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Peri-operative practices by Anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand Academic hospitals

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

Johannesburg, 2020

Declaration

I, Lungile Carol Mwelase declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



5 October 2021

Abstract

Background

Diabetic patients are frequently encountered in theatre by anaesthetists. These patients are at an increased risk of developing peri-operative complications. The aim of this study was to describe the knowledge of peri-operative diabetic management guidelines as well as peri-operative practices of anaesthetists in the Department of Anaesthesiology at the University of the Witwatersrand (Wits).

Methods

A prospective, descriptive, and contextual study was conducted using a self-administered questionnaire developed following review of the literature. The study population consisted of anaesthetists working in the Department of Anaesthesiology at Wits. A convenient sampling method was used and completion of the questionnaire implied consent.

Results

In terms of international peri-operative DM guidelines, only 57 (48.3%) knew about them, even fewer 43 (38.1%) reported implementing them, and only 10 (8.6%) had received training on their use. Despite the poor awareness of these international guidelines, majority of participants' adhered to starvation and fluid management practices as outlined in these guidelines. However, there was inadequate adherence to recommended practices with respect to peri-operative management of oral hypoglycaemic agents.

Conclusion

Most Wits Anaesthetists lack knowledge of peri-operative DM guidelines. Despite this, many did comply with international DM guidelines in terms of starvation and fluid recommendations. However, majority demonstrated poor knowledge of recommended practices with respect to management of oral hypoglycaemic agents. There is a need to improve this knowledge by providing more teaching and assessment.

Acknowledgements

Many thanks to my supervisor, Dr Brian Gardner for the hard work in accomplishing this work. I would also like to thank the Wits Department of Anaesthesia without which the research would not have been possible.

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Abbreviations

ADA	American Diabetes Association
ADS	Australian Diabetes Society
BMI	Body mass index
DISN	Diabetes inpatient specialist nurse
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DNSF	Diabetic National Service Framework
GA	General anaesthesia
HbA1c	Hemoglobin A1c
HONK	Hyperosmolar non-ketotic coma
ICU	Intensive care unit
IDF	International Diabetes Federation
I-G	Insulin-glucose
IV	Intravenous
JBDS	Joint British Diabetes Society
MI	Myocardial infarction
OHA	Oral hypoglycaemic agents
PPC	Post-operative pulmonary complications
RA	Regional anaesthesia
SA	South Africa
SEMDA	Society for Endocrinology, Metabolism and Diabetes of South Africa
SU	Sulphonylurea
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
VRIII	Variable rate intravenous insulin infusion
WHO	World Health Organisation
Wits	University of the Witwatersrand

Statement

This Research Report consists of a literature review, a draft article, a study proposal, and appendices. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations, and Research Reports. The formatting of the draft article may differ from the rest of the Research Report in order to comply with the author guidelines of the South African Journal of Anaesthesia and Analgesia (SAJAA), the journal to which it is intended to be submitted.

Section 1: Review of the literature

1.1 Introduction

Diabetes mellitus (DM) is an extremely common disease worldwide, and in South Africa (1). In health examination surveys, and epidemiological studies conducted by the World Health Organization (WHO), it was discovered that the number of people living with diabetes worldwide increased from approximately 153 million in 1980 to 347 million in 2008 (2, 3). In 2015, the International Diabetes Federation (IDF) estimated that there were approximately 415 million people living with diabetes worldwide and that of these, more than 14 million people were in the African region. The IDF expects that this number will more than double by 2040 (4).

In line with this international global perspective, DM is also becoming a major problem in SA as a result of urbanization, inactive lifestyles, unhealthy eating habits, and an increased prevalence of obesity (1). The IDF estimated that 7% of South Africans were diabetic in 2015, which amounted to 2.28 million cases (4). DM is divided into type 1 diabetes mellitus (T1DM) (insulin-dependent) and type 2 diabetes mellitus (T2DM) (non-insulin dependent). T2DM is a particular concern as it accounts for 90% of diabetics in SA (1). Between 30-85% of patients remain undiagnosed. Because these patients present so late, up to 20% already have complications at the time that they are diagnosed (1). As a result a combined national approach, involving both government and non-governmental organisations, has been suggested to combat the effect of diabetes in SA (1).

The increased incidence of DM has led to an increased presentation of diabetic patients for surgery. A patient with diabetes has a 50% chance of presenting for a surgical intervention in their lifetime, and 20% of all patients presenting for surgical procedures are diabetic (5). The reasons for the increased surgical rate may be unrelated to DM or may be directly related to DM itself as diabetes affects multiple organs systems with micro and macrovascular complications (5). Complications of DM include adverse cardiovascular events, silent ischaemia, coronary artery disease, autonomic neuropathy, nephropathy, as well as general poorer health with increased infection rates (5, 6).

Regardless of how and when they present, diabetic patients are at an increased risk for morbidity and mortality peri-operatively either due to mismanagement of their DM by medical professionals, pre-existing complications of DM, or simply due to the surgery and anaesthesia itself (5). Therefore it is important to assess the baseline knowledge of anaesthetists who are managing DM patients peri-operatively.

This literature review will discuss:

- The definition, classification, and complications of DM.
- The treatment of DM.
- The effects of surgery on a diabetic patient.
- The effects of anaesthesia on a diabetic patient.
- Guidelines for the management of diabetic patients in the peri-operative period, including glucose control, fluid administration, as well as starvation practices.

1.2 Diabetes mellitus background

1.2.1 Definition of diabetes mellitus

According to the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) guidelines, diabetes mellitus is classically defined as: "A group of metabolic diseases with heterogenous aetiologies which are characterised by chronic hyperglycaemia and disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or a combination of both" (1).

1.2.2 Classification of diabetes mellitus

The American Diabetes Association classifies diabetes into four categories (7.8):
1. Type 1 diabetes- An absolute insulin deficiency following β-cell destruction as a result an immune-mediated or idiopathic cause.
2. Type 2 diabetes- A progressive insulin secretory defect with or without associated insulin resistance.
3. Specific types of diabetes- These include genetic β-cell dysfunction, exocrine pancreas abnormalities, endocrinopathies, infections, drug or chemically induced β-cell damage, and genetic defects.

4. Gestational diabetes- Glucose intolerance with new onset or first detection in pregnancy.

1.2.3 Complications of diabetes mellitus

Complications can be divided into acute and chronic complications (9). Acutely, patients can present with a range of complications from dehydration, acidosis, and weight loss to life threatening conditions such as diabetic ketoacidosis and hyperosmolar non-ketotic hypergylcaemic coma (8).

Chronically, if left untreated, hypergylcaemia results in increased morbidity and mortality by damaging small-sized vessels e.g. capillaries (microvascular disease) as well as medium and large-sized vessels i.e arteries and veins (macrovascular disease) (10). Complications of DM result from metabolic and structural derangements, the production of advanced glycation end products, the abnormal activation of signaling cascades, an elevated production of reactive oxygen species, and the abnormal stimulation of haemodynamic regulation systems (10). These mechanisms result in anatomical, structural, and functional changes which lead to multiorgan dysfunction (10). Atherosclerosis is the main finding in macrovascular disease as a result of DM (11). This causes a narrowing of the arterial diameter, which leads to an increased risk of ischaemic heart disease, cerebrovasular accidents, and peripheral vascular disease (11, 12).

In addition, DM can also cause endothelial dysfunction in end organ blood vessels (microvascular disease) leading to several conditions including diabetic retinopathy, nephropathy, and neuropathy (12). Deposition of glucose in joints may predispose to a difficult intubation due to glycosylation of the cervical joints which causes neck stiffness (13).

1.2.4 Treatment of diabetes mellitus

Insulin therapy is the mainstay treatment for T1DM due to the deficiency of endogenous insulin production (1). The different insulins which are available are usually classified according to their duration of action. Their use is tailored to specific dietary needs and the insulin requirements of individual patients (1). Insulin replacement in hospitalised patients can be divided into three components (2,5):

1. Basal insulin which is long acting, and is given to match hepatic liver glucose production. This is given regardless of the patient's food intake.
2. Prandial insulin whichis rapid-acting and is given to cover oral food intake.
3. Supplemental (or correctional) insulin which is rapid acting, and is used to treat hyperglycaemia, aiming for predetermined blood glucose target levels.

Table 1: Insulin preparations and pharmacokinetics (Available in South Africa)

Type	Time to onset of action	Time to peak effect	Duration of action
Rapid-acting analogues Aspart (NovoRapid®) Glulisine (Apidra®) Lispro (Humalog®)	5-15 minutes	30-90 minutes	3.5-4.5 hours
Short-acting regular Actrapid®,Humulin-R®, generic	30-60 minutes	2-3 hours	5-8 hours
Intermediate-acting NPH (neutral protamine Hagedorn) (Humulin-N®,Protaphane®, generic)	2-4 hours	4-10 hours	10-18 hours
Long-acting basal analogues Detemir (Levemir®) Glargine (Lantus®)	2-4 hours	No peak	20-24 hours 16 to 24 hours
Pre-mixed human (biphasic) Regular + NPH (Actraphane®, Humulin 30/70®, Insuman®, generic)	30-60 minutes	Dual peak	10-18 hours
Pre-mixed analogues (biphasic) Pre-mixed aspart (NovoMix®) Premixed lispro (Humalog Mix25®, Humalog Mix50®)	5-15 minutes	Dual peak	10-16 hours

(Adapted from SEMDSA, 2012)

Type 2 diabetics may be managed by diet alone, with oral hypogylcaemic agents, or a combination of oral hypoglyacaemic agents and insulin. In terms of diet, a healthy lifestyle aiming at weight loss is encouraged in patients living with type 2 diabetes. These patients should consume less calories, less saturated and trans fats, less sodium, and should increase physical activity. (1)

Oral hypogylcaemic agents (OHA) include (1, 14):

- Sulphonylureas (SU) e.g. glibenclamide, glipizide, gliclazide, glimepiride, and gliquidone.
- Biguanides which decrease glucose production by the liver and increase glucose utilization peripherally e.g. metformin.
- Thiazolidinediones which increase insulin sensitivity peripherally and impair liver gluconeogenesis e.g. pioglitazone.
- Alpha-glucosidase inhibitors e.g. miglitol.

1.3 The effects of surgery on a diabetic patient

Surgery is a major stressor on the body and complicates the management of DM. As a stressor, surgery contributes to the hyperglycaemia seen in patients peri-operatively, and induces inflammatory and hormonal responses which lead to an increase in the level of inflammatory cytokines. Surgery also results in an increased secretion of catabolic hormones (glucagon and adrenaline) and a decreased secretion of anabolic hormones (i.e. insulin) (15). The hormones released have an anti-insulin effect, and lead to high blood glucose levels (5, 15). The extent of homeostatic disturbance differs according to the patient, the type and length of surgery performed, and other factors such as sepsis, whether surgery was done in the morning, later during the day, or on the afternoon list (5). A combination of these factors will determine whether only minimal or more tight control is required to manage the diabetic patient (5).

Surgery predisposes to elevated blood glucose levels in both diabetic and non-diabetic patients, with diabetic patients more at risk of developing complications (9). Overall, surgery leads to a state of insulin resistance, hyperglycaemia, increased gluconeogenesis, ketogenesis, and an increased risk of infections peri-operatively (15).
Moreover, if haemodyamic instability should occur during the surgical period as a result of peri-operative bleeding or the autonomic instability associated with diabetic patients, then this would hinder the absorption of subcutaneously administered insulin, leading to an increased risk of hyperglycaemia (15).

Furthermore, haemodynamic instability predisposes diabetic patients to silent myocardial ischaemia (MI) as a result of coronary artery disease accompanying the autonomic neuropathy associated with DM (15). In their lifetime, it has been shown that up to 20% of patients with diabetes may experience a silent MI, particularly those with other macrovascular complications (16). In addition, surgery most commonly requires the administration of anaesthesia in order to be performed. This increases the risk of complications peri-operatively because anaesthesia carries its own risks, especially so in patients who are diabetic (15).

1.4 The effects of anaesthesia on a diabetic patient

Anaesthesia may be divided broadly into general or regional techniques (RA). General anaesthesia (GA) has been shown to lead to more perioperative hyperglycaemic events compared to regional anaesthesia (5). This is because, just like surgery, a GA induces a stimulation of the sympathetic nervous system, catabolic hormone and inflammatory cytokine production as well as the impaired secretion of anabolic hormones to a certain extent. The net effect thus leading to insulin resistance and hyperglycaemia peri-operatively (5, 15).

A GA renders a patient unconscious, which may lead to certain complications including hypoglycaemia going unnoticed because the symptoms are more apparent in the awake state (15).

Glycosylation of collagen in the joints, especially the cervical joints, may be encountered in this group of patients leading to 'stiff joint syndrome' (13). This may render these patients difficult to intubate (15). Patients need to be well-hydrated, especially those with diabetic nephropathy. Avoidance of nephrotoxic drugs as well as a dose adjustment of certain drugs is important to avoid further deterioration of renal function, and drug accumulation peri-operatively (16).

An increased body mass index (BMI) which is associated with type 2 diabetic patients increases their risk for post-operative pulmonary complications (PPC) (17). A prospective, observational, and analytical study of 314 general patients undergoing thoracic and abdominal surgeries showed an 11.5 % incidence of PPC. The most commonly encountered complications included respiratory failure, pleural effusion, and pneumonia. Diabetes, hospitalisation for more than five days, and pulmonary disease were noted to be the biggest risk factors for the above mentioned complications (17, 18).

Currently there is no evidence to support the idea that a carefully performed RA is superior to a GA in preventing major complications of surgery, and anaesthesia, in patients with DM (15). This is despite the reduced catabolic state seen with RA compared to that usually associated with a GA (15).

