ORIGINAL RESEARCH

Role of multimodal perioperative management protocol in colorectal cancer surgery

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ABSTRACT

Background-The enhanced recovery after surgery (ERAS) group presenting a comprehensive study of perioperative care for colorectal surgery / colorectal resection is a set of interventions, when combined, lead to early return of gut function, fewer complications and a shorter length of stay. Traditional hospital stay of 10 - 14 days following major bowel resection had been accepted as normal practice up until recently. **Aim**-To study the impact of multimodal perioperative management protocol in patients of colorectal cancer surgery. **Objective**-To measure the outcomes such as hospital stay, complication, 30 days readmission rate in multimodal and control group. **Material and methods**-**Study design**-Prospective randomized control study. **Sample size**-30 patients of Colorectal cancer. **Statistical analysis**-simple randomization by block method, unpaired t-test. **Results**-Out of 30 patients {n=14 in multimodal group and n=16 in control group}, hospital stay of 6.64+/-0.842(median 6-9) and 8.25+/-1.52.(median 6-12)days(p=0.002), complication rate of 13.40% and 20.31%(p=0.019), 30-days readmission rate of 14.28% and 25%(p=0.029) and mortality rate of 7.14% and 12.5% were noted respectively in multimodal and control groups. **Conclusion**- The use of multimodal perioperative management protocol in colorectal cancer reduced the hospital stay, complication rate, readmission rate and mortality significantly as compared to the control group.

Keywords – Colorectal cancer, Perioperative management, Multimodal management, ERAS, hospital stay

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INTRODUCTION

Patients undergoing colorectal surgery, where resection of bowel is involved, can have a complication rate of between 15% and 20% [1–3]. Such complications can prolong postoperative hospital stay by 6 to 10 days [4]. The financial burden imposed on health care systems due to prolonged hospital stay after colorectal surgery can be significant. In an effort to reduce the length of hospital stay after colorectal surgery, Kehlet et al. [5] were the first to describe in detail a specific protocol called “fast-track” or “enhanced recovery after surgery” protocol which had the potential to reduce hospital stay to a mean of 4 days. Many protocols have been put forward by hospital groups which consist of varying individual preoperative, intraoperative, and postoperative fast-track elements such as preoperative counseling and feeding, no bowel preparation, perioperative high oxygen concentrations, active prevention of hypothermia, no routine use of nasogastric tubes and drains [6–14]. Wind et al [15] conducted a metaanalysis of six studies (three RCTs and three CCTs) with a total of 512 patients which showed a reduction in primary hospital stay and morbidity for patients in fast-track programs after elective colorectal surgery. However, in 2000, Basse and Kehlet described a clinical pathway to accelerate recovery after colonic resection which dramatically cut down length of stay. Their study described a median stay of 2 days with a readmission rate of 15%[16-17]. The aim of our study is to attenuate the surgical stress response, accelerate recovery, decrease complications and to minimize hospital stay, readmission rate and mortality.

MATERIAL AND METHODS

Design – Prospective randomized control study.

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Setting – Patients who are undergoing elective colorectal cancer surgery in SMS hospital in year 2016 -17

Sample Size – Sample size was calculated to be 30 in both multimodal and control groups. The study was powered 80% ($\alpha = 0.05$, $\beta = 0.80$) to assuming the difference in mean duration of nasogastric tube removal and early feeding to be 1.1 days and SD = 1 in multimodal and control group. Hence for study purpose 30 subjects were required. Randomization of patients was done by Simple block randomization method.

Selection Criteria

Inclusion criteria- a) patients who underwent elective colorectal resection for cancer with informed consent.

Exclusion criteria – a) Metastatic disease, **b)** Clinical depression, **c)** Combined procedures with other surgical speciality d) patients who does not give consent **e)**patients who underwent Neoadjuvant chemoradiotherapy.

