type 1 diabetes) or the cells of the body not responding properly to the insulin produced (type 2). The International Diabetes Federation estimates that as of 2015, 415 million people have diabetes worldwide, representing 8.3% of the adult population.[4] The global burden of the disease is expected to increase.[5]

Urbanization, affluence, access to healthcare and longer life expectations are variables that longitudinally may correlate with the twin conditions of diabetes mellitus and cataract.[6] Ophthalmologists and anaesthetists can therefore expect a significant and increasing number of perioperative patients with composite conditions, presenting for elective cataract surgery. Current standard of surgical care involves removal of the cataractous lens via phacoemulsification on an ambulatory or day case basis. Cataract surgery is a short procedure that is routinely performed under local or regional (loco-regional) anaesthesia. This patient population is mostly elderly with several pre-existing comorbid conditions including diabetes mellitus. The metabolic and endocrine response to short surgical procedures that are performed under loco-regional anaesthesia is muted.[7]

There are several guidelines pertaining to either perioperative cataract surgery management or perioperative diabetes management.[8–10] Nonetheless, many issues remain unanswered and, to our best knowledge, there are no international consensus statements or guidelines pertaining to perioperative glucose control for cataract surgery under local anaesthesia. There are several questions which need answering; 1) What are the medical dangers and implications of uncontrolled diabetes? 2) Which is more important - HbA1c or random blood glucose before surgery? 3) What is the optimal concentration of blood glucose before surgery? 4) Do we need to control perioperative hyperglycaemia? The authors attempt to address pertinent aspects on these questions in this editorial based on the current available literature.

Medical dangers and implications of uncontrolled diabetes

Long-term hyperglycaemia has significant deleterious health effects. People with diabetes are at increased risk of developing macrovascular disease (stroke and myocardial infarction) and microvascular disease (nephropathy, neuropathy, and retinopathy). Autonomic neuropathy, which is common in this patient population, may increase haemodynamic lability including inhibition of the cardiovascular response to hypotension. In addition, it may cause gastroparesis, thus increasing the risk of regurgitation and pulmonary aspiration.

Patients with diabetes are prone to acute hyperglycaemia and/or hypoglycaemia in the perioperative period. Preoperative fasting, anxiety and withholding of anti-diabetic medications, and anaesthetic and surgical stress responses may lead to perioperative hyperglycaemia. Perioperative hyperglycaemia is a predictor of adverse outcomes. Acute hyperglycaemia may lead to dehydration (from osmotic diuresis), diabetic ketoacidosis (predominant in type-1 diabetes) and a non-ketotic hyperosmolar states (predominant in type-2 diabetes). In addition, postoperative hyperglycaemia is an independent risk factor for surgical complications such as surgical site infection, delayed wound healing, and need for reoperation.[9]

There is much evidence to show that good long-term control of blood glucose will reduce the likelihood of long-term complications such is retinopathy/maculopathy, infections, and the need for cataract surgery.[11] However, the evidence is weaker when asked the question whether perioperative glucose control might influence surgical outcomes, as there is no published evidence on the adverse effects of high intraoperative blood glucose on outcome after cataract surgery.

From a theoretical point, how might high blood glucose affect the outcome of cataract surgery? Some surgeons might worry about the risk of sight-threatening perioperative complications such as choroidal haemorrhage, or early postoperative complications such as endophthalmitis and cystoid macular oedema (CMO), which can cause blurring of central vision. There is little evidence to link high blood glucose with any significant increase in risk of these complications. Case-control studies did not find a positive association between diabetes status and the likelihood of choroidal haemorrhage.[12] The risk of developing postoperative endophthalmitis in patients with diabetes is very low and its causal relationship with perioperative hyperglycemia remains controversial,[13 14] While diabetes *per se* is postulated as a risk factor for CMO after cataract surgery[15] and worsening of retinopathy, there is little evidence to suggest that high perioperative blood glucose is a risk factor.

