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SPLIT DOSE VERSUS SINGLE DOSE OF SODIUM SULPHATE SOLUTION IN COLONIC PREPARATION OF PATIENTS UNDERGOING COLONOSCOPY

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ABSTRACT

Colonoscopy is the gold standard diagnostic procedure for colonic disease. Excellent bowel cleansing is critical for this procedure. If the bowel preparation is not up to par, polyps and lesions can be missed; the colonoscopy may take longer or the whole process may need to be repeated or rescheduled. It should be easy to perform to allow carrying out both inpatient and outpatient. The search for the optimum colon cleansing regimen continues to be a challenge. Each of the currently available regimens has limitations in efficacy, patient tolerance and or safety. The patients who are being referred for colonoscopy will be enrolled in the study and randomized to one of the bowel preparation regimes (either split dose - solution divided in doses given a night before the procedure and 6 hrs prior to the procedure or single dose - given a day before the procedure). Adequate bowel preparation is essential before colonoscopy. Choosing an agent can be confusing, especially with so many agents available in the market today. The method of choice regarding the modality of administration that is bowel preparation solution given in single dose or split doses will depend on its overall safety, efficacy and tolerability. For arriving to any concrete conclusion though the sample size is less nevertheless it is sufficient enough to lay the foundation of a larger study with large sample size. A split-dose regimen may increase the overall efficiency of colonoscopy by improving the quality of bowel preparation and potentially the detection of flat lesions, and CRC screening.

Key Words: Colonoscopy, Split dose and Single dose regimen.

INTRODUCTION

Colonoscopy is the primary method for evaluating the colon, but diagnostic accuracy and therapeutic safety of colonoscopy depend on the quality of colon cleansing.

The defining characteristics of high-quality colonoscopy is the examination of the entire Colon, optimal cleaning of the colon with no gross or histological alteration of the colonic mucosa and endoscope withdrawal time of 6-10 min from cecum to rectum.

Inadequate bowel preparation can result in missed lesions, aborted procedures, and increased discomfort as well as a potential increase in complication rates, thereby necessitating a repeat colonoscopy. Therefore, improvements in bowel preparation tolerability are paramount for increasing patient compliance which in turn can lead to improved outcomes of colonoscopy [1].

A good colon preparation depends partly on correct choice of the same, but also upon dietary restriction. Knowledge of all these products, with their advantages and limitations, we can make a better selection for each patient which greatly influence the results.

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Though it is well documented that a good-quality bowel preparation before colonoscopy improves the rate of detection of colonic polyps but the best method of colon cleansing is, however not clear. Currently we have several options for preparing patients for colonoscopy but split dosing of bowel preparations for colonoscopy has recently emerged as an important factor in bowel cleansing efficacy and may also impact patient tolerability [2].

MATERIALS AND METHODS

TOTAL PATIENTS ENROLLED

20 patients following single dose regimen (male & female)
20 patients following split dose regimen (male & female)

A total of 40 patients were recruited for this study after going through the Informed Consent Process and signing the Informed Consent Form.

INCLUSION -EXCLUSION CRITERIA

This was a single-blinded, prospective, randomized study of adult patients, both male and female (but no healthy volunteers) undergoing routine elective colonoscopy.

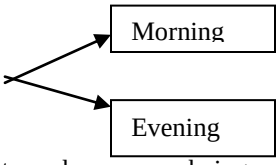
Inclusion Criteria

- All patients with an appropriate indication to colonoscopy were considered eligible.

Exclusion criteria

- Pregnant or lactating women
- Age less than 18 years
- Prior Colectomy or colon surgery
- Significant gastric outlet obstruction or ileus, known
- Suspected bowel obstruction or perforation
- Severe chronic renal failure

ARMS



- **Split dose**
- **Single dose**

The patients who were being referred for colonoscopy were enrolled in the study and randomized to one of the bowel preparation regimes split dose or single dose.