Plan of action

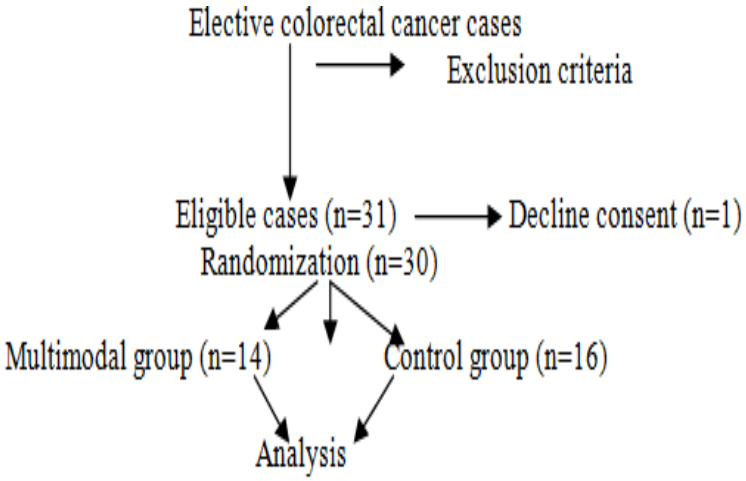

Figure - flow chart of plan of action

Statistical analysis- Continuous data of the multimodal and control group was expressed in the form of proportion or percentage and analyzed by unpaired t-test .

Methodology -The patients who received intravenous fluid restriction, unrestricted oral intake with prokinetic agents, early ambulation, early nasogastric tube removal, early enteral feeding and pre operative antibiotic prophylaxis were included in the multimodal group. The control group included patients who didnt receive the multimodal care during perioperative period.

RESULTS AND OBSERVATIONS

Distribution of Post operative parameters in both groups

S.No.	Post op parameters	Multimodal group(n=14) Mean(2SD) days	Control group (n=16) Mean(2SD) days	p value
1	NG removal	1.35(1.99)	2.06(1.54)	0.038
2	Post op mobilization	1.0(0.78)	1.68(1.40)	0.003
3	Bowel sounds	1.92(0.95)	2.64(1.20)	0.001
4	Flatus	2.42(1.02)	3.31(1.40)	0.001
5	Motion	2.78(1.78)	4.0(2.42)	0.004
6	Oral feeding	2.21(1.73)	3.06(2.07)	0.021
7	Normal /solid diet	3.85(1.32)	4.81(2.09)	0.007
8	Urine catheterization	2.71(1.22)	3.37(2.05)	0.044
9	Fluid restriction	2.42(1.09)	3.65(1.07)	0.001
10	Hospital stay	6.64(1.68)	8.25(3.04)	0.002

*NG-nasogastric tube, op-operative, n=number of patients, SD=standard deviation

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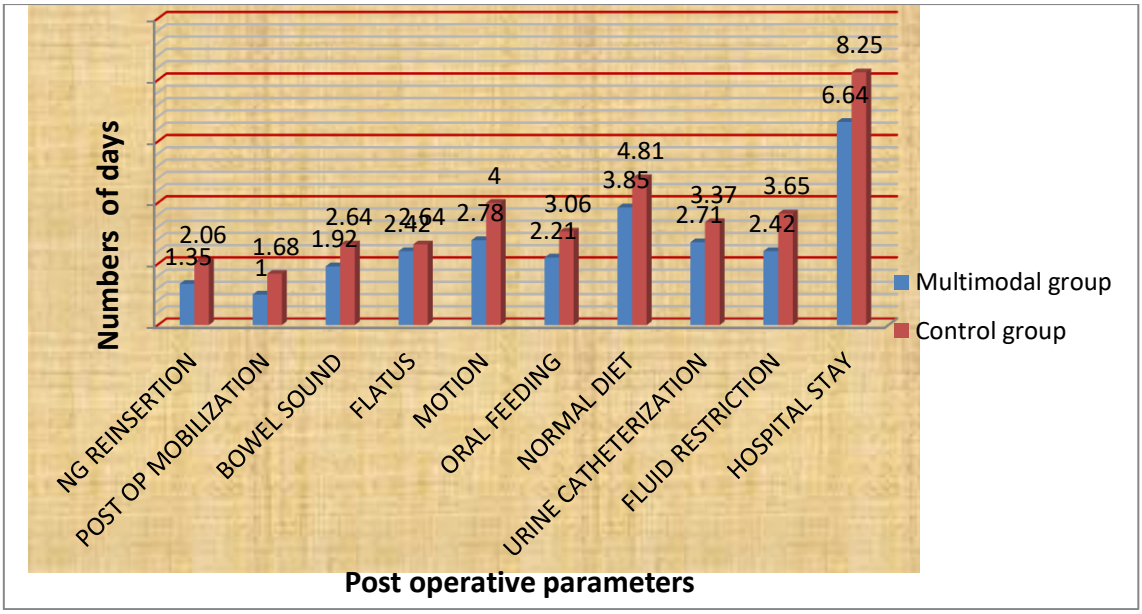
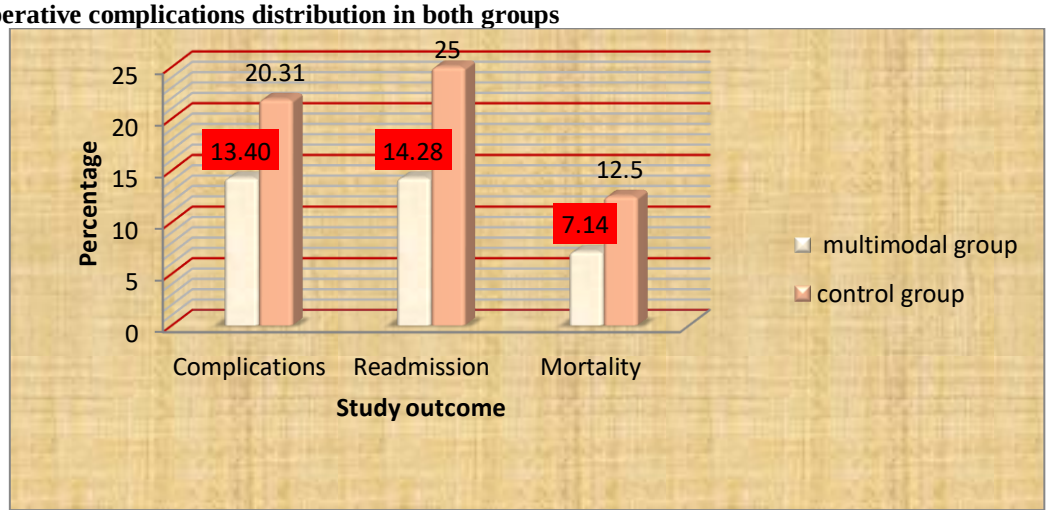