An advantage of RA over GA is that patients are often able to resume their meals and OHA sooner post-operatively (16, 19). On the other hand, RA should be administered with extra caution in patients with DM as they are at an increased risk of having an underlying autonomic neuropathy (15). This may lead to severe haemodynamic instability with profound hypotension if a sympathectomy should ensue from a RA (15). Regardless of whether patients are offered a GA or a RA, they are all still required to be starved peri-operatively. This may predispose patients to develop both hypoglycaemic or hyperglycaemic complications (16, 19).

Starvation means that patients are fasted for a certain period of time pre-operatively to avoid pulmonary aspiration of gastric contents. Patients with diabetes are more prone to aspiration as a result of their increased risk of underlying gastroparesis secondary to autonomic neuropathy. Diabetics with gastroparesis need a more prolonged fasting duration. However, starving patients for a long period of time may lead to a catabolic state and insulin resistance with resultant hypergylcaemia (16).

Depending on the duration of starvation, patients may become hypoglycaemic which may have detrimental effects including a neurological deficit, confusion, or even coma and death (20). Therefore, during the starvation period before surgery, the blood glucose level needs to be appropriately managed. In some instances patients may only be successfully managed by starting an insulin-glucose infusion, or they may need the provision of another source of glucose intravenously (16).

Intravenous (IV) fluids given peri-operatively when starving diabetic patients should help to maintain blood glucose concentrations within an acceptable range (19). IV fluids may also serve as a glucose substrate which will prevent the body from going into a catabolic state, thus preventing proteolysis, lipolysis, and ketogenesis. Moreover, IV fluids also help maintain serum electrolytes within normal limits and optimise intravascular volume (19).

Potential effects of hyper and hypoglycaemia on surgical patients include (18):

- Multi-organ dysfunction, particularly involving the cardiovascular system (with an increased oxygen demand/supply mismatch).
- Metabolic disturbances.
- Fluid and electrolyte imbalance.
- Wound infection.
- Post-operative sepsis.
- Endothelial dysfunction.
- Renal dysfunction.
- Cerebral ischaemia.
- Diabetic ketoacidosis (DKA).
- Hyperosmolar non-ketotic coma (HONK).

Hypoglycaemia may cause a significant neurological deficit to occur (20). Therefore, the main goal in the peri-operative management of diabetic patients, is the avoidance of severe hyperglycaemia and hypoglycaemia (8, 15). This goal can only be achieved by following appropriate guidelines to safely manage diabetic patients.

1.5 Peri-operative management guidelines for diabetic patients

At the start of this study the most comprehensive available guidelines for the management of adult patients with diabetes were from the Joint British Diabetes Societies (JBDS) 2011 and the Australian Diabetes Society (ADS) 2012 (16, 19). The JBDS guidelines were developed from a collaboration between several physician consultants in diabetes, consultant anaesthetists, a senior diabetes nurse, a head of patient safety for medication and medical devices, a diabetes specialist nurse, and a professor in surgery (19). These guidelines are based on the best available evidence, best clinical practice, as well as patient experience (19). The ADS guidelines were compiled using the opinions of several endocrinologists who are part of the Australian Diabetes Society group (Vincent Wong, Glynis Ross, Jennifer Wong and David Chipps) (16).

Although there are a few discrepancies between the JBDS and ADS guidelines, they are both clear when it comes to the major areas which need focus, and which will make an impact in reducing the peri-operative morbidity and mortality of patients with DM. These main areas are glycaemic control, starvation, and fluid management practices (16, 19).

The available American Diabetes Association (ADA) guidelines do not adequately cover the peri-operative management of patients with DM (7). The available South African DM guidelines are not specifically intended for use by anaesthetist but rather for DM management in general by all health care workers, hence they provide inadequate guidance with respect to the peri-operative management of DM patients (1).

The three key areas outlined in the JBDS and ADS guidelines will be addressed, incorporating input from the ADA guidelines.

1.5.1 Peri-operative glycaemic control

One key aspect in determining adequate diabetic control prior to surgery is to check the haemoglobin A1c (HbA1c) level (21). This test reflects the average blood glucose level over the previous 60-120 days (22). It is difficult to dictate an acceptable value for HbA1c peri-operatively. A HbA1C level below 8.5% is believed to be associated with a decreased risk of complications (23). A study by Nicholas et al. (22) showed a positive correlation between HbA1c values of greater than 9.0 % and an increased mortality rate within the first 365 days in type 2 diabetics. Several other studies, across various major surgical departments, have also shown poor surgical outcomes in patients with high levels of HbA1c (>9.0) peri-operatively (15).

The ADS guidelines advocate for tighter control of both the HbA1c and glucose levels compared to the JBDS guidelines (16, 19). The ADS guidelines (16) state that a HbA1c ≥ 7% may lead to a higher number of post-operative wound infections, however they do also acknowledge that it will not be feasible to postpone all elective surgery based on this alone. Therefore, they have made an allowance for a recommended pre-operative HbA1c goal of <8%. The ADS guidelines also recommend postponing elective surgery in patients with an HbA1c of >9% (16). The JBDS guidelines (19) recommend that patients presenting for elective surgery should have a pre-operative HBA1c of <8.5% depending on individual circumstances. This is a bit more lenient than the ADS guidelines (16, 19).

The ADS guidelines recommend targeting a peri-operative blood glucose level between 5-10 mmol/L, whereas the JBDS guidelines recommend targeting a level between 6-10 mmol/L (16, 19). Furthermore, the JBDS considers a glucose range of 4-12 mmol/L as acceptable (19). On the other hand, the ADA recommends that blood glucose levels be maintained between 4.4-10 mmol/L (7).

Apart from avoiding marked hyperglycaemia and hypoglycaemia, there is no further consensus in the literature as to how tightly peri-operative glucose control needs to be managed (21).

An exception to this are intensive care unit (ICU) patients and patients with acute MI. Studies have shown that targeting a blood glucose level between 4.4-6.1 mmol/L in cardiac surgery, and in ICU patients, may reduce mortality (21). The importance of individualising treatment based on the patient, the planned surgery, and the diabetes type has been emphasised (24).

Post-operative blood glucose level targets may depend on the clinical scenario (1). A study done in one surgical ICU showed that critically ill patients do better with intensive insulin therapy, maintaining their average blood glucose levels between 4.4-6.1 mmol/L (25). This was evidenced by a decreased rate of sepsis, as well as a decreased need for dialysis and blood transfusion requirements (25). However, a later follow up study done in another medical ICU showed no improvement of mortality rates when patients were treated with intensive insulin therapy, even though there was an improvement of morbidity rates with earlier discharge from ICU (26). The NICE-SUGAR study, which was an international randomized trial involving 6104 critically ill patients, compared intensive glucose control to conventional glucose control. This study found that intensive glycaemic control (4.5-6.0 mmol/L) was associated with an increased mortality compared to patients with conventional blood glucose level targets of <10 mmol/L (16, 27). The reason for the increased mortality in the group treated with intensive glucose control was severe hypoglycaemia (blood glucose of <2.2 mmol/L), with no significant difference found between surgical and medical ICU patients (27). Until further studies are done to advocate for tighter blood glucose control in ICU patients, the ADS guidelines accept a target blood glucose level between 5-10 mmol/L (16).

In terms of pre-operative monitoring, the ADS guidelines (16) recommend that blood glucose should be checked 3-4 times daily for a few days before the planned surgery. When the pre-operative blood glucose level is stable and well controlled, then both the ADS and the JBDS guidelines recommend one hourly blood glucose level checks intra-operatively (16, 19).

Medically, both the ADS and JBDS guidelines have moved away from the use of the traditional sliding scale. This is because the traditional sliding scale has been shown to be ineffective in maintaining normoglycaemia (16, 19). The reason being that it focuses on treating hyperglycaemia already present instead of preventing hyperglycaemia from occurring in the first place (16). The current recommendation by these bodies is to give an insulin infusion in appropriately selected patients (see below) (16, 19). The ADS guidelines have recommended giving both insulin and glucose intravenously or subcutaneously by insulin infusion pumps, while the JBDS guidelines recommend the use of a variable rate intravenous insulin infusion (VRIII) as shown in Table 2 below (16, 19).

Patient selection is emphasised in the JBDS guidelines when it comes to the use of a VRIII. Patients who are considered for a VRIII include:

- Patients who will miss more than one meal.
- Patients with T1DM, who have not received any background insulin.
- Patients who have poorly controlled diabetes.
- Patients who are inadequately prepared and coming in for emergency surgery (19).

Table 2: A variable rate intravenous insulin infusion regime (VRIII)

Bedside capillary blood glucose (mmol/L)	Initial rate of insulin infusion (units per hour)
<4.0	0.5 (0.0 if a long acting background insulin has been continued)
4.1-7.0	1
7.1-9.0	2
9.1-11.0	3
11.1-14.0	4
14.1-17.0	5
17.1-20	6
>20	Seek diabetes team or medical advice

(Adapted from JBDS,2011)

For patients who are either normally managed with insulin or OHA there are detailed tables containing peri-operative adjustments for all specific types of insulins and OHAs and how, and when, to take them for different situational permutations (e.g. type and length of surgery, morning or evening list, and other factors). Examples of these are attached as Tables III and IV as per the JBDS guidelines, and Figures 1 and 2 as per the ADS guidelines.

1.5.2 Peri-operative starvation

The main goal when it comes to starvation practices is to minimise the time that patients are starved, to avoid a catabolic state from developing. To achieve this, the avoidance of prolonged starvation periods pre-operatively as well as the resumption of meals as soon as possible post-operatively is essential (16, 19). The ADS (16) guidelines recommend the prioritisation of diabetic patients to be done on the morning list so as to shorten their starvation time. This prioritisation of DM patients is echoed in the JBDS (19) guidelines. Patients are allowed to re-start their normal diabetes medication as soon as they are able to take their first meal (16, 19).

1.5.3 Peri-operative fluid management

The ADS and the JBDS guidelines recommend starting fluids pre-operatively to prevent a catabolic state from developing (16, 19). The careful selection of intravenous fluids is important (16, 19). The JBDS guidelines have more comprehensive tables guiding fluid management than the Australian guidelines. The type of fluid administered depends on the electrolyte status of the patient as well as whether or not the patient is on a VRIII (16, 19). There is currently insufficient evidence to dictate the optimal fluid management for a diabetic patient undergoing surgery (19).

The JBDS guidelines have divided fluid management according to whether the patient requires a VRIII or not. The recommended IV fluid (which is balanced) for patients requiring a VRIII is glucose 5% in saline 0.45% pre-mixed with either potassium chloride 0.15% (20 mmol/l) or potassium chloride 0.3% (40 mmol/l), depending on the presence or absence of hypokalaemia (K^+< 3.5 mmol/l), administered at a correct infusion rate (19).

The NICE guidelines recommend a maintenance range of 25–50 mls/kg/day (approximately 83 ml/hr for a 70-kg patient) (28). Solutions which will lead to iatrogenic hyponatraemia should be avoided. These include glucose 5% in water solution and solutions containing 0.18 % saline (19).

Hartmann's solution is recommended to optimise intravascular volume status for patients without a VRIII. Unlike 0.9% normal saline, the use of Hartmann's solution avoids causing a hyperchloraemic metabolic acidosis (19). If a patient requires prolonged post-operative fluids (> 24 hr), then a VRIII should be administered and a solution containing glucose 5% in saline 0.45% pre-mixed with potassium chloride should be given as described above at an appropriate rate (19). The JBDS also recommends that hospitals should stock these solutions, despite the fact that they are three times more expensive than the standard 5% glucose solutions, in the hope that the price will eventually decrease with frequent use (19).

Post-operatively, both the ADS and the NHS JBDS guidelines recommend that patients who are treated with OHA's prior to surgery should resume these agents as soon as the patient is ready to take adequate meals (at least 50% of their usual diet) (16, 19). If patients are unable to take adequate meals, the JBDS recommends reducing the dose of sulphonylureas (19). It is recommended that metformin be restarted only once the estimated glomerular filtration rate is > 50 mls/min/1.73m^2 (19). Patients should be kept on a VRIII or on an insulin-glucose (I-G) infusion while they are only taking clear fluids (16).

When transitioning DM patients from a VRIII or an I-G infusion to their usual insulin regime, it is important to bear in mind that their insulin requirements may fluctuate due to the stress response to surgery, pain and inadequate food intake. Hence these patients need to be monitored frequently to achieve set blood glucose targets (16, 19). Both the ADS and the JBDS guidelines recommend that once the patient starts with food intake there should be an overlap between the VRIII or I-G infusion and the patient's normal subcutaneous insulin (16, 19).

The JBDS guidelines recommend that for patients on basal bolus insulin, the subcutaneous fast acting acting insulin should be restarted with the food intake and to then stop the VRIII 30-60 minutes later (19). While the ADS guidelines recommend that after giving the patient's usual subcutaneous (SC) insulin dose with the first meal, the I-G infusion can be stopped 1-2 hours later (16).

For patients who are also on long-acting insulin, only the short acting insulin should be given as above with the first meal because the long acting insulin is not discontinued pre-operatively (19). The JBDS guidelines recommend that patients who are treated with long-acting insulin at night only (and who are then meant to resume their meals in the morning) be given half the usual insulin dose in the morning. It is also recommended that these patients have background insulin present and be given the normal insulin dose at night (19). The ADS guidelines recommend giving one third of the usual dose with breakfast, and to then give a normal dose at night (16).

