



The Effect of Laxative Use in Length of Hospital Stay and Complication Rate in Patients Undergoing Elective Colorectal Surgery within an ERAS Setting

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Abstract

Background: Enhanced Recovery after Surgery (ERAS) is a multimodal approach that aims to decrease the surgical stress and speed up the post-operative recovery. The use of laxatives is one of the ERAS elements which aim to reduce post-operative ileus and stimulate gut motility. With our study, we aim to evaluate if the addition of laxatives would make any difference in the Length of Hospital Stay (LoS) and in complications, among patients, within an ERAS setting, undergoing elective colorectal resections without stoma formation.

Materials and Methods: A prospectively collected database of 220 patients, undergoing elective colorectal resections between August 2015 and June 2017 was analyzed. The study population was divided in two groups. Both groups were within an ERAS setting, but in the first group (group A), we used laxatives from postoperative day 1. The second group (group B) did not use laxatives. Patients who required stoma formation or patients with a documented complication were excluded from the analysis for LoS, but all patients were included in the analysis for complications. Our primary goal was to evaluate the LoS in each group and secondary to evaluate the post-operative complications. Non-parametric tests were used. P Values <0.05 were considered to be statistically significant. The analysis was done for the overall LoS in each group and also separately for lap right hemicolectomies, lap left hemicolectomies and open or complicated resections.

Results: 220 patients were analyzed (100 patients in group A and 120 in group B). Patients demographics (age, sex, BMI), were similar between the groups. The overall median LOS was 4 days for group A (range 2 to 6) and 5 days for group B (2 to 7)) p<0.05). LoS was statistically significant less in all subgroup analyses. Sixteen patients had complications in group A (16%) and 22 in group B (18%, 3%), but this did not reach statistical significance (p=0.64).

Conclusion: Use of laxatives from day one post-operatively, could be a safe and effective measure to reduce LoS in patients undergoing uncomplicated elective colorectal surgery, without stoma formation.

Keywords: ERAS; Length of stay; Laxatives; Prolonged post-operative ileus; Post-operative complications

Abbreviations

ERAS: Enhanced Recover After Surgery; LoS: Length of Stay; PPOI: Prolonged Post-Operative Ileus

Introduction

The enrolment of colorectal patients in Enhanced Recovery after Surgery (ERAS) protocols and its benefits are well supported by current literature and broadly implemented across healthcare systems worldwide, including the National Health System of England (NHS). ERAS is a multimodal approach, with evidence supporting that it reduces Length of Hospital Stay (LoS) and post-operative complications. Additionally, it could also improve mortality and re-admission rates as shown in latest studies [1].

The adherence in ERAS elements plays an important role in the success of the protocol and

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Figure 1: ERAS Protocol.

increasing compliance, independently improves outcomes [2]. The most common post-operative complication in colonic and rectal resections is Prolonged Post- Operative Ileus (PPOI). PPOI is defined as absence of bowel motion for more than 6 days post-operatively. The current studies suggest that this percentage is around 12.7% in colonic resection and more than 30% in rectal and complex pelvic resections (exenterations) [3]. In order to minimize incidence of PPOI and, ultimately, reduce the LoS, the enhanced recovery protocols include various elements, both intra-operatively, such is reduction of opioids and intravenous administration of fluids and post-operatively, such is introduction of regular diet immediately, alvimopam, chewing gum and laxatives. The aim of this study is to evaluate if laxatives could be used in reduce length of hospital stay and complications in patients after elective colorectal surgery within an ERAS setting.

Patients and Methods

A prospectively collected database of 220 patients, undergoing elective colorectal resections between August 2015 and June 2017 was analyzed. The study population was divided in two groups. Both groups were within an ERAS setting, but in the first group (group A), we used laxatives from postoperative day 1. The second group (group B) did not use laxatives. Patients who required stoma formation or patients with a documented complication were excluded from the analysis for LoS, but all patients were included in the analysis for complications. First, we tried to evaluate the LoS in each group. Secondly, the post-operative complications. The hypothesis was that the addition of laxatives from post-op day 1, within an ERAS setting, could reduce the LOS without increasing complications.

Patient's characteristics such as age, BMI, sex, ASA grading, did not differ significantly between the groups Median age of the patients in group A was 62 years (35 to 84) and group B was 63 years (33 to 83). Group A included 100 patients who had their operations

from August 2016 to July 2017, and the second group included 120 patients, who had their operations between August 2015 to July 2016.

The achieved power of the test was post-hoc calculated. More specifically, after the implementation of laxatives, for the patients that received laxatives (n=100) the mean and standard deviation was 3.89 and 1.34 respectively while for the other group was 4.93 and 1.14. This gave us an effect size of 0.858 and under setting the p-value to 0.05 for the hypothesis testing; the power was calculated to be 0.99 through the G-power Software for a Mann-Whitney-U-test of means comparison.

