Protocol

An audit of the prevalence of abnormal fasting blood glucose levels in patients presenting for elective surgery at a selection of Western Cape government hospitals.

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Introduction and study rationale

Diabetes Mellitus (DM) is a major concern in South Africa, with an estimated prevalence (by the International Diabetes Federation [IDF]) of 7% in adults between the ages of 20-79 (IDF, 2015). A study in the Western Cape showed a crude prevalence of diabetes of 28.2%, with undiagnosed type 2 DM (DMII) present in 18.1%. (Erasmus et al., 2012). The true prevalence is not known, and undiagnosed DM is a growing burden.

Poorly controlled DM is known to have an adverse effect on the perioperative clinical course with an increase in the length of hospital stay and increased morbidity and mortality (Barker et al., 2015, Underwood et al., 2014). As anaesthesiologists and perioperative medicine practitioners, perioperative glycaemic control falls within our scope of practice. We know there are patients presenting for elective surgery with undiagnosed DMII and impaired fasting glucose levels, however, we are not sure of the prevalence rates. The motivation for this study was thus, to examine fasting blood glucose levels in elective, non-cardiac, non-obstetric preoperative patients at seven hospitals across the Western Cape. The study will be conducted over the course of one week, to establish the prevalence of both diagnosed and undiagnosed DMII, as well as impaired fasting glucose.

A fasting blood glucose level (defined as a glucose test taken after eight or more hours of no caloric intake) (Sebranek et al., 2013) is a recognised diagnostic test for DMII; patients scheduled for elective surgery are starved for a minimum of six hours. However, a large number of patients are starved for a greater period of time; therefore the majority will fulfil the criteria for a fasting blood glucose test. In this regard, the immediate preoperative period represents an ideal time to check blood glucose levels.
In addition, data will be collected regarding patient comorbidities, as well as evidence of diabetic target organ damage. It is hoped that this collected data will help raise the awareness regarding the contribution of diabetes to the burden of disease, and may aid in establishing an effective perioperative referral system in the screening, diagnosis, and referral for further management of DM.

The aim of this study is to identify the prevalence of abnormal fasting blood glucose levels in preoperative patients in the Western Cape.

Primary outcomes:

a. Incidence of DM and intermediate hyperglycaemia.

Secondary outcomes:

1. Establish prevalence of adequate control of DM (HbA1C).
2. Establish prevalence of compliance with therapy.
3. Establish proportion of patients with complications of diabetes.

Methods

Study Design

This will be a prospective, observational study of adult, non-cardiac, non-obstetric, elective surgical patients conducted over a period of one week.

Study Population

The study population comprises all adult non-cardiac, non-obstetric patients presenting for elective surgery over a period of one week at following sites: Groote Schuur -, Somerset -, Paarl -, Victoria -, Mitchell’s Plain -, Worcester - and George Hospital. The study population sample size is estimated to be 500 patients, from a recent study on hypertension carried out at these hospitals.

Inclusion criteria:

• Adult patients presenting for non-cardiac, non-obstetric, elective surgery
Exclusion criteria:

- Paediatric surgical patients
- Cardiac surgical patients
- Obstetric patients
- Emergency surgery

Study Methods

All patients will be assessed as part of the routine preoperative evaluation, usually occurring the day before the surgery is scheduled. Informed consent will be obtained by the anaesthetist from eligible patients who agree to participate in the study. The patient will be given the option to withdraw from the study at any time. If a patient chooses not to participate, surgery will proceed as scheduled. Information will be gathered directly from the patient, as well as from the folder and documented on the data Case Report Form (CRF).

At the preoperative assessment, clinical data will be collected and recorded on the CRF. This will include whether the patient is a known diabetic or has intermediate hyperglycaemia. In addition, patients medications, comorbidities, and the planned surgery will be documented.

On the day of surgery, before induction of anaesthesia, all patients will have a finger prick blood glucose level done by point of care glucometry, if there is not a documented fasting blood glucose value in their ward file. In patients of unknown diabetic status, should the preoperative value be >7 mmol/l, blood will be drawn when IV access is established, for HbA1C measurement.

