Section: Radiotherapy

Original Research Article

TO STUDY THE EFFECT OF CHEMOTHERAPY AFTER CONCURRENT CHEMO RADIATION ON PATHOLOGICAL TUMOR RESPONSE IN LOCALLY ADVANCED CARCINOMA RECTUM

B. Sheela[1], Prakash[2], C.Sanjeevakumari[3], Lohitha[4], Ashwini[4], Nanditha[4]

[1]Associate Professor, Department of Radiotherapy, MNJ Cancer Hospital/ Osmania Medical College, Red Hills, Lakdikapul, Hyderabad, Telangana, India.
[2]Assistant Professor, Department of Radiotherapy, MNJ Cancer Hospital/ Osmania Medical College, Red Hills, Lakdikapul, Hyderabad, Telangana, India.
[3]Professor, Department of Radiotherapy, MNJ Cancer Hospital/ Osmania Medical College, Red Hills, Lakdikapul, Hyderabad, Telangana, India.
[4]Senior Resident, Department of Radiotherapy, MNJ Cancer Hospital/ Osmania Medical College, Red Hills, Lakdikapul, Hyderabad, Telangana, India.

Received : 04/07/2023
Received in revised form : 11/08/2023
Accepted : 25/08/2023

Keywords:
Neoadjuvant concurrent chemoradiotherapy (NCRT), Colorectal cancer (CRC), neoadjuvant Chemotherapy (NACT).

Corresponding Author:
Dr. Lohitha,
Email: drlohita111mbbs@gmai.com

DOI: 10.47009/jamp.2023.5.5.165

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (5); 851-857

Abstract

Background: The current standard treatment of locally advanced rectal carcinoma is [NCRT] followed by LAR/APR followed by postoperative adjuvant chemotherapy after which is a multimodality approach. Local recurrence rates range from 25% to 50% for patients with T3–T4 and/or node-positive cancer. The aim is to study the effect of chemotherapy after concurrent chemo radiation on pathological tumor response in locally advanced carcinoma rectum in tertiary cancer centre. **Materials and Methods:** It is prospective comparative study done in 30 patients presenting to the department of Radiotherapy with locally advanced carcinoma rectum fulfilling the inclusion criteria were recruited for the study and assigned randomly in two Groups, consists 15 patients per group. In this study acute toxicities have been evaluated in both groups during chemoraditation and chemotherapy according to CTCAE Version 5. **Result:** Toxicities during chemoradiation in both groups are almost similar in experimental group during chemotherapy toxicities are grade 2 - 3.which are tolerable with good compliance .radiological and pathological response are almost similar in both groups. **Conclusion:** Addition of neoadjuvant consolidation chemotherapy after CRT is a safe approach that may lead to better response and increased compliance with systemic chemotherapy regimen and reducing systemic metastasis, although not significant.

INTRODUCTION

Colorectal cancer (CRC) remained as the major world-wide health problem. It is ranked at 3rd most frequently diagnosed cancer and it is the 2nd most leading cause of cancer death in USA. Colorectal cancer is the 3rd most common cancer in the men (10.6%) and it is 2nd most common in women (9.4%) worldwide with nearly 2 million new cases recorded in 2020 (GLOBOCON 2020). According to these colorectal cancers are the 3rd most commonly diagnosed cancer in both sexes. Colorectal cancer is the 3rd most common cancer in males with incidence of 10.6% following lung and the prostate cancer.

Colorectal cancer is the 2nd most common cancer in females with incidence of 9.4% following breast cancer. In India rectal carcinoma is the 9th most common with an Annual Incidence Rates of 4.1/100000 in males. For women rectal cancer does not come in top ten cancers, where as colon cancer ranks at 9. The incidence of colorectal cancer at MNJ Cancer Hospital is approximately 236 cases newly diagnosed rectal cancers out of total attending 8563 patients at MNJ during the period of 2021-2022 year with the incidence rate being 2.75%.[1]

The standard care for the Rectal carcinomas is multidisciplinary approach with preoperative chemo-radiotherapy is currently considered as the standard therapy for the patients with locally advanced rectal carcinoma. Pathological complete response (pCR) following neoadjuvant treatment for locally advanced rectal cancer (LARC) is associated with better survival, less local recurrence, and less distant failure. Furthermore, pCR indicates that the rectum may have been preserved. This study gives an overview of adding chemotherapy and its effects on pCR after concurrent chemo radiation in locally advanced rectal carcinoma (LARC) and analyzes how these perform in achieving pCR as compared with the standard of care.

