Adequacy Rate of Magnesium Citrate Bowel Preparation in a Large Retrospective Cohort

MOHD AMER ALSAMMAN, MD; STEPHANIE LEUNG, MD; ABDELMONIEM MOUSTAFA, MD; MOHAMED ABEID, MD; GRAYSON L. BAIRD, PhD; SAMIR A. SHAH, MD, FACG

ABSTRACT

INTRODUCTION: Magnesium Citrate (MC) is not FDA approved as a colonoscopy preparation. Advantages include low cost, small volume and accessibility without prescription. We retrospectively evaluated bowel preparations used in a private gastroenterology practice. The sample size is the largest for any similar studies (n =19,173).

METHODS: Electronic Medical Records were queried for colonoscopies between 2010-2016. Bowel preps, indications (screening vs. other) and preparation adequacy were all recorded. Adequacy rates were calculated and compared using generalized linear modeling. Data were analyzed using SAS.

RESULTS: The most common prep used was MC 2 bottles; screening (n=6,064, with 98.94% adequacy) and non-screening (n=3,251, with 99.29% adequacy), followed by MC 3 bottles; screening (n=2,757 with 90.35% adequacy), and non-screening (n=1,925 with 92.92% adequacy).

CONCLUSION: MC bowel preparation is adequate, well tolerated, and inexpensive. In a large retrospective analysis, it compares favorably to other preparations.

KEYWORDS: bowel preparations, colonoscopy, magnesium citrate

INTRODUCTION

Adequate bowel preparation is vital for high quality colonoscopy. Optimal bowel cleansing shortens the time of the procedure and increases polyp detection rate. Conversely, suboptimal bowel preparation may lead to inadequate visualization of the colon, missing polyps and repeat procedures with its associated financial and time burdens on patients and the healthcare system.[1,2,3] According to both American and European societies of gastrointestinal endoscopy, cost, safety and tolerability are important attributes of an optimal bowel prep.[4,5]

Concern about bowel preparation was the most common reason cited by people older than age 50 years for not having a colonoscopy.[6] Magnesium citrate (MC) is an osmotic agent that achieves bowel cleansing by increasing intraluminal fluid volume and stimulating bowel motility.[7,8] MC has the advantage of being of low volume which increases tolerability, and it is inexpensive, costing around $2 for a two bottle prep. Both factors are important concerns to patients. Brand name bowel preparations can cost at least 10 times and up to 100 times the price of MC.

Few published studies compared tolerability and efficacy of magnesium citrate to polyethylene glycol (PEG). Rapier et al compared two different MC preps to PEG; although bowel cleansing rates were lower in MC arms, it did not reach statistical significance and there was no evidence of a difference in tolerability between groups.[9] Aurora et al found that PEG and oral sodium phosphate were superior to MC.[10] In a more recent study by Gu et al, MC showed significantly higher tolerability compared to PEG (P = 0.014) and a higher adequate bowel cleansing rate 90.6% vs 48%.[11]

Several studies have evaluated the safety and efficacy of MC demonstrating no evidence of a difference or higher tolerability and bowel cleansing compared with PEG. However, small sample size is an important limitation common among these studies. We evaluated bowel preparations including MC used in an endoscopy center of a community gastroenterology private practice. We hypothesized that MC bowel preparations would be at least as effective as other available bowel preparations and have the advantage of substantial reduction of cost.

METHODS

Design and sample

Bowel preparations data were documented along with adequacy of the prep in a private, community-based, single specialty gastroenterology practice in Providence, RI. IRB approval was obtained. The Electronic Medical Records using the endoscopic report writer (MDReports) was queried for patients who underwent colonoscopies between 2010 to 2016. Colonoscopies were performed by eight different board-certified gastroenterologists in the group. The bowel prep used, indication for the colonoscopy (screening vs. other indications) and preparation adequacy were queried for analysis retrospectively. Cases where the prep type or quality of the prep was not recorded were excluded. At our endoscopy center no patient navigator or phone applications were

utilized; however, both verbal and printed instructions were provided to the patient by nurses and medical assistants. The majority of our patients spoke English. For the minority who spoke either Spanish or Portuguese, an interpreter was utilized along with instructions in Spanish.

