EVALUATION ON THE RESULTS OF XELOX REGIMEN FOR ADJUVANT CHEMOTHERAPY OF STAGE II, III COLON ADENOCARCINOMA

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ABSTRACT

Background: *XELOX regimen has been proven in adjuvant chemotherapy for colorectal carcinoma. To evaluate the efficacy and safety of XELOX regimen in Vietnamese is very necessary.* ***Patients and method****: 136 adenocarcinoma colorectal cancer patients treated with XELOX regimen.* ***Ressults:*** *3 years disease-free survival(DFS) was 86.7%, 3 years overall survival (OS) was 82.4%. Average disease-free survival was 35.8 months, average overall survival was 37.9 months. 79.4% treatment-related toxicitiy, among which toxicity of grade 3-4 were 16.9%. The side-effects of XELOX regimen in adjuvant chemotherapy in colon cancer is manageable.* ***Conclusions:*** *Efficacy of XELOX regimen in adjuvant chemotherapy in colon cancer treatment is high, the side-effects of XELOX regimen in is manageable.*

Key word: *XELOX, colorectal, efficacy and safety.*

I. INTRODUCTION

Colorectal cancer is one of the leading cancers in Vietnam and worldwide. According to Globocan 2012, every year, there are, about 1.361.000 new cases of colorectal cancer of which 694.000 deaths worldwide, ranged as the third most common cancer and third leading causes of cancer deaths [1]. Capecitabine is an oral prodrug of fluorouracil which has been demonstrated as efficace as FUFA regimen in adjuvant chemotherapy for colon cancer treatment [2]. The NO16968 trial, comparing effect of adjuvant chemotherapy with XELOX regimen from FUFA regimen for colon cancer stage III, had a 3 year DFS 70.9 % (XELOX) and 66.5 % (FUFA), p=0.0045 [3]. We carried out this study in order to evaluate the results and toxicities of XELOX regimen in the adjuvant treatment for high-risk stage II and III colon cancer with research objectives: Evaluate the results and side effects of XELOX regimen for adjuvant chemotherapy of high risk stage II and stage III colon adenocarcinoma.

II. OBJECTS AND METHODS OF STUDY

2.1. Objects

136 high risk stage II and stage III colon adenocarcinoma patients were treated at Cantho oncology and K hospitals from January 2012 to December 2016.

2.1.1. Selective criteria

High risk stage II and stage III colon adenocarcinoma

Stage II colon adenocarcinoma and one the of following factors: (1) Grade 3.4; (2) bowel obstruction or perforation; (3) T4; (4) lymphatic/vascular/perineural invation ; (5) < 12 lympho nodes examined;

No history of precious chemotherapy or radiation therapy. KPS ≥ 70; Sufficient clinical and subclinical information.

Adjuvant chemotherapy with XELOX regmen 6-8 cyclye at least 12 weeks after surgery.

Follow-up untill the death or to the end of studied time

2.1.2. Exclusion criteria

Colon cancer patients without adenocarcinoma;Colon cancer patients had the second cancer, liver failure, kidney failure, hear failure, myelosuppression or pregnant women.

2.2. Methods of study

2.2.1. Study design: intervention study without control group.

Patients surgically treated will be classified as high-risk stage II or stage III, receive XELOX regimen for adjuvant chemotherapy. After the end of treatment, follow-up every 3 months to evaluate their outcome. If these patient can not come to hospital, we would collect information by phone, letter (questionnaire form).

The end of the study : the end of the study in one of the following reasons: Dead or disappeared; The end of studied time.

2.2.2. The steps of carrying out

Examination and evaluation of patients before treatment. Adjuvant chemotherapy: Oxaliplatin 130mg/m^2, IV infussion with glucose 5% on day 1 plus oral capecitabine 1.000mg/m^2 twice/daily on days 1-14 every 3 weeks. Evaluating the results of follow-up: If patients relapsed, further treatment would be considered such as patiative chemotherapy with or without combination target therapy, radiationtherapy, surgery or paliative care and continue to follow-up the patient. Evaluate the results of treatment: Recurrence, 3 years disease-free survival and 3 years overall survival. Toxicity, side effects were identified WHO criteria. Compare survival time with prognostic factors.

2.2.3. Data analysis

Research data will be analyzed by STATA 8.0. Analyse overal survival with method Kaplan - Meier. Compare the differences between survival time according to quantitative variants by Log-ran test, and independent prognostic factors affecting survival time were to identified by cox regression model.