The JBDS recommends that patients who take twice daily fixed dose SC insulin should restart their SC insulin before breakfast or supper, and not at any other time, and their VRIII should be stopped 30-60 minutes after the first SC insulin dose (19). The ADS guidelines recommend that the patient is transitioned from the I-G infusion after breakfast and for their normal insulin or OHA to be given before breakfast, especially if the patient is treated with premixed or intermediate insulin. This is because the staff complement is greater and any unstable blood glucose levels can be managed better at this time of day (16)

For patients who have undergone major surgery, it is recommended that their usual diabetes treatment prior to operation be restarted after stopping the I-G infusion and that supplemental insulin be provided to achieve predetermined blood glucose levels (16). Close monitoring of blood glucose levels is also emphasised (16).

When it comes to clinical practice, diabetes management still seems to be based on the clinical experience of the individual practitioner as well as the institutional norm rather than on what has been proven and documented in the literature (19).

This may be because international guidelines, and specifically the JBDS guidelines, place a lot of emphasis on patient education. Patient management and successful implementation of these guidelines relies heavily on the services of specific diabetes trained nurses (19). The JBDS guidelines emphasise the existence of a "Diabetic National Service Framework" (DNSF) which includes an onsite diabetes inpatient specialist nurse (DISN) and a diabetologist (19). Not all international centres possess sufficient resources to offer such a service, making the JBDS guidelines difficult to implement in other countries.

With this being said, it was discovered through a national survey done in the United Kingdom (UK) that even 50% of acute UK hospitals did not have a DISN (19). Therefore, carrying out a DNSF in its entirety may not be feasible in many hospitals where diabetes management remains mostly the responsibility of doctors. Another challenge raised by the guidelines is the poor access to the recommended fluids for diabetics peri-operatively. A VRIII and specialised fluids may be too expensive for certain hospitals (19). Even though hospital managers are urged to enforce these guidelines, the JBDS guidelines can only aim to guide and are often not able to be followed word for word (19).

1.6 Summary

There is a paucity of data with respect to South African Anaesthetists knowledge of guidelines, and their practices with respect to perio-operative management of diabetic patients.

The ADS and JBDS guidelines are the only recent comprehensive international guidelines available in the literature (16, 19). The ADA has 2012 guidelines but their peri-operative guidance is unclear. Even more disturbing is that national guidelines, from SEMDSA, were last updated in 2017 and are inadequate (1). The peri-operative management of diabetic patients is mentioned in just one paragraph and does not include an actual recommended practice (1). There is an absence of guidelines at national academic hospitals. According to the JBDS guidelines, one of the four major contributors to adverse outcomes when managing diabetic patients was an absence of institutional guidelines (19). It is advised

that medical professionals who treat this group of patients, do so by using a standardised, rational approach to managing all blood glucose variations peri-operatively (29).

It is therefore impertative that the the knowledge and practices of anaesthetists at Wits be assessed to ensure good patient outcomes.

Table 3: Procedure for peri-operative management of oral medication

Tablets	Day before going into hospital	Day of surgery	
		If your surgery is in the morning	If your surgery is in the afternoon
Acarbose	Take as normal	Omit morning dose if you have been told to fast from midnight.	Take your morning dose if eating breakfast. Do not take your lunchtime dose.
Meglitinide (repaglinide or nateglinide)	Take as normal	Omit morning dose if you have been told to fast from midnight.	Take your morning dose if eating breakfast. Do not take your lunchtime dose.
Metformin If you are due to have contrast media this may need to be stopped on the day of the procedure and not taken for a further 48 hours (your doctor should tell you this in advance)	Take as normal	If taken once a day – do not stop. If taken twice a day- do not stop. If taken three times a day omit your lunchtime dose only.	If taken once a day – do not stop. If taken twice a day do not stop. If taken three times a day omit your lunchtime dose only.
Sulphonylureas (glibenclamide, glipizide, gliclazide/gliclazide MR, glimepiride, gliquidone)	Take as normal	If taken once a day in the morning – omit this dose. If taken twice a day, omit the morning dose. If taken once a day in the morning – omit this dose.	If taken twice a day, omit both doses.
Thiazolidinediones (Pioglitazone)	Take as normal	Take as normal	Take as normal
DPP-IV inhibitors (Sitagliptin, saxagliptin, vildagliptin)	Take as normal	Omit your morning dose.	Omit your morning dose.
You should restart taking your normal tablets the morning after surgery. However, your blood glucose may be higher than usual for a day or so.			
If you are taking Byetta® (exenatide) or Victoza® (liraglutide) by injection these medications should not be taken the day of surgery and restarted once once you start eating and drinking normally.			

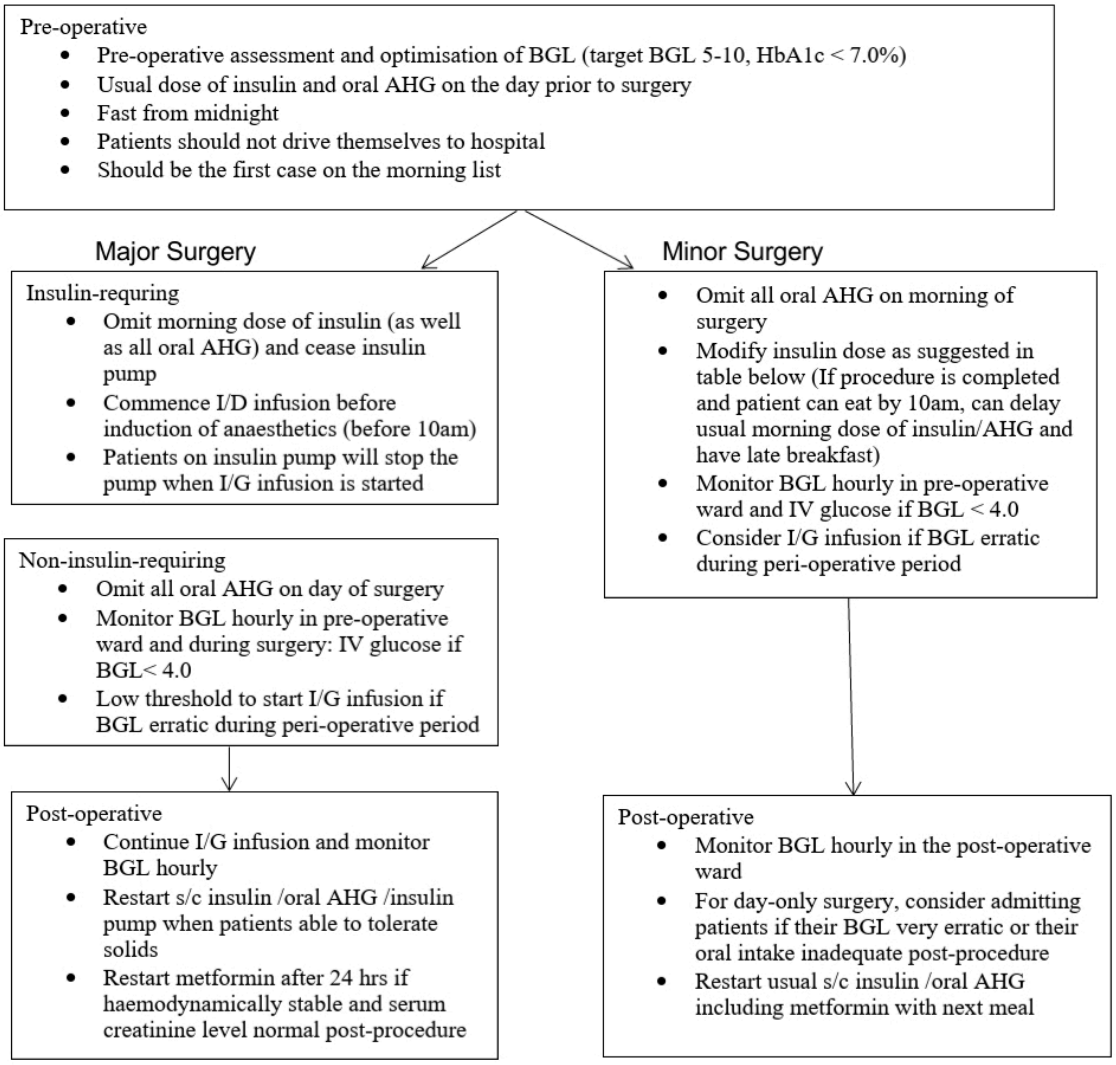
(Adapted from NHS Joint British Diabetes Societies, 2011)

Table 4: Procedure for peri-operative management of insulin

Insulins	Day before going into hospital	Day of surgery	
		If your surgery is in the morning	If your surgery is in the afternoon
Once daily (evening) (Lantus®/Glargine or Levemir/Detemir®) Insulatard® or Humulin I®	No dose change	No dose change necessary.	No dose adjustment necessary.
Once daily (morning) (Lantus®/Glargine or Levemir/Detemir®) Insulatard® or Humulin I®	No dose change	Take your normal dose. Your blood glucose will be checked on admission.	Take your normal dose. Your blood glucose will be checked on admission.
Twice daily (Novomix 30®, Humulin M3®, Humalog Mix 25®, Humalog Mix 50®)	No dose change	Halve the usual dose. Your blood glucose will be checked on admission. Resume your normal insulin with your evening meal.	Halve the usual dose. Your blood glucose will be checked on admission. Resume your normal insulin with your evening meal.
3, 4, or 5 injections Daily	No dose change	Do not take your morning dose of short acting insulin if no breakfast is eaten. If you normally take a long acting basal insulin in the morning you should take your normal dose. If you normally take a pre-mixed insulin the dose should be halved. Do not take your lunchtime dose. Resume your normal insulin with your evening meal.	Take usual morning insulin dose(s). Do not take lunchtime dose. Your blood glucose will be checked on admission. Resume your normal insulin with your evening meal.
You should restart taking your normal insulin the morning after surgery (procedure). However, your blood glucose may be higher than usual for a day or so.			

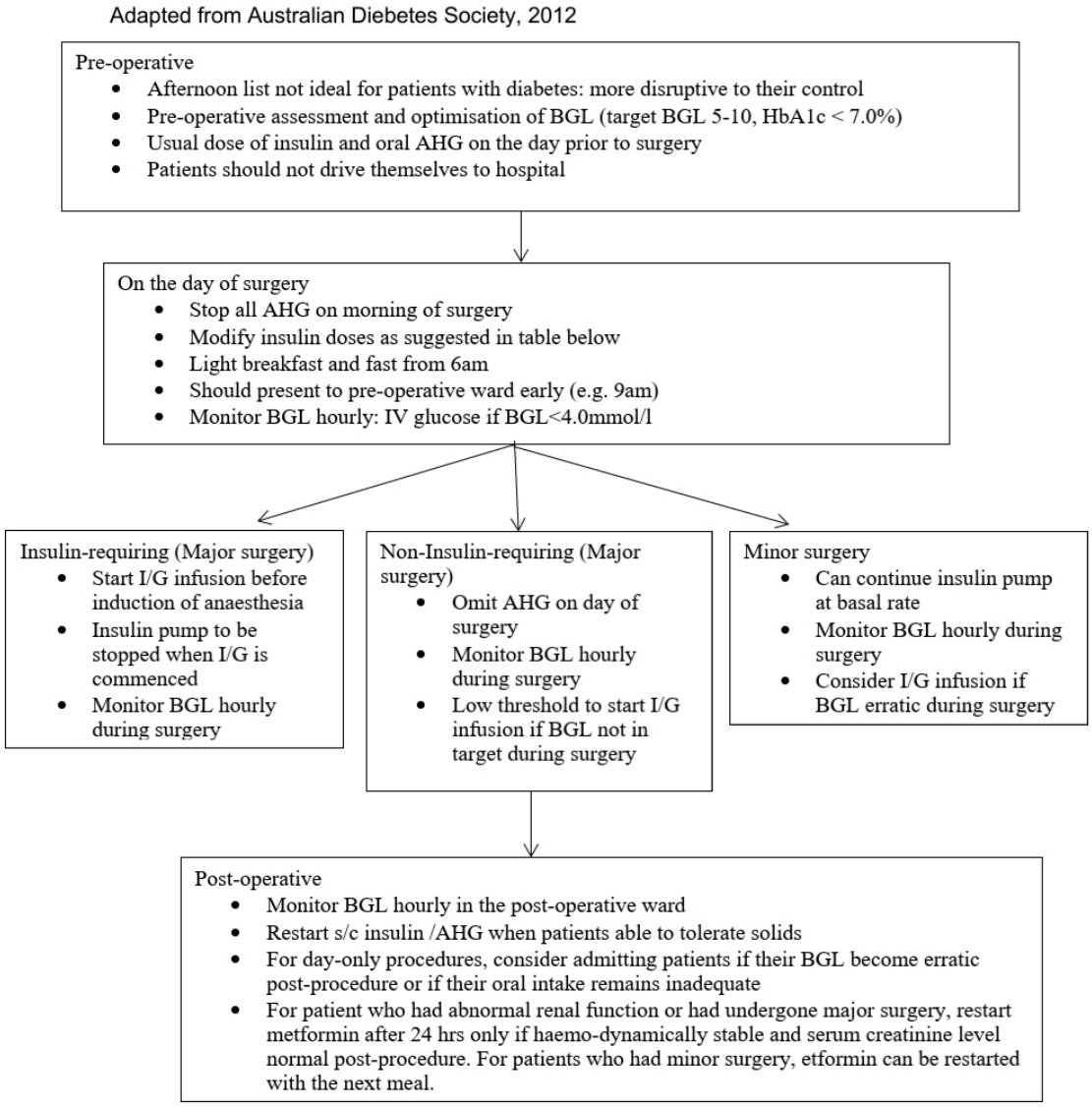
(Adapted from NHS Joint British Diabetes Societies,2011)

Adapted from Australian Diebetes Society, 2012



BGL: blood glucose level, AHG: antihyperglycaemics, I/D: insulin-dextrose, I/G: insulin-glucose, s/c :subcutaneous

Figure 1: Summary of peri-operative protocol for patients on the morning list



BGL: blood glucose level, AHG: antihyperglycaemics, I/D: insulin-dextrose, I/G: insulin-glucose, s/c: subcutaneous

Figure 2: Summary of peri-operative protocol for patients on the afternoon list

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Section 2: Author's guidelines

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Acknowledgements

In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

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The following are sample references:

1. Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar;132(3):429-34.
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Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research.

