Published in final edited form as:

Dig Liver Dis. 2014 January ; 46(1): 56–61. doi:10.1016/j.dld.2013.07.020.

THE IMPACT OF OPIATE PAIN MEDICATIONS AND PSYCHOACTIVE DRUGS ON THE QUALITY OF COLON PREPARATION IN OUTPATIENT COLONOSCOPY

Vladimir M. Kushnir, MD, Pavan Bhat, MD, Reena V. Chokshi, MD, Alexander Lee, MD, Brian B. Borg, MD, C. Prakash Gyawali, MD MRCP, and Gregory S. Sayuk, MD, MPH
Division of Gastroenterology, Washington University School of Medicine, St Louis, Missouri, USA

Abstract

Background—Suboptimal colon preparation is a significant barrier to quality colonoscopy. The impact of pharmacologic agents associated with gastrointestinal dysmotility on quality of colon preparation has not been well characterized.

Aims—Evaluate impact of opiate pain medication and psychoactive medications on colon preparation quality in outpatient undergoing colonoscopy.

Methods—Outpatients undergoing colonoscopy at a single medical center during a 6-month period were retrospectively identified. Demographics, clinical characteristics and pharmacy records were extracted from electronic medical records. Colon preparation adequacy was evaluated using a validated composite colon preparation score.

Results—2600 patients (57.3±12.9 years, 57% female) met the inclusion and exclusion criteria. 223 (8.6%) patients were regularly using opioids, 92 antipsychotics, 83 tricyclic antidepressants and 421 non-tricyclic antidepressants. Opioid use was associated with inadequate colon preparation both with low dose (OR=1.4, 95%CI 1.0-2.1, p=0.05) and high dose opioid users (OR=1.7, 95%CI 1.1-2.9, p=0.039) in a dose dependent manner. Other significant predictors of inadequate colon preparation included use of tricyclics (OR=1.9, 95%CI 1.1-3.0, p=0.012), non-tricyclic antidepressants (OR=1.5, 95%CI 1.1-2.0, p=0.013), and antipsychotic medications (OR=2.2, 95%CI 1.4-3.4, p=0.001).

© 2013 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.

Address all correspondence to: Gregory S. Sayuk, MD, MPH, Division of Gastroenterology, Washington University School of Medicine, 660 South Euclid Ave, Campus Box 8124, St Louis, Missouri 63110, Phone: 314-454-8201, Fax: 314-454-5107, GSAYUK@wustl.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Presented in preliminary form at the Annual Meeting of the American Gastroenterological Association, 2012, San Diego

Author Contributions:

Gregory S. Sayuk, C. Prakash Gyawali, Vladimir M Kushnir: study design, data collection, data analysis, manuscript preparation.
Pavan Bhat, Reena V. Chokshi, Alexander Lee, Brian B. Borg: data collection, manuscript preparation.

Conflict of Interest: None of the authors have any financial disclosures related to this manuscript.

Conclusions—Opiate pain medication use independently predict inadequate quality colon preparation in a dose dependent fashion; furthermore psychoactive medications have even more prominent effects and further potentate the negative impact of opiates with concurrent use.

Keywords

Colonoscopy; Cathartics; Psychotropic Drugs; Opiate Pain Medications

Background

Colon preparation is found to be inadequate in up to 33% of colonoscopies; leading to aborted procedures, increased procedure duration, greater patient discomfort, and potentially higher complication rates and healthcare costs.[1-6] Additionally, inadequate colon preparation decreases efficacy of colonoscopy as a screening modality, with up to 40% of polyps and 27% of advanced adenomas being missed when preparation is inadequate.[7-10]

In the past decade, efforts to improve the quality of colon preparation largely have focused on improving the efficacy and tolerability of osmotic based colon preparation regimens.[11] Consequently, more effective and palatable regimens have been developed, including low-volume and split-dose preparation.[11-13] Despite these improvements, inadequate preparations still are encountered in 10-20% of patients.[7, 14-16] Focus hence has shifted to patient-related factors, including psychoactive and opiate medication (OPM) use.[1-3]

The link between opiates and slowed colon transit is well established, with over 80% of patients treated with opiate pain medications reporting constipation. Likewise, psychoactive medications (antidepressants and atypical antipsychotics) have been strongly associated with gastrointestinal hypomotility and constipation. [17-23] Understanding the influence of these medications on colon preparation quality is essential, as use of OPM and psychoactive agents has grown exponentially in the past 20 years.[24-26] However the impact of these classes of medications on quality of colon preparation remains incompletely understood.