III. RESULTS

From January 2012 to December 2013, we had collectted 136 high risk stage II and stage III colon adenocarcinoma patients, the results as following:

3.1. Characteristics of patients

Age: mean : 54.1±11.8; range: 25-76. 77 (56.6%) male and 59 (43.4%) female. male/female=1.3/1; Stage: stage II 80 (58.8%); stage III 56 (41.2%); Histopathology: rough shape 46 (33.8%); adenocarcinoma 111 (81.6%). mild differentiation 95 (69.9%). The number of lympho nodes examined: meanly 6.8; more than 12 lympho nodes were 26 (19.1%). Nodes positive 41.2% among which 1-3 nodes positive were 29.8%. Surgically therapeutic situation: emergency surgery 25 (18.4%), 13 (9.6%) patients recieved 6-7 cycles.

3.2. Evaluation on the results of treatment

Median follow-up 40.6± 7.2 months, 5 patients (3.7%) were lost the trace after following-up more than 24months.

3.2.1. Toxicity

Treatment related toxicities were documented in 108 patients (79.4%), among which toxicity of grade 3-4 were 16.9%.

Table 3.1: Gastrointestinal, neurological and muco-cutaneous toxicities

Toxicities	Grade 1-2 n (%)	Grade 3-4 n (%)	All n (%)
Nausea-vomoting	28(20.6)	0	28(20.6)
Diarrhea	23(16.9)	0	23(16.9)
Mucosa ulcer	2(1.5)	0	2(1.5)
Stomatitis	15(11.0)	0	15(11.0)
Peripheral neurotoxicites	22(16.2)	0	22(16.2)
Hand-foot syndrome	24(17.7)	0	24(17.7)

Comment: Gastrointestinal, neurological and muco-cutaneous toxicities were almost grade 1-2.

Table 3.2: Toxicities of hematology, liver and kidney

Toxicity	Grade 1-2 n (%)	Grade 3-4 n (%)	All n (%)
Neutropenia	65(48.2)	10(7.4)	75(55.6)
Febrile leukonia	2(1.5)	0	2(1.5)
Anemia	10(7.4)	1(0.7)	8(8.1)
Thrombocytopenia	32(23.5)	12(8.8)	44(32.3)
SGOT/SGPT ↑	17(12.5)	0	17(12.5)
Ure/Creatinin ↑	2(1.5)	0	2(1.5)

Comment: Toxicities of hematology mainly were grade 1-2, only 16.9% patients on grade 3-4. Toxicities of liver and kidney almost were grade 1-2.

3.2.2. The results of treatment

At the time of analysis, 25 patients (19.1%) had relapsed, among which 19 patients (14.5%) died. The location of recurrence is liver in 10 patients (36%).

Table 3.3: Disease-free survival and overall survival

Results	N	Mean (months)	Percentage (%) (%)	CI 95%
3 years DFS	131	35.8	82.4	0.75-0.88
3 year OS	131	37.9	86.7	0.79-0.91