In split dose - solution divided in doses given a night before the procedure and 6 hrs.Prior to the procedure. In single dose the bowel preparation solution was given a day before the procedure.

The nurse carefully explained how they should be taken, emphasizing the importance of complete intake of the solution in order to ensure a safe and effective procedure.

Apart from instructions, the nurse also informed the patients as to potential side effects of the preparation solution as well as the drawbacks of an aborted procedure or missed lesion.

The following dietary advice was given to patients: on the day before colonoscopy, to have a light breakfast and lunch but a semi liquid dinner (clear soup, yoghurt,) before taking the bowel preparation solution [3].

For both types of preparation, no solid food was allowed instructed to be taken nothing by mouth from midnight, on, before the procedure from the start of the bowel preparation. All patients were then asked to report to colonoscopy unit where they underwent a colonoscopy.

COLONOSCOPY AND ENDPOINT MEASUREMENT

On the morning of colonoscopy, immediately before the procedure, a nurse questioned each patient about his/her experience by using a standardized questionnaire (Percentage of participant response to Acceptability and Tolerability Questionnaire), composed of a set of questions with answers. Patients were asked about compliance, tolerance, additional fluid intake, acceptability, and willingness to repeat the same type of bowel preparation if necessary. The gastroenterologist was not allowed to listen to the questioning or to see the questionnaire at any time before colonoscopy and assessment of the degree of bowel cleansing.

Colonoscopies were performed by experienced gastroenterologist unaware of the treatment allocation. The primary endpoint was the degree of colon cleansing [4].

Any adverse events related to bowel preparation

- Nausea
- vomiting, bloating
- abdominal pain
- headache

Were recorded and all participants were monitored for adverse events during colonoscopy.

ASSESSMENT OF BOWEL PREPARATION

Bowel cleansing was assessed by colonoscopist who was unaware of the preparation methods.

Two methods were followed to assess the bowel preparation.

AronchickScale: 4step rating scale

- Inadequate
- Fair
- Good (>90% mucosa seen significant suctioning required for adequate visualization)
- Excellent (>90% mucosa seen, mostly liquid stool, minimal suctioning needed for visualization).

Though Aronchick scale is a well validated scale to measure the degree of colon cleansing but the use of terms such as “excellent,” “good,” “fair,” and “inadequate,” these terms lacked the standardized

definitions. Therefore, the Boston Bowel Preparation Scale (BBPS) was used simultaneously to provide a much needed standard for rating the quality of bowel preparation for colonoscopy [5].

Boston Bowel Preparation Scale (BBPS)

The BBPS is a valid and reliable measure of bowel preparation. It may be well-suited to colonoscopy outcomes research because it reflects the colon's cleanliness during the inspection phase of the procedure. Three segments of the colon (left, transverse, right) are ranked based on cleaning:

- **0** = Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.
- **1** = Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid.
- **2** = Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well.
- **3** = Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid.

Each region of the colon receives a "segment score" from 0 to 3 and these segment scores are summed for a total BBPS score ranging from 0 to 9. Therefore, the maximum BBPS score for a perfectly clean colon without any residual liquid is 9 and the minimum BBPS score for an unprepared colon is 0. If a colonoscopist aborts a procedure due to an inadequate preparation, then any non-visualized proximal segments are assigned a score of 0.Representative images were selected to aid in comprehension of the points making up the Segment scores [6].

SAMPLE SIZE CALCULATION AND STATISTICAL ANALYSIS

In order to have a satisfactory concordance among the personnel involved in the assessment of the degree of bowel cleansing, prior to study initiation designated observers performed a calibration exercise on 30 colonoscopies by using the scoring system adopted in the study [7].

Out of total 60 patients assessed for eligibility ,the sample size of only 20 patients in each group were taken due to time bound limitations of the course work, so any statistical analysis of the data could not be performed.

However the studies has been well represented by using various figures and graphs and in future wish to continue to study with a larger sample size and use statistical tools like t tests and variance analysis for multiple comparison data [8].