Adequacy was documented based on a numeric grade, [0 = excellent (equals 9 on Boston Bowel Preparation Scale (BBPS)), 1= good (equals 7,8 on BBPS), 2 = fair (equals 6 on BBPS), and 3 = poor (less than 6 on BBPS)]. Excellent, good and fair were considered adequate and poor was not. During the time of study, BBPS was not being used/recorded but now is and hence the translation to the equivalent BPPS score. All bowel preparations were given in a split dose fashion. An adequate prep resulted in following guidelines for next interval colonoscopy. On the other hand, inadequate preparation resulted in an earlier repeat of colonoscopy (less than a year).

Table 1. Adequacy rates of different preparations both screening and non-screening

Screening				Non-Screening			
Prep (n)	Mean	Lower Mean	Upper Mean	Prep (n)	Mean	Lower Mean	Upper Mean
Combo (n= 2613)	99.08%	98.65%	99.38%	Combo (n= 1347)	99.48%	98.92%	99.75%
Golytely 4L (n= 98)	95.92%	89.66%	98.45%	Golytely 4L (n= 39)	92.31%	78.75%	97.49%
Mg C 2 (n= 6064)	98.94%	98.67%	99.16%	Mg C 2 (n= 3251)	99.29%	98.95%	99.53%
Mg C 3 (n= 2757)	90.35%	89.51%	91.13%	Mg C 3 (n= 1925)	92.99%	91.92%	93.92%
Miralax (n= 142)	93.08%	62.02%	99.35%	Miralax (n= 51)	100.00%	0.00%	100.00%
Moviprep (n= 132)	100.00%	0.00%	100.00%	Moviprep (n= 21)	100.00%	0.00%	100.00%
Nuletely 4L (n= 117)	100.00%	0.00%	100.00%	Nuletely 4L (28)	100.00%	0.00%	100.00%
Suprep (n=160)	99.38%	95.71%	99.91%	Suprep (n= 48)	100.00%	0.00%	100.00%

Statistical Methods

Adequacy was modeled using a binomial distribution (numeric grade: 0 = excellent, 1 = good, 2 = fair, and 3 = poor) and a binary distribution (adequate (0, 1, and 2) vs. inadequate (3)) between Preparation groups (combination-which was a 4 liter PEG + MC 2, Golytely, MC 2 – 2 bottles of MC + 2 Dulcolax, MC 3 – 3 bottle of magnesium citrate, Miralax (including Miralax with Dulcolax and 1 bottle MC), Moviprep, Nulytely, Suprep) by screening and non-screening colonoscopy using generalized linear modeling (GLM). An adequate prep resulted in following guidelines for next interval colonoscopy. We considered an adequacy threshold rate of 90% (at least 90% of all colonoscopies in any group had at least fair or better test) to be clinically useful. All modeling was accomplished using SAS Software 9.4 (SAS Inc., Cary, NC) with the GLIMMIX procedure. Bonferroni adjustments were used when comparing preparation types. All interval estimates were calculated using 95% confidence.

RESULTS

As shown in **Table 1**, the most common prep used was MC 2 for both screening (n=6,064, with 98.94% adequacy rate) and non-screening (n=3,251, with 99.29% adequacy rate), followed by MC 3 (n=2,757 with 90.35% adequacy rate, and n=1,925 with 92.92% adequacy rate) and then combination prep (n=2,613 with 99.08% adequacy rate and n=1,347 with 99.28% adequacy rate). All other preps occurred in fewer than 160 screening patients and 51 non-screening patients, respectively; Golytely 4L (n=98 for screening, with 95.92% adequacy AND n=39 for non-screening, with 92.31% adequacy rate), Miralax (n=142 for screening, with 93.08% adequacy rate AND n=51 for non-screening, with 100% adequacy rate), Moviprep (n=132 for screening, AND n=28 for non-screening, with 100% adequacy rate for both groups), Nulytely (n=117 for screening AND n=28 for non-screening, with 100% adequacy rate for both groups), and Suprep (n=160 for screening with 99.28% adequacy rate AND n=48 for non-screening with 100% adequacy rate). The total number of patients who received these preps and had adequate grades was n=18,793.