In the world, colorectal cancer accounts for 10% of all cancer types and is the second leading cause of cancer-related fatalities.[2] Total mesorectal excision (TME) and postoperative adjuvant chemotherapy following neoadjuvant concurrent chemoradiotherapy (NCRT), which uses a multimodal strategy, are the current standard treatments for locally advanced rectal malignancy. Patients with T3-T4 and/or node-positive malignancy had local recurrence rates that range from 25% to 50%.[3] With Neoadjuvant concurrent chemoradiotherapy, the chance of local recurrence is greatly decreased.[4] The rate of distant metastases is still estimated to be as high as 30%, and the survival benefit of NCRT has not been proven.[5] As a result of inadequate management of micrometastases, this has prompted researchers to look for new, alternative approaches in neoadjuvant therapy for controlling distant metastases and improving survival rates.

Patients who experience a pathological complete response (pCR) after NCRT have higher survival rates, and numerous studies have demonstrated the significance of pCR as a prognostic indicator for NCRT-treated rectal cancer patients. The rate of pCR in these investigations ranged from 15% to 30%.[6,7] As a result, numerous studies have been done to improve pCR rates by altering perioperative treatment plans. To raise the rate of pCR and hence boost survival rates, numerous researchers have experimented with various chemotherapy regimens. The outcomes of combining chemotherapy to neoadjuvant radiotherapy (NART), which increases the radiation effect as a radio sensitizer, served as the foundation for these initiatives. The anticancer efficacy of NCRT in particular, though, is still unknown. There hasn't been a single chemotherapy drug that has considerably improved the pathological complete response up until this point. Increasing the duration of chemotherapy may be a rational method to improve the efficacy of NCRT, the rate of pCR, and the likelihood of survival. In order to establish tumour response to concurrent chemoradiotherapy (CRT) and recover from CRT-related toxicity, there is a six- to eight-week rest interval following the conclusion of conventional NCRT therapy before surgery. After administering the same chemotherapy for three further cycles during the recovery period after the conclusion of six weeks of 5-fluorouracil (5-FU)-based CRT, Habr-Gama et al. reported a 65% clinical complete response rate. They hypothesized that further treatment could raise the pCR rate while potentially having an anticancer effect and radiosensitizing effects.[8]

In this situation, an alternate strategy would be to administer a safe, efficient, low-toxic, and affordable chemotherapy regimen to patients with rectal cancer getting neoadjuvant therapy during the "rest" phase after CRT is finished. With this method, chemotherapy will be able to radiosensitive patients in the best possible way and provide any potential antitumor effects at a systemic dose. It is anticipated that this approach may result in a decrease in tumour size and nodal involvement, as well as an improvement in the percentages of pathological complete responses and survival. In this study, we looked into the impact of addition of chemotherapy on tumour response and survival rates before to surgery.[9-11]

Delivering Chemotherapy in the neoadjuvant setting has the promise to remedy many of the pitfalls associated with adjuvant Chemotherapy approaches that resulted in poor compliance. With the high incidence of postoperative complications and treatment- related toxicities limiting adjuvant Chemotherapy compliance across multiple trials, neoadjuvant Chemotherapy (NACT) may allow for greater treatment compliance. Avoiding Chemotherapy in the postoperative setting might also reduce overall toxicity rates. Earlier delivery of full-dose, systemic therapy to eliminate micrometastatic disease has the potential to decrease the risk of disease progression during treatment and improve disease- related outcomes. Others have noted that positioning surgery as the final step in the treatment algorithm for LARC could allow for earlier reversal of a diverting stoma postoperatively.[12-14] With NAC, Total Neoadjuvant therapy (TNT) for rectal cancer can also facilitate the selection of patients who may benefit from organ preservation, or a watch- and-wait approach, for their cancer. In this context, NAC added to neoadjuvant CRT might help further identify patients for whom surgical resection can be safely omitted.