The statistical analysis was done using SPSS (Statistical Package for the Social Sciences), Mann-Whitney-U test and chi-squared test. This non- parametric analysis was done for the median Length of Stay (LoS) and complication rate. Additionally, subgroup analysis for Laparoscopic Right Hemicolectomies (LRH), Laparoscopic Left Hemicolectomies (LLH) and open or complicated resections was performed. Patients who required stoma formation or patients with a documented complication were excluded from the analysis for LoS, but all patients were included in the analysis for complications.

Ethical Considerations

ERAS protocol is a well established and approved method of standardized care in our Trust over the past 10 years. Permission was granted by the Clinical Effectiveness department (Figure 1). However, over the past years it has been under-utilized. Therefore, this study has implemented the use of laxatives, within the established ERAS protocol, as a service improvement element of the current trust guidance.

Results

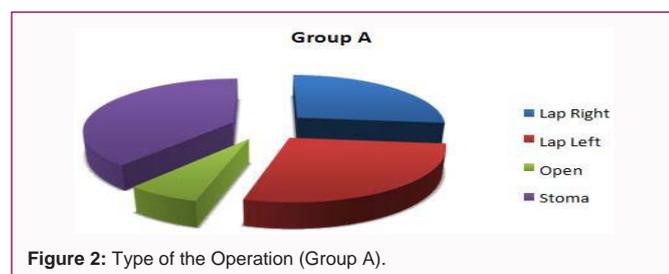
The demographic characteristics were similar in the 2 groups.

Table 1: Characteristics of the 2 Groups.

	Group A	Group B
Number of patients	100	120
Gender	60 M/40F	79 M/41F
Age (Median)	66 (44 to 87)	61 (48 to 83)
Complications (%)	16	22
Lap R Hemi	24	17
lap left resection	25	34
Open resection	6	5
Stomas	22	30
Included in analysis for LoS	55	56
Excluded from the analysis for LoS (complications, stomas, social reasons)	45	64

Table 2: Group Comparison for LoS.

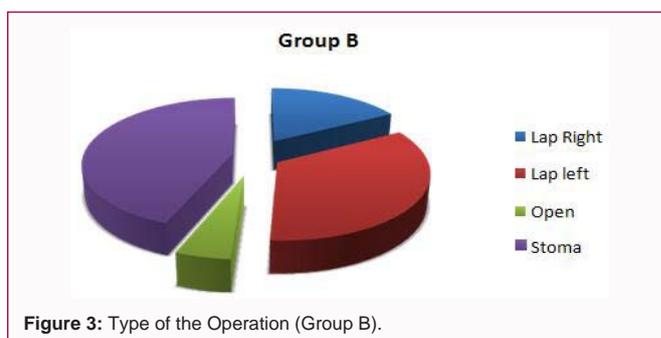
Type of surgery	Group A (100 pts) LOSH (Days-Median)	Group B (120 pts) LOSH (Days- Median)	P-Value (Mann-Whitney U test)
Laparoscopic Anterior Resections	4	5	<0.014
Lap Right Colectomies	3	5	<0.001
Open Colectomies	6	6	<0.931
Total	4	5	<0.001



They are 60 male and 40 females in group A, with a median age was 66 (43 to 87) and ASAII. In group B, we had 79 males and 41 females, with a median age of 61 (35 to 83) and ASAII as well. Also the type of the operations and stoma formation and delays in LoS for social reasons were similar. The Table 1 below outlines the previously described.

The median LoS was 4 days for group A and 5 days for group B (Range: 2 to 6 days for group A, 2 to 7 days for group B, $p < 0.001$). This result, was statistically significant in all subgroup analysis (three vs. five days for laparoscopic right sided colectomies, $p < 0.001$, and four vs. five days for laparoscopic left sided colectomies, $p < 0.014$), apart from open/complicated resections, where the median LoS was 6 days for both groups ($p = 0.931$).

The complication rate, which was in accordance to Clavien-Dindo classification [5], was less for group A; 16 patients had complications (16%), and 22 patients (18.3%) from the second group; however, this did not reach statistical significance ($p = 0.64$ - x-square test, respectively). 8% of patients from Group A went home on post-operative day 2. No patients from group B went home before day 3. No patients, without a documented complication, from Group A were discharged on day 7. With regards to Prolonged Post-Operative ileus, group A had an incidence of 6%, significantly lower compared to group B's 15% incidence ($p < 0.001$). In the Figures below is the distribution, between the type of the operation between the 2 groups, which were no differ statistically significant (Figure 2 and 3). The same applies to the leak rate, which was again, not statistically significant



different.

