Ultrasonographic Assessment of Gastric Emptying Following Water Ingestion in Healthy Volunteers – Feasibility Study

Study Protocol

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Plain English Summary

Patients who have a procedure performed under general anaesthetic are required to fast from food for at least six hours, and fluids for at least two hours before the operation (the six/two rule). A general anaesthetic involves inducing loss of consciousness with medication, so that awareness is lost and the operation can proceed. If the stomach is full, then there is risk of regurgitation of stomach contents into the lungs as anaesthesia commences. This occurs due to the relaxation of muscles brought on by the medication, and can have severe consequences. Understandably, given the potential for serious harm, anaesthetists are rigid in their requirements for patients to adhere to the six/two rule.

The problem with fasting for surgery is that patients may experience discomfort. The longer a patient fasts the more dehydrated they become, and the more likely they are to experience symptoms of thirst, dizziness, headache or nausea. Often a delay in the start of surgery can lead to extended periods of fasting.

There is increasing published evidence that some fluids may leave the stomach earlier than expected – well within the two-hour window traditionally advised. If fluid has left the stomach it cannot be regurgitated. Different fluids may leave the stomach at different times, however, there have been no recent studies that examine how quickly water leaves the stomach.

Our study will assess how quickly water leaves the stomachs of healthy volunteers. We will give participants water and scan their stomachs with ultrasound to see how long it takes for the water to exit. If water exits the stomach rapidly, and in a shorter time frame than the two-hour window currently used, we may eventually be able to allow patients to drink water closer to the time of their operation, reducing their discomfort and increasing satisfaction without any increased risk of aspiration.

Background

Current national and international guidelines require that patients are subjected to a fasting period of six hours for solids and two hours for clear fluids prior to surgery under general anaesthesia to minimise the risk of aspiration of gastric contents.[1] In addition to the adverse effects of fasting on patient comfort, the development of 'enhanced recovery pathways' for surgery has raised awareness of the importance of optimal perioperative fluid balance and haemodynamic status.[2] Whilst it is difficult to link different fasting regimens to clinical outcomes, there is general agreement that it is beneficial to minimise fasting times where possible. Surgical intervention exposes patients to significant physiological stress and with the current guidelines most patients are subjected to dehydration and hunger at some stage preoperatively. Furthermore, if the conventional two hour fasting guideline for clear fluids can be safely reduced this could contribute to increased patient comfort and reduced feelings of thirst. It is estimated that over 2.7 million patients received a general anaesthetic in the UK in 2013,[3] thus the implications of fasting affect a large part of the population.

The volume of fluid in the stomach – the gastric volume, a surrogate marker for risk of aspiration – can be measured rapidly and non-invasively using ultrasound imaging with widely available equipment. Studies have shown that estimated volumes using ultrasound correlate well with assessment by other modalities, with a recent review supporting the use of cross-sectional area measurement with ultrasound in determining gastric volume.[4,5]

Recently there has been interest in challenging conventional fasting times, particularly for non-clear fluids (milky drinks and carbohydrate drinks).[6,7] However, to date there have been no studies involving administering water alone and assessment with ultrasound.