MATERIALS AND METHODS

It is prospective comparative study done in Department of Radiotherapy, MNJ Institute of Regional Cancer Centre/Osmania Medical college, Hyderabad study December 2020 to Novermber 2022. 30 patients presenting to the department of Radiotherapy with locally advanced carcinoma rectum fulfilling the inclusion criteria were recruited for the study and assigned randomly in two Groups, consists 15 patients per group. Approval from the institute ethical committee was obtained on 10-12-2020. All the patients recruited for the study were explained in detail about the study, the type of treatment and the advantages and disadvantages of the treatment. Once the patient had understood and their queries answered informed consent was obtained from the patient, agreeing for their participation in the study.

Inclusion Criteria

Patients age >18yrs <70yrs Patients of both sexes ECOG score 0-2 with Histological proven Carcinoma Rectum and carcinoma rectum planned for neo adjuvant chemo radiation

Exclusion Criteria

ECOG >2 Patients with distant metastases and who had undergone surgery for Carcinoma Rectum

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Procedure

Patients were selected for the study in OPD department as per the inclusion criteria, after taking proper consent will undergo Pre-treatment Workup was done as Complete History, Complete physical examination including digital rectal examination.

All routine work up Includes CBP, RFT, LFT, RBS, Serum electrolytes, HIV, HbsAg., Colonoscopy, Histopathological examination, MRI Abdomen and pelvis, Chest X Ray and CEA.

Treatment Protocol

Patients will be randomly assigned into two Arms- A (EXPERIMENTAL ARM) & B (CONTROL ARM). In EXPERIMENTAL ARM A – Patients will undergo treatment Radiotherapy 50.4Gy in 28 fractions (1.8Gy per fraction) along with Concurrent Chemotherapy daily Capecitabine for 5 to 6 weeks followed by Chemotherapy with 3 weekly CAPEOX (Capecitabine plus oxaliplatin) for 3 cycles followed by surgery after 6 weeks.

In Control Arm B - Patients will undergo treatment Radiotherapy 50.4Gy in 28 fractions (1.8Gy per fraction) along with Concurrent Chemotherapy daily Capecitabine for 5 to 6 weeks followed by surgery after 6 weeks.

Acute toxicities were evaluated during Chemoradiotherapy in both arms and during chemotherapy in experimental arm. Radiological response with MRI was assessed before surgery in both arms and compared among both arms according to RECIST 1.1 criteria.[23] Pathological Response was evaluated after surgery in both arms and compared among both arms according to modified ryan tumor regression score.[24]

RESULTS

Total 30 patients were included in the study. These 30 patients are randomly assigned into two Arms A & B, where each group contain 15 patients each.

Table 1: Baseline Characteristics

			ARM		P value
			Experimental	Control	
Age in mean +/-SD years			49.13 ± 10.7	53.3 ± 8.5	0.15
Gender	Male	n	11	10	0.21
		%	73.3%	66.7%	
	Female	n	4	5	
		%	26.7%	33.3%	
Total		n	15	15	
		%	100.0%	100.0%	
Performance Status					
ECOG	1	n	6	2	
		%	40.0%	13.3%	2.72
	2	n	9	13	
		%	60.0%	86.7%	

There is no significance with age and gender in both groups.

Table 2: Distribution according to performance status staging

			ARM		P-value
			Experimental	Control	
T	T3	n	9	8	0.13.
		%	60.0%	53.3%	
	T4	n	6	7	
		%	40.0%	46.7%	
N	N0	n	2	3	
		%	13.3%	20.0%	
	N1	n	9	7	
		%	60.0%	46.7%	0.75.
	N2	n	4	5	
		%	26.7%	33.3%	

There is no significance in performance status staging.

Table 3: Distribution according to N-staging histopathology.

			ARM		p- value
			Experimental	Control	
Histology	Well Differentiated Adenoca	n	6	6	
		%	40.0%	40.0%	
	Moderately differentiated adenoca	n	7	7	0.72
		%	46.7%	46.7%	
	Poorly differentiated adenoca	n	2	2	
		%	13.4%	13.3%	
Total		n	15	15	
		%	100.0%	100.0%	

There is no significance to N-staging histopathology.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 4: Distribution according to histology histological grading.

			ARM		p-value
			Experimental	Control	
Grade	G1	n	6	6	
		%	40.0%	40.0%	
	G2	n	7	7	0.10
		%	46.7%	46.7%	
	G3	n	2	2	
		%	13.3%	13.3%	
Total		n	15	15	
		%	100.0%	100.0%	

There is no significance to histology histological grading.

Table 5: Distribution according to histological grade tumor location

			ARM		p-value
			Experimental	Control	
Tumor Location	Lower Rectum	n	1	2	
		%	6.7%	13.3%	
	Lower Rectum And Anal Canal	n	1	2	
		%	6.7%	13.3%	
	Mid & Lower Rectum	n	5	0	
		%	33.3%	0.0%	0.50
	Mid Rectum	n	3	5	
		%	20.0%	33.3%	
	Upper & Mid Rectum	n	2	0	
		%	13.3%	0.0%	
	Upper Rectum	n	1	6	
		%	6.7%	40.0%	
	Upper, Mid & Lower Rectum	n	2	0	
		%	13.3%	0.0%	
Total		n	15	15	
		%	100.0%	100.0%	

There is no significance to histological grade tumor location.

Table 6: Distribution of tumor location tumor response post NCRT and NACT (radiological response)

			ARM		p-value
			Experimental	Control	
Radiological Response: According to Recist 1.1 criteria	Complete response	n	0	0	
		%	0	0	
	Partial response	n	12	14	0.47
		%	80.0%	93.3%	
	Defaulted	n	2	1	
		%	13.3%	6.7%	
	Expired post CT	n	1	0	
		%	6.7%	0.0%	
Total		n	15	15	
		%	100.0%	100.0%	

Table 7: Tumor response post-surgery (pathological response)

Pathological response tumor regression score (Modified Ryan Score)	Groups			
	Experimental Arm		Control Arm	
	N	%	N	%
0	0	0.00	0	0.00
1	0	0.00	0	0.00
2	12	80.00	12	80.00
3	0	0.00	2	13.33
Defaulted	2	13.33	1	6.67
Expired Post CT	1	6.67	0	0.00
P-value	0.31			

Table 8: Pathological T downstaging in experimental arm

Pathological T downstaging – experimental arm		TNM staging post treatment- T			
		t1	t2	t3	t4
TNM staging (pretreatment)- T	t3	4	3	0	0
	t4	1	4	0	0
Total		5	7	0	0
Pathological-T downstaging – control arm					
TNM staging (pretreatment)- T	t3	3	3	1	0
	t4	0	3	2	2
Total		3	6	3	2

In experimental group: Expired Post CT: 1, Defaulted: 2: Total patients analysed: 12.
Control group: Defaulted: 1: Total patients analysed: 14.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 9: Pathological t downstaging between two arms.

	Experimental Arm	Control Arm
T Downstage +	12 (80%)	13 (86.66%)
T Downstage -	3 (20%)	2 (13.33%)
P-Value	0.624.	
N Downstage +	10 (66.66%)	9 (60%)
N Downstage -	5 (33.33%)	6 (40%)
P-Value	0.704	

Table 10: Pathological N downstaging between two arms

Pathological N downstaging – experimental arm		TNM staging post treatment- N		
		n0	n1	n2
TNM staging (pretreatment)- n	n0	1	1	0
	n1	7	0	0
	n2	2	1	0
Total		10	2	0
TNM- staging (pretreatment)- n of control arm	n0	3	0	0
	n1	4	2	0
	n2	4	1	0
Total		11	3	0

Expired Post CT: 1: Defaulted: 2: Total patients analysed: 12
Defaulted: 1: Total patients analysed: 14.

Table 11: Toxicities during NCRT in both groups

Toxicities of experimental arm	GRADES							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Dermatitis	4	26.67	2	13.33	0	0.00	0	0.00
Anaemia	1	6.67	0	0.00	0	0.00	0	0.00
Neutropenia	2	13.33	2	13.33	0	0.00	0	0.00
Thrombocypenia	0	0.00	0	0.00	0	0.00	0	0.00
Nausea	3	20.00	3	20.00	1	6.67	0	0.00
Vomiting	3	20.00	2	13.33	0	0.00	0	0.00
Diarrhea	2	13.33	3	20.00	1	6.67	0	0.00
Stomatitis	0	0.00	0	0.00	0	0.00	0	0.00
Peripheral Sensory Neuropathy	2	13.33	1	6.67	0	0.00	0	0.00
Blood Bilirubin Increased	4	26.67	0	0.00	0	0.00	0	0.00
ALP increased	0	0.00	0	0.00	0	0.00	0	0.00
ALT Increased	0	0.00	0	0.00	0	0.00	0	0.00
Creatinine elevated	0	0.00	0	0.00	0	0.00	0	0.00
Proteinuria	0	0.00	0	0.00	0	0.00	0	0.00
Haematuria	0	0.00	0	0.00	0	0.00	0	0.00
Hand-Foot Syndrome	0	0.00	0	0.00	0	0.00	0	0.00
Toxicities of control arm								
Dermatitis	3	20.00	4	26.67	1	6.67	0	0.00
Anaemia	0	0.00	0	0.00	0	0.00	0	0.00
Neutropenia	1	6.67	2	13.33	0	0.00	0	0.00
Thrombocypenia	0	0.00	0	0.00	0	0.00	0	0.00
Nausea	3	20.00	4	26.67	0	0.00	0	0.00
Vomiting	4	26.67	2	13.33	0	0.00	0	0.00
Diarrhea	3	20.00	3	20.00	2	13.33	0	0.00
Stomatitis	0	0.00	0	0.00	0	0.00	0	0.00
Peripheral Sensory Neuropathy	0	0.00	0	0.00	0	0.00	0	0.00
Blood Bilirubin Increased	4	26.67	1	6.67	0	0.00	0	0.00
ALP increased	0	0.00	0	0.00	0	0.00	0	0.00
ALT Increased	1	6.67	0	0.00	0	0.00	0	0.00
Creatinine elevated	0	0.00	0	0.00	0	0.00	0	0.00
Proteinuria	0	0.00	0	0.00	0	0.00	0	0.00
Haematuria	0	0.00	0	0.00	0	0.00	0	0.00
Hand-Foot Syndrome	0	0.00	0	0.00	0	0.00	0	0.00

Toxicities during NCRT are significant when compared in grade of toxicity.

Table 12: Toxicities during NACT in experimental arm

TOXICITIES	GRADES							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Anaemia	0	0.00	0	0.00	0	0.00	0	0.00
Neutropenia	1	6.67	2	13.33	0	0.00	0	0.00
Thrombocypenia	0	0.00	0	0.00	0	0.00	0	0.00

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Nausea	5	33.33	3	20.00	1	6.67	0	0.00
Vomiting	3	20.00	2	13.33	0	0.00	0	0.00
Diarrhea	2	13.33	1	6.67	1	6.67	0	0.00
Stomatitis	2	13.33	2	13.33	0	0.00	0	0.00
Peripheral Sensory Neuropathy	4	26.67	4	26.67	1	6.67	0	0.00
Blood Bilirubin Increased	7	46.67	2	13.33	0	0.00	0	0.00
ALP increased	2	13.33	1	6.67	0	0.00	0	0.00
ALT Increased	5	33.33	0	0.00	0	0.00	0	0.00
Creatinine elevated	4	26.67	0	0.00	0	0.00	0	0.00
Proteinuria	0	0.00	0	0.00	0	0.00	0	0.00
Haematuria	0	0.00	0	0.00	0	0.00	0	0.00
Hand-Foot Syndrome	5	33.33	0	0.00	0	0.00	0	0.00

Toxicities during NACT in experimental arm is significant when compared in groups.

DISCUSSION

This study mainly focus on addition of chemotherapy after neoadjuvant Chemoradiotherapy and before surgery may increase pathological response in patients with locally advanced rectal cancer, and may provide the opportunity to follow this group of patients without surgery in the future, in terms of showing real-life data. We hope that it can shed light on other studies to be conducted in this respect.

In this present study total 30 patients are recruited and randomly assigned to two groups A (experimental arm) & B (Control arm), 15 patients for each group. Group A received Neoadjuvant Concurrent chemoradiation followed by 3 cycles of Chemotherapy with CAPEOX Regimen followed by surgery while Group B received Neoadjuvant Concurrent chemoradiation followed by surgery. Group B considered as control arm for the comparision. Out of 15 patients in Group A, 2 patients were defaulted after neoadjuvant concurrent chemoradiation and 1 patient expired post chemotherapy. In Group B, Out of 15 patients 1 patient defaulted for surgery. Therefore in Group A total 12 patients underwent surgery and in Group B 14 patients underwent surgery. On the Basis of Intention To Treat (ITT), all patients were included in the analysis.

In this study mean age was 49 years in experimental arm and 53 years in control arm. The western literature reported that rectal carcinoma is more prevalent in people above 50 years of age. In this study also maximum patients were in range of 40 to 60 years. The early age of presentation in this study may due to changing pattern of disease characteristics and modification in lifestyle and dietary changes.

In the present study, there were 21 males and 9 females. Male to female ratio 2.3:1, which is near equal to German trial with 2.4:1 supporting to this study.[15] In this study the Radiolological response done after completetion of neoadjuvant therapy in both arms. All patients who underwent response assessment have partial response. But there is no statistical significant difference between the two groups in terms of Radiological Tumor response rates (Chi-Square: 1.48, P Value: 0.47).

In this study in experimental arm 12 patients had partial response with modified ryan tumor regression score 2. 2 patients are defaulted after neoadjuvant chemoradiotherapy and 1 patient expired post chemotherapy. In Control arm 12 patinets had partial response with modified tumor regression score 2. 2 patients had poor response with modified ryan tumor regression score 3. No patient had complete pathological response in both arms. But there is no statistical significant difference between the two groups in terms of Pathological Tumor response rates. (Chi-Square: 5.86, P Value: 0.31).

T downstaging: In experimental Arm, T stage down staged from cT3 to pT1 in 4 patients, cT3 to pT2 in 3 patients, cT4 to pT1 in 1 patient, cT4 to pT2 in 4 patients. In Control Arm, T stage down staged from cT3 to pT1 in 3 patients, cT3 to pT2 in 3 patients, cT4 to pT2 in 3 patients, cT4 to pT3 in 2 patients. 2 patients in control arm had no T down staging.

N downstaging: In experimental Arm, N stage down staged from cN1 to pN0 in 6 patients, cN2 to pN0 in 2 patients, cN2 to pN1 in 1 patient. 2 patients had no change in N stage and 1 patient had N upstaged in 1 patient. In Control Arm, N stage down staged from cN1 to pN0 in 4 patients, cN2 to pN0 in 2 patients, cN2 to pN1 in 1 patient. 2 patients had no change in N stage.

In a Phase II randomized study conducted by kim et al,[16] on comparision of Consolidation Chemotherapy after Preoperative Chemoradiation versus Chemoradiation alone for Locally Advanced Rectal Cancer, Disease downstage rate in consolidation chemotherapy arm is 36.4% and in control arm 21.2% with P value 0.077(not significant). In our study we analysed T and N downstaging in both arms according to intention to treat analysis. On comparision T downstaging in experimental arm is 80% and in control arm 86.66% with P value 0.624 (not significant). N downstaging in experimental arm is 66.66% and in control arm 60% with P value 0.705 (not significant).