RESULTS

Taste of the preparation was also rated as good or acceptable by about 80% of the people though for our study it is not of much concern as the bowel preparation solution used (*coloprep)* is already a tested product in the

Study participant allocation is recorded in Figure 4. Of the 60 patients assessed for eligibility, 10 were excluded for contraindications (2 for severe chronic renal failure, 4 for age below 18 years, 1 for recent colon surgery, and 3 for severe hypertension). A total of 50 patients were included and randomized to the split-dosage schedule (N 24) or to the single dosage schedule (N 26). 3 patients had protocol deviation (1 patient had his bowel preparation ended 1 day earlier than indicated,2 patients drank the solution in small, fractioned doses over 24 hours). Furthermore, an additional 5 patients were excluded from analysis for incomplete report forms as to the type of preparation used, 2 withdrew themselves from the study. Therefore, a total of 40 randomized patients male and female inclusive were finally analyzed (20 in the split-dosage group and 20 in the single dosage group).

EFFICACY

Study compliance was better in split dose intake schedule as compared to single dose.

Complete preparation that is, drinking of the full amount of fluid indicated was accomplished by 95% and 80 % of patients respectively.

The split-dosage regimen produced markedly superior cleansing results over the single dosage. regimen Table 1 as analyzed by Aronchick Scale [9].

Overall, a good/excellent degree of bowel cleansing was recorded in 80% of patients allocated to the split dosage regimen versus 50% of patients allocated to the single dosage regime.

The split-dosage regimen provided a significantly superior degree of bowel cleansing in all colon segments, as calculated from the Boston Bowel Cleansing Scale (BBPS) Graph 2.

The total BBPS score in case of split dose on an average has been above 6 whereas in case of single dose regimen around 3.It has been also observed that the split dose solution resulted in significantly less fecal material in right colon compared to single dose regimen. Furthermore, the bowel fluid was typically translucent in the split-dosed group, whereas the fluid was opaque in the group taking the solution the day before the procedure [10].

It has been observed that male patients are at higher risk of poor bowel cleansing. The reason for this may be probably due to the non-compliances or poorer adherence to bowel preparation instructions which is because of the lesser healthcare attitude (less health consciousness compared to women) amongst men [11].

TOLERABILITY

Both preparations were well-tolerated, with none reporting side effects. Preparation related symptoms of cramping, bloating, nausea, and vomiting was generally mild and infrequent.

market with an established study regarding the acceptability of taste [12].

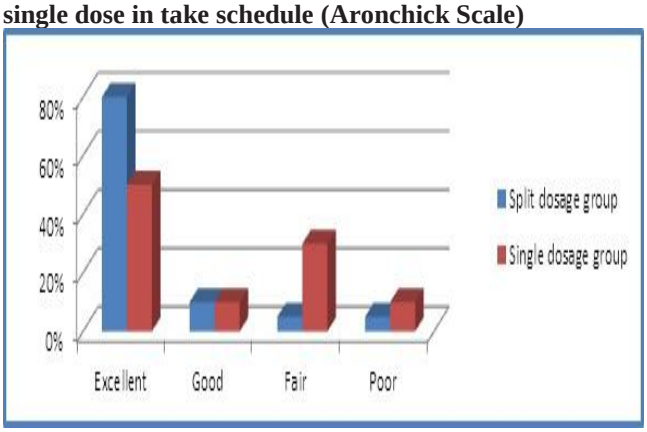
A split-dosing schedule helps to ensure that an appropriate time interval has elapsed between the two doses which in turn provide greater opportunity for patients to ingest additional fluid and maintain hydration thereby increasing the chances of tolerability.

A concern arises regarding the split-dose regimen that patients may not be willing to comply with the early morning administration of the second dose. But data suggests that most patients are relatively satisfied with a split-dosing regimen and are willing to wake early if convinced the timing of the second dose will enhance the outcome of their colonoscopy [13].

