The assessment of response to adjuvant chemotherapy with CMF in triple negative breast cancer

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Abstract

Introduction: Breast cancers are divided into at least 4 sub Types on the Basis of gene expression profiles and expression of receptors as measured by IHC (Immunohistochemical). Triple negative breast cancer (TNBC) is more chemosensitive yet, it is much harder to detect than other sub types. At present lack of highly effective therapeutic targets for TNBC, Leaves standard chemotherapy, as the only medical treatment but it is not remarkably efficient. CMF (cyclophosphamide-MTX-5-fu) chemotherapy is effective in some sub types of TNBC.

Patients and methods: A Total of 40 patients with TNBC who had undergone surgical resection because of primary Invasive Breast cancer were studied from 2009 to 2011. Twenty patients in treatment group received four cycles of modified CMF after standard chemotherapy and 20 patients in group control Received standard chemotherapy (Antracycline / Taxane), Patients were Regularly Followed up every 3 months for median observation 13.3 mo.

Results: In our study the prevalence of TNBC was %13.5 The average age of patients 49.5 years Their clinical and histopathological characteristics include: 90% Invasive Ductal carcinoma, 55.35% LN(Lymph node) pos. 61.3% P53 Pos , 74.5% Ki67 ≥ 20 , 68% grade III. There was No statistical differenced between control and treatment group in OS, DFS and PD median Followed up 13.3 mo.

Conclusion: The results of study indicate that the adjuvant therapy with regimen CMF in TNBC patient after standard chemotherapy with Antracyline / Taxane- Base no affected out come in patient in Median follow up 13.3 mo.

Key word: chemotherapy, CMF, TNBC

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Introduction

Breast cancer is a Heterogeneous Disease of gene expression, Morphology, clinical course and Response to Treatment.

Gene expression and IHC profiling divides Breast cancer in to four sub Types. Triple Negative Breast cancer is one these sub types which is defined by alack of expression of estrogen and progesterone receptors (ER and PgR) as well as human epidermal growth factor receptor (HER-2).

Prevalence is 10-27% of Total Breast cancer. This sub type is more aggressive from clinical and pathology point of view. It appears in women at younger ages and in higher stages of the disease which leads to visceral versus osseous metastases in and in give early metastasis. There is poorer survival and no chance target therapy.

Cytotoxic therapy remains as the main therapy in TNBC patients. Many studies report on the usefulness of this therapy.

Neoadjuvant therapy is effective in TNBC patients than in non TNBC and it more creates more perfect pCR, which cause their Long recovery.

TNBC heterogeneous disease has many sub types such as: sub Type with Mutation BRCA1, sub Type Basaloid, sub Type with mutation pro Retinoblastoma with good response to CMF regimen Du to More sensitive to agent DNA damage agent effective to pathway sentetase Thymidilate Antracyclines and Taxanes that these drugs have verified effect. platinumes

have these effects. Inhibitors EGFR, Bevacizumaband EGFR in clinical Trail. Yet in these patients Regimen containing Taxanes and antracyclines remains as important medicinal regimen but was not more exclusive than non TNBC patients. (1, 2, 3)
The purpose of this study was thus, to investigate the effects of Taxanes/Antracyclines with CMF chemotherapy.

Methods and material
This interventional clinical trial was performed on patients with stage I-III breast cancer .Twenty TNBC patients were analyzed from May 2009 to June 2011. All patients had surgery in order to primary invasive breast cancer. They were under chemotherapy with Antra cycline/ Taxane- Base useful Regimen were Ac→T and TAC. Then they received four cycles of modified CMF. After having chemotherapy the patients got treatment with radiotherapy.
Median follow up in treatment group was13.3 mo (Range 8-24 mo). Twenty TNBC patients were control group. They were under chemotherapy with Antra cycline/ Taxane-Base after surgery. The patients' information is in Table 1.
In the study Inclusion criteria includes: 1- age≥18 year. 2- New case. 3- Negative metastase (stage I-III) and the Exclusion criteria includes: 1- abnormality in Tests of Renal and Liver. 2- Dysfunction Heart.