In a retrospective cohort study of Cui et al. demonstrating the efficacy of consolidation chemotherapy (between neoadjuvant CRT and operation) in patients with locally advanced rectal cancer, they showed increased pCR responses. In this study, 63 patients received 2 cycles of XELOX consolidation chemotherapy. In our study, while pathological response according to modified ryan tumor regression score was 2 which implies partial response seen in 80 percent patients.[17]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

In this study by Tuta M et al,[18] tumor downstage was 45.8%in the group that received consolidation and 24.6%in the group that did not.[8] In our study, T downstage observed in 66.66% of patients while N downstage seen in 60% of patients who received consolidation chemotherapy.[18]

In this study acute toxicities have been evaluated in both groups during chemoraditation and chemotherapy according to CTCAE Version 5.[25] Toxicities during Chemoradiation in both groups are almost similar. Toxicities in Experimental arm during chemotherapy are evaluated. Haematological toxicities like anaemia, neutropenia and thrombocytopenia are evaluated. Grade 1 neutropenia seen in 1(6.67%) patient and Grade 2 neutropenia seen in 2 (13.30%) patients.

GI toxicities like nausea, vomiting, diarrhea and stomatitis have been evaluated. Grade 3 Nausea seen in 1(6.67%) patient, Grade 2 vomiting in 2 (13.30%) patients, Grade 3 diarrhea in 1 (6.67%) patient, and Grade 2 stomatitis in 2 (13.30%) patients.

Peripheral sensory neuropathy was seen in most of the patients with Grade 1 in 4 (26.67%) patients, Grade 2 in 4 (26.67%) patients and Grade 3 in 1 (6.67%) patient.

Liver parameters like Blood bilirubin increased, ALP increased, ALT increased are also evaluated. Grade 1 Blood bilirubin increased in 7 (46.67%) patients, Grade 1 ALP increased in 2 (13.30%) patients and ALT increased in 5 (33.30%) patients. Renal parameters like serum creatinine elevated in 4 (26.67%) patients, Grade 1 Hand-foot syndrome seen in 5 (33.33%) patients.

On comparision with a phase 2 randomised trial by Kim et al,[16] grade > 3 toxicities in test arm is 9.4% and in control arm 3.6%. In our study Grade 3 toxicities in test arm is 33.33% and in control arm 20%. This cannot be generalized as it is a study with small sample size.[19]

Limitations

- Study findings could not be generalized as it is single institution study with small sample size.
- Radiological response assessment required better protocol-based imaging studies for the assessment.

CONCLUSION

This study showed that the addition of neoadjuvant consolidation chemotherapy after CRT is a safe approach that may lead to better response and increased compliance with systemic chemotherapy regimen and reducing systemic metastasis, although not significant. The time until surgery with neoadjuvant consolidation chemotherapy may provide the chance to follow the patient without surgery in addition to increasing the tumor response. For this purpose, randomized prospective studies with a large number of patients are needed.