In known diabetics, a sample will be taken for HbA1C, regardless of the preoperative fasting blood glucose level, unless there is an HbA1C measurement in the previous 3 months. However, should the patient management have been modified based on the HbA1C result, a repeat HbA1C measurement would be performed. These patients will then be stratified into four categories (based on the WHO diagnostic criteria) (WHO, 2011):

- Low fasting glucose level: <2.8 mmol/l
- Normal fasting glucose level: 2.9-6.0 mmol/l
• Impaired fasting glucose: 6.1-6.9 mmol/l
• Diabetic: ≥7.0 mmol/l

The study protocol can be summarised in the following flow diagram.
All consenting patients

Diabetic Patients

No recent HBA1C; No ward FBG results
- Finger-prick
  - HBA1C regardless

No recent HBA1C; Ward FBG results
- HBA1C regardless

Recent HBA1C*
- No HBA1C*

Unknown status

No ward FBG
- Finger-prick
  - >7 mmol/L
    - HBA1C
  - <7 mmol/L
    - HBA1C

Ward FBG
- Finger-prick
  - >7 mmol/L
    - HBA1C
  - <7 mmol/L
    - HBA1C

*Recent HBA1C (within the previous 3 months). If patient management has been modified in the previous 3 months, a repeat HbA1C measurement would be performed.
Ethical considerations

This study is a large-scale clinical audit. All data will be recorded by anaesthesia registrars and consultants on a separate CRF designed for the purpose of this study, during the in-theatre time of the patient. Patient identifying data will not be captured on the CRF, and thereby data will be kept confidential. The aforementioned are all documented routinely during the anaesthetic, and will not influence patient management or theatre practice, but rather reflects current clinical practice. The study is purely observational and therefore no additional interventions will take place and no adverse events are anticipated as a result of participation in this study. Standard theatre safety precautions and clinical practice will apply.

DMII is a disease in which the long-term outcomes are very dependent on the management of the condition. Therefore, all patients who are identified as having abnormal fasting glucose levels (who are not known with diabetes or impaired glucose tolerance), will be referred to their local clinic/general practitioner for further workup and management. Furthermore, any patient identified with DM will receive further patient education in the form of a patient information leaflet (available in English, Afrikaans and Xhosa).

Data management and analysis

All data will be captured on a CRF and entered into an Excel chart. Data will be collected by anaesthesia registrars and specialists. Data will be handled by the research team as described, and will be kept anonymous, as no patient-identifying details will be recorded on the CRFs. Completed CRFs will be kept in the UCT Department of Anaesthesia and Perioperative Medicine (D23, New Groote Schuur Hospital).

Statistical analysis

Continuous variables will be described as mean and standard deviation if normally distributed or otherwise median and interquartile range (IQR). Comparisons of continuous variables between groups will be performed using unpaired t-tests or the Mann Whitney U test as appropriate. With a sample size of approximately 500 patients, and an expected prevalence of diabetes of approximately 30%, we expect to be able to determine the prevalence within a 95% confidence interval of approximately 9% i.e. 25 to 34%. We believe this study will provide a fairly robust estimate of the prevalence of diabetes in the elective surgical population in the Western Cape.
The Statistical Package for the Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA) will be used for data analysis.

**Reporting of results**

Study results will be recorded and submitted in the form of an MMed dissertation to the University of Cape Town, for assessment as per postgraduate requirements. These results will also be made available to the public and submitted for publication in recognised academic journals. Prior to the start of the study, individual institutional approval and provincial approval from Western Cape Department of Health will be obtained. DM is a treatable condition that contributes significantly to the overall burden of disease in South Africa. Patients participating in our study who are diagnosed with DM will be referred to their local clinic or general practitioner for further management and education. This will take the form of a letter informing the referral physician of the findings.

**Conduct of Study**

The collection of data is scheduled to take place from during a week in October. A week before commencement, all the medical officers, registrars and specialist in the Department of Anaesthesia at participating hospitals will be briefed about the study and their level of involvement. The purpose and execution of the study as well as the researchers’ expectations will be clearly communicated to the various participating hospitals. Posters will be displayed in the theatre complex to ensure adherence to the protocol. The elective surgery lists at each participating hospital will be collected by the medical officer, registrar or specialist the day before scheduled surgery, in order to conduct the preoperative evaluation and recruitment. A CRF will be issued for each patient on the elective list to be completed on the preoperative round according to the researchers instructions. All the information documented on the data form is routinely available in the patients hospital folder. The data from the CRF will be transferred to an electronic data sheet which is password protected. No personal information will be displayed on this form.
Upon arrival in theatre on the day of surgery the CRF will be identified in the patients folder. Postoperatively, all the completed data forms will be collected in the recovery room by the researcher or research assistant.

Data collection forms from all participating hospitals will be collected by the researchers after completion of the study period, and stored in a locked office in the Department of Anaesthesia and Perioperative Medicine at Groote Schuur Hospital.

Resources and costing
The major costs for the study is the laboratory investigations that will be requested as part of the study. The cost of fasting blood glucose determination and HBA1C will be funded by Departmental resources.