The goal of the present study was to evaluate the influence of OPM and psychoactive medications on the quality of colon preparation in a cohort of outpatients undergoing screening and diagnostic colonoscopy, while controlling for other factors known to negatively impact the quality of colon preparation.

Methods

Patients

Consecutive adult outpatients (>18 years old) undergoing colonoscopy at our tertiary care center between June and December 2007 were retrospectively identified from the institutional endoscopic database (Provation MD, Minneapolis, MN). A manual chart review was performed and the pre-endoscopy history was extracted from each patient's electronic medical record; demographics (age, gender, race, weight, height), clinical data (past medical and surgical history, indication for colonoscopy, gastrointestinal symptoms at the time of colonoscopy), and colonoscopy details (quality of colon preparation, sedation used, endoscopic findings, final diagnosis, post procedure recommendations, and pathology

reports) were abstracted. Patients were excluded if procedure documentation was incomplete or if the colonoscopy was performed on an inpatient basis. The Institutional Review Board of Washington University School of Medicine/ Barnes Jewish Hospital approved review of clinical data for the purpose of this study.

Medication Use History

Pharmacy records were obtained from outpatient medication reconciliation forms, routinely collected as part of pre-endoscopy assessment. All medications used within one week of colonoscopy were extracted from the medication reconciliation form, including dose, frequency of use, and indication for use. Psychoactive medications of interest included antidepressants, benzodiazepines and antipsychotic agents. Antidepressants were further sub-classified as tricyclic antidepressant (TCA, including amitriptyline, desipramine, doxepin, imipramine, nortriptyline) and non-TCA agents (selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, other classes). Antipsychotic agents and benzodiazepines were recorded separately. OPM dose was recorded in milligrams per day of parent opiate compound and subsequently converted to oral morphine equivalents (OME) for further analysis using a standard algorithm (Table S1).[27-30] Opiate dose was then categorized as follows: no OPM, low dose OPM (<40 OME per day) and high dose OPM (>40 OME per day) (Table 1).

Colon Preparation Regimens and Quality

During the study period, polyethylene glycol (PEG) based colon preparation regimens were used at our center, either of 4L polyethylene glycol (PEG), 2 L PEG with ascorbic acid, or MiraLAX prep [PEG 3350 without electrolytes (MiraLAX; Schering-Plough Healthcare Products, Inc, Kenilworth, NJ) with 64 oz. of sports drink consumed on the evening prior to colonoscopy, with a clear liquid diet earlier in the day. An alternative sodium phosphate-based regimen was used at the discretion of the referring physician, typically reserved for patients without prior history of cardiac or renal disease.

Colon preparation quality, as judged by the endoscopist, was extracted from the endoscopy report, during the period of the study bowel preparation quality was recorded for all procedures using the Aronchick scale. Specifically, during colonoscopy, preparation quality was designated an ordinal value on an Aronchick scale (1=excellent, 2= good, 3= fair, 4= inadequate, 5= unsatisfactory).[31] In order to more accurately assess the overall quality of colon preparation a composite score was calculated utilizing a previously described formula, which accounts for the impact of colon preparation on follow up recommendations and the subjective confidence of the endoscopist in the adequacy of colon preparation.[2] The composite score was computed as a sum of the following variables:

1. Ordinal Aronchick score, which for the purposes of this analysis was dichotomized as adequate (0=excellent or good) or inadequate (1= fair, inadequate, unsatisfactory).
2. Change in post procedure follow up recommendations due to quality of colon preparation. Follow up interval specified in the colonoscopy report were compared to the accepted American Gastroenterological Association, American College of

Gastroenterology and American Society for Gastrointestinal Endoscopy guidelines. Recommendations for follow up were dichotomized, such that recommended follow-up sooner than would be advised by the guidelines was given a score of 1, while follow up interval in accordance with guidelines was given as score of 0.