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8. It must be clear where every figure and table should be placed in the text. If possible, tables and figures must be placed in the text where appropriate. If too large or impractical, they may be featured at the end of the manuscript or uploaded as separate supplementary files.
9. All photographs must be at 300dpi and clearly marked according to the figure numbers in the text. (Figure 1, Table II, etc.)
10. All numbers below ten, without percentages or units, must be written in words.
11. Figure numbers: Arabic, table numbers: Roman

Section 3: Draft article

Peri-operative practices by Anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand Academic hospitals

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Keywords: peri-operative practices, diabetes mellitus, management guidelines anaesthesia

Abstract

Background

Diabetic patients are frequently encountered in theatre by anaesthetists. These patients are at an increased risk of developing peri-operative complications. The aim of this study was to describe the knowledge of peri-operative diabetic management guidelines as well as peri-operative practices of anaesthetists in the Department of Anaesthesiology at the University of the Witwatersrand (Wits).

Methods

A prospective, descriptive, and contextual study was conducted using a self-administered questionnaire developed following review of the literature. The study population consisted of anaesthetists working in the Department of Anaesthesiology at Wits. A convenient sampling method was used and completion of the questionnaire implied consent.

Results

In terms of international peri-operative DM guidelines, only 57 (48.3%) knew about them, even fewer 43 (38.1%) reported implementing them, and only 10 (8.6%) had received training on their use. Despite the poor awareness of these international guidelines, majority of participants adhered to starvation and fluid management practices as outlined in these guidelines. However, there was inadequate adherence to recommended practices with respect to peri-operative management of oral hypoglycaemic agents.

Conclusion

Most Wits Anaesthetists lack knowledge of peri-operative DM guidelines. Despite this, many did comply with international DM guidelines in terms of starvation and fluid recommendations. However, majority demonstrated poor knowledge of recommended practices with respect to management of oral hypoglycaemic agents. There is a need to improve this knowledge by providing more teaching and assessment.

Background

Diabetes mellitus (DM) is a common metabolic disorder worldwide, and in South Africa (SA).[1,2] It is estimated that in 2015 7% of South Africans (2.28 million) were diabetic.[3] The majority of diabetics in South Africa remain undiagnosed, hence about 20% of patients will have complications by the time that they present in the peri-operative period.[3] As a result, a national approach involving both government and non- governmental organisations has been suggested to combat the effect of diabetes in SA.[3]

The increased incidence of DM has meant that the surgical patient population with DM has increased. A patient with diabetes has a 50% chance of presenting for a surgical intervention in their lifetime, and 20% of all patients presenting for surgical procedures are diabetic.[4, 5] Moreover, this particular group of patients is at an increased risk of morbidity and mortality peri-operatively either due to mismanagement of their DM by medical professionals, pre-existing complications of their DM, or due to the surgery and anaesthesia (as both may lead to hyperglycaemia).[4]

The effects of prolonged hyper- and hypoglycaemia on perioperative outcomes have been well studied. These include multi-organ dysfunction, particularly involving the cardiovascular system (with an increased oxygen demand/supply mismatch), metabolic disturbances, fluid and electrolyte imbalances, wound infections, post-operative sepsis, endothelial dysfunction, renal dysfunction, cerebral ischaemia, diabetic ketoacidosis (DKA), hyperosmolar non-ketotic coma, as well as neurological deficits.[6, 7] Therefore, the main goals of management of patients with diabetes in the peri-operative period are to avoid severe hyperglycaemia and also hypoglycaemia. These aims can be achieved by following appropriate guidelines to safely manage this group of patients.

The current and most comprehensive guidelines for the management of patients with diabetes in the literature are from the National Health Services (NHS) Joint British Diabetes Societies (JBDS) (British and United Kingdom) and Australian Diabetes Society (ADS).[8, 9]

At the time of data collection the NHS Joint Diabetes Societies 2011 guidelines and the Australian 2012 guidelines were the most up to date and comprehensive guidelines available in the literature. Hence, they were used to formulate our questionnaire and were used to assess the practice of participants in our study. Although there are a few discrepancies between these guidelines, the three main areas of focus which they both agree upon are glycaemic control, starvation practices, and fluid management practices.[8,9] At our institution the peri-operative management of diabetic patients is not guided by formalised guidelines or protocols, thus it is unknown whether or not these patients are managed appropriately. We therefore undertook a study with the aim of describing the knowledge and the use of diabetic management guidelines in practice, using international guidelines as an standard because no comprehensive South African peri-operative guidelines existed at the time of data collection.

Methods

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and the Graduate Studies Committee of Wits (Clearance certificate NO. M161118). Convenient sampling was used and the sample size was realised by the response rate. A prospective, contextual, descriptive research design was followed. The study population consisted of anaesthetists working as the University of the Witwatersrand Department of Anaesthesiology over a period of four months. At the time of the study the department consisted of 208 anaesthetists. All anaesthetists at academic meetings were approached and a minimum response rate of 60% (125) was considered acceptable.[10] Questionnaires (Appendix B) were distributed at the start of departmental academic meetings and returned into a sealed box upon completion. A total of 140 questionnaires were handed out and 125(89.3%) were returned representing a survey response rate of 60.1%. Of these returned questionnaires, 122 were completed while 3 were left blank and were excluded from the data analysis but included in the data response rate as per protocol. Data was entered into a Microsoft Excel® spreadsheet and described using frequencies and percentages.

Results

The data presented includes, demographics, awareness and knowledge of diabetic management guidelines, and the practices of Wits anaesthetists in the peri-operative period when managing diabetic patients. The findings are described using descriptive statistics and percentages are rounded off to one decimal place. Demographic characteristics of the participants are presented in Table 5.

Table 5: Demographics of participants

Demographics	**n (%)**
Gender	
Male	39 (32.2%)
Female	82 (67.8%)
Age	
25-30	38 (31.7%)
31-35	44 (36.7%)
36-45	28 (23.3%)
>45	10 (8.3%)
Designation	
Community service	1 (0.8%)
Medical Officer	23 (19.3%)
Registrar	59 (49.6%)
Consultant	36 (30.3%)
Years of experience	
<6 months	6 (5.1%)
6months-5 years	57 (48.3%)
5 years-10years	37 (31.3%)
>10 years	18 (15.3%)

The knowledge, awareness and implementation of diabetic management guidelines

Although nearly half of all participants inidicated that they were aware of local and international general management and peri-operative guidelines, less than half implemented guidelines in the workplace, and less than 20% of participants had received formal training with respect to management guidelines. Participants' knowledge, awareness, and implementation of South African general management guidelines, SouthAfrican peri-operative management guidelines, and International peri-operative management guidelines are presented in Figures 3-5.

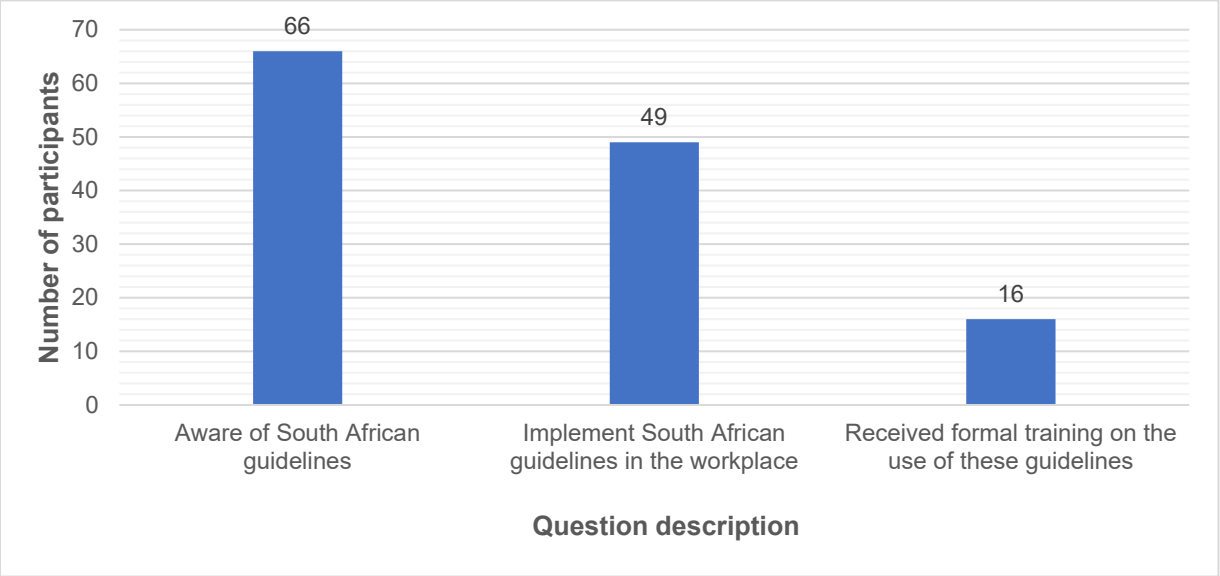


Figure 3: Awareness, implementation, and training with respect to South African diabetes mellitus general management guidelines

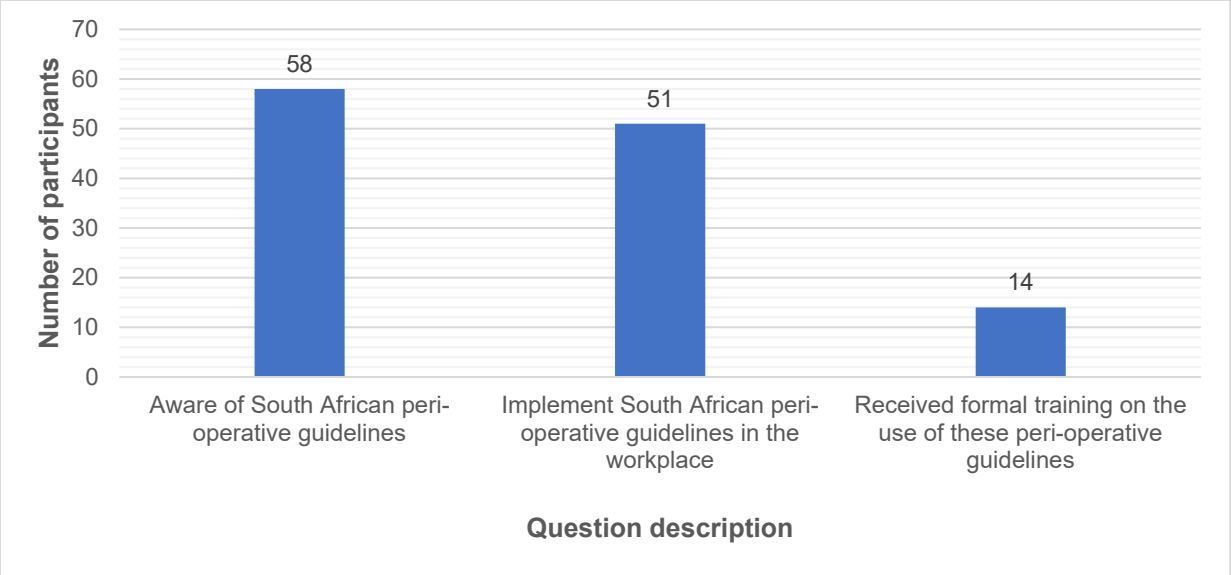


Figure 4: Awareness, implementation, and training with respect to South African peri-operative diabetes mellitus management guidelines

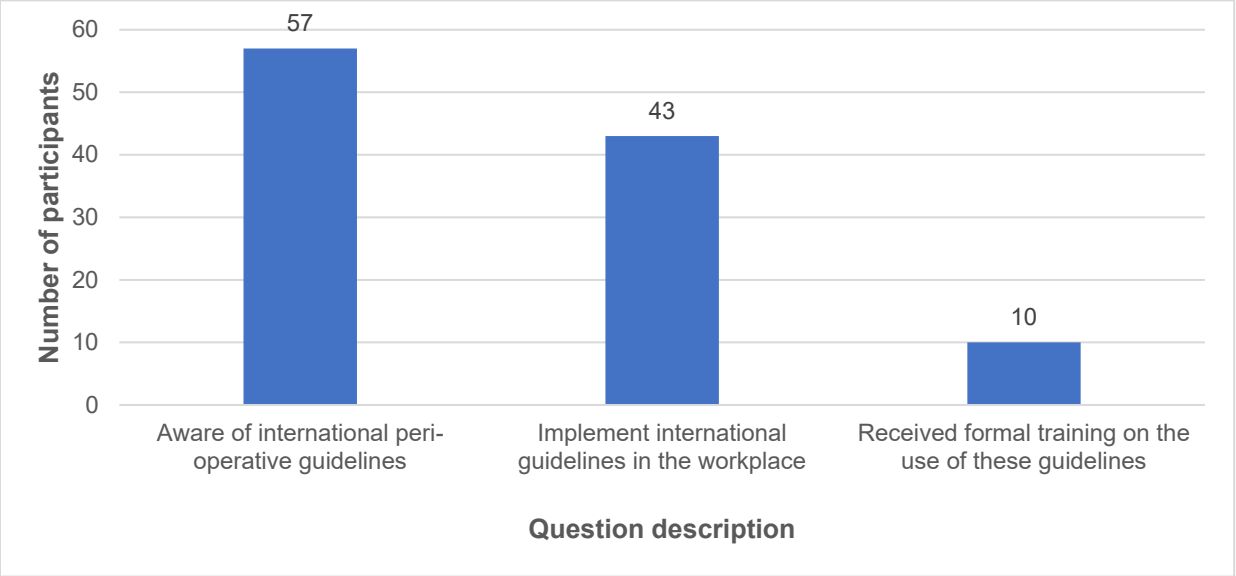


Figure 5: Awareness, implementation, and training with respect to international peri-operative diabetes mellitus management guidelines

Even though South African peri-operative guidelines do not exist, more than 40% of participants claimed to know and implement them at the workpalce, while less than 20% reported having received formal training.