Reporting of results
The results of the study will be submitted as an MMed dissertation to the University of Cape Town as part of postgraduate study requirements. The results will be submitted for publication in a recognised academic journal.

Bibliography:


University of Cape Town

Department of Anaesthesia and Perioperative Medicine

EPIC 1

Evaluating Perioperative Interventions to improve patient outcomes 1

An audit of the prevalence of anaemia in patients presenting for elective surgery in selected hospitals in the Western Cape

Research proposal for MMed dissertation in Anaesthesiology and Perioperative Medicine

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Synopsis

This is a proposal for the study “The prevalence of preoperative anaemia in patients presenting for elective surgery.” Preoperative anaemia is considered an independent risk factor for poorer patient outcomes, with increases in morbidity and mortality as well as prolonged length of hospital stay (Kassebaum et al., 2014, Munoz et al., 2015a). One third of patients presenting for surgery will be anaemic, according to the World Health Organization (WHO) criteria (WHO, 1968). However, the importance of this finding in the preoperative period is often overlooked and not corrected prior to surgery (Munoz et al., 2015a). The leading cause of preoperative anaemia is iron deficiency. Iron deficiency anaemia is common in developing countries and results mostly from nutritional deficiency (White, 2017).

Preoperative anaemia is a modifiable risk factor and should be identified early and treated appropriately to improve patient outcomes. There are various modalities available for the prevention and correction of preoperative anaemia. According to the author’s assessment of the literature, there is no published data in South Africa pertaining to the prevalence of preoperative anaemia and the association with iron deficiency.

Study aims and objectives

The purpose of this observational study is to identify the prevalence of preoperative anaemia among patients presenting for elective surgery in the Western Cape.

Primary outcome:

a) Prevalence of anaemia.

Secondary outcomes:

a) Prevalence of iron deficiency anaemia.

b) Proportion of patients that have:
   i) Blood group and screen for antibodies.
   ii) Blood cross-matched.
   iii) Blood in operating theatre.
Background and rationale for the study

The WHO defines anaemia as insufficient red blood cell mass, with Haemoglobin (Hb) concentrations of <12.0 g/dl in females and <13.0 g/dl in males (WHO, 1968). According to the WHO criteria, the global prevalence of anaemia is 32.9% (Kassebaum et al., 2014).

Preoperative anaemia is an important modifiable risk factor associated with increased postoperative morbidity and mortality (Munoz et al., 2015a, Musallam et al., 2011), including an increased risk of postoperative complications such as increased hospital length of stay, ICU admissions, wound infections and readmission to hospital (Munoz et al., 2015a).

In patients presenting for surgery, one third will be anaemic at preoperative assessment, with even higher rates amongst specific surgical groups, for example colorectal and gynaecological patients (Shander, 2014). According to data from the US National Health and Nutritional Examination Survey (NHANES), the prevalence is higher in females and increases with age, affecting 1.5% of males and 12.2% of females aged 17-49 years, more than 10% in age group >65 years and more than 20% in age group >85 years.

The British Committee for Standards in Haematology guidelines highlight three main reasons to identify and treat preoperative anaemia: 1) to identify underlying undiagnosed diseases, for example malignancy, 2) to reduce the likelihood of allogeneic blood transfusions (ABT) and 3) to avoid patient exposure to unnecessary effects of anaemia and transfusion. Audits on transfusion practices is scheduled to take place in the United Kingdom. Management of preoperative anemia will be included as one of the Key Performance Indicators in these audits (5).

Preoperative anaemia is a strong predictive factor for perioperative ABT and the associated complications. Early detection and treatment of preoperative anaemia is a key intervention in the reduction of patient risk due to anaemia-related adverse outcomes after surgery (Munoz et al., 2015a). A 2017 consensus statement by Muñoz et al. recommends that all patients with planned surgery with a transfusion risk of >10% or estimated blood loss >500 ml and a preoperative Hb <13 g/dl, should receive early workup and treatment. If surgery is elective it should be postponed until the Hb is >13 g/dl. This includes obstetric- and gynaecological procedures (Munoz et al., 2011). Minor surgery can be performed as scheduled while investigations for anemia are underway (10) (11).

Although the WHO classification is widely accepted, recent literature suggests that female patients should also have a Hb >13 g/dl prior to surgery if moderate to high blood loss is expected (Munoz et al., 2017). This is because women have a larger relative red blood cell loss during surgery compared
to males (Gombotz, 2007). Females with a preoperative Hb of 12 g/dl have a two-fold risk of blood transfusion compared to men with an Hb of 13 g/dl.