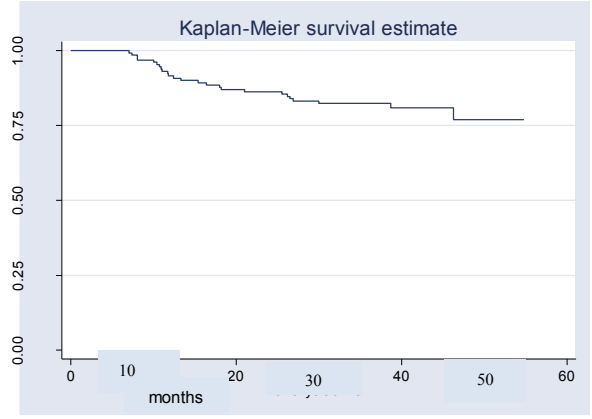

Figure 3.1: Disease-free survival

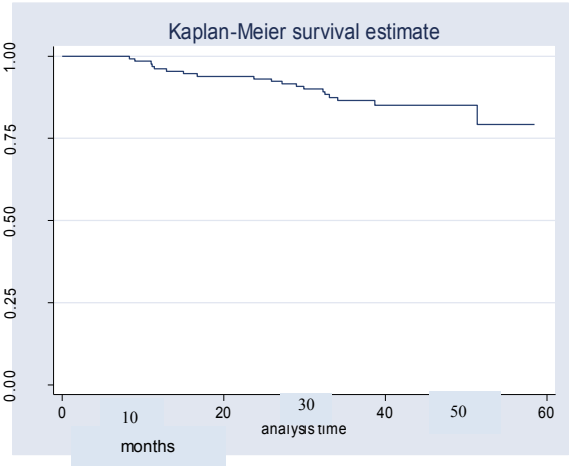

Figure 3.2: Overall survival

IV. DISCUSSION

Median follow-up 40.6 months. 136 patients, we follow-up 131 patients (96.3%), 05 patients (3.7%) after 24 follow-up we cuold not contact them, they may change their addresses, telephone number...

4.1. Evaluation on some toxicities of chemotherapy

In this study, the toxicities of XELOX regimen for colon adenocarcinoma, often less severe, were 79.4% of all grades, among which 16.9% of grade 3 and 4, no treatment-related to toxicity mortality. Nausea-vomoting: garde 1-2 20.6% were most often seen. We prevented with primperan 10 mg, ondansetron 8mg before adjuvant chemotherapy; diarhea grade 1-2 16.9% were manageable; mucosal ulcer grade 1-2 1.5%, manifested only with mild mucositis, few cases with true mouth mucosa ulcer; Epigastric pain are symptoms of gastric mucositis, patients often manifested symtoms of belch, agita, epigastric pain were accounted 11.0%. Peripheral neurotoxicity 16.2%, hand-foot syndrome 17.7% (almost grad 1& 2 and totally recoverred after the management)

Hematological toxicities (neutropenia: 7.4%; leukopenia with fever: 1.5%; thrombocytopenia: 8.8%). Neutropenia: neutropenia 55.6%, among which, 7.4% patients were gade 3-4. Majority of these patients were recoverred after 1 week; for grade 3-4 neutropenia, we medicated Filgrastim 2-3 days, about febrile neutropenia 1.5%, we had to medicate Filgrastim and broad spectrum antibiotics for 5-7 days. Thrombocytopenia 32.3%, grade 3-4 thrombocytopenia 8.8%. Mostly patients recoverred, some paitents had to need platelet transfusions. Anemia grade 1-2 7.4%; for amenia grade 3: 0.7%, we need to do the blood transfusions.

According to a other study, 70 Stage III colon adenocarcinoma patients were treated with XELOX regimen for adjuvant chemotherapy. The toxicities comprised: neutropenia 41.3%, of which 11.3% amenia of grade 3 -4; decrease of hemoglobine 19.3%; 6.7% thrombocytopenia; diarrhea 20% comprising 1.2% of grade 3; peripheral neuropathy 52.5%, comprising 40% of grad 1 and Hand-foot syndrome 15%, of which 2.5% were grade 3-4 [4].

Schmoll et al studied on a multicenter, randomized trial of 938 patients treated capecitabine plus oxaliplatin (XELOX) as adjuvant therapy for patients with stage III: the neurotoxicities 78% comprised 11% grade 3-4, nausea and vomiting were 43% and 66%

respectively, among which, grade 3-4 were 6% and 5%, diarrhea 19%, hand-foot syndrome 29%, of which 5% were grade 3-4, leukopenia 27% with grade 3-4 were 9%; epigastric pain 17%. Totally, 94% patients had related to, at list, one toxicity and 55% patients were in grades 3-4[5]. These results are also similar to our study. Hematological toxicity, neurotoxicity of our study were fewer than toxicities of FOLFOX, FLOX regimen [6].

4.2. The results of treatment

At the time of analysis, median follow-up 40.6± 7.2 months, 5 patients (3.7%) were absent after 24months of follow-up. At the time of analysis, 25 patients(19.1%) had relapsed or died, among which 19 patients(14.5%) died. The liver is first site recurrence 10 patients (36%). According to Andre T., stage II, III colon adenocarcinoma receiving adjuvant chemotherapy, the recurrence rate were 21.1% (FOLFOX), 26.1% (FU/FA)[7]. Joon J H, stage II and III colon adenocarcinomas treated with FOLFOX4 and FOLFOX6 adjuvant chemotherapy, the recurrence rate were 17.1%, in which liver matastasis 21.4%[8]. Recurred, metastased patients almost continued to receive XELIRI, FOLFIRI or capecitabine regimens as chemotherapy, a few patients received chemotherapy combined with cetuximab, bevacizumab or paliative care and follow-up.