Distribution of Postoperative complications in both the groups

S.No.	Complications	Multimodal group (n=14)						Control group(n=16)						p value
		AR n=4		APR n=4		Hemi colectomy n=6		AR n=4		APR n=6		Hemi colectomy n=6		
		n	%	n	%	N	%	n	%	n	%	n	%	
1	Wound infection	1	25	1	25	1	16.67	1	25	2	33.33	2	33.33	0.019
2	Anastomotic leak	1	25	0	0	0	0	1	25	0	0	1	16.67	
3	Urinary /sexual dysfunction	0	0	2	50	0	0	1	25	3	50	0	0	
4	Stoma complication	0	0	1	25	0	0	0	0	2	33.33	0	0	
5	Chest infection	1	25	0	0	1	16.67	2	50	1	16.67	1	16.67	
6	Cardiac	1	25	1	25	0	0	2	50	1	16.67	0	0	
7	PONV	1	25	0	0	2	33.33	2	50	1	16.67	1	16.67	
8	Mortality	1	25	0	0	0	0	1	25	0	0	1	16.67	

*PONV-post operative nausea and vomiting, AR-anterior resection, APR-abdominal perineal resection

Postoperative complications distribution in both groups



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Comparision of multimodal perioperative protocol in various Randomized control studies

Study	Preoperative counselling	Bowel preparation	Preoperative Feeding	Fluid restriction	Minimal invasive incision	NG removal	No use of drain	Post operative mobilization	Post operative feeding	urine catheter	Systemic use of morphine	Antibiotic prophylaxis
Anderson ADG et al (2003)	+	_	+	_	+	+	+	+	+	_	_	+
Delney CP et al(2003)	+	+	_	+	_	+	_	+	+	+	+	_
Gatt M et al(2005)	+	_	+	_	+	+	+	+	+	_	_	+
KhooCK et al(2007)	+	+	_	_	_	+	_	+	+	_	_	_
Present study	+	+	+	+	+	+	_	+	+	+	_	+

Comparision of results of various Randomized control studies

Study	Year	Design	No. of patients (n)		Hospital stay(days) Mean(2SD)		Mortality %		Readmission %	
			MG(n)	CG(n)	MG	CG	MG	CG	MG	CG
Anderson ADG[6]	2003	RCT	14	11	4 (1.8)	7(2.1)	0	9	0	0
Delney CP[8]	2003	RCT	31	33	5.4 (2.5)	7.1 (4.8)	-	-	10	18
Gatt M[10]	2005	RCT	19	20	6.6 (4.4)	9 (4.6)	5	0	5	20
Khoo CK[13]	2007	RCT	35	35	5 (8.5)	7 (14.35)	0	6	9	3
Present	2017	RCT	14	16	6.64 (1.68)	8.25 (3.04)	7.14	12.5	14.28	25