Iron deficiency is the leading cause of anaemia worldwide, with the highest incidence in Sub Saharan Africa and Asia (Stoltzfus, 2003). These areas account for 85% of the global anaemia burden amongst high risk populations, according to the WHO (WHO, 2002). Iron deficiency anaemia (IDA) is the most common cause of preoperative anaemia (Kassebaum et al., 2014, Musallam et al., 2011). In a recent multicentre study of patients undergoing major elective surgery reported the same cut off value for anaemia (<13 g/dl) were used for males and females. A third of the patients were anaemic, of which over two thirds had absolute IDA or iron sequestration (White, 2017). Although South African data on IDA is scarce (Nojilana B, 2007), it is a risk factor that contributes significantly to the burden of disease in South Africa particularly in the perioperative period.

The diagnosis of iron deficiency anaemia is based on laboratory testing of Hb, mean corpuscular volume (MCV), serum ferritin and transferrin saturation (TSAT). Other tests also exist, but the above are most commonly available and affordable tests used for the diagnosis. Ferritin is the main iron storage protein in the body and is the most useful test to determine iron status in the absence of inflammation (Kotze, 2015). Serum Ferritin has a 92% sensitivity and 98% specificity for absolute iron deficiency if the levels are <30 mcg/l (Munoz et al., 2017, Munoz et al., 2011, Musallam et al., 2011).

Transferrin is the only iron transporter in the body (Munoz et al., 2011). Transferrin saturation (TSAT) is measured by serum iron/ total iron binding capacity (TIBC). TSAT< 20% is a reliable indicator of iron deficiency and suggests inadequate supply of iron to sustain normal erythropoiesis(9)(12)(17)(14). Ferritin and TSAT can indicate whether absolute iron deficiency, iron sequestration, or low iron stores for surgery is present (Auerbach and Adamson, 2016, Munoz et al., 2015b).

Despite the morbidity associated with blood transfusions, it remains the most frequently used treatment for perioperative anaemia, with up to one third of all transfusions being administered in the surgical period (Clevenger and Richards, 2015, Norgaard et al., 2014).

Preoperative iron replacement therapy, especially intravenous iron, has been successfully implemented to increase preoperative Hb levels and reduce allogeneic blood transfusions among certain patient groups, for example patients undergoing orthopaedic surgery (White, 2017). Early recognition and management of preoperative anaemia provides perioperative physicians with an
opportunity to optimise patients before surgery, thereby reducing ABT and potentially enhancing early recovery. Although the prevalence of preoperative anaemia in South Africa is not well known, the high prevalence of nutritional deficiencies and chronic diseases such as HIV/AIDS may predispose our patients to a high prevalence of preoperative anaemia.

Methodology:

Study Design
This will be a prospective observational study of adult, non-cardiac, elective surgical patients conducted over a period of one week.

Study Population
The study population comprises all adult non-cardiac patients presenting for elective surgery at Groote Schuur-, Somerset-, Paarl-, Victoria-, Mitchell’s Plain-, Worcester-, and George Hospital over a period of one week.

The sample size is based on a recent study (HASS). We expect to recruit 500 patients in 1 week. With an estimated incidence of anaemia of 30% we estimate that 150 patients will be investigated for iron deficiency as described above.

Inclusion criteria:

- Adult patients (>18yrs)
- Non-cardiac patients
- Elective surgery

Exclusion criteria:

- <18 years of age
- Obstetrics patients

Setting

Elective surgical patients at Groote Schuur-, Somerset-, Paarl-, Victoria-, Mitchell’s Plain-, Worcester, and George Hospital over a period of one week (Monday to Friday, 07:30 to 17:00).
Study Methods

All patients will be assessed as part of the routine preoperative evaluation, usually occurring the day before the surgery is scheduled. Informed consent will be obtained by the anaesthetist from eligible patients who agree to participate in the study. The patient will be given the option to withdraw from the study at any time. If a patient chooses not to participate, surgery will proceed as scheduled.

Information will be gathered directly from the patient as well as from the folder and documented on the data collection form. If the patient has had a Hb level measured within the preceding 3 months, this value will be documented. If more than one Hb level has been determined during this period, the most recent result will be used in the study. If a patient has not had a Hb level documented within this period, a finger-prick Hb test prior to inserting the IV line will be done. If this Hb level, or the previously documented Hb is low according to the WHO criteria, a blood specimen will be obtained when inserting the IV line. If the patient arrives in the operating theatre with a IV line in situ, an additional venepuncture will be performed to obtain the blood sample. The collected blood will be sent to NHLS for Hb, MCV, serum ferritin and transferrin saturation(TSAT) testing. According to the results each patient will be classified as having: i) no anaemia, ii) anaemia without iron deficiency, or iii) iron deficiency anaemia.