Suko and colleagues[16] assessed the effect of rapid preoperative glycaemic correction, defined as reducing the HbA1c from $>9\%$ (75 mmol mol^{-1}), by at least 3%, in the three months before surgery. Paradoxically, this seems to increase the risk of postoperative progression of retinopathy and maculopathy. The authors concluded that the practice should be avoided in patients with moderate to severe non-proliferative diabetic retinopathy.[16] A review article entitled 'prevention of CMO after cataract surgery in nondiabetic and patients with diabetes' did not identify any studies that had looked at the effects of perioperative glucose control on CMO rates.[17]

The literature points to a trend for increased likelihood of some eye complications in patients who have diabetes. However, the role of short-term blood glucose control is not well understood. We are not aware of any large, robust studies that have looked at outcomes for patients who have high blood glucose intraoperatively. The Joint Colleges (The Royal College of Anaesthetists and The Royal College of Ophthalmologists) guidelines 2012 for ophthalmic anaesthesia under local anaesthesia,[18 19] stated that at present there is insufficient evidence to recommend cancelling the surgery above a certain high blood glucose concentration and the clinical judgement should prevail.

Which is more important—HbA1c or random blood glucose before surgery?

HbA1c is considered as an indicator of long-term glycaemic control, as it reflects the average glycaemic concentrations over the previous three to four months. Adequate glycaemic control may be associated with a lower incidence of systemic and surgical complications, decreased mortality, and shorter duration of hospital stay.[20] However, a recent systematic review concluded that elevated HbA1c concentrations were not associated with increased postoperative morbidity and mortality after noncardiac surgery.[21] Notably, the studies included in this systematic review were heterogeneous and of less robust quality. Thus, while we wait for higher level evidence, whenever possible, HbA1c concentrations should be obtained in all persons with diabetes. For day case surgeries, if HbA1c concentrations are not available, it may be substituted with average daily blood glucose concentrations.[22] However, a single value of random blood glucose concentration may not always be useful, particularly if it is above normal values.

What is the optimal concentration of blood glucose before surgery?

There are no studies evaluating the blood glucose concentrations above which elective surgery should be delayed.[8] However, it is clear that perioperative hyperglycaemia (blood glucose concentrations >140–180 mg dL^{-1} (>7.8–10.0 mmol L^{-1}) increases postoperative surgical complications for various non-cataract and non-cardiac surgeries.[22 23] Intuitively, patients who exhibit symptoms and signs of acute hyperglycaemic emergencies (e.g. severe dehydration and haemodynamic instability, ketotic state, and non-ketotic hyperosmolar state) should have their surgery irrespective of the procedure postponed.

A review of outcomes after noncardiac surgery found that HbA1c of 7% was associated with a significantly lower incidence of postoperative infections.[21 24] Therefore, if the patient has hyperglycaemia on the day of surgery, but has had 'good' long-term glycaemic control (i.e. an HbA1c that is age appropriate and not associated with increased perioperative harm, usually $<8.5\%$

(69 mmol/mol), or a preprandial blood glucose concentration of 108-180 mg/dl (6.0-10.0 mmol L^{-1}), but with an acceptable range of 72-216 mg/dL (4.0-12.0 mmol L^{-1}), it may be appropriate to proceed with the surgical procedure. The most likely cause of hyperglycaemia in this instance could be the inappropriate withdrawal of antidiabetic drugs and/or exaggerated stress response.[24] The UK guideline recommends that preoperative HbA1c of <8.5% (69 mmol mol^{-1}) should be considered as acceptable for surgery.[21]

Patients undergoing cataract under topical or regional anaesthesia are generally awake, therefore, they can resume their regular antidiabetic medications in the immediate postoperative period.[10] Furthermore, symptoms and signs of hypoglycaemia and hyperglycaemia could be recognised early, avoiding the occurrence of acute hypo- or hyperglycaemic complications. Similar advice has been offered by the Joint Royal Colleges guidelines, [19] as long as it is appreciated that there can be no conversion to general anaesthesia or moderate to deep sedation during the procedure. According to a survey in the UK, the majority of patients were not starved before loco-regional techniques and food and fluids were allowed until the time of surgery, to avoid undesirable effects of thirst, dehydration, headache, dizziness, fainting or feeling faint, nausea and the possible occurrence of hypoglycaemia.[25]

To reiterate, the concern in patients with poorly controlled diabetes is the potential for surgical complications and poorer outcomes: including infection, postoperative inflammation, and delayed wound healing.[26–28] Therefore, the decision to proceed with surgery should be made in conjunction with the surgeon.