Table 1. Frequency of excellent, good, fair and poor bowel cleansing in patient Undergoing split dose vs. single dose in take schedule (Aronchick Scale)

Degree of cleansing	Split dosage group No. (%)	Single dosage group No. (%)
Excellent	80 %(16 of 20 patients)	50 % (10 of 20 patients)
Good	10% (2 of 20 patients)	10% (2 of 20 patients)
Fair	5 % (1 of 20 patients)	30% (6 of 20 patients)

Graph 1. Frequency of excellent, good, fair and poor bowel cleansing in patient Undergoing split dose vs. single dose in take schedule (Aronchick Scale)



Graph 2. The segment scores are summed for a total BBPS score ranging from 0 to 9 for split and single dose regimen. The maximum BBPS score for a perfectly clean colon without any residual liquid is 9 and the minimum BBPS score for an unprepared colon is 0.

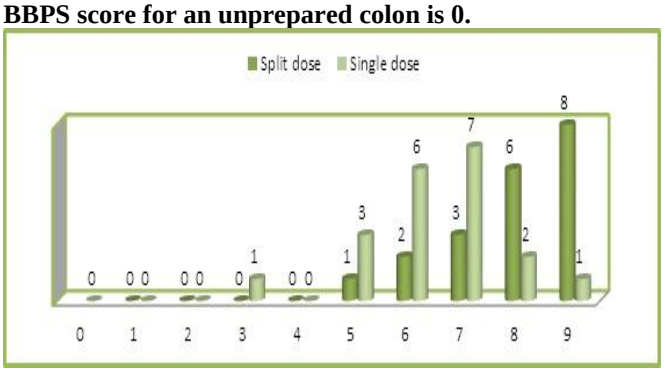


Figure 1. Split-dosing regimen. NBM = nothing by mouth

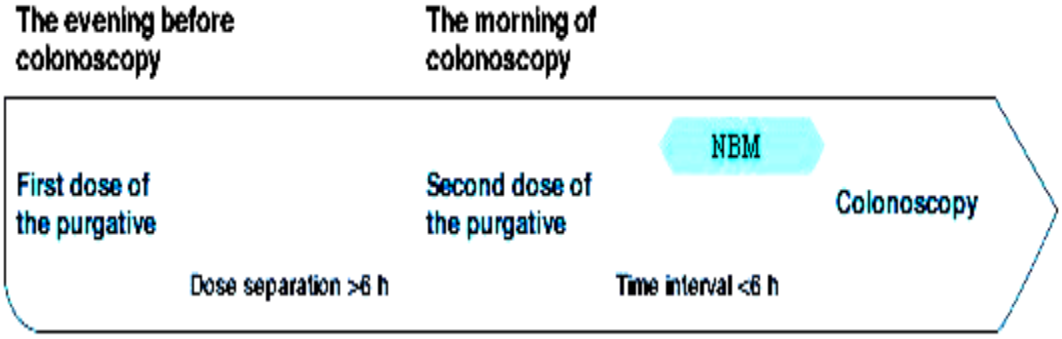
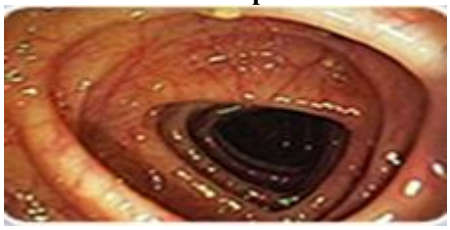


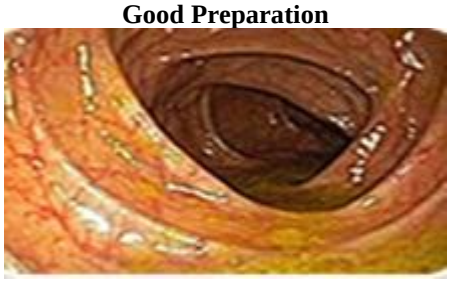
Figure 2. Representative images of Aronchick Scale