At the time of analysis, followed-up 40.6 months, the proportion of 3 years disease-free survival (DFS) were 82.4%; median duration of disease-free survival were 35.8 months. 3 years overall survival (OS) were 86.7%, median duration of overall survival (OS) 37.9 months. 25 patients (19.1%) had recurred or died, among which 19 patients(14.5%) died. The liver is first site recurrence 10 patients (36%).

Table 4.1: Survival according to stage II-III

Author	Median follow-up (months)	3 years DFS (%)	3 years OS (%)
Andre T (2004,n=2.246)[7]	37.9	78.2	87.7
KueblerIP (2007,n=2407)[9]	42.5	76.5	
Joon J H(2011, n=82)[8]	37	82.9	87.5
This study (2016,n=136)	40.6	82.4	86.7

V. CONCLUSIONS

Adjuvant chemotherapy XELOX regimen brings a high survival time for stages II, III colon adenocarcinoma. The proportion of 3 years disease-free survival (DFS) were 82.4%; median duration of disease-free survival: 35.8 months. 3 years overall survival (OS) were 86.7%, median duration of overall survival (OS): 37.9 months. The toxicities of XELOX regimen for colon adenocarcinoma patients, often less severe, were 79.4% of all grades, among which 16.9% of grade 3 and 4.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M et al (2013). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide. International Agency for Research on Cancer. Lyon
2. Steven K. et al (2015). Cancer of the colon, Cancer Principles and practice of oncology edited by Vincent T Devita VT et al, 10th edition, Wolters Kluwer, Philadephia, 1167-1222
3. Haller DG, Tabernero J, at al (2011). Capecitabine plus oxaliplatin compared with Fluorouracil and Acid folinic as Adjuvant therapy for stage III colon cancer, J Clin Oncol, 29. Pp.1-9.
4. Hang Nguyen Thi Thuy (2013). Some clinical, paraclinical characteristic and toxicity of xelox regimen in adjuvant chemotherapy for stage III colon cancer, Ha Noi Madical University.

5. Schmoll H, et al (2007). Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer, J Clin Oncol 25:2007, p.102-109.
6. Gill S, Loprinzi CL, Sargent DJ, et al (2004). Pooled analysis of fluorouracil-based adjuvant therapy for stage II and III colon cancer: who benefits and by how much? J Clin Oncol, 22, 1797.
7. Andre´ T, Boni C, Navarro M, et al (2009). Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial, J Clin Oncol 27:3109- 3116
8. Jeon HJ, Woo JH, Lee HY, at al (2011). Adjuvant chemotherapy using the FOLFOX regiment in colon cancer, Journal of the Korean Society of Coloproctology, 27. Pp.1-8.
9. Kuebler JP, Wieand HS, O'Connell MJ et al (2007). Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. J Clin Oncol, 25, 2198.

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DEPRESSION AND SUICIDAL IDEATION AMONG SECONDARY SCHOOL STUDENTS IN CAN THO CITY: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: *There is a rapidly growing public awareness of depression and suicide, among pupils at Vietnamese secondary schools. This study aims to determine the prevalence of depression, and suicidal ideation; and identify risk factors related to depression.* ***Methods:*** *A cross-sectional study was conducted among 1161 secondary students during September-December 2011. A structured questionnaire was use to assess depression, and suicidal ideation.* ***Results:*** *The prevalence estimates of symptoms reaching a threshold comparable to a diagnosis of depression were 41.1%. Suicide had been seriously considered by 26.3% of the students, 12.9% had made a suicide plan while 3.8% had attempted suicide. Major risk factors related to depression were physical or emotional abuse by the family and high educational stress.* ***Conclusions:*** *Depression and suicidal ideation are common among secondary school students. They have strong significant associations with physical or emotional abuse in the family and high educational stress.*

Keywords: *Mental health, Depression, Suicide, Adolescents, Student, Can Tho*

I. INTRODUCTION

Mental health disorders are among the most important public health issues globally. Estimates of the global burden of disease place mental illness in the top three of diseases in terms of years lost due to disability [1]. The mental health of adolescents and young people is a crucial issue because of the general burden of mental illness and