In the absence of higher level evidence, survey of practices may influence the current opinion about perioperative glycaemic control for cataract surgery. A cross-sectional self-administered questionnaire was obtained from 129 ophthalmologists and anaesthetists,[29] a blood glucose threshold concentration $\geq$ 17 mmol L^{-1} (306 mg dL^{-1}) prompted the majority of doctors (86–93.8%) to adopt a treat-and-defer strategy, and a threshold of $\geq$ 23 mmol L^{-1} (414 mg dL^{-1}) prompted most (86%–96.9%) to cancel the cataract surgery. Survey respondents were found to be more concerned about intraoperative hyperglycaemia than hypoglycaemia.

Do we need to control perioperative hyperglycaemia?

Some of the reasons for this variability may be because of confusion between recommendations for major surgical procedures requiring general anaesthesia,[30] [31] and the cataract surgical population. Furthermore, in recent years intensive insulin therapy (IIT) has attracted much attention in ophthalmology. IIT in patients with type 1 diabetes was associated with a substantial reduction in the long-term risk of ocular surgery.[11] A systematic review and meta-analysis have shown that treatment with IIT for two to three weeks can induce a glycaemic remission and can improve the underlying pathophysiology in early type 2 diabetes mellitus.[32] However, the safety and efficacy of IIT (mechanism not fully understood) has also been questioned by others because of severe hypoglycaemia and other adverse events.[32] Contrary to the benefits of IIT, postoperative progression of maculopathy was significantly more common in the group that underwent rapid correction of poor glycaemic control before surgery compared with those who did not.[16] [33-36] These authors recommended that a rapid correction of blood glucose concentrations before surgery may not be always useful for preventing postoperative complications, and, in fact, it may cause postoperative progression of both retinopathy and maculopathy in patients who already have moderate to severe non-proliferative diabetic retinopathy.

The recommended interventions to control the perioperative blood glucose concentration vary significantly, these include subcutaneous injection (bolus or continuous/infusion),[37] i.v. injection (bolus or continuous/infusion) and insulin pump therapy. The 2010 Society of Ambulatory Anesthesia consensus statement on perioperative blood glucose management in persons with diabetes undergoing day case surgery[8] indicated that subcutaneous rapid-acting insulin may be preferred over regular insulin for its efficacy safety, costs and logistical administration. Subcutaneous administration would result in less fluctuation in blood glucose concentration, which may have the consequence of patient harm. Of note, the continuous insulin administration techniques may be unsuitable and cumbersome for very short duration ambulatory cataract surgery. The logistics of who is responsible for the glycaemic optimisation - primary care, or secondary care, and how long one should wait to reassess glycaemic control for elective surgery is beyond the remit of this editorial.

Joint British Diabetes Societies Guidelines[20] and American Diabetic Association[38] recommend that blood glucose concentrations should be maintained between 140–180 mg dL^{-1} (7.8–10.0 mmol L^{-1}) during the perioperative period. The incidence of hypoglycaemia is significant and the consequences of hypoglycaemia are worse than the benefits of IIT (i.e. near normal blood glucose concentration of 70–110 mg dL^{-1} (3.9–6.1 mmol L^{-1}). A number of small studies in persons with type 1 and type 2 diabetes comparing different methods of achieving glycaemic control during minor and moderate surgeries, did not demonstrate any adverse effects of maintaining perioperative glycaemic concentrations between 90–198 mg dL^{-1} (5–11 mmol L^{-1}).[39]

In conclusion, the twin problems of diabetes and cataracts are formidable peaks in the healthcare landscape. Anaesthetists and ophthalmologists continue to grapple with the concerns of the extreme highs and lows of glycaemic control in elderly patients with diabetes during cataract surgery. The causal relationship of perioperative hyperglycaemia resulting in poorer surgical outcomes remains inconclusive. Recent systematic reviews calls into question the utility of HbA1c—an indicator of three-month glycaemic control—as a predictor of postoperative morbidity and mortality.

As a result of the low risk nature of cataract surgery under loco-regional anaesthesia techniques, stringent criteria for blood glucose concentrations that trigger surgery postponement may not be warranted, albeit robust clinical evidence remains lacking. In the same vein, tight intraoperative glucose control may likewise not be beneficial in mitigating surgical complications. There is a loud undeniable clarion call for well-designed studies to answer these important questions pertaining to glycaemic control during cataract surgery – for currently we are truly none the wiser.