Statistical methods
Data analysis was done using SPSS16. Both descriptive statistics such as frequency, percentage mean and SD as well as, inferential statistics such as t- test, chi square and Fisher exact test use to analyze data. The Level of significance was defined as $p \leq 0/05$. The sample size in this study was 20 cases.

Results
The mean age in treatment and control groups was50 and 48 respectively, and in total patients 49.5 year. (Range 29-63). 90% of the patients were ductal carcinoma from the histological points of view. 44% of patients were positive LN, and in control group 66.7% were positive LN. Regarding tumor size in treatment group T_1=15.6%, T_2= 68%, T_3=15.8%. In control group, T_1=15.6%, T_2=85%, T_3=5% and in total T_1=12.9%, T_2=76.4%, T_3=10.4%. Examining ki 67>20, show these values: in treatment group 35%, control group 15.8% and total 25.4%. Regarding p53 in treatment group 52.6%, control group 70% and in total 61.3% patients have positive p53. From point of view grade Tumor were in patients group grad I=0%, grad II=35%, grad III=65% and control group grad I=0%, grad II=45%, grade III=55%.
It is worth mentioning that one patient after four months of chemotherapy developed skin and liver metastasis extensively which ends with her death after 6 months of therapy. Another patient in course 2 of CMF was affected by grade III nausea and vomiting which caused to stop the treatment. From 20 patients in control groups one patient was affected by bone metastasis. As regards OS, DFS, PD medicinal event there was no significant difference between two groups.

Discussion
TNBC cancers have more aggressive behavior and worse prognosis. They have medicinal strategy and are lesser preventative than cancers with hormonal receptor positive.[4, 7] in the present study the prevalence of this sub type was 13.5%. mean age of patients was 49.5% year. 60% of patients were high grade histologic (grade III). 55.35% of patient were LN positive, %76.5 of patient had tumor size of T_2, %9 Ductal carcinoma 61.3% p53 positive and ki67>20 was seen in %74 of patients.
The results of this is similar to ones reported by Ytaka et al in 2010, where the prevalence was reported to be 11-17% that is percentage is comparable with our study. The mean age in TNBC was 53 and non TNBC was 57 year. In this study in TNBC metastasis to LN was 57.7%, the average size of tumor 3cm, p53 positive 71%, high histologic grade 68%, 60 ki 67>30, 60% and in non TNBC this currency was 46%, 1cm, 14.2%, 16%.[1] In another study carried out by Di Leo et al, among patients with TNBC Antracycline- Base therapy was superior to CMF in terms of DFS with borderline statistical significance which is not comparable with our study.[5] Trail TACT that was per formed by Ellis et al in 2009 Regime ECF-Taxoter compared with ECF – CMF to out come of TNBC and non TNBC patients has

effected and the results of this study comparable with our result.[3] In another study Cheang MC et al (2008)Regimen CMF was more useful than Regimen containing of Antracycline in sub type Basal-Like breast cancer.[6] In our study TNBC was analyzed and sub type of BCLC was not analyzed separately. In one study performed by Dr. Trere et al in 2009, from among 518 TNBC patient under study the prevalence of TNBC was 10.2% and 145 patients taken 6 courses Chemotherapy with Modified CMF. DFS in TNBC were %75, Luminal A 46%, HER-2 positive 50%. Loss pRB in TNBC were 37.7% and non TNBC 2.3%. Loss PRB is the main factor for response to chemotherapy. pRB is sensitive to DNA damage and drugs effect in thymidylate sentetase such as 5-Fu and MTX. In patients with Loss pRB, DFS. in Follow up 109 mo, 100% and another groups 50%. Also in this study in TNBC patients P53 positive was 58.5%, grade III 77.4%, ki67>20 83%. The results of the study comparable with our study.[2,7]

Conclusion

The results of this study reveals that adjuvant therapy with Regimen CMF in TNBC patients after standard chemotherapy with antra cycline/ Taxane- Base had no effects (OS, DFS, PD) in short time follow up. In this study as well as another study [8], in TNBC patients large tumor size, high LN pos, high grade and high mitotic tumor were seen.

Considering the small size and short follow up periods taken in this study, to gain more valid Conclusion, we call for more studies done in this regard with greater sample size and longer follow up periods.

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