Clinical Significance of Beclin-1 Dependent Autophagy Induced by Imatinib in Chronic Myeloid Leukemia Patients

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Abstract

Background and objectives: The introduction of imatinib as one of the tyrosine kinase inhibitors (TKI) has revolutionized the treatment of chronic myelogenous leukemia (CML), representing the first target specific drug. Autophagy is a constitutive homeostatic mechanism for intracellular recycling and metabolic regulation. The role of autophagy in cancer is very complex, it is tumor suppression mechanism yet it enables tumor cell survival in stress. The aim of the present study was to assess autophagy induced by imatinib therapy through beclin-1 gene in CML patients, and to evaluate beclin-1 gene expression in relation to patients' clinical and hematological response.

Subjects and methods: The present study was carried out on 50 subjects, 35 newly diagnosed CML patients who were classified into 2 groups: (Group I) including 17 CML patients and (Group II) including 18 CML patients in accelerated phase, and 15 apparently healthy subjects served as controls (Group III). All patients were treated with imatinib and followed up after six weeks of treatment. Each patient was subjected to complete history taking, clinical examination along with laboratory investigations in the form of liver & renal function tests, random blood glucose, ESR, CBC & examination of Leishman-stained peripheral blood and Bone marrow aspiration and examination of Leishman-stained smears. The diagnosis was confirmed by detection of BCR-ABL gene expression by quantitative RT-PCR. Beclin-1 gene expression in peripheral blood samples was assessed as well *via* quantitative RT-PCR for all subjects along with its reassessment in follow-up samples for all patients.

Results: All patients in the study have achieved complete clinical and hematological response after six weeks of the beginning of imatinib therapy along with a highly significant increase in beclin-1 gene expression levels after treatment, ($P<0.001$) than before treatment in both patients groups I & II. There was no significant difference between group I & group II, regarding beclin-1 gene expression results after treatment ($p=0.631$). There was a high statistically significant negative correlation between beclin-1 gene expression before treatment and BCR-ABL gene expression results ($r=-0.844$ & -0.822) in group I and II respectively.

Conclusions: We concluded that beclin-1 dependent autophagy is increased after the beginning of imatinib therapy indicating induction of autophagy in CML patients, along with complete clinical and hematological response.

Keywords:

Introduction

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Range	(134-1000)	(145-409)	0.003*
Mean ± SD	506.4 ± 241.4	284.4 ± 91.0	

Hb, haemoglobin; TLC, total leucocytic count. * P value is significant (when P<0.05), ** P value is highly significant (when P<0.001)

Ethical Considerations

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