Declaration of interest

None declared.

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The suffering and satisfaction of Schrödinger's cat

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A well-known thought experiment poses the question, if a tree falls in a forest and nobody is within earshot, has it made a sound? In quantum physics, the tale of Schrödinger's Cat is a philosophical paradox pertaining to apparently contradictory concurrent realities. For the anaesthetist, there are analogous conundrums relating to intraoperative awareness and perioperative discomfort. If a patient has distressing intraoperative experiences, but has no explicit recall, has the patient actually been traumatized? When perioperative symptoms reflecting suffering are prevalent, but patients are apparently satisfied, is the quality of perioperative anaesthetic care simultaneously beyond and requiring reproach?

In this issue of the British Journal of Anaesthesia Walker and colleagues[1]focus on early patient reported outcomes after anaesthesia throughout the UK. This seminal study is impressive in its conception, execution and findings. That 97% of eligible organizations (257 hospitals) contributed data is a staggering feat that was made possible by the participatory culture engendered by the National Institute of Academic Anaesthesia, by the tradition of impactful national audit projects in Anaesthesia, and by the camaraderie that has historically characterized the UK's National Health Service (NHS). Similarly, the high proportion (93%) of eligible adult patients completing postoperative surveys speaks to their respect for the NHS and their willingness to be active collaborators in the quality improvement process. It is unlikely that clinician auditors would achieve comparable hospital and patient involvement in most other countries. The investigators must specifically be congratulated for garnering the support and involvement of junior doctors and students. This not only contributed to the success of this ambitious project, but also exposed tomorrow's clinicians and leaders to the rewards of relevant and impactful clinical research.

From the vantage of quality assessment, the striking revelation by Walker and colleagues[1] was that more than a third of patients reported severe discomfort in at least one measured domain, with burning thirst, acute pain, and excessive drowsiness being most common. Other relatively common potentially anaesthesia-related complications included nausea and vomiting; hoarseness and sore throat; cold and shivering; and confusion.[1] Many of these symptoms might be modifiable. For example, in this study, regional anaesthesia was associated with less postoperative pain and drowsiness.[1] Finally, when asked to identify the worst thing about their operation, the leading responses were anxiety (33%) and severe pain (17%), both relevant to anaesthetic conduct.[1] There is thus a clear signal that the quality of perioperative anaesthetic care probably can and should be improved.

However, the authors also report substantial dissociation between the prevalence of negative perioperative symptoms and patient dissatisfaction, with only 5% of patients reporting that they were dissatisfied with any aspect of their anaesthetic care. This might partly be explained by patients' expectations regarding the inevitability of certain unpleasant symptoms. If patients anticipate that they are likely to experience discomfort, it is perhaps unsurprising that their thirst, pain and drowsiness do not curtail their satisfaction, and they are content that the anaesthetist has discharged her duties in a satisfactory fashion. An important caveat is that it does not necessarily follow that patients were fully satisfied on the grounds that they were not dissatisfied. This is exemplified by the fact that only 62% of patients reported that they were very satisfied with pain control. One might also speculate that patients would not be quite as sanguine in their appraisal if they had more explicit memories of early postoperative discomfort, or if they had been asked about satisfaction after a longer time interval, when less fleeting and more serious complications might become apparent. Finally, given that non-respondents were generally higher risk with more co-morbidities than respondents, it is likely that serious complications were more common in this group.

As the authors state, the prevalence of severe symptoms in this cohort provides impetus for further study aimed at their prevention. However, this would be a complex undertaking, especially as improvements in some domains are likely to be associated with worse outcomes in others. The importance of some reported symptoms such as drowsiness and thirst in relation to operative outcomes more broadly is not firmly established, especially when considering other outcomes that were not measured. Many of the early postoperative adverse symptoms assessed in this study are fleeting, and might not have long-term ramifications. Addressing these without assessing the baseline prevalence of and associated impact upon more serious outcomes may be counterproductive. For example, aggressively trying to prevent thirst might lead to problems with excessive fluid administration. Some techniques that mitigate excessive