THE EFFECT OF CARBOHYDRATE LOADING ON GASTRIC RESIDUAL VOLUME AND HUNGER SCORE:

A SINGLE BLIND, RANDOMISED CONTROLLED TRIAL STUDY

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LIST OF ABBREVIATIONS

ERAS	Enhanced Recovery After Surgery
HUSM	Hospital Universiti Sains Malaysia
JEPeM	The Human Research Ethics Committee of USM
OGDS	oesophagogastroduodenoscopy
VAS	Visual analog scale
GRV	Gastric residual volume
SD	Standard deviation
IQR	Interquartile range
BMI	Body mass index
GERD	Gastroesophageal reflux disease

ABSTRAK

Penyelidikan Klinikal Rawak: Kesan minuman karbohidrat terhadap isipadu baki gastrik dan keselesaan pesakit

Abstrak

Latar belakang

Penggunaan minuman karbohidrat sebelum pembedahan adalah salah satu langkah penting dalam protokol “Enhanced Recovery After Surgery (ERAS)” yang bertujuan untuk mempercepatkan pemulihan pesakit selepas pembedahan. Semasa pembedahan dan puasa yang berpanjangan, badan bertindakbalas dengan merembeskan hormon stress yang turut menyebabkan rintangan insulin dan katabolik.

Objektif

Keberkesanan minuman karbohidrat berbanding dengan air kosong terhadap isipadu baki gastrik dan keselesaan pesakit

Metodologi

Ini adalah kajian klinikal terkawal rawak yang melibatkan pesakit dari satu pusat kajian sahaja iaitu di Unit Endoskopi, Hospital Universiti Sains Malaysia (HUSM) dari Mei 2019 hingga Mac 2020. Pesakit sukarela yang berumur lebih daripada 18 tahun akan

dirawakkan kepada kumpulan karbohidrat (237 ml sumber) dan plasebo(250 ml air kosong). Turutan rawak tersebut adalah dihasilkan oleh komputer dan susulan pesakit diberikan dalam sampul surat yang bernombor dan tertutup. Minuman akan diberikan 2 jam sebelum prosedur esofagogastroskopi (OGDS). Semasa prosedur OGDS, semua kandungan gastrik akan disedut ke dalam botol takungan dan direkodkan sebagai isipadu baki gastrik untuk dibuat perbandingan. Keselesaan pesakit (kelaparan, dahaga, kegelisahan, keletihan dan kelemahan) akan dinilai mengguna skala analog visual (VAS) sebelum and selepas mengambil minuman.

Keputusan

78 pesakit telah dianalisa dengan pembahagian yang sama antara dua kumpulan. Purata usia peserta kajian adalah 49 tahun dengan sisihan piawai sebanyak 14.3 tahun. Purata (Sisihan piawai) isipadu sisa gastrik dalam kumpulan karbohidrat adalah 58.54 (52.98) mls, manakala 13.97 (14.93) mls dalam kumpulan plasebo. Jumlah sisa gastrik didapati lebih banyak dalam kumpulan karbohidrat ($p < 0.001$) berbanding dengan plasebo. Kumpulan karbohidrat menunjukkan penurunan ketara dalam skor skala analog visual (VAS) kelaparan ($p = 0,043$) dan dahaga ($p = 0,021$). Skor VAS untuk kegelisahan, keletihan dan kelemahan didapati bertambah baik dari masa ke masa dalam kumpulan karbohidrat berbanding dengan kumpulan plasebo, tetapi pengurangan tersebut tidak signifikan secara statistik.

Kesimpulannya

Penggunaan minuman karbohidrat menyebabkan isipadu sisa gastrik yang lebih tinggi berbanding air kosong tetapi ia memberikan skor keselesaan yang lebih tinggi kepada pesakit.

ABSTRACT

THE EFFECT OF CARBOHYDRATE LOADING ON GASTRIC RESIDUAL VOLUME AND THE PATIENTS' WELL-BEING: A SINGLE-BLINDED, RANDOMISED CONTROLLED TRIAL.