Excellent Preparation



>90% of mucosa seen, mostly liquid stool, minimal suctioning needed for adequate visualization

Good Preparation



>90% of mucosa seen, mostly liquid stool, significant suctioning needed for adequate visualization

Fair Preparation

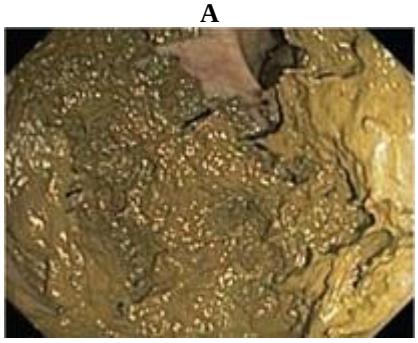
>90% of mucosa seen, mixture of liquid and semi-solid stool, which could be suctioned and/or washed

Poor /in adequate preparation

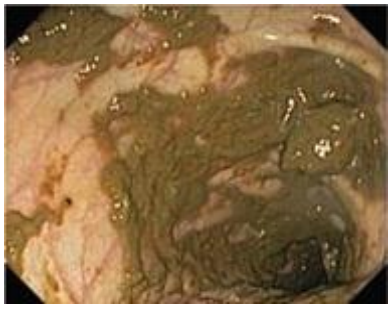
<90% of mucosa seen, mixture of semi-solid stool, which could not be suctioned and/or washed

Figure 3. The Boston Bowel Preparation Scale (BBPS). **A,** segment score 0: unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared. **B,** segment score 1: portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid. **C,** segment score 2: minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well. **D,** segment score 3: entire mucosa of colon segment seen well with no residual staining, small fragments of stool and/or opaque liquid.

