Abstract

Department of Community Medicine, College of Medicine, University of Baghdad for his kind help and valuable advise in statistics.

Summary

Background and objectives: several factors render Chronic myeloid leukemia an interesting subject for study by researchers. They include marked progress in understanding its molecular biology, the discovery of Philadelphia chromosome and the development of new drug generation, the tyrosine kinase inhibitors (TKI).

Break point cluster region – Abelson murine leukemia translocation gene is present in ninety-five percent of chronic myeloid leukemia patients and involving ninety percent of a granulocyte in most cases.

Aim of the study: The aim of this study was to apply the technique of interphase fluorescence in situ hybridization (FISH) technique and detect Break point cluster region – Abelson murine leukemia translocation and P53 alteration, to assess if there is any significant relationship and to detect Ataxia Telangiectasia Mutated gene (ATM), and isochromosome of the long arm of chromosome seventeen(17q) and Myeloperoxidase (MPO) gene.

Materials and methods: This is a prospective study in which 104 newly diagnosed chronic phase chronic myeloid leukemia having not received
a prior tyrosine kinase inhibitors were included together with 30 normal adult subjects as a control group. Two prognostic relative risk scores were used to calculate the predicted response to treatment, including the Sokal score and the European Treatment and Outcome Study score. The patients were divided into two groups, twenty-four patient (fifteen male and nine female) were studied by using ethylene diamine tetra acetic acid anticoagulant and eighty patients were studied by using sodium heparin as anticoagulant.

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Results: All patients in both groups had a positive Break point cluster region –Abelson murine leukemia translocation signal in their peripheral blood specimen but the percentage of positive cells varies between two groups of patients being 86.6% for patients in the heparin group and 11.33% for patients in the ethylene diamine tetra acetic acid group. The majority of patients were in the high risk group in both relative risk scores. Significant statistical association was found between the European Treatment and Outcome Study score and spleen size, lymphocyte%, basophils% and bone marrow Myeloid: Erythroid ratio. In the ethylene diamine tetra acetic acid group of patients there was a significant statistical relationship between Fluorescence in situ hybridization test with their white blood cells count, platelet count and bone marrow Myeloid: Erythroid ratio. In the heparin group of patients, two patients were excluded because they were Fluorescence in situ hybridization negative, seventy-eight patients included in this study (forty three male and thirty five female). The mean white blood cell count count of these patients was 189.5 x 109/l. The Fluorescence in situ hybridization score of these patients was 70-90% (mean 86.6%). Protien fifty three isochromosome(17q) FISH test was also applied to nineteen of our patients (13 male and 6 female), ten of them show positive results. No significant statistical relationship was found between P53 i(17q) with the gender of patients.

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A statistically significant relationship was found between P53 i(17q) and
Sokal relative risk score while no significant statistical correlation was found with the EUTOS relative risk score. No statistically significant difference was observed between the study sample and the control group regarding the P53/ATM gene signals. All patients were started treatment on Tyrosine kinase inhibitor imatinib mesylate in a dose of 400mg/day and were followed for six to nine months of treatment, thirty six patients of them became Fluorescence in situ hybridization negative after treatment while twenty seven of them remain Fluorescence in situ hybridization positive after treatment. Comparison of the clinical characteristics and laboratory parameters before starting treatment between those group of patients who became Fluorescence in situ hybridization negative and those who continue to be Fluorescence in situ hybridization positive was statistically significant regarding the spleen size and the percentage of bone marrow granulocytes. Conclusion: Fluorescence in situ hybridization test is a reliable technique in the detection of Break point cluster region –Abelsone murine leukemia translocation in chronic myeloid leukemia patients pre and post therapy to assess the cytogenetic response. It is important both in the diagnosis and follow up. Both Sokal and the European Treatment and Outcome Study scores are useful prognostic parameters in CML patients. Protein fifty three isochromosome (17q), Ataxia Telangiectasia Mutated gene and myloperoxidase gene abnormalities are important genes to be screened in Iraqi CML patients.