ORIGINAL ARTICLE

Response of Capecitabine and Oxaliplatin Chemotherapy in Metastatic Colorectal Carcinoma

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ABSTRACT

Objective: To evaluate the frequency of objective response of Capecitabine and Oxaliplatin (CAPOX) in patients with metastatic colorectal cancer.

Study Design: A descriptive case study.

Place and Duration of Study: The Study was conducted at the Oncology Department, Hameed Lateef Hospital Lahore, Pakistan from 17th July 2019 to 16th January 2020.

Methods: A total of 80 participants aged 20-80 who were diagnosed with metastatic colorectal carcinoma were selected for the study. After baseline investigations and examination, all the patients were advised chemotherapy comprising oral capecitabine and oxaliplatin for 6 cycles. For assessment of the response, CT scans were done by the radiological department and reported after chemotherapy.

Results: 3 (3.8%) showed complete response, 32 (40%) showed partial response, 26 (32.5%) showed no response, and 19 (23.8%) patients showed disease progression after six cycles of chemotherapy. (43.8%) patients had objective responses, and 45 (56.2%) patients showed no objective response.

Conclusion: chemotherapy yields promising activity for treating metastatic colorectal cancer.

Keywords: *Carcinoma, Chemotherapy, Colon Cancer, Metastatic Carcinoma.*

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Introduction

Colorectal cancer is a common type of cancer with high rate of mortality. It is primarily located in colon. Left-sided colon cancer are infiltrating lesions that encircle the lumen and cause obstruction, while right-sided cancers are exophytic, bulky, and polyploidy projecting into the lumen.[1] The location of the tumor has an important role in determining disease prognosis, right-sided cancers usually present at later stages and have worse prognoses.[2,3] A study reported that left sided colon cancer was significantly associated with reduced risk of mortality, independent of cancer stage.[4] A study done in Pakistan reported the differences between right and left cancers with respect to clinical presentation behavior and histopathology. Left-side cancers are less severe and present better clinical outcomes in comparison with right-side cancer.[5]

The first-line chemotherapy for the treatment of colorectal cancer includes CAPOX (capecitabine plus oxaliplatin). 5-Fluorouracil (5-FU) is mainly administered systemic drug for colorectal cancer.[6] Oxaliplatin is used along with flouropyramidin, and a study reported that CAPOX led to better outcomes than flouropyrimidines alone.[7] A multicenter study reported that therapy with

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CAPOX resulted in 54% objective response and 6% disease progression. 70% population survived after 1 year and survival rate after 2 years was 30%. The results showed that CAPOX has good safety profile and is effective.[8]

Another study compared CAPOX and FUOX (infusion 5fu plus oxaliplatin) in the first-line treatment of MCRC. 37% of patients responded to treatment, 29% showed no response, and the disease increased in 21% of CAPOX patients and 46% of FUOX patients. The results show the effectiveness of XELOX for the treatment of metastatic colorectal cancer.[9] This study aims to evaluate the frequency of objective response of CAPOX in patients with metastatic colorectal cancer.

Methods

The descriptive case study was conducted at the Oncology Department, Hameed Lateef Hospital Lahore, Pakistan, from 17th July 2019 to 16th January 2020 after obtaining approval from the hospital Ethical Committee Board held on dated: 18th June 2019, vide letter no: 13/125. A total of 80 participants aged 20-80 years diagnosed with metastatic colorectal carcinoma were selected for the study through consecutive sampling. Pregnant and breast-feeding women, patients with severe toxicity from chemotherapy, patients with a history of chemotherapy or radiotherapy, and those with ECOG Performance Status 4< were excluded.Patients coming through the department's OPD who fulfilled the criteria were enrolled, and written informed consent was taken. After baseline investigations and examination, all patients were advised chemotherapy comprising oral capecitabine and oxaliplatin for 6 cycles. For assessment of the response, CT scans were done from the radiological department and reported after chemotherapy. The presence of objective response was also labeled.

All the data was analyzed by SPSS version 20. Quantitative parameters were calculated as mean and standard deviation. Qualitative variables like gender, disease-free survival, ECOG status, and progression-free survival were calculated by frequency and percentage. Stratification was done with respect of age, gender, ECOG status and right and left side involvement. *Chi-square* test was applied after stratification. A *P*-value ≤ 0.05 was taken as significant.

Results

The mean age of the patients was 54.88±14.08 years. 49 (61.2%) patients were male and 31 (38.8%) patients were female. 7 (8.8%) patients had ECOG status 0, 34 (42.5%) patients had ECOG status 1, 19 (23.8%) patients had ECOG status 2, 12 (15%) patients had ECOG status 3 and 4 (8%) patients had ECOG status 4. (Table-1).

3 (3.8%) patients had a complete response, 32 (40%) patients had a partial response, 26 (32.5%) patients had stable disease, and 19 (23.8%) patients had progressive disease after six cycles of chemotherapy. (43.8%) patients had objective responses, and 45 (56.2%) patients showed no objective response. (Table-2). Stratification of age, gender, side, and ECOG status is shown in table-3.

Discussion

Colorectal cancer is a major cause of morbidity and mortality and has a wide range of symptoms, including fecal blood, changed bowel habits, dragging feeling in the abdomen, and sensation of abdominal mass. The prognosis and presentation of the disease are affected by demographic factors, including age, comorbid conditions, type of tumor, and ethnic group. In addition, the location of colorectal cancer also has implications for the course of the disease. Its treatment regimen includes 5-fluorouracil-based chemotherapy, which is used to manage severe cancers.