MG-multimodal group, CG-control group, RCT-randomized control trial

DISCUSSION

In our study, it was found that the mean duration of return of bowel sounds was 1.92+/-0.95 days vs.2.64+/-1.20 days in Mutimodal Vs control group, patient passed motion in about 2.78+/-1.78 days as compared to 4.0+/-2.42 days in control group and tolerance to normal diet (3.85+/-1.32 vs.4.81+/-2.09) days. This was found to be significantly better in multimodal group as compared to the control group. This has been found to be in concordance with Arenal JJ et al [1] who concluded return of bowel movements in (1.7±0.89 vs. 3.27±1.3)days, normal pattern of defecation (3.4±0.77 vs. 4.38±1.18) days and time of tolerance of solid diet in (2.48±0.85 vs. 4.77±1.81)days. The mean duration of nasogastric removal in the 2 groups was found to be (1.35+/-1.99 vs.2.06+/-1.54)days and passing of flatus was in (2.42+/-1.02 vs.3.31+/-1.40) days. These differences were again found to be significant which is comparable with Reissman et al [24]. The early feeding in the 2 groups i.e. 2.21+/-1.73 vs. 3.06+/-2.07 days respectively was comparable with Anderson et al [6]. It, thus, concluded that patients in the optimization group tolerated a regular hospital diet significantly earlier than controls (48 versus 76 h; $P < 0.001$). Next parameter compared was the hospital stay and it was found to be 6.64+/-1.68 vs.8.25+/-3.04 days in the multimodal and control group respectively. These results were comaparable with Anderson ADG et al [6] where hospital stay was (4+/-1.8 vs 7+/-2.1days, p was 0.002), Delaney CP et al [8] with stay of (5.4 vs. 7.1 days; $p = 0.02$), Gatt M et al [10] showing hospital stay of (6.6 +/-4.4 vs 9 +/-4.6days, $p = 0.027$), Khoo CK et al [13] with (5 vs. 7 days; $p < 0.001$) and Yang et al [18] had (6.0 ± 1.0 vs 11.7 ± 3.8 days, $p < 0.001$). It was seen that maximum hospitalization was found in study done by Khoo CK et al [13] while the minimum was found in Anderson ADG et al [6]. The mean duration of catheterization in our study was 2.71+/-1.22 vs.3.37+/-2.05days in the 2 groups which concordance with Gatt M et al [10] with a p value of 0.022, hence has been found to be significant. The mean intravenous fluid required/used was calculated to be (2.42+/-1.22 vs.3.37+/-2.05) litres in our study which is comparable with Mackay et al [21] who concluded that the median total intravenous fluid intake in the restricted group was 4.50 (4.00-5.62) litres as compared to 8.75 (8.00-9.80)

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litres in the standard group (p< 0.001). The overall complication rate in our study was found to be 13.40% and 20.31% in multimodal and control groups respectively with p=.0019 which was statistically significant. This is in accordance with Brandstrup et al [22] who concluded that the restricted intravenous fluid regimen significantly reduced postoperative complications both by intention-to-treat (33% versus 51%, P = 0.013) and per-protocol (30% versus 56%, P = 0.003) analyses. The number of cardiopulmonary complications were 7% and 24% (p = 0.007) and tissue-healing complications were 16% and 31% (p = 0.04) respectively in the 2 groups which were found to be statistically significant. Similar results have been noted by Noblett et al [26] who concluded that major postoperative complications were 2% versus 15% in the 2 groups of their study with p = 0·043. In our study, readmission rate was calculated as 14.28% and 25% in the multimodal and control groups respectively with p =0.029. This was similar to Christensen et al [20] who found a readmission rate of 15% in the fast-track group and 16% in the control group patients. Similarly, Gustafsson et al [23] concluded readmissions was significantly reduced with increasing adherence to the ERAS protocol (>90%) compared to low ERAS adherence (<50%). Our study also took into consideration the mortality rate which was recorded as 7.5% in multimodal and 12.5% in control group. Similar results have been put forth by Anderson ADG et al [6] (0% vs9%), Gatt M et al [10] (5% vs 0%) and Khoo CK et al [13] (0% vs 6%) respectively.

CONCLUSION

Enhanced recovery programs is shown to be effective in reducing overall hospital stay and readmission without compromising patient safety or increasing morbidity. There is good evidence that multimodal management protocol form the mainstay of elective colorectal surgery.

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