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Background

Carbohydrate loading is one of the key steps in Enhanced Recovery After Surgery (ERAS) protocol which aims to expedite post-operative recovery. Body response to surgery and prolong fasting by releasing of stress hormone and inflammatory marker leads to insulin resistance and catabolic state.

Objective

Effectiveness of carbohydrate loading versus plain water on gastric residual volume and patient's well being.

Methodology

This is a single centre, single-blinded, parallel, placebo-controlled, stratified randomized controlled trial at Endoscopy Unit, Hospital Universiti Sains Malaysia(HUSM) from May 2019 to March 2020. Patients older than 18 years old were randomly assigned to either carbohydrate loading (237mls of resource) or control group (250mls of plain water). Randomization sequence was computer generated and allocation sequence was sealed in sequentially numbered and opaque envelopes. The drinks were served 2 hours prior to OGDS procedure. During the OGDS, all the gastric contents were aspirated into a reservoir bottle and recorded as gastric residual volume for comparison later. The patients' well-being (hunger, thirst, anxiety, tiredness, and weakness) were assessed using visual analogue scale (VAS) before (pre) and after (post) drink consumption.

Results

78 patients were randomised and analysed with equal allocation between groups. Their mean age was 49 years old with standard deviation (SD) of 14.3 years old. The means (SD) gastric residual volume in carbohydrate loading group was 58.54(52.98)mls, whereas 13.97(14.93)mls in plain water group. There was significantly more gastric residual volume in carbohydrate group ($p<0.001$). Carbohydrate loading group

significantly showed reduction in VAS score of hunger (p=0.043) and thirst (p=0.021). There was improvement of VAS score for anxiety, tiredness, and weakness over time in carbohydrate loading group compared with plain water group, but not statistically significant.

Conclusion

Carbohydrate loading is associated with higher gastric residual volume compared to plain water. However, they were associated with significantly better well-being.

Dr Michael Pak-Kai Wong: Supervisor

Dr Mohd Nizam Md Hashim: Co- Supervisor

CHAPTER 1

INTRODUCTION

Carbohydrate loading is one of the measures in ERAS (enhanced recovery after surgery) protocol which aims to improve patient outcome(Carmichael et al., 2017). Body response to surgery and prolong fasting by releasing of stress hormone and inflammatory marker leads to insulin resistance and catabolic state. Production of glucose via gluconeogenesis and inability of usage of glucose by peripheral tissues due to insulin resistance cause hyperglycaemia post operation which is associated with increased morbidity and mortality postoperatively (Gustafsson et al., 2008; Kratzing, 2011; Tran et al., 2013). Carbohydrate loading is usage of carbohydrate rich beverage prior to operation which shift body metabolic from fasted state into fed state and subsequently improve insulin resistance especially during postoperative period(Tran et al., 2013).

Pulmonary aspiration is a fatal complication for patient undergoes general anaesthesia. It is due to aspiration of acidic gastric content during intubation and subsequently leads to pneumonitis(Nason, 2015). Practicing nil by mouth for minimum of 6 hours had been replaced by allowing solid food until 6 hours prior to and clear fluid 2 hours prior to operation in recent guideline(Kratzing, 2011). According to previous study, patients are at risk of develop pulmonary aspiration if the gastric content >25ml (>0.4ml/kg) and the pH<2.5(Dalal et al., 2010). With this cut off level, 30-60% of fasted patient are at risk of developing pulmonary aspiration(Dalal et al., 2010). Fasting group showed significant more gastric residual volume compared to intake of 150mls of water, and it is safe to

take 150mls water without increase risk of aspiration(Dalal et al., 2010). Apart from those factors, delay gastric emptying in patient who has diabetic mellitus, dyspepsia, history upper gastrointestinal surgery or intestinal obstruction can predispose to pulmonary aspiration also(Asai, 2004).