It will also be documented on the data collection form if the following action has been taken: i) blood group and screen for antibodies, ii) blood crossmatch, or iii) blood products ordered for the operating theatre.

Ethical considerations

This study is a large scale clinical audit. All data will be recorded by anaesthesia registrars and consultants on a separate case report form designed for the purpose of this study, during the in-theatre time of the patient. Patient identifying data will not be captured on the case report form, and thereby data will be kept confidential. The aforementioned are all documented routinely during the anaesthetic, and will not influence patient management or theatre practice, but rather reflects current clinical practice. The study is purely observational and therefore no additional interventions will take place and no adverse events are anticipated as a result of participation in this study. Standard theatre safety precautions and clinical practice will apply. Should a patient require further medical care based on either of the medical conditions identified, or the severity of the medical conditions, normal clinical practice will be followed to ensure adequate medical care of the patient. Furthermore, any patient
identified with anaemia and or diabetes will receive further patient education in the form of a patient information leaflet (available in English, Afrikaans and Xhosa) and referral letter to primary health clinic/physician for follow-up and further management.

Data management and analysis

All data will be captured on a Case Report Form and entered into an Excel chart. Data will be collected by anaesthesia registrars and specialists. Data will be handled by the research team as described, and will be kept anonymous, as no patient-identifying details will be recorded on the case report forms. Completed Case Report Forms will be kept in the UCT Department of Anaesthesia and Perioperative Medicine (D23, New Groote Schuur Hospital).

Statistical analysis

Continuous variables will be described as mean and standard deviation if normally distributed or otherwise median and interquartile range (IQR). Comparisons of continuous variables between groups will be performed using unpaired t-tests or the Mann Whitney U test as appropriate. With a sample size of approximately 500 patients, and an expected prevalence of anaemia of approximately 30%, we expect to be able to determine the prevalence within a 95% confidence interval of approximately 9% i.e. 25 to 34%. We believe this study will provide a fairly robust estimate of the prevalence of anaemia in the elective surgical population in the Western Cape.

The Statistical Package for the Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA) will be used for data analysis.

Reporting of results

Study results will be recorded and submitted in the form of an MMed dissertation to the University of Cape Town, for assessment as per postgraduate requirements. These results will also be made available to the public. Prior to the start of the study, institutional approval and provincial approval from Western Cape Department of Health will be obtained.

Anaemia and iron deficiency anaemia are treatable conditions that contribute significantly to the overall burden of disease in South Africa. Patients participating in our study who are diagnosed with anaemia will be referred to their local clinic or general practitioner for further management and education. This will take the form of a letter informing the referral physician of the findings. The most common cause of iron deficiency anaemia in developing countries is poor nutritional status. Patients
will receive a take home pack with information on the prevention of the condition along with a referral to the local clinic to receive appropriate nutritional support/supplementation.

**Conduct of Study**

The collection of data is scheduled to take place from 16-20th October, 2017. A week before commencement, all the medical officers, registrars and specialist in the Department of Anaesthesia at participating hospitals will be briefed about the study and their level of involvement. The purpose and execution of the study as well as the researchers’ expectations will be clearly communicated to the various participating hospitals. Posters will be displayed in the theatre complex to ensure adherence to the protocol.

The elective surgery lists at each participating hospital will be collected by the medical officer, registrar or specialist the day before scheduled surgery, in order to conduct the preoperative evaluation and recruitment. A Case Report Form (CRF) will be issued for each patient on the elective list to be completed on the preoperative round according to the researchers’ instructions. All the information documented on the data form is routinely available in the patient’s hospital folder. The data from the CRF will be transferred to an electronic data sheet which is password protected. No personal information will be displayed on this form.

Upon arrival in theatre on the day of surgery the CRF will be identified in the patient’s folder. Postoperatively, all the completed data forms will be collected in the recovery room by the researcher or research assistant.

Data collection forms from all participating hospitals will be collected by the researchers after completion of the study period, and stored in a locked office in the Department of Anaesthesia and Perioperative Medicine at Groote Schuur Hospital.

**Resources and costing**

The major costs for the study are the laboratory investigations that will be requested as part of the study. The cost of the diagnostic tests, posters and data collection forms will be funded by Departmental resources.
Reporting of results

The results of the study will be submitted as an MMed dissertation to the University of Cape Town as part of postgraduate study requirements. The results will be submitted for publication in a recognised academic journal.

References:


