

A prospective study of the impact upon serum electrolyte and magnesium levels of using magnesium sulphate for bowel preparation for colonoscopy.

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Background

Magnesium sulfate is a potent osmotic laxative that has been in use as a bowel cleansing agent in the form of Epsom salts for nearly 400 years. It has been in established use as a bowel preparation agent prior to colonoscopy and colorectal surgery^{1,2} and to induce complete intestinal purgation as part of the treatment of drug overdose³.

In 2007, dried magnesium sulfate was presented to the Australian market for the first time in capsule format for the purposes of bowel preparation and constipation treatment. It is being used with increasing frequency because of its enhanced palatability.

Palatability, safety and adequacy of bowel preparation after magnesium sulfate capsules had been compared with standard Colon-Lytely bowel preparation in a trial conducted at SCGH in 2005⁴. Capsules proved safe, were more palatable but provided less satisfactory bowel cleansing at a dose of 38.75gm dried magnesium sulfate.

The dose of dried magnesium sulfate required for consistently good bowel cleansing is 61.75gm. A similar dosage has previously been studied in the clinical setting in the area of drug overdose³ and was found to be safe.

The purpose of this study is to assess the safety of the currently recommended (and widely prescribed) dosage of magnesium sulfate capsules in current gastrointestinal practice by measuring its impact upon serum urea and electrolytes as well as serum magnesium levels.

Trial Objectives

The main aim of this study is to assess the safety of ingesting 61.75g of magnesium sulfate in the form of Colocap Balance™ capsules as a bowel cleaning preparation for colonoscopy.

The specific objectives include:

- To assess the difference in serum magnesium levels of patients before and after ingesting 61.75g of magnesium sulfate in the form of Colocap Balance™ capsules as a bowel cleaning preparation for colonoscopy.
- To assess the difference in serum Urea and Creatinine levels of patients before and after ingesting 61.75g of magnesium sulfate in the form of Colocap Balance™ capsules as a bowel cleaning preparation for colonoscopy.
- To assess the difference in serum electrolyte levels of patients before and after ingesting 61.75g of magnesium sulfate in the form of Colocap Balance™ capsules as a bowel cleaning preparation for colonoscopy.
- To evaluate the efficacy of Colocap Balance™ using the surgeon's evaluation of the quality of the bowel clean using the validated Ottawa Scale.
- To evaluate the patients' overall acceptability of Colocap Balance™, using their reports of palatability, ease of use (compliance) and tolerability (side effects).

Trial Design

This study will be a single arm, open design where all participants will receive the same treatment (65 capsules of Colocap Balance™), and undergo the same assessments. Participants will be asked to have two blood tests, one taken prior to beginning the treatment, and one during the colonoscopy procedure in order to compare the levels of certain minerals in the bloodstream as a result of the preparation. All consented, elective colonoscopy patients, except those with renal insufficiency and current chronic inflammatory bowel disease, will be eligible to participate in the study, assuming they meet the local safety criteria set by the Investigator site.

The study will involve a sample of 100 consented, colonoscopy patients, recruited by Investigators at St John of God Hospital, Subiaco and Murdoch.

Procedure

1. All patients identified as being eligible for the study will be introduced to the study by the Investigators, and consented (see Appendix 1). Patients who attend a pre-colonoscopy consultation will be consented during the consultation, and given their preparation and pathology request form during the visit. On leaving the clinic they will be asked to proceed to the hospital pathology department to have their first blood test.
2. Open Access patients, and private patients identified as eligible for the study, but who have already attended their consultation will be phoned and asked if they wish to participate in the study. Those who agree will be asked to attend

the clinic for a brief visit during which they will be consented by a doctor, receive their treatment, and be asked to proceed to the pathology collection centre for their blood test.

3. Patients will take their Colocap Balance bowel preparation at home as instructed.
4. Patients will attend the clinic for their scheduled colonoscopy, and complete the patient assessment form in the waiting room. The specialist will perform the colonoscopy and complete the efficacy assessments on the form provided. During the procedure a second blood will be taken from the patient.

Preparation under Investigation

All patients participating in the study will receive Colocap Balance™, and will be given a bottle of 65 capsules each containing 950mg of dried magnesium sulfate, and provided with instructions for use (see Appendix 2).

Safety Assessment

Participants will have two venous blood samples collected (approximately 2 teaspoons). The first sample will be taken prior to starting the bowel preparation, and the second during the colonoscopy procedure (after the preparation has been completed). Samples will be tested for electrolytes, magnesium, urea and creatinine levels.

Assessment of Efficacy

Participating specialists will rate the quality of the bowel preparation using the Ottawa Bowel Preparation Assessment Tool (Rostom et al, 2004) (REF) based on regional cleanliness and residual fluid volume (see Appendix 3). Adequacy of bowel cleaning will be assessed using a five point scale from excellent to very poor for the right, mid and recto-sigmoid bowel segments. Residual fluid will be assessed on a three point scale from no fluid to large volume. The fluid score and regional cleanliness score will be combined into a total score from 0 to 14.

Assessment of Patient Acceptability

All patients will receive a questionnaire (see Appendix 4) which will be completed in the clinic, prior to the colonoscopy procedure. The questionnaires will record patient compliance with the preparation, fluid consumption, assessment of palatability, and tolerability (side effects).

Confidentiality

All test results will be reviewed by the treating specialist and any unexpected abnormalities detected by the Investigator will be brought to the attention of the specialist in question. All test results held by the Investigator will be stored securely until the completion of the study and will thereafter be destroyed in accordance with the appropriate legislation.

Data Analysis

All patient data (demographics, patient acceptability and specialists' efficacy assessment) will be combined and analysis performed using descriptive statistics and appropriate inferential tests.

Blood results collected before and after bowel preparation will be compared within-subject for each factor under consideration (magnesium, electrolytes, urea and creatinine), and statistical analysis (Student t-test) will determine if the preparation causes significant changes.

References:

1. Huddy SPJ, Rayter Z, Webber PP, Southam JA. Preparation of the bowel before elective surgery using a polyethylene glycol solution at home and in hospital compared with conventional preparation using magnesium sulfate. *Journal of the Royal College of Surgeons of Edinburgh*, 1990, 35, 16 – 20.
2. Kiely EM. Bowel preparation in children using magnesium sulphate. *South African Journal of Surgery*, 1980, 18, 19 – 22.
3. Morris ME, LeRoy S, Sutton SC. Absorption of magnesium from orally administered magnesium sulfate in man. *Clinical Toxicology*, 1987, 25, 371 – 382.
4. Nikoletti S et al (2005). Edith Cowan University Centre for Nursing Research. A single blinded randomised controlled trial to compare magnesium sulfate capsules with Colon-Lytely as a bowel preparation for patients undergoing colonoscopy.

Appendix 1. A Study to Assess the Safety of Magnesium Sulfate as a Preparation for Colonoscopy

You are being invited to take part in this study. Before you decide it is important for you to understand why the study is being done and what it will involve. Please take time to read the following information carefully, and ask your doctor to explain anything you do not clearly understand.

What is the purpose of the study?

This practice routinely recommends Colocap Balance™ as the principal agent for bowel cleansing prior to colonoscopy. Although this agent was only first made available in 2007, the active component – magnesium sulfate – has been in common use as a purgative and laxative (in the form of Epsom salts) for many years.

Your participation in this study is sought so that we can provide further evidence of the safety of Colocap Balance™ by determining if levels of certain minerals in the bloodstream are affected by the preparation.

What does this study involve?

You will be asked to undergo two blood tests, one before you start the preparation, and the second during the colonoscopy procedure. The results of these tests will be compared to determine if there are any differences between before and after the bowel preparation. You will also be asked to complete a brief questionnaire about taking Colocap Balance™.

To date, experience with Colocap Balance™ across Australia has been extremely positive. Patients regularly indicate that they prefer taking these capsules to other bowel preparation agents. The only adverse reactions that have been reported so far have been very occasional nausea and even less occasional vomiting, reactions that are also seen with other bowel preparation agents.

There will be no out-of-pocket cost to you for these extra blood tests. The bowel preparation agent, Colocap Balance™ will be provided to you at no cost.

The St John of God Health Care Ethics Committee has given ethical approval for the conduct of this study. If you have any concerns or complaints about the study please contact the Executive Officer on (08) 9382 6940 on a confidential basis. Your concerns will be drawn to the attention of the Committee who is monitoring the study.

If you agree to participate in this study, please sign below and print your name and the date.

I have read the outline of this study printed above and agree to participate in this study. I understand that I will need to have a blood test taken before the preparation begins and that another blood test will be taken from me during the colonoscopy. I understand that I can withdraw from this study if and whenever I wish to do so. If I choose not to participate in this study, this will not affect the level of care I receive.

Name of participant Date Signature

Name of Investigator Date Signature

Appendix 2. Colocap Balance Colonoscopy Preparation Information

The preparation commences on the day before your procedure.

On this day **NO** solid food is to be eaten at all. You may drink clear, non-alcoholic fluids only and **it is very important to drink as much as possible**. You may include jelly (not red or green), sugar drinks and clear broth to maintain your strength. Please record the volume of fluid you drink from the time you start the preparation until the time of the procedure.

You will need to take 65 capsules in all.

You will need to continue taking capsules until your bowels are properly 'clean'. You can tell that they are clean when your output (the liquid coming from your bowels) is clear, lemon-coloured fluid with no solid particles.

The capsules can be taken one at a time, they may also be easily swallowed as a 'handful' of 5 capsules.

If your colonoscopy is scheduled for the morning.

The day before the procedure:

3.30pm Swallow the first 5 capsules. You should 'wash down' these capsules by drinking a large glass – at least 250ml – of clear, non-alcoholic liquid of your own preference (soft drink, water or clear juice).

Take 5 more capsules every 15 minutes with at least 250ml more to drink with each lot of 5 capsules until all the capsules have been taken.

You should continue to drink clear, non-alcoholic fluids after completing the capsule preparation. After midnight you MUST NOT have anything further to eat or drink until the colonoscopy procedure is completed.

If your colonoscopy is scheduled for the afternoon.

The day before the procedure:

4.30pm Swallow the first 5 capsules. You should 'wash down' these capsules by drinking a large glass – at least 250ml – of clear, non-alcoholic liquid of your own preference (soft drink, water or clear juice).

Take 5 more capsules every 15 minutes with at least 250ml more to drink with each lot of 5 capsules until all the capsules have been taken.

On the day of your colonoscopy:

6.30am Take 5 more capsules and at least 250ml more to drink every 15 minutes until all the capsules are taken.

At 10am on the morning of your colonoscopy, you may drink one more large glass of liquid, and you MUST NOT have anything further to eat or drink until the colonoscopy procedure is completed.

Colonoscopy Preparation Bowel Preparation Assessment

Name _____ Date: _____

Reason for Colonoscopy: _____

Time of Colonoscopy: Morning / Afternoon

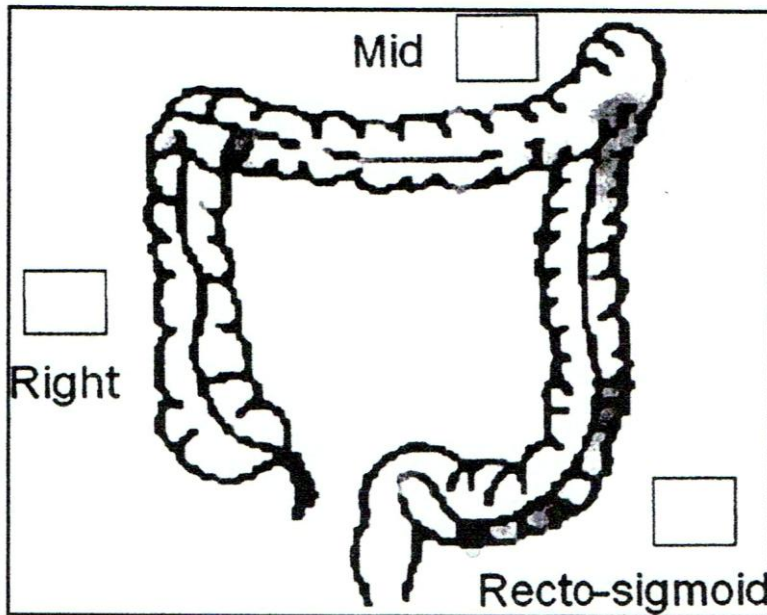
Assessment (based on Rostom et al Gastrointest Endosc 59;4:2004)

• **Regional score per segment (Zero to four):**

- 0 = perfect preparation (excellent)
- 1 = mild staining but mucosa seen (good)
- 2 = suction needed to see colonic wall (fair)
- 3 = wash and suction needed (poor)
- 4 = unable to see colonic wall (very poor)

• **General fluid score (Zero to two)**

- 0 = No fluid
- 1 = Moderate volume
- 2 = Large volume



Total Regional Score (range 0-12)	_____
Fluid Score (range 0-2)	_____
Total Score (Min 0 Max 14)	_____
Sig/Initials	_____

Colonoscopy Preparation Patient Tolerability Questionnaire

Name _____ Date: _____

Medical History. Please circle applicable answer

Sex:	Male	Female			
Age:	Under 40	40-49	50 - 59	60 - 70	Over 70
How often do your bowels normally open?	Less than twice a week	2-3 times per week	Daily	2 times per day	More than twice a day

Ingestion of the colonoscopy preparation. Please circle applicable answer

How palatable (easy / pleasant) to ingest was the Preparation?	Very Palatable	Palatable	Mildly Unpalatable	Unpalatable	Very Unpalatable
How many capsules did you take?	Less than 40	Between 40 and 49	Between 50 and 59	Between 60 and 64	65
Approximately how much did you drink since starting the preparation?	Less than 2 Litres	2-3 Litres	3-4 Litres	4-5 Litres	Greater than 5 litres
Is this your first colonoscopy?	YES	NO			
If No, was THIS preparation.....	Preferred	Same	Worse		

Reaction to colonoscopy preparation. Please cross (X) applicable boxes

	None	Very Mild	Mild	Moderate	Severe
Nausea					
Vomiting					
Bloating					
Abdo Pain or Cramp					
Headache					
Dizziness					
Soreness of back passage					

Please indicate on the line the overall tolerability of the bowel preparation medication used.

Not Tolerated at all

Thank you for completing this questionnaire.

Totally Tolerated