50g of carbohydrate is needed to stimulate insulin release to reduce perioperative insulin resistance(Kratzing, 2011). Carbohydrate rich beverage contained polymer (maltodextrin) instead of other monomer beverage is used as carbohydrate loading currently because its low osmolality leads to increase gastric emptying rate(Gunner, 2012).

Other benefit provided by carbohydrate loading were improved patient's wellbeing in the aspect of thirst, hunger and anxiety (Gustafsson et al., 2008; Hausel et al., 2001).

Most studies conducted showed carbohydrate loading prior to operation is safe and benefit(Brady et al., 2003; Dalal et al., 2010; Hausel et al., 2001) However, most of studies conducted to measure gastric volume is through aspiration via nasogastric tube. The objective of the study is to assess the effect of carbohydrate loading and clear fluid on the gastric residual volume after 2 hours of consumption using direct aspiration via OGDS and its effect towards the patient's well- being (hunger, thirst, weakness, tiredness, anxiety).

CHAPTER 2

STUDY PROTOCOL

2.1 DOCUMENT SUBMITTED FOR ETHICAL APPOVAL

The effect of carbohydrate loading on gastric residual volume and hunger score: A single blind, randomised controlled trial study

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Department of Surgery

Health Campus University Science Malaysia (USM)

Supervisor:

Dr Michael Wong Pak Kai

Co-supervisor:

Dr Mohd Nizam Bin Md Hashim

Introduction

ERAS (enhanced recovery after surgery) protocol is a standardised perioperative care procedure which aim to improve patient outcome (Carmichael *et al.*, 2017). It can be divided into preoperative, intraoperative and postoperative components. One of the measures in preoperative care component is carbohydrate loading. Carbohydrate loading is usage of carbohydrate rich beverage prior to operation to improve insulin resistance post operation (Faria *et al.*, 2009). Body response to surgery and prolong fasting by releasing of stress hormone and inflammatory marker (Kratzing, 2011). This led to insulin resistance and catabolic state (Kratzing, 2011). Production of glucose via gluconeogenesis and inability of usage of glucose by peripheral tissues due to insulin resistance cause hyperglycaemia post operation (Kratzing, 2011). This catabolic state and insulin resistance are associated with increased morbidity and mortality postoperatively (Gustafsson *et al.*, 202308; Tran *et al.*, 2013). By giving carbohydrate loading prior operation shift body metabolic from fasted state into fed state (Tran *et al.*, 2013).

Recent guideline had recommended to allow solid food until 6 hours prior to and clear fluid 2 hours prior to operation in replace to fasting of minimum of 6 hours (Kratzing, 2011). However, most of the centres still practice nil by mouth for minimum of 6 hours due to worried of pulmonary aspiration. According to previous study, patient are at risk of develop pulmonary aspiration if the gastric content >25ml (>0.4ml/kg) and the pH<2.5 (Dalal *et al.*, 2010). Pulmonary aspiration is a fatal complication for patient undergoes general anaesthesia. It is due to aspiration of acidic gastric content during intubation and subsequently leads to pneumonitis (Nason, 2015). There are several normal physiological reflex mechanism to prevent aspiration of gastric content but they were abolished by the drugs used during general anaesthesia (Robinson and Davidson, 2014). Apart from residual gastric volume and pH, delay gastric

emptying in patient who has diabetic mellitus, dyspepsia, history upper gastrointestinal surgery or intestinal obstruction can predispose to pulmonary aspiration also (Asai, 2004).

According to study, amount of carbohydrate that can stimulate insulin release is 50g (Kratzing, 2011). Carbohydrate rich beverage contained polymer (maltodextrin) is used as carbohydrate loading currently because its low osmolality compared with other monomer beverage (Nygren *et al.*, 1995). Low osmolality leads to increase gastric emptying rate (Nygren *et al.*, 1995). However, absorption of small bowel for glucose from digested maltodextrin is rapid, which affect blood sugar level especially in diabetic patient (Hofman *et al.*, 2016).