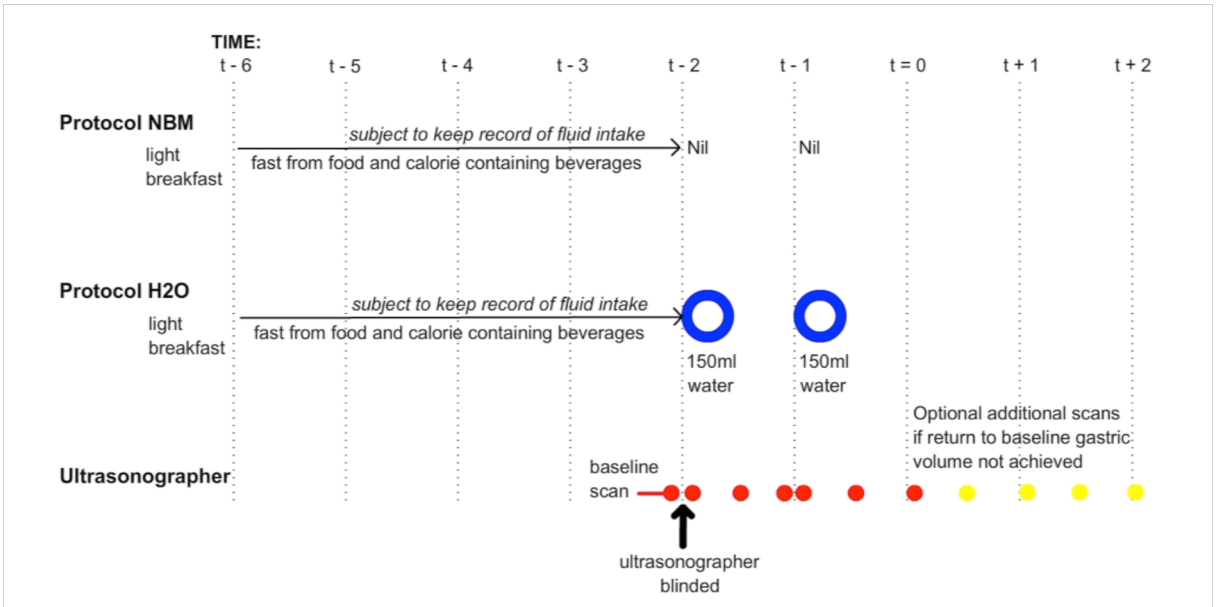
Aims

- Primary aim: To establish if it is possible to use ultrasound to collect data on gastric volume in volunteers following 2 study protocols called 'Protocol NBM' and 'Protocol H_2O'.
- To determine if volunteers can be recruited, how long the protocols last and whether there are any unknowns that require answering prior to designing a full trial.
- To use the primary outcomes in each protocol and their standard deviations to estimate the sample size required for a full trial.

Trial Design

This is a feasibility study, with features that may assist in the design of a pilot/full study. The volunteers will abstain from eating and drinking calorie containing beverages for 4 hours, and then be randomised to being nil by mouth 'Protocol NBM' or to have 2x150ml drinks of water 'Protocol H_20'. The trained researcher performing the ultrasound measurement of gastric volume will be blinded as to which intervention has occurred. On a subsequent session >1 week later, the volunteer will repeat the fast and follow the alternative intervention e.g. randomised crossover interventional study. Participants in this feasibility study will act as their own controls by undertaking both protocols. This study is preliminary work to establish proof of concept. The future objective, after subsequent ethics applications, will be to repeat the study in patients undergoing operations under local anaesthesia and then general anaesthesia

Figure 1: Protocol Overview



Outcome Measure

The primary outcome is the gastric volume measured at specific intervals following protocols of either nil by mouth 'Protocol NBM' or having 2x150ml drinks of water 'Protocol H_20', and the standard deviation of that measure. The ability of a full trial to establish a difference in primary outcome between 'Protocol NBM' and 'Protocol H_20' is dependent on the size of any difference measured, and the standard deviation.

Recruitment and Sample Size

Fifteen healthy volunteers will be recruited in a variety of ways including, but not limited to, poster advertisement in the Musculoskeletal Research Unit. At this stage of recruitment, participants will be informed that gastric emptying will be measured during the study, and that ultrasound will be used to obtain the measurement.

Inclusion Criteria

- Adult (aged over 18 years)
- Ability to attend on two separate days to complete both protocols – 'day A' and 'day B'.

Exclusion Criteria

- Participants must not be pregnant, not be trying to get pregnant and not think they may be pregnant
- Participants must not be taking medication that may influence appetite and/or digestion of food (except oral contraceptive pills).
- Participants must not have a history of any medical condition that may affect appetite and/or digestion of food e.g. previous gastro-duodenal surgery, diabetes mellitus, advanced liver or renal disease, recent gastrointestinal infection (within one month).

- Conditions that affect ability to obtain accurate data with ultrasound e.g. obesity (BMI>35), previous gastro-duodenal surgery

Attendance

On day A participants will be randomised via computer software to either undertake 'Protocol NMB' (conventional fasting) or 'Protocol H_2O' (drinking water). On day B (which should be at least a week later) the participant will undertake the other protocol not yet completed. Where possible the participants will complete the two protocols at approximately the same time on each day (morning or afternoon). The two attendance days A and B will be separated by at least 1 week and no more than 2 months.

Consent

Before participants take part in the study, it is important to ensure they are adequately informed about the procedures used in the study, the mandatory participation criteria and the level of staff training on 2D ultrasound.

Participants will be emailed an information sheet to read prior to taking part in the study informing them that ultrasound will be used to measure gastric emptying during the study and i) what ultrasound is ii) what to expect from the scan iii) what risks are associated with ultrasound.