In addition, no grade for each bowel preparation fell under 2 or "fair," as illustrated in **Figure 1**. As seen in **Table 2**, exploratory comparisons revealed combination was better than Golytely for non-screening, and combination was better

Figure 1. Graph showing all the preparations we evaluated to be adequate. It also shows that MgC 2 performed better than MgC 3. This applies for both screening and non-screening groups.
MgC 2: Magnesium Citrate 2 bottles with Dulcolax.
MgC 3: Magnesium Citrate 3 bottles.

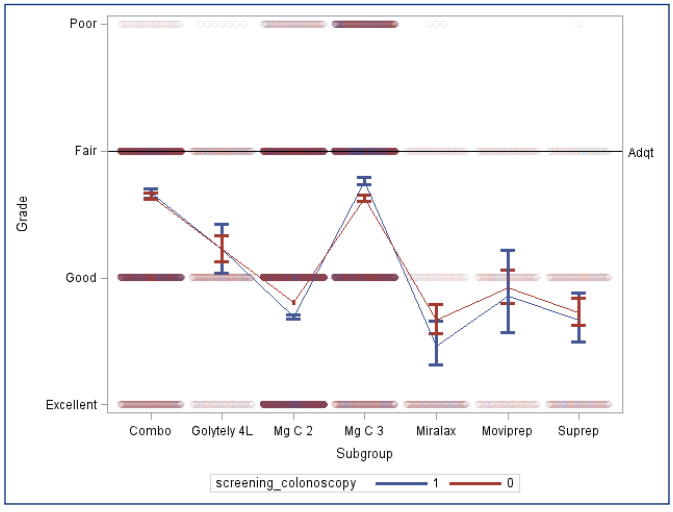

Table 2. Comparing Mg C 2 and Mg C 3 to other preparations, in screening and non-screening groups

Prep 1 (Screening)	Prep 2	P Value
Mg C 2	Mg C 3	**<.0001**
	Golytely 4L	**0.0085**
	Miralax	0.0192
	Moviprep	0.9393
	Nuletely 4L	0.9428
	Combo	0.5595
	Suprep	0.6006
Mg C 3	Golytely 4L	**0.0738**
	Miralax	**0.095**
	Moviprep	0.9255
	Nuletely 4L	0.9299
	Osmoprep	0.1945
	Combo	1.65
Prep 1 (Non- Screening)	**Prep 2**	**P Value**
Mg C 2	Mg C 3	**<.0001**
	Golytely 4L	**0.0001**
	Miralax	0.9636
	Moviprep	0.9763
Mg C 3	Golytely 4L	0.8695
	Miralax	0.9547
	Moviprep	0.9705
	Nuletely 4L	0.9659
	Combo	**<.0001**
	Suprep	0.9545

than MC 3 for both screening and non-screening. In addition, MC 2 was better than Golytely for non-screenings and higher than MC 3 for both screenings and non-screenings.

DISCUSSION

Our retrospective study shows that MC is adequate as a bowel preparation for screening, surveillance and diagnostic colonoscopies. PEG preparations have historically been the standard of care for bowel cleansing and FDA-approved preparations have usually been compared to 4L PEG. We summarize the available bowel preparations that are FDA approved. In addition, we included data that are used by the FDA, as well as data from large trials, reviews, and meta-analysis evaluating different bowel preparation in **Table 3**.

In our outpatient endoscopy center, all bowel preparations used met the mean adequacy threshold of > 90% effectiveness. This high rate of effective bowel preparations for various preparations may suggest selection bias in terms of patients booked as outpatients in a private practice ASC, staff and physician education of patients for effective bowel preparations, or possible other factors.