There is still no proper guideline regarding usage of carbohydrate loading in diabetic mellitus patient prior to operation in view of possibility of delay gastric emptying and poor glycaemic control after loading (Gustafsson *et al.*, 2008).

Other than metabolic effect, carbohydrate loading also improve patient's wellbeing in the aspect of thirst, hunger and anxiety in most of the study (Gustafsson *et al.*, 2008; Hausel *et al.*, 2001).

Most studies conducted showed carbohydrate loading prior to operation is safe and benefit. However, most of studies conducted to measure gastric volume is through aspiration via nasogastric tube. This study conducted is to assess effect of carbohydrate loading (maltodextrin with whey protein) to gastric volume 2 hours after ingestion via aspiration while doing OGDS (direct visualisation) and patient's wellbeing (hunger, thirst, weakness, tiredness, anxiety) for all patient planned for OGDS.

Literature review

Enhanced recovery after surgery (ERAS) protocol is also known as fast track protocol. It is an evidence-based protocol with multimodal perioperative care pathway (Carmichael *et al.*, 2017). It is designed to improve patient outcome after treatment and care. There are several standardised practices can be done preoperatively, intraoperatively and postoperatively in order to achieve pain free postoperation, return bowel function in shorter time, improve wound healing and shorten hospitalisation (Carmichael *et al.*, 2017; Noblett *et al.*, 2006). With the ERAS protocol developed, overall complication rate and length of hospitalisation reduced as compared to conventional practice (Adamina *et al.*, 2011). Patient's satisfication is also improved and cost of hospitalisation is reduced (Carmichael *et al.*, 2017; Kratzing, 2011). Apart from surgeon, cardio-thoracic surgeon or gynaecologist also practice according to this protocol (Kaska *et al.*, 2010).

Body response towards injury or surgical trauma can be divided into ebb and flow phase (Faria *et al.*, 2009). Ebb phase is response of body in order to maintain hemodynamic stability. After ebb phase, body enter flow phase, where catabolic state started. This response is mediated by stress hormone and release of cytokines (Kratzing, 2011). Stress hormones and cytokines cause consumption of glycogen reservoir, increase gluconeogenesis and insulin resistance of peripheral tissues (Faria *et al.*, 2009). All of these contribute to hyperglycaemic after injury. Peripheral insulin resistance also leads to proteolysis, inability to utilise glucose as source of energy and subsequently reduced muscle function (Kratzing, 2011). All of these happened even after minor operation (Helminen *et al.*, 2009) and the condition worsen if added prolonged fasting (Faria *et al.*, 2009; Weledji *et al.*, 2017). Hyperglycaemia and insulin resistance are associated with post operation complication. Intensive insulin therapy had shown to give a better outcome (Kratzing, 2011).

Carbohydrate loading is recommended as preoperation measure in ERAS protocol because it induce insulin release and shift body metabolism from fasting to feed state (Tran *et al.*, 2013). Previous study showed that 50g of carbohydrate is needed to produce this effect. Hence, carbohydrate loading with 100g carbohydrate on the night before operation and 50g of carbohydrate 2 hours prior operation were used (Kratzing, 2011).

Traditionally, adequate fasting time with a minimum of 6 hours is required before operation in order to prevent pulmonary aspiration during general anaesthesia. Lately, allow clear fluid for up to 2 hours prior operation is recommended as it improve patient's wellbeing and it is safe (Kratzing, 2011). However, not all solution is safe to be used as carbohydrate loading. Type of food (solid or fluid), the volume of fluid, particle size and composition of the fluid can affect gastric emptying rate (Dalal *et al.*, 2010; Nygren *et al.*, 1995). With the presence of carbohydrate and protein, gastric emptying rate is shorter than fluid contain fat or cellulose (Dalal *et al.*, 2010). Polymer carbohydrate such as maltodextrin has low osmolality which cause rapidly passage of fluid through stomach if compare with monomer fluid (Nygren *et al.*, 1995). According to previous study, 400cc of carbohydrate rich solution (12.0% carbohydrate, maltodextrin) was used and it took about 90minutes to pass through stomach (Nygren *et al.*, 1995). Hence, carbohydrate loading with polymer is recommended in order to provide large dose of carbohydrate which able to stimulate insulin release and not produce significant gastric residual volume prior to anaesthesia.