Participants' diabetes mellitus peri-operative management practices

Participants' peri-operative management practices with respect to starvation, fluid management, and glycaemic control are presented in Figures 6-12.

In genraal, particants' adhered to international peri-operative guidelines when in comes to starvation and fluid management practices as presented below in Figures 6 and 7.

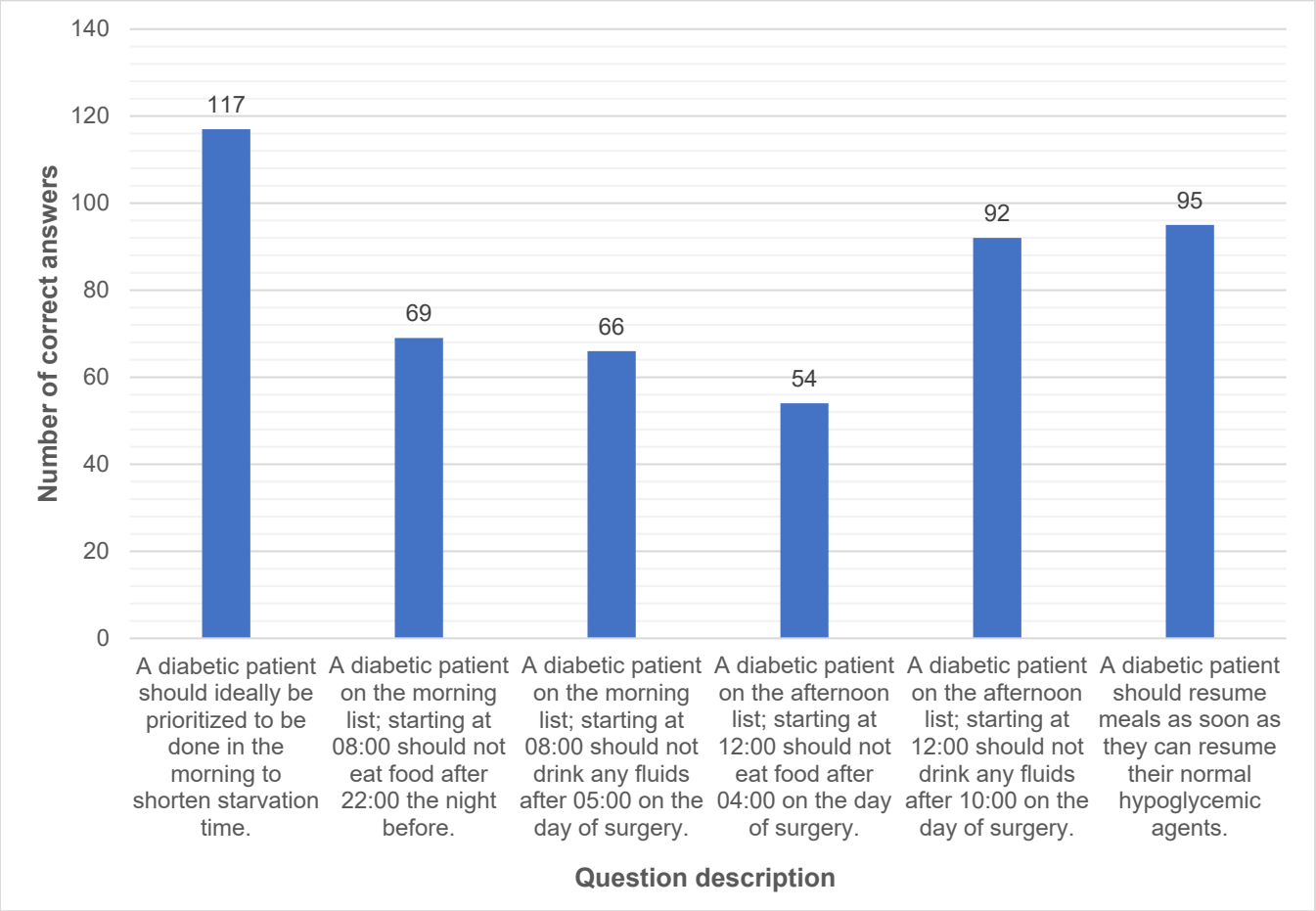


Figure 6: Participants' practices with regards to pre-operative starvation

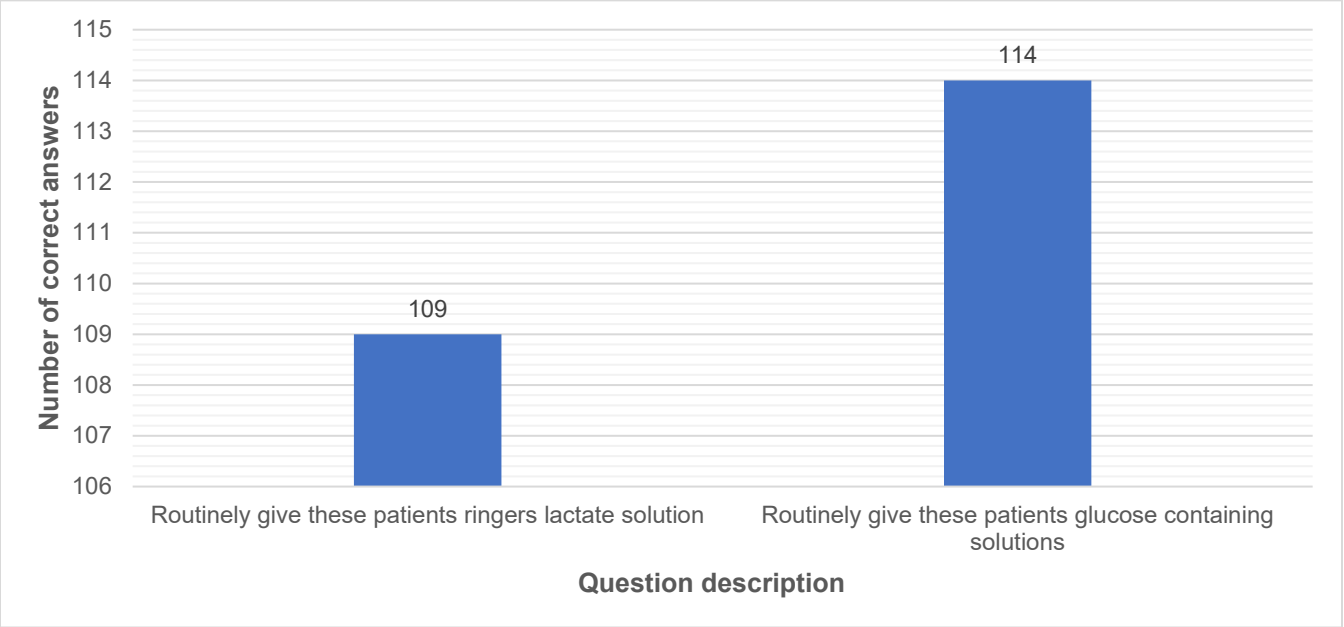


Figure 7: Participants' choice of fluids for patients

Participants' practices with respect to pre-operative, intra-operative, and post-operative glycaemic control mostly adhered to either UK or Australian guidelines. However, majority demonstrated poor knowledge of recommended practices with respect to management of oral hypoglycaemic agents as seen in Figure 9.

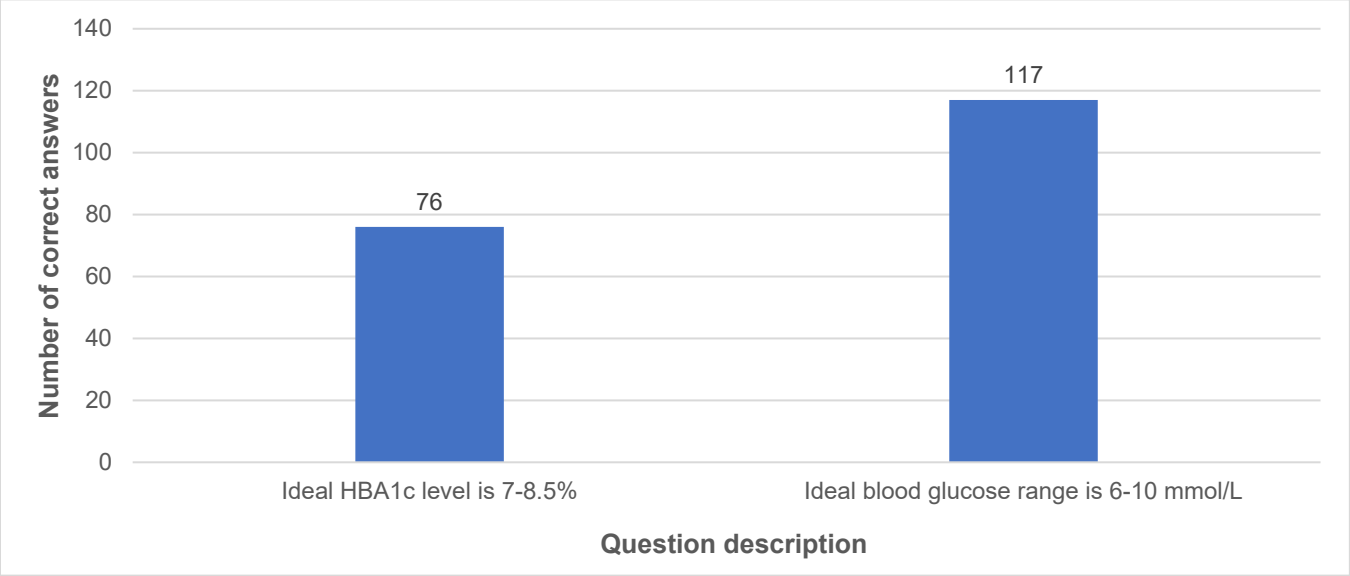


Figure 8: Participants' practices with regards to pre-operative glycaemic control

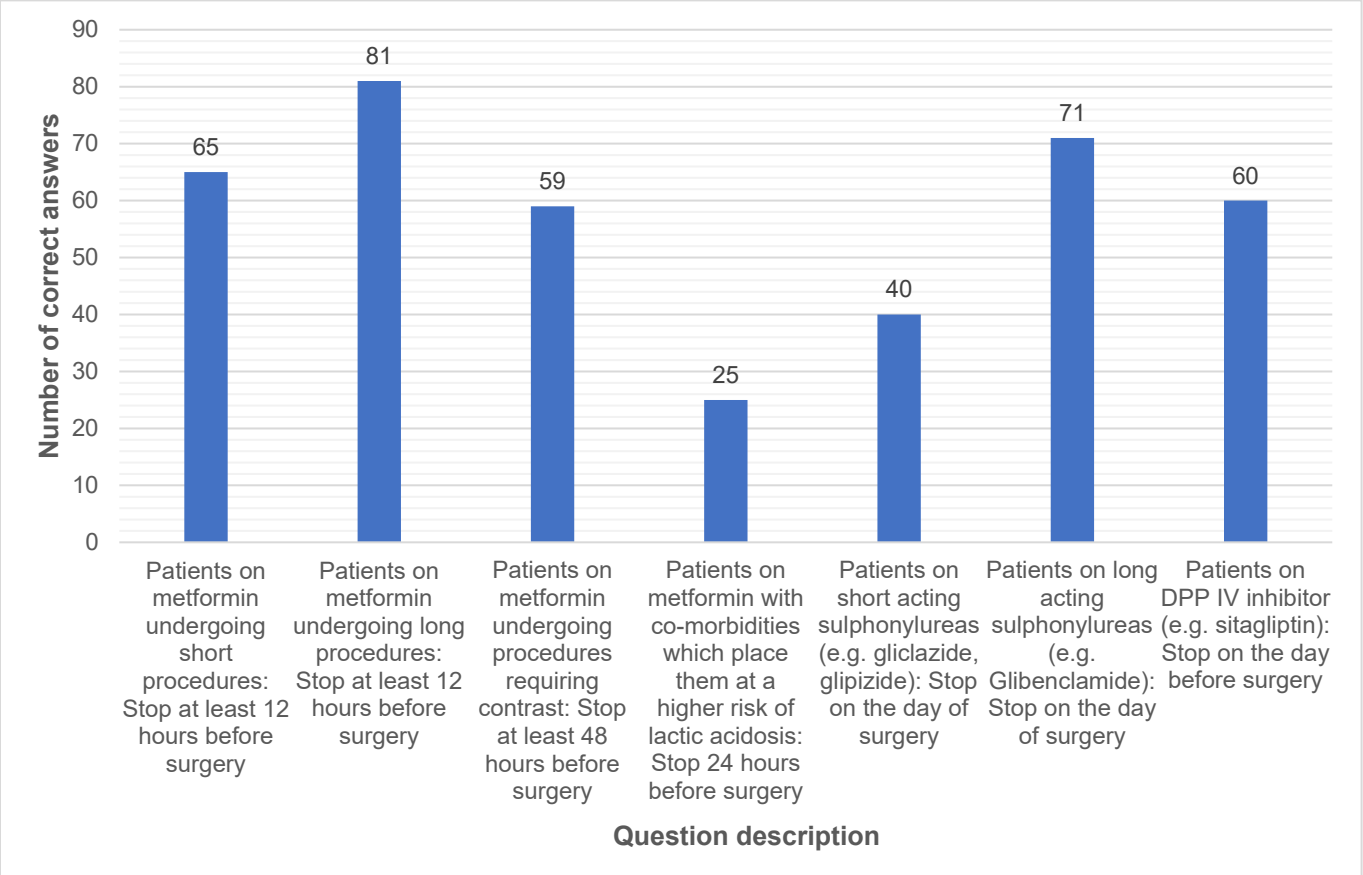


Figure 9: Participants' practices with respect to oral hypoglycaemic agent(s)