During the period of the study, we were not routinely using a validated bowel preparation such as the Boston Bowel Preparations Score (BBPS). Over the last few years, we have used the BBPS as a validated measure. Thus, we can translate our scale as follows: excellent= BBPS 9, good= BBP 8, fair= BBPS 6-7, poor/inadequate= BBPS < 6.

Adenoma detection rates (ADR) were monitored by individual physicians and the practice as a whole beginning in 2008. Since 2015, there was data available from the groups' formal participation in GIQuIC, a nationally recognized quality benchmarking initiative. From the beginning of 2015 through the end of 2016, the endoscopy center's overall ADR rate for screening colonoscopies including serrated lesions was 51.09% (1550/3034) with a gender breakdown of 57.85% in males (825/1426) and 45.09% in females (725/1608). This significantly is above quality benchmark thresholds and suggests an overall high quality exam regardless of preparation used.

Interestingly, we found that 2 bottles of MC with 2 Dulcolax tablets was better than 3 bottles, and we hypothesized that this could be due to intolerance to larger volume of MC, possible selection bias in choosing MC 3 for selected patients, and that a subset of patients who received the 3 bottles prep likely did not finish it entirely (many patients would report anecdotally that they were nauseated by the time they were scheduled to take the third dose and were not able to take the entire third dose). Nonetheless, despite that caveat, MC 3 still appeared to be adequate. Furthermore, it is likely that the same bowel prep was chosen for a follow-up procedure if it previously gave an adequate prep, whereas if the prep was inadequate, a more vigorous prep such as a combination prep might have been selected for the follow-up procedure. This may result in a "stacking effect" for the MC 2 or other preps, making them appear better in the time period studied.

Combination preparation, which is a combination of Golytely or Nulytely with MC, did worse in terms of adequacy than 2 bottles of MC preparation. However, this could be due to selection bias as a probable factor as typically combination preps were given to patients who had failed other preps previously or were known to have chronic constipation.

MC is significantly less expensive than other available bowel preparations–and has better tolerability due to low volume. Several studies have shown that MC has great tolerability as high as 100% in a prospective trial by Gu et al.[11] Also, studies have shown that high- and low-volume preparations are equally effective.[12]

Limitations of our study include the retrospective design and comparison of preparations that have varying numbers and that are not randomized. Specifically, these estimates and observed differences (and even lack of differences) should be interpreted with caution as the type of bowel preparation patients received was due to clinical judgment, not randomization. As such, observed differences (and lack of differences) could be due to the bowel preparation itself, the selection mechanism as to who received which bowel preparation, or the combination of the two. Also, no

Table 3.

	4L PEG/4L Nulytely	Moviprep	Miralax	Suprep	Mag Citrate	Suclear	Prepopik	Osmoprep (48g)	Osmoprep (60g)	Plenvu
FDA	N/A	(n=153) 88.9% (CI 9.8, 1.3)	N/A	(n=180) 97% (CI -2%, 5%)	N/A	*Study 1* (n=176) 90% (CI 84%, 94%) *Study 2* (n=185) 94% (CI 89%, 97%)	*Study 1* (n=304) 84.2% (CI 3.4%, 16.2%) *Study 2* (n=284) 83.0% (CI -2.9%, 9.6%)	(n=236) 95%	(n=233) 97%	(n=275) 92% (CI 4.5%, -4.0%)
Metanalysis (1)	(n=458) 90.8% (CI 0.43,0.98)	N/A	(n=738) 89.7% (CI 0.43,0.98)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (2)	(n=934) 83% (CI 0.78, 0.89)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (3)	(n= 1049) 81% (CI 2.45 ,4.89)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (4)	(n=6593), 87.4% (84.1,90.7)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (5)	(n=430) 84 % (CI Reference)	(n=267) 91.1% (CI 0.85,2.44)	(n=2,499) 92.5% (CI 1.24,2.49)	(n=426) 90.6% (CI 0.86, 2.16)	(n=48) 90.6% (CI 0.57,4.17)	N/A	N/A	N/A	N/A	N/A
RCT (6)	N/A	N/A	N/A	N/A	[MC alone]; (n=160) 67% VS [MC with Senna] (n=182) 95%	N/A	N/A	N/A	N/A	N/A
RCT (7)	(n=191) 90% (0.68, 3.00)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (8)	(n=93) 92% (0.21, 1.46)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (9)	(n=76) 81% (0.14, 0.61)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (10)	(n=210) 81% (0.69, 1.87)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (11)	(n=59) 78% (0.66, 5.42)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