Discussion

The implementation of Enhanced Recovery after Surgery (ERAS) in 1997, as a multimodal approach to control postoperative pathophysiology and rehabilitation, reduces morbidity, fastens the recovery and shortens the length of hospital stay, in patients after major abdominal surgery. All this, is evidence-based and covers the entire perioperative period and is formulated into a standardized protocol [6].

A met analysis from Zhuang et al. [7] in 2013, which included 13 Studies and 1910 patients, showed a decrease in LoS of 2, 39 days and complication rate, without increasing re-admission rates or mortality. The success of the protocol though is compliance dependent. Therefore, when compliance increases within an ERAS setting and also, when minimally invasive surgery is been used, the outcomes improve; these factors are independent. Discharge patients within 72 h after elective colorectal resections, can be safely achieved for a large proportion of patients without compromising short-term outcomes [7]. There is a large, multi-institutional North American data registry, which was published in October 2017, which showed that high adherence to Enhanced Recovery Protocols resulted in earlier recovery, decreased complications, and shortened the length of hospital stay. Specifically, motivated patients, who stuck to the protocols, tolerated oral diet faster (2.4 days vs. 5.4 days), their bowel

function returned to normal at 1.9 days vs. 3.7 days, and oral pain control started sooner (2.7 days vs. 5.0 days ($P < 0.001$)) [8].

Despite the use of enhanced recovery protocols, Prolonged Postoperative Ileus (PPOI), which is defined as absence of bowel motions of more than 7 days, remains a significant problem after colorectal resections; its incidence is 12.7% in colon resections and 30% in rectal resections. It is worst in right colectomies. New regimens for better prophylaxis are needed, and further research on PPOI treatment is important.

Laxatives, as previously described, are oral agents that are used for multiple purposes, such as stimulation of gut motility and reduction of constipation in acute i.e. opioid use or chronic conditions. While generally, there is a preference for different types of laxatives, based on condition treated, for PPOI there is no preference [9,10].

Gianpiero's et al. study supports that laxatives can reduce the length of hospital stay [11]. Also, Zingg et al., studied the effect of bisacodyl and found that it positively affects LOS, without increasing complications and published it in *Int J Col Disease* in 2007 [12]. A systematic review and meta-analysis of randomized controlled trials, states that the use of laxatives within an ERAS setting reduces the LOS and complication rate in liver resections [13]. Other studies on the management of postoperative constipation in anorectal surgery conclude that laxatives help with post-op and also, they improve the bowel function after minimally invasive urogynecological surgery [14]. Additionally, bisacodyl in radical hysterectomy can reduce LOS of 1 day. There is a role of magnesium in earlier return of bowel motility following liver resections; studies have shown that it can reduce LoS by 1 day [15].

There were some studies, suggesting that the use of laxatives after colorectal resections, can increase the anastomotic leak rate, however, there was never strong evidence to support this, thus the Enhanced Recovery After Surgery (ERAS) Society Group, in their recommendations, which were published in *World J Surg* 2013 recommend the use of laxatives as one of the postoperative elements to reduce postoperative ileus. The previously published studies, use different types of laxatives as each category acts in a different way to promote bowel motility and relief of constipation; no definite evidence up to now, to for the use of one category better than the others [16].

Despite the supporting evidence for the use of laxatives for reducing PPOI and ultimately reduce LoS, the American Society of Colon and Rectal Surgeons (ASCRS) and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) in their latest Guidelines, published in 2017, recommend the use chewing gum and alvimopan as elements to prevent postoperative ileus, and not the use of laxatives [16].

Our study states favorable outcomes against the previously mentioned studies, regarding the LoS. Because this is an observational study, it has multiple biases and limitations and most importantly, lacks randomization. However, the group populations were not significantly different in demographic characteristics and operation type. Therefore, it gives promising results and it could be used as a base for more research on the topic.

Conclusion

ERAS protocols have proven benefit in reducing LoS and complication rate; however, they are compliance dependent; the

higher the compliance, the more likely is these protocols to succeed. When we add laxatives, automatically, we increase the compliance, since we comply, with one more element. We believe, that their use, from postoperative day one, could be a safely and effectively reduce length of stay, in the group of colorectal

Patients, who undergo uncomplicated resections, without stoma formation. Patients with right colostomies benefits more and there is no convincing literature that they could affect anastomotic leak rate however, since previously published data does not show elicited clear evidence, further, prospective studies and RCTs are necessary in order to establish clarity amongst colorectal surgery evidence and expand laxative use in within ERAS protocols at a worldwide scale.

Declarations

Ethics approval and consent to participate

- The Enhanced Recovery after Surgery Protocol is the standard practice in Newcastle Hospitals, for at least 12 years, so a new approval was not needed.
- All patients are treated within the pathway, so no need for patient's approval was needed either. All patients received a booklet with details about their care, within the ERAS, in their first visit in outpatient's clinic, where a detailed discussion was always done.
- The study was not involving animals.

Availability of data and materials

- The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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