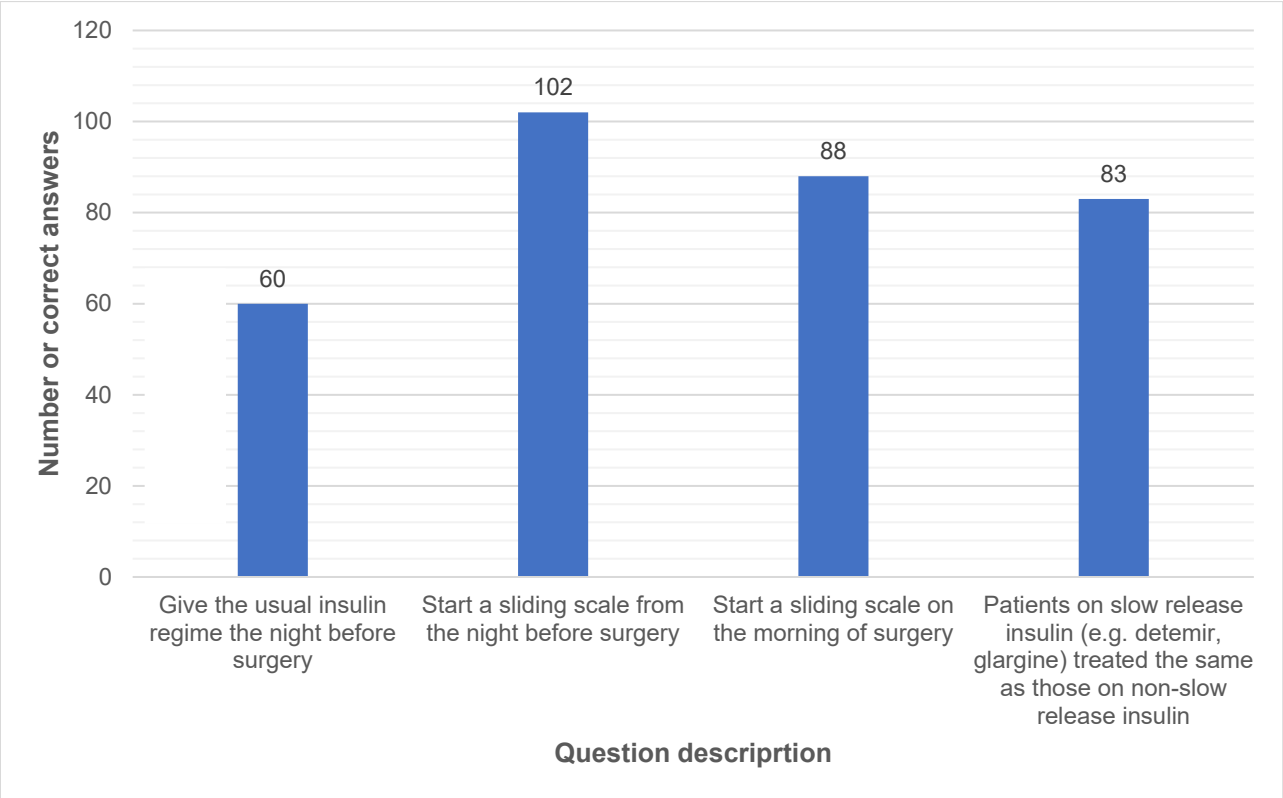


Figure 10: Participants' practices with respect to management of insulin

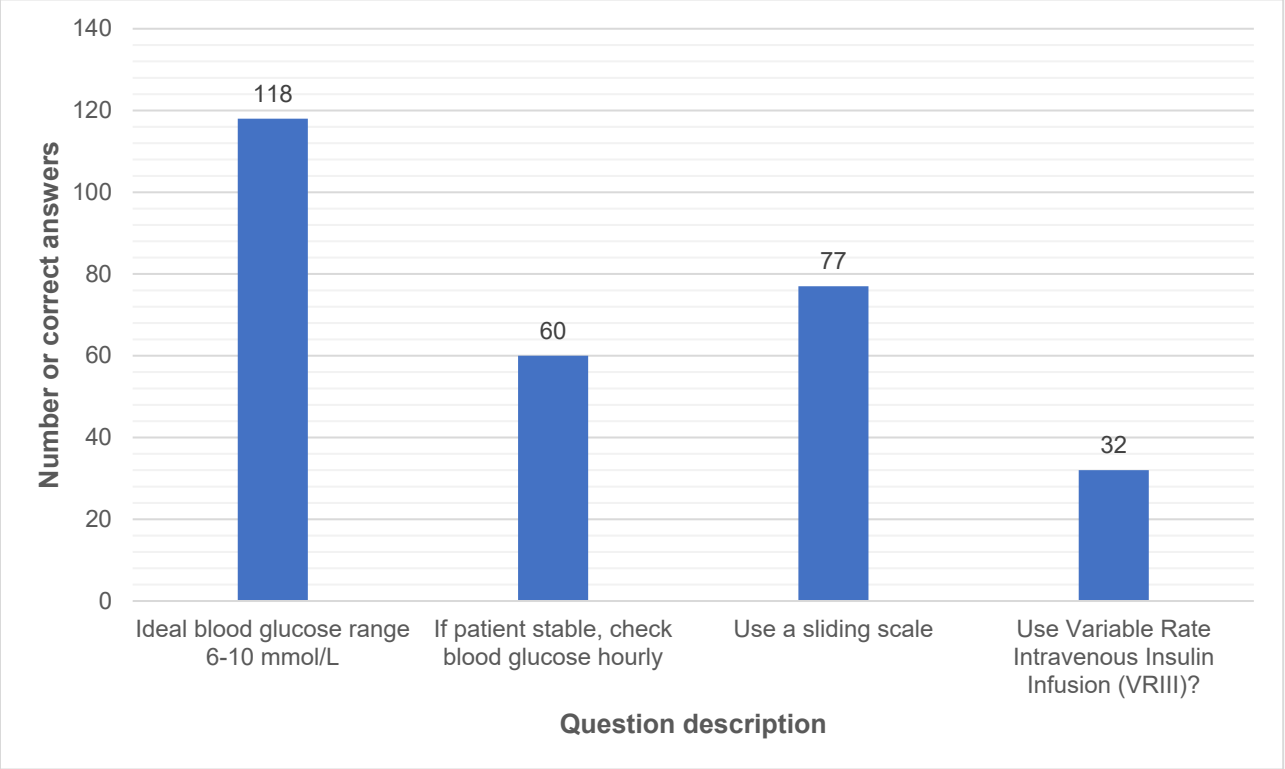


Figure 11: Participants' practices with respect to intra-operative glycaemic control

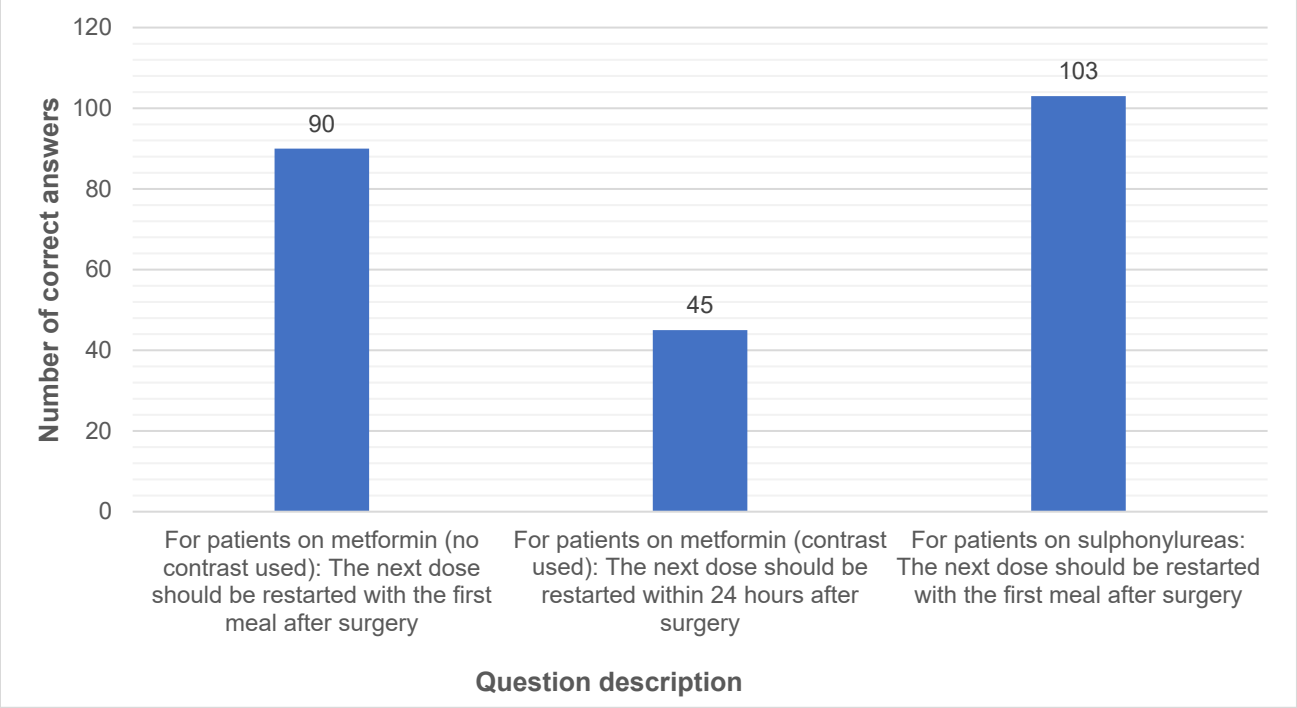


Figure 12: Participants' practices with respect to post-operative glycaemic control

Discussion

There are currently no formal national or institutional guidelines with respect to the peri-operative management of South African diabetic patients. The current Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) guidelines are limited and incomplete.[11] According to the JBDS [8] guidelines, one of the four major contributors to adverse outcomes when managing diabetic patients in the peri-operative period is the absence of institutional guidelines. There is a paucity of data with respect to the knowledge, awareness, and implementation of peri-operative guidelines for the management of diabetic patients among South African anaesthetists.

In the literature there were no similar studies done on this topic which would allow us to compare our results with international or local data. In this study, less than half of participants demonstrated knowledge and awareness of SA and international peri-operative guidelines, their implementation of guidelines was poor, and less than 20% of participants had received formal training with respect to these guidelines. Even though SA peri-operative DM guidelines do not exist, almost half of participants clamied to know them. Majority of participants knew about general SA diabetes mellitus guidelines, however these do not guide practice peri-operatively.

We further explored the three main areas of focus identified by the international guidelines on how to manage diabetic patients in the peri-operative setting. When it came to starvation the main goal according to the guidelines is to minimise the time that patients are starved. Therefore, avoidance of prolonged starvation periods pre-operatively, prioritising diabetic patients on the list and the early resumption of meals post-operatively is essential.[8,9] Majoriy of participants adhered to guildeines when it came to these recommended starvation practices.

The careful selection of fluids is important in order to maintain blood glucose concentrations within an acceptable range. Intravenous (IV) fluids help maintain serum electrolytes within normal limits and optimise the intravascular volume.[8] When it comes to fluid management; both the JBDS and the ADS guidelines generally recommend that diabetic patients should be given Hartmann's solution i.e. Ringer's lactate solutions whereas glucose containing solutions should be avoided peri-operatively.[8,9] More than 90% of participants adhered to these recommendations.

With regards to glycaemic control practices, the questions that had the most correct responses included, the ideal HBA1c level (>60%), ideal blood glucose range (>95%), and management of patient treated with insulin (50% and above). The management of oral hypoglacaemics had the worse scores with more than half of the particants giving incorrect answers overall. These low scores may be attributed to a lack of training and testing of anaesthetists regarding peri-operative management of diabetic patients and that guidelines knowledge is not emphasised in the department.

Diabetic patients are frequently encountered in theatre and more importantly, 90% of diabetic patients in our SA setting have type 2 DM which is mostly managed using oral hypoglycaemic agents.[1] Mismanagement of DM by health professional is one of the major causes of increased risk for morbidity and mortality peri-operatively, largely as a result of uncontrolled hyperglcaemia.[4] This suggests that more emphasis needs to be placed on oral hypoglacaemics training of anaesthetists in the department.