1: Am J Gastroenterol. 2014 Oct;109(10):1566-74. doi: 10.1038/ajg.2014.238. https://www.ncbi.nlm.nih.gov/pubmed/25135007 (all RCTs were screening)

2: Gastrointest Endosc. 2014 Oct;80(4):566-576.e2. doi: 10.1016/j.gie.2014.05.320 https://www.ncbi.nlm.nih.gov/pubmed/25053529 (all indications)

3: Clin Gastroenterol Hepatol. 2012 Nov;10(11):1225-31. doi: 10.1016/j.cgh.2012.08.029 https://www.ncbi.nlm.nih.gov/pubmed/22940741

4: Clin Gastroenterol Hepatol. 2019 Nov 1. pii: S1542-3565(19)31246-7. doi: 10.1016/j.cgh.2019.10.044. https://www.ncbi.nlm.nih.gov/pubmed/31683057

5: Am J Gastroenterol. 2019 Feb;114(2):305-314. doi: 10.14309/ajg.0000000000000057. https://www.ncbi.nlm.nih.gov/pubmed/30730859 (all indications)

6: World J Gastroenterol. 2009 Apr 14; 15(14): 1759–1763. doi: 10.3748/wjg.15.1759. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2668782 (all indications) (no confidence interval reported)

7: Dis Colon Rectum. 1994 Mar;37(3):229-33; discussion 233-4. https://www.ncbi.nlm.nih.gov/pubmed/8137669

8: Am J Gastroenterol. 2003 Oct;98(10):2187-91. https://www.ncbi.nlm.nih.gov/pubmed/14572566

9: Endoscopy. 2005 Jun;37(6):537-41. https://www.ncbi.nlm.nih.gov/pubmed/15933926

10: Can J Gastroenterol. 2011 Dec;25(12):657-62. https://www.ncbi.nlm.nih.gov/pubmed/22175055

11: Gastrointest Endosc. 1998 Feb;47(2):167-71. https://www.ncbi.nlm.nih.gov/pubmed/9512283

patient satisfaction surveys in terms of individual preps were conducted. Overall facility satisfaction surveys consistently demonstrated high performance with scores over 95% in terms of the facility, scheduling, communication, staff and care received. Data were collected previously but then time constraints prevented analysis until later, when the project was taken up by Dr. AlSamman. Strengths of our study includes prospective documentation and a very large sample size – much larger than previously reported studies examining MC preparations. Although no formal power analysis was conducted to compare the differences between bowel preparations, the primary outcome – estimation of the adequacy rates of MC – were calculated using large sample sizes. Our experience supports the conclusion that MC preparations are adequate for both screening and diagnostic colonoscopies. In addition, MC is the least expensive preparation available. Though not FDA approved in the USA as a bowel preparation, given our experience and previous data, we feel MC should be considered a viable option for bowel preparation. Nonetheless, we should continue to exercise caution for patients who have chronic kidney disease, cirrhosis, and congestive heart failure. Despite the large sample size of our study, nonetheless, confidently generalize our findings given the retrospective nature of our analysis and nonrandomized design. Given its low cost, it is unlikely that any company would perform the prospective trial needed to obtain FDA approval. Hence, future guidelines should consider our experience and other published data on MC when updating bowel preparation guidelines.