3. Endoscopist confidence in the adequate visualization of colonic mucosa was extracted from the reports. The endoscopy report writer allowed a drop down menu for the endoscopist to designate whether quality of preparation allowed for visualization of polyps < 5 mm in size. This was also coded in a binary manner, with 0 indicating preparation adequate to detect polyps < 5 mm in size and 1 indicating preparation that was not adequate to detect polyps < 5 mm in size.

The above components were added together and a composite score of 0 designated an adequate colon preparation, while a composite score of 1 designated an inadequate colon preparation. Colonoscopy was designated incomplete if the endoscopist failed to reach the base of the cecum.

Statistical Analysis

Normally distributed data are reported as mean $\pm$ standard deviation, skewed data as median and interquartile range (IQR). Grouped continuous variable data were compared using two-tailed Student's t tests and Mann-Whitney U tests, where appropriate. Intergroup comparisons between categorical variables were made using the Chi-squared test and Fisher's exact test. A multivariable logistic regression model was created utilizing the colon preparation composite score as the outcome variable in order to determine independent predictors of inadequate colon preparation. The potency of the multivariable model for predicting inadequate colon preparation was evaluated with a C statistic. Following development of the multivariable model, tests for interactions between variables of interest were performed. A p value of <0.05 was required for statistical significance in each instance. All analyses were performed using SPSS version 19.1 software (IBM, Armonk, New York).

Results

Patient Characteristics

During the six-month study period, there were 2857 colonoscopies performed at our endoscopy center by 29 endoscopists who performed a median of 66 procedures each. Of this, 257 patients were excluded, due to inpatient status at time of colonoscopy in 234 cases and incomplete documentation in 23 cases. A total of 2600 patients (57.3 $\pm$ 12.9 years, 57.0% female) met all inclusion and exclusion criteria. Baseline patient characteristics are detailed in Table S2. Colorectal cancer screening or surveillance was the primary indication for colonoscopy in 67.7% (table S2). Diabetes mellitus (17.8%), neurologic disease (5.6%), and psychiatric disease (20.4%) were the most frequent comorbidities, and 17.1% reported constipation as a symptom.

Medication Use

At the time of colonoscopy, 223 (8.6%) of patients were regularly using OPM. In these patients, the median OME dose was 20 mg (IQR 20-40 mg) of oral morphine per day. The

majority of OPM users (67.7%) were on low dose OPM [equivalent to <40 mg oral morphine per day] (Table 1). Among psychoactive agents, non-TCA antidepressants were most frequently encountered (16.2%), and use of TCA (3.2%), antipsychotic agents (3.5%) and benzodiazepines (6.5%) were lower in frequency.

Colon Preparation Quality and Polyp Detection

Polyethylene glycol (PEG) based colon preparation regimens were used by 87.6% of patients. Colon preparation quality as assessed by the composite score was adequate in 1966 (75.6%) and was inadequate in 634 (24.4%). Colonoscopy was incomplete in 3.9%, significantly more often when colon preparation was inadequate (10.7%) than with an adequate preparation (1.7%, $p<0.001$). Polyp detection rate was 42.0% for the study cohort, with a trend toward higher polyp detection when colon preparation was adequate (43.0% vs. 38.9% with inadequate preparation, $p=0.071$). Early repeat colonoscopy was recommended due to poor quality of bowel preparation in 332 (12.8%) patients.

Univariate Analysis

Colon preparation was inadequate significantly more often in OPM users (37.2%) compared to OPM non-users (23.2%, $p<0.001$). A gradient of colon preparation quality was observed in relationship to OPM use, inadequate quality colon preparation frequency increasing from 9% in OPM non-users, to 15% in low dose OPM users and 22% in high dose OPM users ($p<0.001$ across groups, Figure 1). Users of TCAs, non-TCA antidepressants, benzodiazepines and antipsychotic medications also were significantly more likely to have inadequate colon preparation when compared to non-users ($p<0.009$ for each, Table 1). Bowel preparation regimen used was a highly significant the quality of colon cleansing; with 2 Liter PEG being more effective than 4 Liter PEG or sodium phosphate based regimen ($p<0.001$ across groups, Table 1). Other factors significantly associated with inadequate colon preparation on univariate analysis included male gender, non-Caucasian race, higher BMI, hypertension, neurologic comorbidities (e.g. stroke, parkinsonism, multiple sclerosis), depression, constipation, diabetes mellitus ($p<0.01$ for each, Table S2).

Multivariate Analysis

Factors independently associated with inadequate colon preparation on univariate analysis were further evaluated; a multivariate logistic regression model was created, containing demographic, clinical and procedure variables significantly associated with inadequate colon preparation on univariate analysis (Table 3). The overall model was statistically significant (likelihood ratio Chi-square=180.5, $df=20$, $p<0.001$) with a C statistic of 0.67. In this model, OPM use was associated with inadequate colon preparation in a dose dependent manner, with both low dose OPM (OR 1.4, 95%CI 1.0-2.1, $p=0.05$) and high dose OPM (OR 1.7, 95%CI 1.1-2.9, $p=0.039$) being significant predictors of inadequate colon preparation. Other medication use that significantly predicted inadequate colon preparation included non-TCA antidepressants (OR 1.5, 95% CI 1.1-2, $p=0.013$), TCAs (OR 1.9, 95% CI 1.1-3.0, $p=0.012$) and antipsychotic medications (OR 2.2, 95% CI 1.4-3.5, $p=0.001$), with antipsychotic medications demonstrating the highest ORs. Clinical and procedure related predictors independently associated with inadequate colon preparation included male gender, non-Caucasian race, history of diabetes mellitus or neurologic disease, sodium phosphate-based

or 4 L PEG based colon preparation and procedure indication other than screening or surveillance (Table S3).

Interactions between use of various psychoactive medications and OPM were tested, and no interaction effects were observed. To further examine this, the cumulative adjusted ORs for inadequate colon preparation were calculated in patients with concurrent psychotropic medication usage, stratified by OPM dose. A cumulative gradient was seen in all categories tested, the lowest ORs seen in non-users of OPM, and the highest ORs in high dose OPM users (Figure 2). Among the covariates studied in this analysis, antipsychotic medications had the strongest predictive ORs for inadequate colon preparation in conjunction with opiate use.

Discussion

In this large retrospective cohort study, we report that use of opiates and psychoactive medications independently predict inadequate quality of colon preparation at colonoscopy. Further, we report that the effect of OPM on the quality of colon preparation is dose dependent, with a significantly higher likelihood of inadequate preparation in high dose opiate users. These results add to the growing literature identifying predictors of inadequate colon preparation, and further emphasize the need to explore individualized colon preparation regimens that account for patient demographics, clinical characteristics and medication use in determining which patients can benefit from a more aggressive approach to colon preparation.

Inadequate colon preparation is a significant barrier to quality colonoscopy generally, and colorectal cancer screening programs in particular. Indeed inadequate preparation of the colon has been linked to prolonged procedure time, missed adenomas and shortened surveillance intervals in patients undergoing screening colonoscopy.[2, 5, 9] Consequently, inadequate colon preparation is a significant driver of endoscopy costs, which in the current reimbursement environment falls largely on physicians and health systems.[6] Thus, attention is appropriately being focused on identifying factors associated with inadequate colon preparation. Several investigators have described the association between disease states and medications associated with intestinal hypomotility and inadequate colon preparation.[1, 2, 32] However, prior to the present study, the degree of influence of specific classes of medications causing intestinal hypomotility on quality of colon preparation had not been systematically explored.

The link between opiates and gastrointestinal hypomotility has been well established. The primary drivers of opiate-induced hypomotility are the μ opiate receptors, largely located in the stomach and proximal colon, the two areas that may be critical to patient tolerance of ingested cleansing agent and clearance of the agent from the colon, respectively.[33] Activation of intestinal μ opiate receptors by exogenous opiates leads to non-propulsive peristalsis as well as increased tone in gastrointestinal sphincters (e.g. pylorus), which in turn lead to delayed intestinal transit and increased fluid absorption.[25] Pre-clinical and clinical studies have demonstrated that the relationship between gastrointestinal dysmotility and opiates is dose-related and cumulative, with more profound dysmotility when opiates

are used on a continuous basis.[34, 35] Thus, our finding that opiates increase the risk of inadequate colon preparation in a dose-dependent manner is in keeping with the current understanding of opiate-induced gastrointestinal dysmotility. Extrapolating from our findings and the pathophysiology of opiate-induced gastrointestinal dysfunction, we hypothesize that optimizing the quality of colonoscopy preparation in opiate users would require a strategy focusing both on stimulating peristalsis and increasing the volume of fluid within the gastrointestinal tract. Alternatively, specific opiate antagonists targeting the gastrointestinal tract need to be studied as adjuncts to colon preparation regimens in this patient population.

Our findings of the effects of antidepressant medications on colon preparation quality also are of clinical interest. Ness *et al.* initially described a relationship between tricyclic antidepressants and inadequate colon preparation quality, an effect presumed to be mediated by the anticholinergic effects of this class of medications.[17, 32] We also report a significant relationship between use of non-TCA antidepressants and inadequate colon preparation. While this class of medications has not been conspicuously linked to constipation in clinical practice, the role of serotonin in gastrointestinal motility and sensation is well established. Indeed, both major classes of non-TCA antidepressants, selective serotonin reuptake inhibitors (SSRI) and serotonin-norepinephrine reuptake inhibitors (SNRI) have been linked to increased colonic compliance as well as decreased postprandial colonic tone in human studies.[20, 36] We hypothesize that a serotonin-mediated increase in colonic compliance leads to retention of purgative solution in the colons of patients taking SSRI/SNRIs, resulting in inadequate colon preparation for colonoscopy. At the same time, the relationship between antidepressant medications and colon preparation quality may be mediated by the underlying affective psychiatric disturbance itself; in the case of depression, this may lead to decreased patient mobility and compliance with the purgative regimen.

Finally, we found that antipsychotic medication use was the strongest risk factor for inadequate colon preparation; with antipsychotic users being 2.4 times more likely to have inadequate colon preparation. Like tricyclic antidepressants, this class of medications has an established association with gastrointestinal hypomotility, in this case mediated by the dopaminergic and antiserotonergic properties of this class of medications.[22, 37] Patients who are taking antipsychotic medications may be more sedentary due to extrapyramidal side effects as well as negative symptoms of psychiatric disease. Both of these factors could potentially exacerbate gastrointestinal hypomotility and lead to inadequate colon cleansing at the time of colonoscopy. Thus, for these patients we speculate that colon preparation is likely to be aided by the addition of pro-motility agents to traditional colon preparation regimens.

The findings of our study were largely in agreement with the current literature for traditional risk factors for inadequate colon preparation (Table 3).[1-3, 32, 38, 39] As in several prior reports, diabetes mellitus was a strong predictor of inadequate colon preparation.[1, 2] Increased BMI was strongly associated with inadequate colon preparation on univariate analysis, but BMI did not survive as an independent predictor on multivariate analysis in the current study (OR=1.0, CI 0.9=1.0). This may relate the fact that we only included

outpatients the study cohort; outpatients generally have better mobility and are better able to comply with preparation instructions, which may have counteracted the effects of obesity on colon preparation. The lack of association between age and inadequate colon preparation is in line with a majority of studies in the present literature.[3, 32, 40] Our data is also consistent with prior literature with respect to bowel preparation volume and quality of bowel cleansing; with 2 Liter PEG based regimens outperforming 4 Liter PEG and sodium phosphate based regimens.[39] Finally, our findings add to the substantial body of evidence linking short duration of time from last dose of purgative agent to start of colonoscopy with quality of colon preparation.[3, 40] While split dose preparation was not used at our center at the time of the study, our finding that preparation quality was significantly better for morning versus afternoon colonoscopies implies that split dose preparation would have been helpful in our population.

The primary limitation of this study relates to its retrospective design. Specifically, quality of colon preparation was assessed via interrogation of the medical record, and at the time of the study preparation quality was recorded in terms of the Aronchick score rather than a more established instrument such as the Boston Bowel Preparation Scale.[41] However, colon preparation quality was prospectively recorded for all patients who were included in the study, and our large number of endoscopists further decreases the potential for bias. Additionally, to reduce the impact of interobserver variability we utilized a composite colon preparation score as the primary outcome measure; this score accounted for all reported variables that related to colon cleansing quality, including ability to visualize polyps < 5 mm in size as well as shortened follow up intervals for repeat screening/ surveillance colonoscopy. This approach to assessing colon preparation quality is supported by our finding of a trend toward decreased polyp detection rate in patients with inadequate colon preparation and is in line with the existing literature (Hendry et al, *Colorectal Dis* 2007; 9: 745 – 8). Further, the clinical nature of the present study prevents us from speculating on the potential mechanisms leading to inadequate colon preparation. Finally, during the study period split preparation was not utilized in our GI unit and all procedures were performed with bowel preparation being administered the evening prior to the procedure. However, our findings are in line with the current understanding of the effects of pharmacologic agents and systemic conditions on gastrointestinal motility, and we believe that colon preparation can be improved by individualizing purgative regimens based on patient-specific factors.

In conclusion, we report for the first time that opiates adversely affect colon preparation quality in a dose dependent fashion. We also found that use of antipsychotic and antidepressant medications have similar negative effects, with inadequate preparation observed in a full one-half of antipsychotic medication users. We believe that these factors warrant further consideration in efforts to optimize colon preparation for colonoscopy. These findings should be utilized to shape additional prospective work to investigate the efficacy of purgative regimens individualized on the basis of specific patient level factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported in part by (NIHMS320979) (VMK) and (K23 DK84113) (GSS).

References

1. Hassan C, Fuccio L, Bruno M, et al. A predictive model identifies patients most likely to have inadequate bowel preparation for colonoscopy. *Clin Gastroenterol Hepatol*. 2012; 10:501–506. [PubMed: 22239959]
2. Borg BB, Gupta NK, Zuckerman GR, et al. Impact of obesity on bowel preparation for colonoscopy. *Clin Gastroenterol Hepatol*. 2009; 7:670–675. [PubMed: 19245852]
3. Lebowitz B, Wang TC, Neugut AI. Socioeconomic and other predictors of colonoscopy preparation quality. *Dig Dis Sci*. 2010; 55:2014–2020. [PubMed: 20082217]
4. Crispin A, Birkner B, Munte A, et al. Process quality and incidence of acute complications in a series of more than 230,000 outpatient colonoscopies. *Endoscopy*. 2009; 41:1018–1025. [PubMed: 19856246]
5. Froehlich F, Wietlisbach V, Gonvers JJ, et al. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc*. 2005; 61:378–384. [PubMed: 15758907]
6. Rex DK, Imperiale TF, Latinovich DR, et al. Impact of bowel preparation on efficiency and cost of colonoscopy. *Am J Gastroenterol*. 2002; 97:1696–1700. [PubMed: 12135020]
7. Marmo R, Rotondano G, Riccio G, et al. Effective bowel cleansing before colonoscopy: a randomized study of split-dosage versus non-split dosage regimens of high-volume versus low-volume polyethylene glycol solutions. *Gastrointest Endosc*. 2010; 72:313–320. [PubMed: 20561621]
8. Lebowitz B, Kastrinos F, Glick M, et al. The impact of suboptimal bowel preparation on adenoma miss rates and the factors associated with early repeat colonoscopy. *Gastrointest Endosc*. 2011; 73:1207–1214. [PubMed: 21481857]
9. Chokshi RV, Hovis CE, Hollander T, et al. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. *Gastrointest Endosc*. 2012; 75:1197–1203. [PubMed: 22381531]
10. Oh YS. What are we missing when colon preparation is inadequate? *Gastrointestinal endoscopy*. 2012; 75:1204–1205. [PubMed: 22624811]
11. Di Palma J, Rex D. Advances in bowel preparations: new formulation and clinical results. *Gastroenterol Nurs*. 2011; 34(Suppl 2):S2–8. [PubMed: 21989190]
12. Parente F, Marino B, Crosta C. Bowel preparation before colonoscopy in the era of mass screening for colo-rectal cancer: a practical approach. *Dig Liver Dis*. 2009; 41:87–95. [PubMed: 18676211]
13. Mamula P, Adler DG, Conway JD, et al. Colonoscopy preparation. *Gastrointest Endosc*. 2009; 69:1201–1209. [PubMed: 19481646]
14. Rex DK, Di Palma JA, Rodriguez R, et al. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc*. 2010; 72:328–336. [PubMed: 20646695]
15. Di Palma JA, Rodriguez R, McGowan J, et al. A randomized clinical study evaluating the safety and efficacy of a new, reduced-volume, oral sulfate colon-cleansing preparation for colonoscopy. *Am J Gastroenterol*. 2009; 104:2275–2284. [PubMed: 19584830]
16. Kilgore TW, Abdinoor AA, Szary NM, et al. Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials. *Gastrointest Endosc*. 2011; 73:1240–1245. [PubMed: 21628016]
17. Leroi AM, Lalaude O, Antonietti M, et al. Prolonged stationary colonic motility recording in seven patients with severe constipation secondary to antidepressants. *Neurogastroenterol Motil*. 2000; 12:149–154. [PubMed: 10771496]
18. Chial HJ, Camilleri M, Burton D, et al. Selective effects of serotonergic psychoactive agents on gastrointestinal functions in health. *Am J Physiol Gastrointest Liver Physiol*. 2003; 284:G130–137. [PubMed: 12488239]

19. Coates MD, Johnson AC, Greenwood-Van Meerveld B, et al. Effects of serotonin transporter inhibition on gastrointestinal motility and colonic sensitivity in the mouse. *Neurogastroenterol Motil.* 2006; 18:464–471. [PubMed: 16700726]
20. Tack J, Broekaert D, Corsetti M, et al. Influence of acute serotonin reuptake inhibition on colonic sensorimotor function in man. *Aliment Pharmacol Ther.* 2006; 23:265–274. [PubMed: 16393306]
21. Cha DS, McIntyre RS. Treatment-emergent adverse events associated with atypical antipsychotics. *Expert Opin Pharmacother.* 2012; 13:1587–1598. [PubMed: 22304541]
22. De Hert M, Dockx L, Bernagie C, et al. Prevalence and severity of antipsychotic related constipation in patients with schizophrenia: a retrospective descriptive study. *BMC Gastroenterol.* 2011; 11:17. [PubMed: 21385443]
23. Verma S, Fogel J, Beyda DJ, et al. Chronic methadone use, poor bowel visualization and failed colonoscopy: a preliminary study. *World J Gastroenterol.* 2012; 18:4350–4356. [PubMed: 22969198]
24. Grunkemeier DM, Cassara JE, Dalton CB, et al. The narcotic bowel syndrome: clinical features, pathophysiology, and management. *Clin Gastroenterol Hepatol.* 2007; 5:1126–1139. quiz 1121-1122. [PubMed: 17916540]
25. Camilleri M. Opioid-induced constipation: challenges and therapeutic opportunities. *Am J Gastroenterol.* 2011; 106:835–842. quiz 843. [PubMed: 21343919]
26. Pratt LA, Brody DJ, Gu Q. Antidepressant use in persons aged 12 and over: United States, 2005-2008. *NCHS Data Brief.* 2011; 76:1–8. [PubMed: 22617183]
27. Grossman, SA.; Nesbit, S. Cancer Pain. In: Abeloff, MD.; Armitage, JO.; Niederhuber, JE.; Kastan, MB.; McKenna, WG., editors. *Abeloff's Clinical Oncology.* 4 edn. Churchill Livingstone Elsevier; Philadelphia, PA: 2008. p. 565-567.
28. Patanwala AE, Duby J, Waters D, et al. Opioid conversions in acute care. *Ann Pharmacother.* 2007; 41:255–266. [PubMed: 17299011]
29. Vickers MD, O'Flaherty D, Szekely SM, et al. Tramadol: pain relief by an opioid without depression of respiration. *Anaesthesia.* 1992; 47:291–296. [PubMed: 1519677]
30. Barkin RL, Barkin SJ, Barkin DS. Propoxyphene (dextropropoxyphene): a critical review of a weak opioid analgesic that should remain in antiquity. *Am J Ther.* 2006; 13:534–542. [PubMed: 17122535]
31. Aronchick CA, Lipshutz WH, Wright SH, et al. Validation of an instrument to assess colon cleansing [abstract]. *Am J Gastroenterol.* 1999; 94:2667.
32. Ness RM, Manam R, Hoen H, et al. Predictors of inadequate bowel preparation for colonoscopy. *Am J Gastroenterol.* 2001; 96:1797–1802. [PubMed: 11419832]
33. Fickel J, Bagnol D, Watson SJ, et al. Opioid receptor expression in the rat gastrointestinal tract: a quantitative study with comparison to the brain. *Brain Res Mol Brain Res.* 1997; 46:1–8. [PubMed: 9191072]
34. Maurer AH, Krevsky B, Knight LC, et al. Opioid and opioid-like drug effects on whole-gut transit measured by scintigraphy. *J Nucl Med.* 1996; 37:818–822. [PubMed: 8965152]
35. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician.* 2008; 11:S105–120. [PubMed: 18443635]
36. Chial HJ, Camilleri M, Ferber I, et al. Effects of venlafaxine, buspirone, and placebo on colonic sensorimotor functions in healthy humans. *Clin Gastroenterol Hepatol.* 2003; 1:211–218. [PubMed: 15017493]
37. Peyriere H, Roux C, Ferard C, et al. Antipsychotics-induced ischaemic colitis and gastrointestinal necrosis: a review of the French pharmacovigilance database. *Pharmacoepidemiol Drug Saf.* 2009; 18:948–955. [PubMed: 19572384]
38. Nguyen DL, Wieland M. Risk factors predictive of poor quality preparation during average risk colonoscopy screening: the importance of health literacy. *J Gastrointest Liver Dis.* 19:369–372. [PubMed: 21188326]
39. Valiante F, Pontone S, Hassan C, et al. A randomized controlled trial evaluating a new 2-L PEG solution plus ascorbic acid vs 4-L PEG for bowel cleansing prior to colonoscopy. *Dig Liver Dis.* 2012; 44:224–227. [PubMed: 22119219]

40. Siddiqui AA, Yang K, Spechler SJ, et al. Duration of the interval between the completion of bowel preparation and the start of colonoscopy predicts bowel-preparation quality. *Gastrointest Endosc.* 2009; 69:700–706. [PubMed: 19251013]
41. Calderwood AH, Jacobson BC. Comprehensive validation of the Boston Bowel Preparation Scale. *Gastrointest Endosc.* 2010; 72:686–692. [PubMed: 20883845]

Figure 1. Bowel preparation quality across narcotic dose categories. The quality of bowel preparation was significantly worse in opiate users, particularly in those patients who were receiving high dose opiate pain medications at time of preparation for colonoscopy ($p=0.009$ across groups)

* OME-oral morphine equivalent.

Figure 2. Odds Ratios for independent effects adjusted for opiate pain medication use categories adjusted for psychoactive medication use

* OPM-opiate pain medication, SSRI-selective serotonin reuptake inhibitor, SNRI-serotonin norepinephrine reuptake inhibitor, TCA-tricyclic antidepressant.

Table 1
Opiate Medication Dose Categories for Commonly Used Analgesics

Low Dose OPM[*]	High Dose OPM[^]
Tramadol 50 mg TID (30 OME)	Fentanyl patch 25 mcg/hr (60 OME)
Hydrocodone 5 mg QID (20 OME)	Methadone 10 mg TID (240 OME)
Oxycodone IR 5 mg QID (30 OME)	Oxycodone ER 60 mg BID (90 OME)

[#] OPM- opiate pain medication, OME- oral morphine equivalent

^{*} Low dose OPM < 40 mg OME per day

[^] High dose OPM > 40 mg OME per day