With advancement in therapy, FOLFOX, a combination of fluorouracil folinic acid and oxaliplatin, has shown excellent results when used for treating colon cancer. It has improved the survival rate and progression-free survival.[10] Similarly, CAPOX, a combination of capecitabine and oxaliplatin, has also shown positive results. Therefore, FOLFOX and CAPOX are now widely used for the treatment of colon cancer. However, CAPOX is more preferable due to its affordability, reduced need for hospitalization, and no requirement of a vascular port.[11]

Table-1: Patients demographics (n=80)

Parameters	n (%)	Percentage
Average age in years mean±SD	54.8 ±14.0	
Age distribution		
20-40 years	13	16.2
41-60 years	41	51.2
61-80 years	26	32.5
Gender		
Male	49	61.2
Female	31	38.8
Position of cancer		
Right	51	63.8
Left	29	36.2
ECOG status		
0	7	8.8
1	34	42.5
2	19	23.8
3	12	15
4	8	10

Table-2: Response after chemotherapy (n=80)

Response	Frequency	Percentage
Complete response	3	3.8
Partial response	32	40
Stable disease	26	32.5
Progressive disease	19	23.8
Objective response	35	43.8

In the current study, 3.8% patients had complete response, 40% patients had partial response, 32.5% patients had stable disease and 23.8% patients had progression disease after 6 cycles of chemotherapy. 43.8% patients had objective response.

Kim et al. conducted a study on the efficacy of XELOX in patients of metastatic colorectal cancer.[12] Around 55% of patients showed an objective response, 31% of patients showed no response, and 7% had progressive disease. Kibudde et al. conducted their study on Capecitabine/Oxaliplatin for treatment in patients of metastatic colorectal cancer.[13] The results of their study showed an objective response in 58% and 52% of younger and older patients. Petriolli et al. conducted their study on the treatment of advanced colorectal carcinoma with oxaliplatin and capecitabine.[14] They observed 38.5% partial response with a high dose of capecitabine and 37.1% partial response with a low dose of capecitabine.

Kim et al. used a combination of oxaliplatin and capecitabine in for treatment of colorectal cancer.[15] They observed the response rate of 54.5% in high dose capecitabine combination group and 42.2% in low dose capecitabine combination group. They concluded that both high dose and low dose capecitabine combination are safe, effective, feasible and tolerable treatment for metastatic colorectal cancer.[15]

Table-3: Stratification with respect to age, gender, side and Eastern Cooperative Oncology Group Performance Status

Variable	Complete response	Partial response	Stable disease	Progressive disease	*Chi Square*-value	*P*-value
Age						
20-40 years	1 (7.7%)	6 (46.2%)	3 (23.1%)	3 (23.1%)		
41-60 years	1 (2.4%)	17 (41.5%)	13 (31.7%)	10 (24.4%)	1.72	0.943
61-80 years	1 (3.8%)	9 (34.6%)	10 (38.5%)	6 (23.1%)		
Gender						
Male	2 (4.1%)	21 (42.9%)	15 (30.6%)	11 (22.4%)	0.52	0.914
Female	1 (3.2%)	11 (35.5%)	11 (35.5%)	8 (25.8%)		
Position of cancer						
Right	1 (1.9%)	15 (28.8%)	22 (42.3%)	14 (26.9%)	10.97	0.012
Left	2 (7.1%)	17 (60.7%)	4 (14.3%)	5 (17.9%)		
ECOG status						
0	2 (28.6%)	5 (71.4%)	0	0		
1	1 (2.9%)	20 (58.8%)	11 (32.4%)	2 (5.9%)		
2	0	6 (31.6%)	11 (57.9%)	2 (10.5%)	0.00	0.0001
3	0	1 (8.3%)	4 (33.3%)	7 (58.3%)		
4	0	0	0	0		

Kim et al., in their study, found objective response in 49% of patients with metastatic colorectal cancer and concluded that a combination of oxaliplatin and capecitabine could be used as first as well as second-line treatment in advanced or metastatic colorectal cancer.[16] Degirmencioglu et al. conducted a study on the efficacy and safety of CAPOX in patients with stage III colon cancer and found the progression of the disease in 27.36% of patients.[10] They concluded that CAPOX is preferred in older patients of metastatic colon cancer. Li et al. conducted their study on a combination of capecitabine and oxaliplatin for the treatment of metastatic colorectal cancer in Spain.[17] They observed objective response in 37% of patients (complete response in 5% of patients and partial response in 32% of patients), stable disease in 29% of patients' progression of disease in 21% of patients. They concluded that XELOX is as effective as FUOX for the treatment of metastatic colorectal cancer.

Our study has some limitations. The study was single-centered and had a limited sample size, which affected the generalizability of the results. Large, multi-center studies on this subject would be useful for the applicability of results to the general population.

Conclusion

CAPOX chemotherapy yields promising activity for the treatment of metastatic colorectal cancer.

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Authors Contribution

AAR: Idea conception, manuscript writing and proofreading

AZ: Study designing, data analysis, results and interpretation, manuscript writing and proofreading

AJ: Idea conception, data collection

RI: Study designing, data collection

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ZI: Study designing, data collection