Upon arrival at the test sessions, participants will be given this information sheet to read again. In addition, they will read the document 'Risks associated with the use of ultrasound' (Appendix A)

Participants will be given the opportunity to ask any questions they may have. Questions will be answered by the researcher.

Before the participants complete the consent form they must be informed that the ultrasound scan is for research purposes only and is not a diagnostic scan and must be made aware of the 'Incidental findings policy' (Appendix B)

Participants will be given two consent forms to complete – one for the researcher and one for the participant to keep. A copy of the consent form will be kept in a site file.

Intervention

Preparation

- Screening questionnaire – participants identified who meet inclusion and exclusion criteria
- Study information and consent process

- Dates and times given for study attendance
- Fasting instructions and times given
- A record of the content and timing of the light breakfast prior to the period of fasting, and amount, type and timing of clear fluids self-administered during the subsequent 4 hour period of free clear fluids, will be kept by the participant
- No alcohol and no major exercise other than 'usual activities' for 24 hours prior to attendance to reduce the risk of dehydration

Intervention

- Abstinence from eating and drinking calorie containing beverages for 4 hours then either oral water administration or nil by mouth for 2 hours, during which ultrasound measurements of gastric volume are made. (see Figure 1 'Protocol Overview' above):
    - **'Protocol NBM':** light breakfast followed by a period of four hours during which the volunteer abstains from eating and drinking calorie containing beverages, followed by a further 2 hours of complete fast (i.e. nil by mouth) during which ultrasound measurements of gastric volume are made.
    - **'Protocol H_2O':** light breakfast, followed by a period of four hours during which the volunteer abstains from eating and drinking calorie containing beverages, followed by two 150ml drinks of water an hour apart, during which ultrasound measurements of gastric volume are made. Ultrasound measurement of gastric volume may optionally continue for a further two hours if return to the starting gastric volume is not achieved.

- Sonographers will be blinded as to which protocol the participant has been allocated. Blinding of participants will not be possible.
- Ultrasound scans will take place prior to any water administration, then at 30 minute intervals, with gastric volume ascertained using the techniques described in references 4 and 5.
- If the baseline gastric volume measured at the beginning of the protocol has not been achieved following two hours then further scans will occur at 30 minute intervals until either the starting gastric volume is achieved or a further two hours

has elapsed

- Participants will be asked to rate their comfort, thirst, hunger and anxiety levels every hour (numerical scale 1 to 10)

Adverse Events

An Adverse Event (AE) is defined as any untoward medical occurrence in a volunteer, not necessarily having a causal relationship.

A Serious Adverse Event (SAE) is defined as any untoward and unexpected medical occurrence or effect that:

- Results in death
- Is life-threatening – refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe
- Requires hospitalisation
- Results in persistent or significant disability or incapacity
- Is otherwise considered medically significant by the investigator

Medical judgment will be exercised in deciding whether an AE is serious. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, will also be considered serious.

It is considered very unlikely that any such event would occur during the course of this healthy volunteer study with a non-invasive investigation.

Unrelated Adverse Events

Adverse events unrelated to the trial procedures are:

- *None known*

Expected Adverse Events

Possible (expected) adverse events related to the trial procedures are:

- In the event that an ultrasound scan reveals a suspected abnormality that was unknown to the Study Research Team and which they suspect might require

treatment, the 'Incidental findings policy' (Appendix B) will be followed.

Reporting Procedures

The Chief Investigator (CI), will notify the study sponsor (University of Bristol) within 72 hours of receiving the SAE and report any related and unexpected SAEs to the main Research Ethics Committee within 15 days of the CI becoming aware of the event.

Contact details for reporting SAEs:

Dr Chris Thompson

Email: at17585@bristol.ac.uk

Statistical Analysis

This is a feasibility study designed to establish whether a complete set of data can be collected following each of the protocols. The primary outcomes in each protocol and their standard deviations will be used to estimate a sample size requirement for a future full trial. 15 cases should provide reasonable precision for this calculation.

Data Storage

All the information collected will be kept strictly confidential and will be used only for the purposes of this project. All names will be removed from the information provided by participants. No names or details that might allow identification of individuals will be reported in any research papers, or to anyone outside the research team. Local data will be temporarily stored with a unique ID on a password-protected computer. All data will then be stored on the University of Bristol secure server accessed through the remote desktop from outside the University.