REFERENCES

1. GLOBOCAN 2020 [Last cited on 14th December 2020]. Available from https://www.uicc.org/news/globocan-2020-new-global-cancer-data.
2. Siegel RL, Miller KD, Fedewa SA et al. Colorectal cancer statistics, 2017. CA Cancer J Clin 2017;67:177–193.
3. V. Valentini, R. G. van Stiphout, G. Lammering et al., "Nomograms for predicting local recurrence, distant metastases, and overall survival for patients with locally advanced rectal cancer on the basis of European randomized clinical trials," Journal of Clinical Oncology, 2011:vol. 29, no. 23, pp. 3163–3172.
4. M. L. Garland, R. Vather, N. Bunkley, M. Pearse, and I. P. Bissett, "Clinical tumour size and nodal status predict pathologic complete response following neoadjuvant chemoradiotherapy for rectal cancer," International Journal of Colorectal Disease, 2014: vol. 29, no. 3, pp. 301–307.
5. J. Wook Huh, K. Hyeong Rok, and J. K. Young, "Clinical prediction of pathological complete response after preoperative Chemoradiotherapy for rectal cancer," Diseases of the Colon and Rectum, 2013:vol. 56, no. 6, pp. 698–703.
6. M. Maas, P. J. Nelemans, V. Valentini et al., "Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data," The Lancet Oncology, 2010vol. 11, no. 9, pp. 835– 844.
7. Ciseł B, Pietrzak L, Michalski W, Wyrwicz L, Rutkowski A, Kosakowska E, et al. Long-course preoperative chemoradiation versus 5 × 5 Gy and consolidation chemotherapy for clinical T4 and fixed clinical T3 rectal cancer: long-term results of the randomized Polish II study. Annals of Oncology [Internet]. 2019 Aug;30(8):1298–303.
8. Cui J, Dou X, Sun Y, Yue J. Consolidation chemotherapy may improve pathological complete response for locally advanced rectal cancer after neoadjuvant chemoradiotherapy: a retrospective study. PeerJ. 2020 Jul 7;8:e9513
9. Lao VV, Grady WM. Epigenetics and Colorectal Cancer. Nature reviews Gastroenterology & hepatology [Internet]. 2011 Oct 18;8(12):686–700.
10. Ponz de Leon M, Rossi G, di Gregorio C, De Gaetani C, Rossi F, Ponti G, et al. Epidemiology of colorectal cancer: the 21-year experience of a specialised registry. Internal and Emergency Medicine. 2007 Nov 29;2(4):269–79.
11. Baker S, Markowitz S, Fearon E, Willson J, Vogelstein B. Suppression of human colorectal carcinoma cell growth by wild-type p53. Science. 1990 Aug 24;249(4971):912–5.
12. Pino MS, Chung DC. The Chromosomal Instability Pathway in Colon Cancer. Gastroenterology [Internet]. 2010 May;138(6):2059–72.
13. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM-K, Putter H, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. The Lancet Oncology. 2011 Jun;12(6):575–82.
14. Roh MS, Colangelo LH, O'Connell MJ, Yothers G, Deutsch M, Allegra CJ, et al. Preoperative multimodality therapy improves disease-free survival in patients with carcinoma of the rectum: NSABP R-03. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology [Internet]. 2009 Nov 1 [cited 2022 Mar 9];27(31):5124–30.
15. Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, et al. Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer. New England Journal of Medicine. 2004 Oct 21;351(17):1731–40.
16. Kim SY, Joo J, Kim TW, Hong YS, Kim JE, Hwang IG, et al. A Randomized Phase 2 Trial of Consolidation Chemotherapy After Preoperative Chemoradiation Therapy Versus Chemoradiation Therapy Alone for Locally Advanced Rectal Cancer: KCSG CO 14-03. International Journal of Radiation Oncology, Biology, Physics [Internet]. 2018 Jul 15;101(4):889–99.
17. Demiray AG, Yaren A, Sungurtekin U, Baltalarlı PB, Demirkan N, Herek D, et al. The Effect of Continuing Chemotherapy after Chemoradiotherapy during the Time to Surgery on Tumor Response and Survival for Local Advanced Rectal Cancer. De Felice F, editor. Journal of Oncology [Internet]. 2022 Sep 15 [cited 2023 Jan 6];2022:1–8.
18. Tuta M, Boc N, Brecelj E, Omejc M, Anderluh F, Ermenc AS, et al. Total neoadjuvant treatment of locally advanced rectal cancer with high risk factors in Slovenia. Radiology and Oncology. 2019 Oct 25;53(4):465–72.
19. Marco MR, Zhou L, Patil S, Marcet JE, Varma MG, Oommen S, et al. Consolidation mFOLFOX6 Chemotherapy After Chemoradiotherapy Improves Survival in Patients With Locally Advanced Rectal Cancer: Final Results of a Multicenter Phase II Trial. Diseases of the Colon & Rectum. 2018 Oct;61(10):1146–55.

ISSN (O): 2687-5365; ISSN (P): 2753-6556