Kaska et al. (2010) conducted a randomized, prospective and blinded clinical trial, in which patients were randomized into three groups: overnight fasting group as control group, intravenous administer glucose preoperatively and preoperative oral consumption of 400cc a specifically composed solution (principally maltodextrin and electrolytes). Gastric residual

volume was examined by aspiration of juice with the aid of a gastric tube inserted temporarily at the beginning of surgery. It showed that the residual volume was 5 ml in all groups without statistically significant differences. However, the values of gastric residual volume perioperatively was smallest in preoperative carbohydrate drink group. Yagci et al. (2008) had conducted similar study, in which patient was randomized into 2 groups that were overnight fasting and carbohydrate drink(800cc on the evening before and 400cc 2 hours prior to operation), it showed no statistically significant difference between two groups with respect to gastric residue contents. Itou et al. (2011) conducted a study which randomized patient into 2 group that were fasting group and ORS group showed similar result. However, study conducted by Dalal et al. (2010) randomized patient into 2 groups that were fasting (group I) and water (group II). It showed that the gastric fluid volume was found to be lesser in Group II (5.5 ± 3.70 ml) than Group I (17.1 ± 8.2 ml) which was statistically significant.

Significant gastric residual volume can predispose to pulmonary aspiration for patient undergo general anaesthesia. Pulmonary aspiration is defined of inhalation of solid or liquid into respiratory tract (Nason, 2015). It occurs 1 in 900 to 1 in 10000 of patient underwent general anaesthesia (Robinson and Davidson, 2014). General anaesthesia is considered safe in most of the cases, but pulmonary aspiration can cause significant airway related mortality and morbidity (Nason, 2015). Entry of acidic gastric content into lung leads to pneumonitis. The severity of the injury to lung parenchymal is depend on gastric volume, pH level of aspirated gastric content and content of the aspirated fluid which cause infection or mechanical airway obstruction (Nason, 2015). Traditionally, patient is considered as high risk of aspiration pneumonia if gastric volume aspirated more than 25cc and pH less than 2.5 (Dalal *et al.*, 2010). There are several normal physiological reflex mechanism presences in order to prevent aspiration which include gastroesophageal junction, upper oesophageal sphincter and protective laryngeal reflex(Robinson and Davidson, 2014). However, these protective reflexes abolished after

general anaesthesia due to the drug used during anaesthesia. Apart from the causes above, systemic disease such as diabetic mellitus also affect gastric emptying time (Asai, 2004).

In addition to metabolic effect due to carbohydrate loading, patient's well being such as hunger, thirst, anxiety can be improved also (Hausel *et al.*, 2001).

Hausel et al. (2001) consucted a randomised control trial. 252 elective abdominal surgery patients were randomized to preparation with a 12.5% carbohydrate drink (CHO), placebo (flavored water), or overnight fasting. The CHO and Placebo groups were double-blinded and were given 800 mL to drink on the evening before and 400 mL on the morning of surgery. 11 different discomfort variables(anxiety, depression, hunger, inability to concentrate, malaise, nausea, pain, thirst, tiredness, unfitness, and weakness) were scored via Visual analog scales. During the waiting period before surgery, the CHO-treated group was less hungry and less anxious than both the other groups ($P \leq 0.05$). CHO reduced thirst as effectively as placebo ($P < 0.0001$ versus Fasted). Trend analysis showed consistently decreasing thirst, hunger, anxiety, malaise, and unfitness in the CHO group ($P< 0.05$). The Placebo group experienced decreasing unfitness and malaise, whereas nausea, tiredness, and inability to concentrate increased ($P < 0.05$). In the Fasted group, hunger, thirst, tiredness, weakness, and inability to concentrate increased ($P < 0.05$).