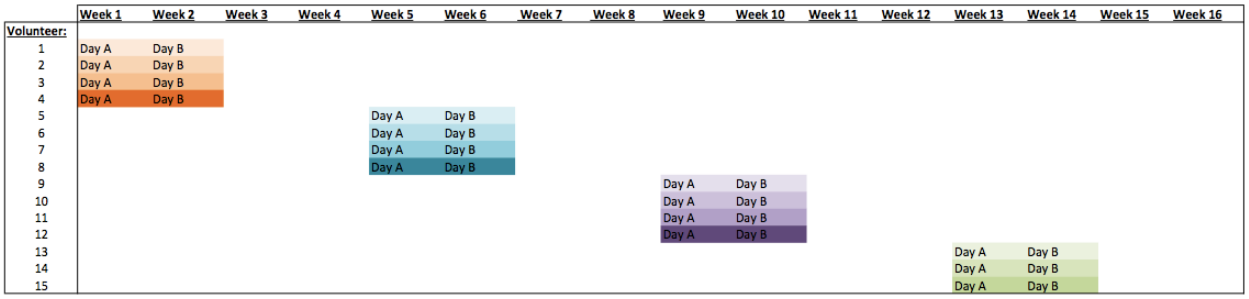
Sponsorship and Insurance

The University of Bristol will provide sponsorship and insurance for the study.

Funding

This project has been awarded a grant of £19775 from the David Telling Charitable Trust, Bristol, UK.

Gantt chart of approximate timeline:



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Appendix A – Risks associated with ultrasound

Risks Associated with the Use of Ultrasound

Ultrasound has been widely used in clinical practice for over 40 years and the international consensus is that there is no discomfort or risk associated with it.
Modern ultrasound scanners, when used in accordance with guidelines published by the British Medical Ultrasound Society, European Federation of Societies for Ultrasound in Medicine and Biology, American Institute of Ultrasound in Medicine, and World Federation for Ultrasound in Medicine and Biology, do not give rise to substantial concerns over safety.

However, certain operating conditions on some equipment are capable of warming tissue to a level where adverse bio-effects may occur. The magnitude of the temperature rise increases with the length of exposure and with the ultrasound output. In addition, it is known that tissues can be damaged close to any gas bodies exposed to high amplitude pulses of ultrasound, for example at the lung surface or with micro-bubble contrast agents.

Certain human tissues are particularly sensitive to ultrasound exposure:

- An embryo less than 8 weeks after conception
- The head, brain or spine of any fetus or neonate
- An eye (in a subject of any age)

Please inform the ultrasound operator if you think you may be pregnant

In this study:

- Sensitive tissues will not be scanned with ultrasound
- Tissues close to gas bodies (lung tissue or micro-bubble contrast agents) will not be scanned with ultrasound
- The operators will scan in accordance to published guidelines
- The operators have received appropriate training from suitably qualified persons at North Bristol NHS Trust

(• This study has been approved by the Faculty of Science research ethics committee) – TBC

Appendix B – Incidental findings policy

Incidental findings arising from ultrasound policy

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The following statement should be included in all information sheets using ultrasound scanning:

"**THIS IS NOT A MEDICAL OR DISEASE DIAGNOSTIC SCAN** and therefore your scan will not be examined for abnormalities. The scan will not benefit you directly, and does not form part of any medical diagnosis or treatment. However, very occasionally, when we look at an ultrasound scan from a healthy volunteer, unexpected potential abnormalities are discovered and if appropriate your GP will be contacted. The staff involved in this research study doing the scanning do not have expertise in medical diagnosis, as they do not have the relevant specialist medical training. You should not regard this scan as a medical screening procedure."

In the event that an ultrasound scan reveals a suspected abnormality that was unknown to the Study Research Team and which they suspect might require treatment, the following procedure must be adopted:

1. So as to avoid distress to participants arising from false alarms, staff of the research team must not disclose their concerns to the participant.
2. The Scanner operator involved must, without delay, report his/her concerns to the Principal Investigator and supply a high quality print displaying the suspected abnormality.
3. The Principal Investigator should, as a matter of urgency, write to the participant's General Practitioner (GP), enclosing the print and describing the cause for concern. It should also state that the participant concerned has not been informed and that the decision as to whether the participant should be informed, and the task of informing the participant is referred to the GP.
4. In the interests of participant confidentiality, the Scanner Operator concerned should not discuss the situation with colleagues other than the Principal Investigator.