The purpose of guidelines is to gather and translate medical research or expert opinion to provide recommendations to support clinicians in order to improve quality of care, patient outcomes and cost effectiveness.[12,13,14] Guidelines are particullay useful in highly prevalent diseases or diseases leading to premature mortality, avoidable morbidity or negative effects on health-relatedquality of life. Studies have shown that despite the presence and awareness of the existence of guidelines they are often not applied.[15] This may result in unnecessary diagnostics as well as inappropriate treatment leading to poor patient outcomes.[16] When introducing guidelines, more focus needs to be put in their development, implementation as well as dissemination strategies.[17] Forrest However more emphasis has now been put on implementation strategies as development of guidelines alone does not improve clinical practice.[15]

A systematic review by Cabana et al showed that the 3 main barriers to health professional not adhering to guidelines are physicians' knowledge (e.g., lack of awareness and lack of familiarity), physicians' attitudes (e.g., lack of agreement and lack of motivation) as well as external barriers (e.g., patient-, guideline- and environment-related factors).[16] Hence, for guidelines to be implemented effectively, these different barriers have to addressed.[15] Strategies to improve implementation were suggested according to these three main barriers. For successful implementation and application of guidelines by physicians, The "Knowledge-Attitude-Behaviour Framework" emphasises the importance of awareness and knowledge of guidelines which then changes attitude and that in turn will influence practice behavior.[17]

Suggested strategies when it came to physician's knowledge included improving dissemination of guidelines, active learning from experts as opinion leaders as well as continuous medical education (CME).[15] When is came to physicians'attitudes, individualised audit and feedback are also considered to be effective strategies.[15] Strategies to improve guidelines related barriers included making guidelines short and user-friendly as possible, having checklists, using tablets, smartphones and mobiles as platforms for the dissemination of guidelines and having decision support systems in place.[15] Whereas when in came to external factors suggestions included, improving organisation of care, usage of protocols, addressing lack of resources, taking into account the type of care setting during the development of guidelines, establishing clear roles in terms of standing orders, financial incentives as well as consideration of local context to allow local adaptation. [15]

Conclusion

Currently, there are no local guidelines with respect to peri-operative management of patients with DM. Despite some participants being aware of guidelines, practice among participants varied, and in some instances was not in alignment with existing guidelines. Implementation of international guidelines may not always be useful in the SA setting due to organisational structure, resource constraints, and our local context. Specific department guidelines need to be developed, implemented, and education with respect to the contents of guidelines as well as repeated education/ CME is required to improve practices, and sustain changes.

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Conflict statement
We declare that we have no financial or personal relationship which may have inappropriately influenced us in writing this paper.

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Section 4: Proposal

Peri-operative practices by Anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand Academic hospitals

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4.1 Introduction and problem statement

Diabetes mellitus (DM) is a common metabolic disorder worldwide, and particularly so in South Africa (SA) (1). In 2015, the International Diabetes Federation (IDF) estimated that there were approximately 415 million people living with diabetes worldwide and that of these more than 14 million people were in the African region (2).This number is expected to more than double by 2040 (2). Globally, a further increased incidence of adults with DM to 69% in developing countries and 20% in developed countries is predicted between 2010 and 2030 (3).

About 7% of South Africans were diabetic in 2015, which amounted to 2.28 million cases (2). Type 2 diabetes accounts for 90% of patients with diabetes in SA. DM is becoming a major problem in SA as a result of urbanization, inactive lifestyles, unhealthy eating habits as well as an increased prevalence of obesity (2). About 30-85% of diabetic patients remain undiagnosed, resulting in about 20% of diabetic patients having complications by the time that they are diagnosed (2). As a result, a national approach involving both government and non-governmental organizations has been suggested to combat the effect of diabetes in South Africa (2).

The increased incidence of DM has meant that the surgical patient population with DM has increased. A patient with diabetes has a 50% chance of presenting for a surgical intervention in their lifetime and 20% of patients presenting for surgical procedures are diabetic (4,5). The reasons for this increase may be unrelated to the DM or directly related to the DM itself as it affects multiple organs systems with micro and macrovascular complications. Regardless of how and when they present, this particular group of patients is at an increased risk of morbidity and mortality peri-operatively either due to mismanagement of their DM by medical professionals, pre-existing complications of the DM, or due to the surgery and anaesthesia (4).

Surgery is a major stressor on the body and complicates the management of DM. As a stressor, surgery is a significant contributor to the hyperglycaemia seen in patients peri-operatively and induces inflammatory and hormonal responses leading to an increase in inflammatory cytokines, catabolic hormones and a decrease in anabolic hormones (e.g. insulin) (6). The extent of homeostatic disturbance differs according to the patient, the type and length of surgery performed, other factors such as sepsis, as well as whether it is done in the morning, or on the afternoon lists. A combination of these factors will determine whether only minimal or tighter control is required to manage the blood glucose (4). Ultimately surgery predisposes to elevated blood glucose levels in both diabetic and non-diabetic patients. With this being said, diabetic patients are more at risk of complications (7). Surgery predisposes to a state of insulin resistance, hyperglycaemia, increased gluconeogenesis, ketogenesis, and an increased risk of infections peri-operatively (6). Moreover, the haemodynamic instability that may occur during the surgical period hinders the absorption of subcutaneous insulin, leading to an increased risk of hyperglycaemia (6). In addition, surgery requires anaesthesia to be performed which further adds to the problem and increases the risk of complications (6).

Anaesthesia can be broadly divided into general or regional anaesthesia. General anaesthesia has been shown to lead to more hyperglycaemic events when compared to regional anaesthesia and hence requires tighter glycaemic control (4). General anaesthesia renders the patient unconscious, which may lead to certain complications, including hypoglycaemia, going unnoticed. Glycosylation of joints, especially in the cervical spine, may be encountered, which may lead to a difficult intubation (6). Moreover, because of the increased incidence of high body mass index in diabetic patients, they are more likely to have post-operative pulmonary complications (8).

Currently there is no evidence to confirm that regional anaesthesia is superior to general anaesthesia in diabetic patients when it comes to preventing major complications of surgery and anaesthesia (6). One advantage of regional anaesthesia is that patients are able to resume their meals and hypoglycemic agents sooner post-operatively. On the other hand, regional anaesthesia should be given with extra caution in patients with diabetes as they are at an increased risk of having autonomic neuropathy (6).

This may lead to severe haemodynamic instability with profound hypotension if a sympathectomy should ensue from a regional technique (6). All patients are required to be starved peri-operatively in order to safely undergo anaesthesia; this may predispose patients to hypoglycaemic or hyperglycaemic complications (6).

Starvation means that patients are fasted for a certain period of time pre-operatively mainly to avoid aspiration. Diabetic patients are more prone to aspiration as a result of their increased risk of gastroparesis due to autonomic neuropathy, and may need prolonged starvation (9). However, starving patients for a long period of time may lead to a catabolic state and a period of insulin resistance with resultant hyperglycaemia (9). On the other hand, patients may become hypoglycaemic which may cause neurological deficits, confusion and even coma or death (3). Therefore during peri-operative starvation, glucose needs to be closely monitored (9).

Fluids are given peri-operatively during the starvation period. This is mainly to maintain blood glucose concentrations within an acceptable range but also to avoid a catabolic state, thus preventing proteolysis, lipolysis and ketogenesis (10). Moreover, fluids help to maintain serum electrolytes within normal limits and optimize intravascular volume (10).

The effects of prolonged hyper- and hypoglycaemia on surgery outcomes have been well studied. These include:

- Multi-organ dysfunction, particularly involving the cardiovascular system (with an increased oxygen demand/supply mismatch)
- Metabolic disturbances
- Fluid and electrolyte imbalance
- Wound infection
- Post-operative sepsis
- Endothelial dysfunction
- Renal dysfunction
- Cerebral ischaemia
- Diabetic ketoacidosis (DKA)
- Hyperosmolar non-ketotic coma (HONK) (8).

As previously mentioned, hypoglycaemia may cause a significant neurological deficit (3). Therefore the main goals of management of patients with diabetes around the peri-operative period are to avoid severe hyperglycaemia and also hypoglycaemia. These aims can be achieved by following appropriate guidelines to safely manage this group of patients.

The current and most comprehensive guidelines for management of patients with diabetes in the literature are from the NHS Joint Diabetes Societies (British and UK) 2011 (10) and Australian Diabetes Society 2012 (9). Although there are a few discrepancies between these guidelines in managing patients with diabetes, they are both clear when it comes to the major areas that need focus and which will make an impact in reducing the morbidity and mortality of patients with diabetes. The main areas of focus are glycaemic control, starvation practices, and fluid management practices (10,9).

Regarding glycaemic control, the Australian guidelines (9) require tighter control of both the HBA1c and glucose when compared to the British guidelines (10). The British guidelines recommend that patients for elective surgery should have a peri-operative HBA1c of less than 8.5% (10) compared to less than 8% in the Australian guidelines (9). Blood glucose target range in the Australian guidelines is 5-10 mmol/L (9) whereas 4-12 mmol/l is considered acceptable by the British guidelines (10). If the blood glucose level is stable and well controlled, then both the Australian and the British guidelines recommend 1 hourly checks peri-operatively (9,10).

Medically, both the Australian (9) and the British (10) guidelines have moved away from the traditional sliding scale. This is because it has been proven ineffective as it focuses on treating hyperglycaemia instead of preventing it from occurring (9). Therefore the current recommendation is to give an insulin-glucose infusion in appropriately selected patients (9,10). Australian guidelines (9) have suggested giving both insulin and glucose intravenously or subcutaneous insulin by infusion pump while the British guidelines (10) suggest a variable rate intravenous insulin infusion (VRIII).

For groups of patients with diabetes who are normally managed with either insulin or oral hypoglycaemic agents (OHA) there are detailed tables containing peri-operative adjustments for specific types of insulins and OHA. Also how and when to take them for different groups of patients (e.g. type and length of surgery, morning or evening list and other factors).

For starvation, the guidelines recommend prioritization of patients with diabetes to be done on the morning list so as to shorten their starvation time (9,10). Fluids should be started to prevent a catabolic state (9,10). Careful selection of fluids is important (9,10). When compared to the Australian guidelines (9), the British guidelines (10) are more comprehensive regarding fluid management. The type of fluid administered depends on the electrolyte status of the patients as well as whether the patient is on VRIII or not (10).

Problem statement

The above mentioned British and Australian guidelines are the only recent comprehensive international guidelines available in the literature.(9). The USA has 2012 guidelines but their peri-operative guidance is unclear. Even more disturbing is that our own national guidelines, from SEMDSA were last updated in 2012 and are inadequate. The only mention of the peri-operative management of diabetic patients was just one paragraph long and did not include an actual recommended practice for our population (11). Attempts to find local guidelines at our academic hospitals were also unsuccessful. According to the British guidelines, one of the four major contributors to adverse outcomes when managing diabetic patients was the lack of institutional guidelines (10). So the question remains; “As Anaesthetists at WITS, how much do we know about managing patients with diabetes and what guides our practice?”

4.2 Aim and objectives

4.2.1 Aim

The aim of this study is to describe peri-operative practices by Anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand (Wits) Academic hospitals.

4.2.2 Objectives

The primary objectives of this study are to:

- describe the practices by Anaesthetists when managing patients with diabetes mellitus in the peri-operative period
- describe the knowledge of diabetic management guidelines in the peri-operative period by Anaesthetists.

4.3 Research assumptions

The following definitions will be used in this study.

Anaesthetist: is any qualified doctor working in the Department of Anaesthesiology including medical officers, registrars and consultants.

Medical officer: is a qualified doctor practising in the Department of Anaesthesiology under specialist supervision. Medical officers with more than 10 years of experience are career medical officers and are regarded as consultants.

Registrar: is a qualified doctor who is registered with the Health Professional Council of South Africa as a trainee anaesthetist.

Consultant: is an anaesthesiologist or career medical officer.

4.4 Demarcation of study field

The study will take place in the Department of Anaesthesiology, affiliated to the Faculty of Health Sciences at Wits. The staff complement is 27 medical officers, 107 registrars and 74 consultants. Wits has the following academic hospitals:

- Charlotte Maxeke Johannesburg Academic Hospital a 1200-bed central hospital
- Chris Hani Baragwanath Hospital a 2888-bed central hospital
- Helen Joseph Hospital a 500-bed regional hospital
- Rahima Moosa Mother and Child Hospital a 338-bed regional hospital
- Wits Donald Gordon Medical Centre a public private hospital with 190 beds

4.5 Ethical considerations

Approval to conduct the study will be obtained from the Human Research Ethics Committee (Medical) and the Postgraduate Committee of the University of the Witwatersrand (Annexure 5.1).

Anaesthetists will be invited to participate in the study at departmental academic meetings. An information letter will be given to the participants (Appendix A) as well as a self-administered questionnaire (Appendix B). The return of a completed questionnaire will imply consent.

Anonymity will be ensured as questionnaires will be collected without any identifying information. A study number will be affixed to each questionnaire. To ensure confidentiality only the researcher and supervisors will have access to the raw data. Data will be stored securely for six years after completion of the study.

This study will be conducted according to the principles of the Declaration of Helsinki and the South African Guidelines for Good Clinical Practice (12,13).

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and the Graduate Studies Committee of the University of the Witwatersrand.

4.6 Research methodology

4.6.1 Research design

A prospective, descriptive design will be followed in this study.

4.6.2 Study population

The study population consists of all the anaesthetic registrars, consultants and medical officers in the Department of Anaesthesiology at Wits.

4.6.3 Study sample

Sample size

The questionnaire will be given to all the accessible Anaesthetists at Wits academic meetings. The sample size will be dependent on the response rate. A minimum response rate of 60% (125) will be acceptable. To increase the response rate, questionnaires will be given at academic meetings on three different occasions to all anaesthetists attending so as to include more anaesthetists who might not be available for certain academic meetings.

Sampling method

In this study, a convenience sampling method will be used. Readily available subjects will be chosen to participate in the study. Data will be collected during academic meetings when the majority of the staff are available.

Inclusion and exclusion criteria

The inclusion criteria for this study are:

- anaesthetists
- employed by the Department of Anaesthesiology at Wits
- willing to participate in the study
- completed questionnaires.

The exclusion criteria in this study are:

- blank questionnaires returned will be excluded from the data analysis, but included to calculate the response rate
- intern doctors as well as doctors from other departments rotating through the department
- medical officers with less than six months work experience in the Anaesthesia department
- anaesthetists on annual or sick leave.