Helminen et al. (2009) conducted a prospective, randomized study, in which 210 patients undergoing general or gastrointestinal surgery were randomly assigned to three groups: overnight intravenous 5% glucose infusion (1000 ml), carbohydrate-rich drink (400 ml) at 6–7 a.m., or overnight fasting. Visual analogue scale was used to assess the subjective feelings of thirst, hunger, mouth dryness, weakness, tiredness, anxiety, headache and pain preoperatively.

During the waiting period before surgery, the carbohydrate-rich drink group was less hungry than the fasting group (P=0.011). No other differences were seen in visual analogue scale scores among the study groups. Trend analysis showed increasing thirst, mouth dryness and anxiety in the intravenous glucose group (P<0.05). The carbohydrate-rich drink group experienced decreasing thirst but increasing hunger and mouth dryness (P<0.05). In the fasting group, thirst, hunger, mouth dryness, weakness, tiredness and anxiety increased (P<0.05).

Glucose from maltodextrin is rapidly reabsorb by intestine and cause elevation of blood glucose rapidly (Hofman *et al.*, 2016). It may impair blood glucose level in diabetic mellitus patient. There is a study about use of carbohydrate loading in diabetic mellitus patient, which showed higher peak glucose level which occur later and take longer time for blood glucose to return to baseline if compare to healthy subject (Gustafsson *et al.*, 2008). Because of the possibility impair blood surgar and delay gastric emptying in diabetic mellitus patietn, use of carbohydrate loading in diabetic mellitus paitent still debate.

Product detail

Resource

Description

Fruit flavoured beverage designed for dietary management in malnutrition and peri-operative to enhance outcomes and recovery. It is lactose and gluten free

Age

≥4 years old

Feature

100% high quality whey protein

Fat free

Clear fluid

Low residue

Indications

carbohydrate loading for peri-operative management

fat intolerance/ malabsorption

clear liquid diet

fat free diet

cancer with treatment

Usage

Oral/tube feeding

Caloric density

1.05kcal/ml

Osmolality

77OmOsm/kg H2O

Flavour

Fruit flavoured

Nutritional information

	Per 100ml	Per 237ml
Energy	105 kcal	250 kcal
Protein	3.8 g	9.0 g
Fat-total	0 g	0.0 g
Carbohydrate	22.6 g	53.6 g
- Sugars	145 g	34.4 g
Dietary Fibre	0 g	0 g
Sodium	32 mg	76 mg
potassium	-	-
phosphorous	72 mg	171 mg
Calcium	-	-
iron	1.3 mg	3.1 mg