A



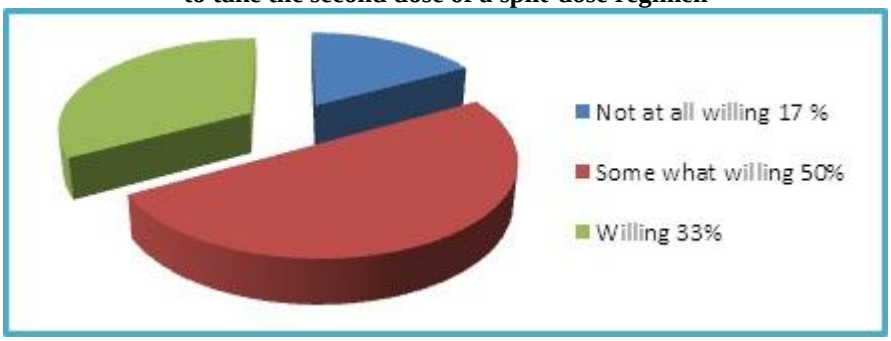
B

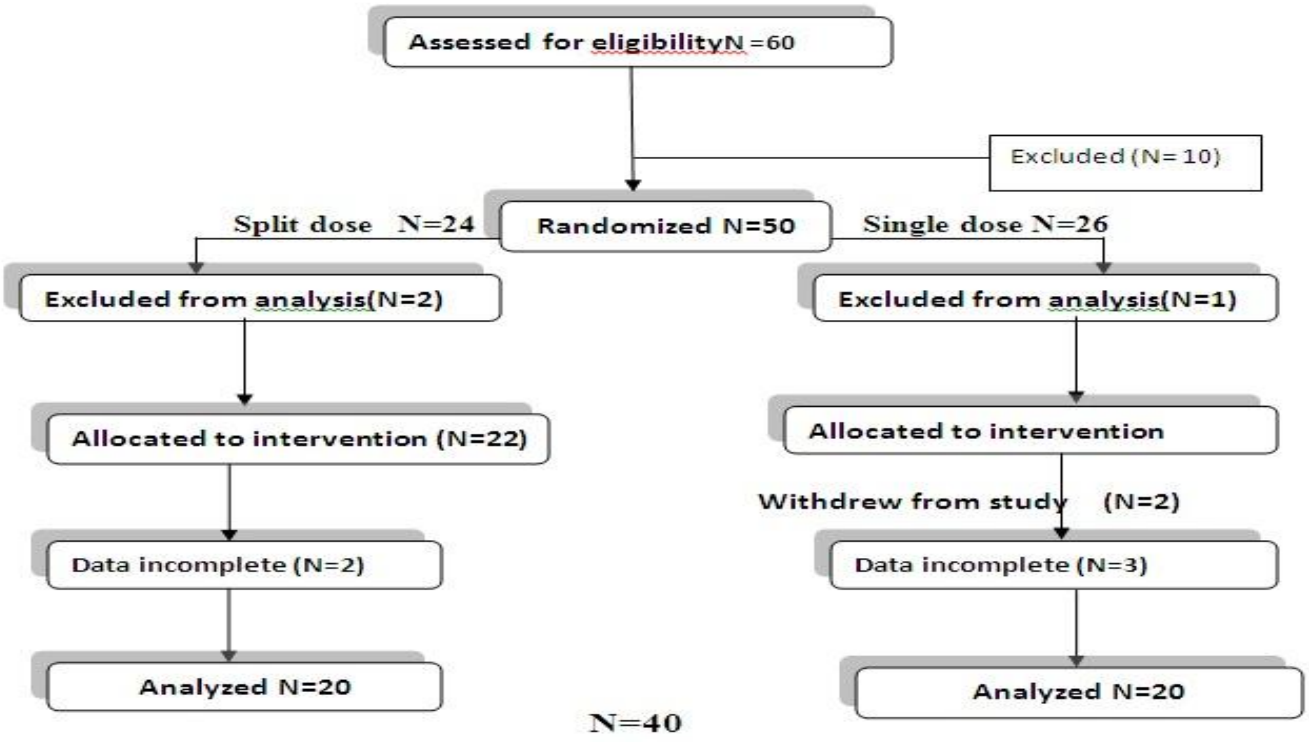


C

D

Figure 4. Results of patient survey. The survey asked patients if they were willing to wake very early in the morning to take the second dose of a split-dose regimen





DISCUSSION

The result of study adds to the fact that split dose regimen is the more effective method of bowel cleansing as compared to single dose regimen in patients undergoing colonoscopy.

Efficacy of the process is also coupled with the excellent safety profile as no Adverse Events of clinical relevance were reported.

Compliance to complete preparation was surprisingly high (95%) as compared to (80%) in single dose regimen. The possible explanation resides in the continuative efforts made by nurses to clearly explain the importance of drinking the full amount of solution in order to achieve a proper cleansing, thus conferring to the patients a strong motivation toward an effective and safe colonoscopy [14].

The taste and volume of preparation may well be an important driving force to improved compliance.

Furthermore, adequate degree of bowel cleansing was observed even when colonoscopy was performed before 6hrs.

Only male patients showed poor bowel cleansing, so to take maximum advantage of the split-dosage schedule, they should undergo afternoon colonoscopies.

No case of aborted or incomplete colonoscopy occurred due to poor bowel preparation following both the schedules.

CONCLUSION

Adequate bowel preparation is essential before colonoscopy. Choosing an agent can be Confusing,

especially with so many agents available in the market today.

The method of choice regarding the modality of administration that is bowel preparation solution given in single dose or split doses will depend on its overall safety, efficacy and tolerability.

For arriving to any concrete conclusion though the sample size is less nevertheless it is sufficient enough to lay the foundation of a larger study with large sample size. Based on evidences of the study it can be well concluded that with the patient acceptance, convenience, and an improved efficacy, split dosing is an effective strategy to optimize colon cleansing and should be considered the standard of care [15].

A split-dose regimen may increase the overall efficiency of colonoscopy by improving the quality of bowel preparation and potentially the detection of flat lesions, and CRC screening.

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