4.6.4 Data collection

Questionnaire development

Following a review of the literature a draft questionnaire was developed by the researcher and reviewed by experts. The questionnaire was validated by a professor and two senior consultant in the department of Anaesthesia at Wits.

The questionnaire (Appendix B) will include questions on the following:

- Demographic data (gender, professional designation, age, years of experience)
- Knowledge of guidelines regarding management of patients with diabetes
- Glycaemic control practices by Anaesthetists
- Starvation practices by Anaesthetists
- Fluid management practices by Anaesthetists.

Data collection

Data collection process

Approval will be sought from the Human Research Ethics Committee (Medical) and the Post Graduate Committee at Witwatersrand before data is collected.

Before the start of the academic meetings at Wits, the chair of the meeting will be asked if the researcher can address the meeting. The researcher will then explain the topic, after which participants will be invited to participate in the study. The anaesthetists will be informed that participation is voluntary and anonymous.

The researcher will then hand out the questionnaires and request that the participants put them in the sealed box for collection upon completion. The researcher will be available to answer questions pertaining to the study and will collect the sealed box once the questionnaires have been returned.

4.6.5 Data analysis

Data will be captured onto a Microsoft Excel® spreadsheet and analysed in consultation with a biostatistician using Statistica version 12. Frequencies and percentages will be used to summarise the results.

4.7 Significance of the study

The prevalence of patients with diabetes mellitus is increasing (2). Anaesthesists frequently encounter this group of patients as part of their daily duties. The importance of using appropriate guidelines has been emphasised to decrease morbidity and mortality when managing this group of patients (10).

The results from this study will give an understanding of current practices by Anaesthetists at Wits when managing patients with diabetes and whether or not they are adhering to guidelines.

4.8 Validity and reliability of the study

The validity and reliability of this study will be ensured by:

- Appropriate research design
- Targeting a representative study sample
- Content validity of questonnaire
    - Face and content validity
    - Comprehensive literature review
    - Senior anaesthesiologists/consultants reviewed
- Sample size determined in consultation with a statistician

- Data collection
    - One data collector
    - Primary researcher present to answer questions, and to prevent data contamination
- Data analysis in consultation with a biostatistician

4.9 Potential limitations

- Contextual design and convenience sampling.
- The existing and comprehensive NHS Diabetes (British and UK) and Australlian guidelines used at the time of data collection may appear outdated as they were developed in 2011 and 2012 respectively. These are the main guidelines that have been consistently used over the last few years when managing patients with diabetes.

4.10 Project outline

4.10.1 Time frame

	May ‘16	June ‘16	Nov ‘16	Dec ’16-Feb ’17	Mar ’17-April ‘17	May ’17-June ‘17	July ‘17
Literature review	X	X					
Proposal preparation	X	X					
Chapter 1,2,3		X					
Post grad submission		X					
Ethics Submission			X				
Data Collection				X			
Data Analysis					X		
Chapter 4,5						X	
Submission							X

4.10.2 Budget

Item	Cost	Number	Total
Paper	R1. 00/page	1000	R1000
Binding	R200/book	3	R600
			R1600

The Wits Department of Anaesthesiology will incur the costs of paper and printing.

4.11 References

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4.12 Appendices

Appendix A: Information sheet

Dear Colleague,

Hello, my name is Lungile Carol Mwelase and I am a registrar in the Department of Anaesthesiology at the University of the Witwatersrand.

I would like to invite you to participate in my study entitled: **Peri-operative practices by Anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand Academic hospitals.**

As Anaesthetists, we are managing patients with diabetes mellitus on a daily basis due to the increased prevalence of diabetes mellitus. This particular group of patients is at an increased risk of morbidity and mortality peri-operatively and appropriate guidelines need to be followed to avoid complications. This creates a need to seek answers regarding our management practices when dealing with diabetic patients and what guides those practices.

Participation in this study is voluntary and consent will be implied on submission of an answered questionnaire. If you decide to participate in the study, the information will be kept anonymous as there will be no personal information required. Questionnaires will be numbered for practical reasons. Only the researcher and supervisors will have access to the raw data to ensure confidentiality.

The questionnaire should take approximately 15 minutes to complete. Please place your completed questionnaire into the sealed box provided. You can withdraw at any stage of the study if you wish to do so.

The study has obtained approval from the Human Research Ethics Committee of the University of the Witwatersrand.

If you have any questions, please feel free to ask me. You can contact me on 011 933 9334 or the Chairman of the Human Research Ethics Committee (Medical) on 011 727 1234.

I would like to thank you for reading this letter, your time is greatly appreciated.

Yours Sincerely
Dr Lungile Carol Mwelase

Appendix B: Questionnaire

Please answer the following questions.

DEMOGRAPHICS				
1. Gender	M		F	
2. Designation	Medical officer	Registrar	Consultant	
3. Age	25-30	31-35	36-45	>45
4. Years of experience in anaesthesia	< 6 months	6 months - 5 years	>5 years- 10 years	> 10 years

5. Please cross either YES or NO to best describe your knowledge and use of South African guidelines regarding the overall medical management of diabetes mellitus.

GUIDELINES	**YES**	**NO**
Do you know of any South African guidelines?		
Do you implement these guidelines at your workplace?		
Did you have any formal training on the use of these guidelines?		

6. Please cross either YES or NO to best describe your knowledge and use of South African guidelines regarding the management of diabetes mellitus in the peri-operative setting.

GUIDELINES	**YES**	**NO**
Do you know of any guidelines?		
Do you implement these guidelines at your workplace?		
Did you have any formal training on the use of these guidelines?		

GUIDELINES	YES	NO

7. Please cross either YES or NO to best describe your knowledge and use of any international guidelines regarding the management of diabetes mellitus in the peri-operative setting.

GUIDELINES	YES	NO
Do you know of any guidelines?		
Do you implement these guidelines at your workplace? Did you have any formal training on the use of these guidelines?		

8. Please cross either YES or NO to best describe your starvation practices in patients with diabetes mellitus when having a surgical procedure.

STARVATION	YES	NO
A diabetic patient should ideally be prioritized to be done in the morning to shorten starvation time.	**	
A diabetic patient on the morning list; starting at 08:00 should not eat food after 22:00 the night before.		**
A diabetic patient on the morning list; starting at 08:00 should not drink any fluids after 05:00 on the day of surgery.	**	
A diabetic patient on the afternoon list; starting at 12:00 should not eat food after 04:00 on the day of surgery.		**
A diabetic patient on the afternoon list; starting at 12:00 should not drink any fluids after 10:00 on the day of surgery.	**	

STARVATION	YES	NO
A diabetic patient should resume meals as soon as they can resume their normal hypoglycemic agents.	**	

9. Please cross either YES or NO to best describe your choice of fluid in patients with well controlled diabetes mellitus when having a minor surgical procedure.

FLUID MANAGEMENT	YES	NO
Do you routinely give these patients ringers lactate solution?	**	
Do you routinely give these patients glucose containing solutions?		**

10. Please cross either a YES or NO to best describe your glycaemic control practices regarding the management of diabetes mellitus in the peri-operative setting.

	YES	NO
PRE-OPERATIVELY		
Ideal HBA1c level 7% - 8.5%.	**	
Ideal blood glucose range 6-10 mmol/L.	**	
For patients on oral hypoglycaemics		
Patients on metformin undergoing short procedures: Stop at least 12 hours before surgery.	**	
Patients on metformin undergoing long procedures: Stop at least 12 hours before surgery.	**	
Patients on metformin undergoing procedures requiring contrast: Stop at least 48 hours before surgery.	**	
Patients on metformin with co-morbidities which place them at a		**

	YES	NO
higher risk of lactic acidosis: Stop 24 hours before surgery.		
Patients on short acting sulphonylureas (e.g. gliclazide, glipizide): Stop on the day of surgery.		**
Patients on long acting sulphonylureas (e.g. Glibenclamide): Stop on the day of surgery.		**
Patients on DPP IV inhibitor (e.g. sitagliptin): Stop on the day before surgery.	**	
For patients treated with insulin		
Give the usual insulin regime the night before surgery.		**
Start a sliding scale from the night before surgery.	**	
Start a sliding scale on the morning of surgery.		**
Are patients on slow release insulin (e.g. detemir, glargine) treated the same as those on non-slow release insulin.		**
INTRA-OPERATIVELY		
Ideal blood glucose range 6-10 mmol/L.	**	
If patient stable, do you check blood glucose hourly?	**	
Do you use a sliding scale?		**
Do you use Variable Rate Intravenous Insulin Infusion (VRIII)?	**	
POST-OPERATIVELY		
For patients on metformin (no contrast used): The next dose should be restarted with the first meal after surgery.	**	

	YES	**NO**
For patients on metformin (contrast used): The next dose should be restarted within 24 hours after surgery.		**
For patients on sulphonylureas: The next dose should be restarted with the first meal after surgery.	**	

Thank you for answering this questionnaire.

** correct responses

Section 5: Annexures

5.1 Ethics approval

R14/49 Dr Lungile Carol Mwelase

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M161118

NAME: (Principal Investigator)	Dr Lungile Carol Mwelase
DEPARTMENT:	Department of Anaesthesiology
PROJECT TITLE:	Peri-Operative Practices by Anaesthetists when Managing Patients with Diabetes Mellitus at the University of Witwatersrand Academic Hospitals
DATE CONSIDERED:	25/11/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Brian Gardner
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	10/02/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in November and will therefore be due in the month of November each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 20 February 2017.

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

5.2 Graduate studies approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

02 April 2017
Person No: 0404399W
PAG

Dr LC Mwelase
Unit 28 Shana Park
41 14th Road
Midrand
1682
South Africa

Dear Dr Mwelase

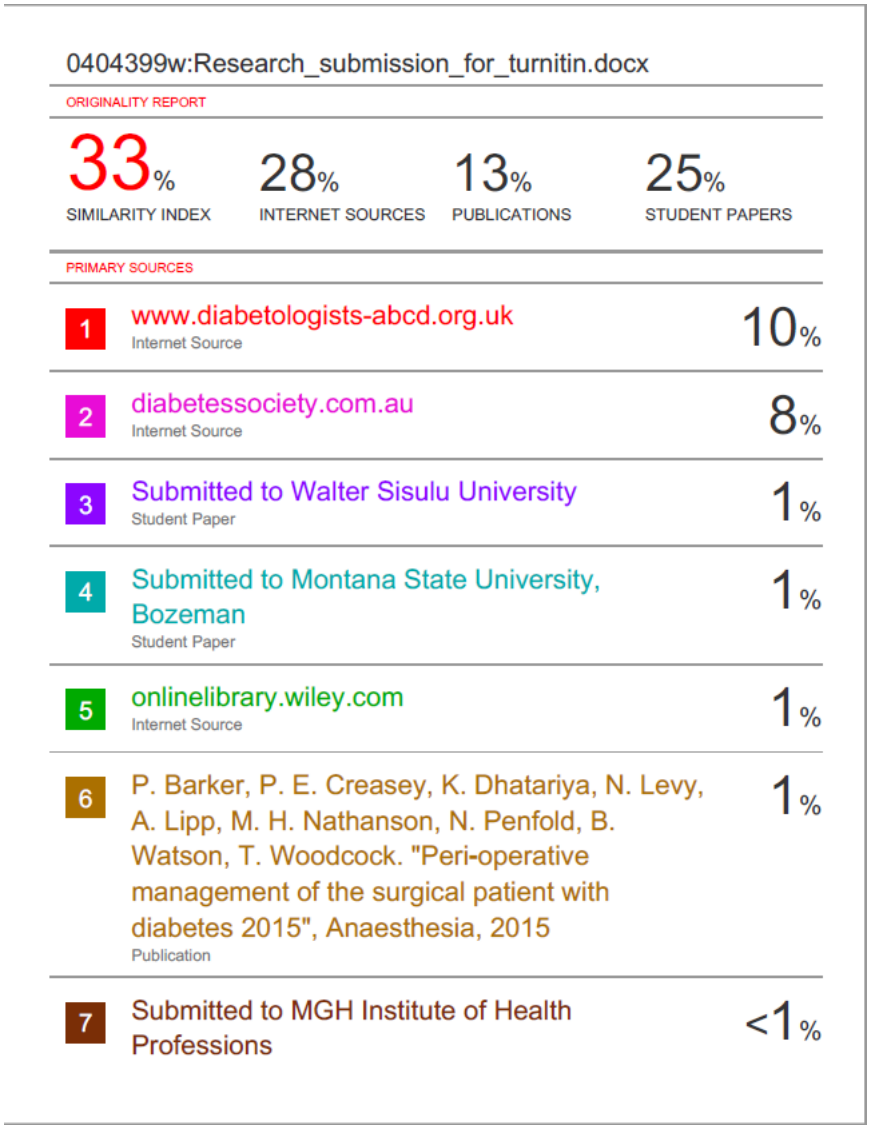
Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Peri-operative practices by anaesthetists when managing patients with diabetes mellitus at the University of the Witwatersrand Academic Hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.3 Turnitin report



0404399w:Research_submission_for_turnitin.docx

ORIGINALITY REPORT

33%	28%	13%	25%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.diabetologists-abcd.org.uk Internet Source	10%
2	diabetessociety.com.au Internet Source	8%
3	Submitted to Walter Sisulu University Student Paper	1%
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6	P. Barker, P. E. Creasey, K. Dhatariya, N. Levy, A. Lipp, M. H. Nathanson, N. Penfold, B. Watson, T. Woodcock. "Peri-operative management of the surgical patient with diabetes 2015", Anaesthesia, 2015 Publication	1%
7	Submitted to MGH Institute of Health Professions	<1%