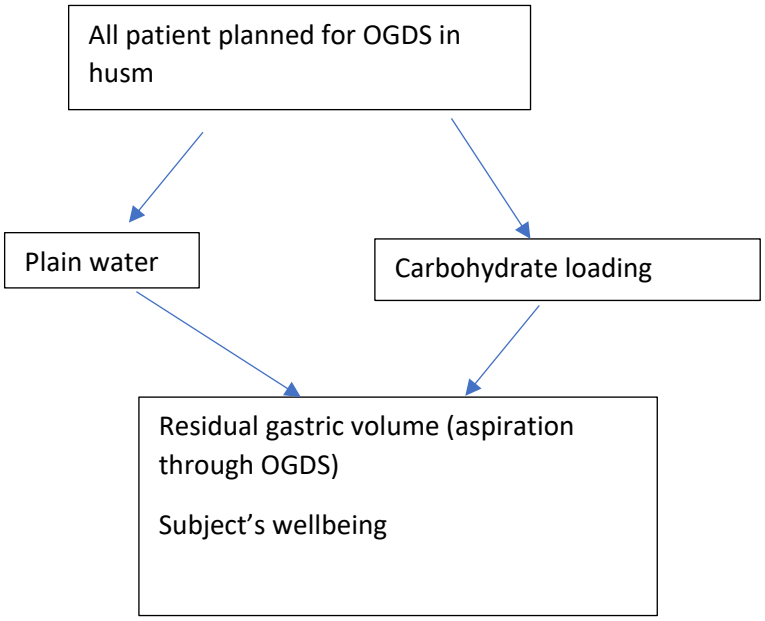
Preparation per serving

237ml

Pack size

237ml

Conceptual framework



Subject planned for OGDS in HUSM will be randomised into 2 group. Plain water is given to group1 of subject and carbohydrate loading is given to group 2 subjects 2 hours prior to OGDS. Residual gastric volume is measure through aspiration via OGDS and subject's wellbeing are assessed for both group of subject prior and after clear fluid have given.

Problem statement & Study rationale

There are a lot of study were conducted to look for the effect of carbohydrate loading worldwide. However, there is limited data about used of carbohydrate and protein as carbohydrate loading. This study conducted by using maltodextrin with whey protein as carbohydrate loading. Method to measure gastric residual volume is via aspiration from direct visualisation with OGDS. This

study also assesses effect of carbohydrate loading (polymer+ whey protein) to patient's well being.

Research Question(s)

1. What is gastric residual volume 2 hours after carbohydrate loading group and control group?
2. What is the effect of carbohydrate loading and control group on subject's wellbeing?

Objectives

General:

- To assess effect of carbohydrate loading in patient planned for OGDS in HUSM

Specific:

- to determine residual gastric volume 2 hours after carbohydrate loading and plain water group
- to explore patient's wellbeing after carbohydrate loading and control

Research hypothesis

First Hypothesis

H1: There is significant association between carbohydrate loading with residual gastric volume

H0: there is no significant association between carbohydrate loading with gastric residual volume

Second hypothesis

H1: there is significant association between carbohydrate loading with subject's wellbeing

H0: there is no significant association between carbohydrate loading with subject's wellbeing

Methodology

Research design

This is a stratified (female, male) with balanced randomisation (1:1), single-blind (blind endoscopist, researcher enrolling and assessing participants), placebo-controlled, parallel-group study

Study area

This study will be conducted in endoscopy room in Hospital University Sains Malaysia in Kubang Kerian

Operative definition

-

Study population

Reference population:

- patient who has planned for OGDS

Source population

- Patient planned for OGDS and attend endoscopy room in HUSM

Study population

- Patient planned for OGDS, attend endoscopy room for in HUSM, fulfilled inclusion criteria and exclusion criteria from April 2019 until December 2019

Subject criteria

Inclusion criteria

- Patient more than 18 years old

Exclusion criteria

- History of upper gastrointestinal surgery
- Intestinal obstruction
- Patient with vomiting
- Mentally disable or who cannot give an informed consent

End points

Primary end point

- Amount of gastric residual volume (ml) that has been aspirated via OGDS 2 hours after plain water or carbohydrate loading group

Secondary end point

- Score (mm) of each parameter from visual analogue scale (VAS) before drink and before OGDS for plain water and carbohydrate loading group

Sample size estimation

Sample size is calculated for all the objectives. However, the one that yield the biggest number is taken as the sample size.

objective 1 is to identify the gastric residual volume between subject with plain water (group A) and carbohydrate loading (group B). Sample size was calculated using comparing two means formula. Sample size is calculate using http://www.openepi.com/SampleSize/SSMean.htm. The

ratio between group A and group B was set as 1. According to article, standard deviation was 18.46. Means difference was set as 12.5.sample size for objective 1 is 35 per group.

Objective 2 is to determined patient's well being for group A and group B. sample size was calculate using comparing paired difference formula. Sample size calculate using http://statulator.com/SampleSize/ss2PM.html#. Expected standard deviation of the paired differences is set as 2 times the expected mean of the paired differences. The sample size is 34 per group

For all sample size calculation, type I error was set at 5% (two tailed), Type 2 error was 20% (to achieve 80% power of study).