References

1. Chokshi RV, Hovis CE, Hollander T, Early DS, Wang JS. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. *Gastrointest. Endosc.* **75**, 1197–1203 (2012).
2. Bechtold ML, Mir F, Puli SR, Nguyen DL. Optimizing bowel preparation for colonoscopy: a guide to enhance quality of visualization. *Ann. Gastroenterol. Hepatol.* **29**, 137–146 (2016).
3. Kluge MA, et al. Inadequate Boston Bowel Preparation Scale scores predict the risk of missed neoplasia on the next colonoscopy. *Gastrointest. Endosc.* **87**, 744–751 (2018).
4. Hassan C, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy* **51**, 775–794 (2019).
5. Johnson DA, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology* **147**, 903–924 (2014).
6. Harewood GC, Wiersema MJ, Melton LJ., 3rd. A prospective, controlled assessment of factors influencing acceptance of screening colonoscopy. *Am. J. Gastroenterol.* **97**, 3186–3194 (2002).
7. Binder HJ. Pharmacology of laxatives. *Annu. Rev. Pharmacol. Toxicol.* **17**, 355–367 (1977).
8. Vradelis S, et al. Addition of senna improves quality of colonoscopy preparation with magnesium citrate. *World J. Gastroenterol.* **15**, 1759–1763 (2009).
9. Rapier R, Houston C. A prospective study to assess the efficacy and patient tolerance of three bowel preparations for colonoscopy. *Gastroenterol. Nurs.* **29**, 305–308 (2006).
10. Arora M, et al. A critical evaluation and a search for the ideal colonoscopic preparation. *Clin. Res. Hepatol. Gastroenterol.* **37**, 200–206 (2013).
11. Gu P, et al. Comparing the Real-World Effectiveness of Competing Colonoscopy Preparations: Results of a Prospective Trial. *Am. J. Gastroenterol.* **114**, 305–314 (2019).
12. Spadaccini M, et al. Efficacy and Tolerability of High- vs Low-Volume Split-Dose Bowel Cleansing Regimens for Colonoscopy: a Systematic Review and Meta-analysis. *Clin. Gastroenterol. Hepatol.* (2019) doi:10.1016/j.cgh.2019.10.044.

Acknowledgment

We acknowledge our colleagues Dr. Edward R. Feller (Brown University) and Dr. Brooks D. Cash (University of Texas Health Science Center, Houston, TX) for reviewing the manuscript and providing important feedback.

Authors

Mohd Amer AlSamman, MD, former Clinical Assistant Professor of Medicine at Alpert Medical School of Brown University; Gastroenterology and Hepatology Fellow, Medstar Georgetown University Hospital, Washington, DC.

Stephanie Leung, MD, former Internal Medicine Resident at Alpert Medical School of Brown University; Division of Hospital Medicine, Assistant Professor of Medicine, University of Kentucky.

Abdelmoniem Moustafa, MD, Division of Hospital Medicine, The Miriam Hospital; Clinical Assistant Professor of Medicine, Alpert Medical School of Brown University.

Mohamed Abeid, MD, Assistant Professor of Gastroenterology, Cairo University, Cairo, Egypt.

Grayson L. Baird, PhD, Assistant Professor in Diagnostic Imaging, Alpert Medical School of Brown University.

Samir A. Shah, MD, FACG, Division of Gastroenterology, Alpert Medical School of Brown University; The Miriam Hospital; Gastroenterology Associates, Inc., Providence, RI.

Disclaimer

The views expressed herein are those of the authors and do not necessarily reflect the views of the affiliated institutions.

Grant Support

None

Disclosures

No financial, professional or personal conflicts of interests to declare on behalf of all authors.

Correspondence

Mohd Amer AlSamman, MD
Medstar Georgetown University Hospital
Division of Gastroenterology, 2 Main Room M2201
3800 Reservoir Road, NW
Washington, DC 20007
513-620-9729
Fax 202-444-1521
alsamman.amer@gmail.com