Corrected sample size is calculated after included 10% of dropout rate. Corrected sample size = calculated sample size/ (1-anticipated drop out rate).

After considering both objective, 1st objective give biggest number of sample size. Hence, 35 subject per group with a total number of 70 subjects are needed to study both objectives. after consider dropout rate, minimum sample size in this study is 39 subjects per group with a total number of 78 subjects.

Sampling method and subject recruitment

Patient scheduled for elective OGDS in HUSM from April 2019 to December 2019 with the complaint of one or more of the following symptoms: Bothersome postprandial fullness, early satiation, Epigastric pain or Epigastric burning are eligible to participate in the study. Patients who fulfilled exclusion criteria (History of upper gastrointestinal surgery, intestinal obstruction, patient with vomiting or mentally disable or who cannot give an informed consent) are ineligible.

If a patient fulfils the inclusion criteria, a suitable medical officer will discuss the trial with patient while reviewing patient in surgical outpatient clinic prior to OGDS. Patient will be approached again on the day of OGDS, if patient agree to participate in study, a written consent will be obtained. If patient refuse to participate in study, appropriate treatment and care still will be provided to patient. The consent form will provide information about the purpose of the study, the procedures to be followed, risks and benefits of participation. If patient agree to participate in the trial, subject will be enrolled in the study. Method of recruitment in this study is direct recruitment of potential study participants.

Stratified permuted block randomization was used. Randomization sequence was created using https://www.sealedenvelope.com/simple-randomiser/v1/lists and is stratified by gender (female and male) with 1:1 allocation. Random block sizes of 6 is used. Subjects are randomized into either preprocedure plain water (group A) or preprocedure carbohydrate loading group (group B). Patients randomized into group A consume 250ml plain water and patients in group B consume 1 packet of resource (237ml, 53.6g carbohydrate and 9g whey protein). Both groups of patients consume the drink over 10 minutes. 2 hours after that, OGDS will be carried out.

Research tools

1. Data collection pro forma
2. Resource beverage (53.6g carbohydrate and 9g whey protein), plain water
3. Visual analogue scale for assessment of patient well being
    - Each scale consisted of ungraded, horizontal lines anchored at two ends.
    - The left end of the scale represented “not at all” which score: 0 and the right end represented and “the most imaginable” which score: 100
    - patients mark an X somewhere along the horizontal line to complete the scale

4. OGDS
5. 2 Suction systems (include suction reservoir, yankauer sucker)

Data collection method

All subjected planned for OGDS with the complain of one or more of the following symptoms: Bothersome postprandial fullness, early satiation, epigastric pain or epigastric burning and fullfill inclusion criteria are selected. Patients will be approached and be explained regarding the study in surgical outpatient clinic prior to OGDS. Patient will be approached again on the day of OGDS, if agree to participate, an informed consent will be obtained. Informed consent will be obtained after explanation regarding the study and procedure again by researcher nurse

Allocation sequence is according computer generated random number list, it was prepared by an investigator with no clinical involvement in the trial. Allocation sequence was concealed from researcher enrolling and assessing participants. Allocation sequence will be sealed in sequentially numbered and opaque envelopes. A manila card will be placed inside envelop to render it impermeable to intense light. To prevent subversion of the allocation sequence, the name and I/C of the participant will be written on a book together with the series number on envelopes. The details in the book will be kept confidentially. After enrolled subject complete all baseline assessment, corresponding envelope will be enclosed by staff (who not involve in study) who prepare the drink. The staff need to ensure that the envelop still sealed when receive it. The staff will prepare the drink into identical container according to the assignment.

Subjects are randomised into 2 group: 1 group with 250cc plain water and another group give 1 packet resource(237ml). Subjects need to finish the drink over 10minutes. After that, subjects are not allow to leave endoscope room before OGDS done to prevent consumption of other drink or food.