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Original Article

Frequency of Hematological Response in Patients with Chronic Myeloid Leukemia (Chronic Phase) with Imatinib After Three Months Presenting to CMH Rawalpindi

Anil Babar, Riaz Ahmed*, Ahmed Raza*, Zulfiqar Ali Amin*, Muhammad Nadeem Piracha*, Anum Zargham, Ibtisam Idrees***

Department of Oncology, Queen Elizabeth Hospital Birmingham England, *Department of Oncology, Combined Military Hospital /National University of Medical Sciences (NUMS) Rawalpindi Pakistan, **Department of Oncology, Fauji Foundation Hospital Rawalpindi Pakistan

ABSTRACT

Objective: To find the frequency of haematological response in patients of chronic myeloid leukaemia (Chronic Phase) after three months of Imatinib Mesylate therapy, presenting to CMH Rawalpindi

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Oncology Combined Military Hospital, Rawalpindi Pakistan, from Jan to Jun 2020.

Methodology: Forty-six patients aged 18 and above within the chronic phase of CML were included. Patients underwent detailed clinical history, examination, baseline investigations, and bone marrow studies at presentation. Enrolled patients were given 400mg of Imatinib, and a complete haematological response was noted at the end of 3 months of therapy.

Results: In our study, the age of patients ranged from 18 to 67 years, with a mean age of 47.2+10.6 years. 33(71.7%)were male, and 13(28.3%) were female. 42(91.3%) patients achieved complete haematological response to Imatinib at three months of therapy. Adverse drug reactions exhibited were oedema 18(39.1%), gastrointestinal disturbance 12(26.1%), anaemia 05(10.9%), and skin reactions 03(6.5%).

Conclusion: This study has concluded that Imatinib Mesylate is highly effective in treating chronic phase CML at the haematological level and can be considered the drug of first choice in CML-CP.

Keywords: Chronic Myeloid Leukemia, Chronic Phase, Imatinib Mesylate.

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INTRODUCTION

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder of the hematopoietic stem cells, characterized by excessive propagation of marrow granulocytes, erythroid precursors, megakaryocytes and connective tissue forming cells.[1] The disease is associated with an oncogenic reciprocal translocation t(9;22) (q34;q11), forming the Philadelphia chromosome. It accounts for 15% of all leukaemia cases worldwide. CML is a biphasic or tri-phasic disease.[2] The disease progresses through three distinctive stages, i.e., chronic phase (CP), accelerated phase and blast crisis.[3] The untreated chronic phase usually evolves into an accelerated or blast phase in three to five years.[4]

Allogenic Stem Cell Transplant is currently considered the only curative therapy for CML and, when feasible, is the treatment of choice.[5] Nowadays, the goal of therapy is to achieve complete haematological and molecular remission and the ultimate cure for the disease. Imatinib, a tyrosine kinase inhibitor, is a revolution in treating CML.[6,7] Imatinib is standard therapy for patients with chronic myeloid leukemia with durable responses in most patients treated in the chronic phase.[8] However, some patients eventually develop resistance, particularly those treated in the advanced stages. Since the introduction of Imatinib in 2000, the annual mortality in CML has decreased from 10%-20% to 1%-2%.[9]

Imatinib marks the ATPase portion of the BCR-ABL tyrosine kinase by mechanism, allowing the cells to divide at a normal rate. The documented haematological remission rate is more than 90%, and the cytogenetic remission rate is around 60%, with the main cytogenetic diminution rate of up to 30% in patients in the chronic phase of CML.[10] In acquaintance with the above statistics, CML has been changed from a life-threatening disease to a chronic illness over a decade. This study was to report the haematological response and side effects of Imatinib in CML patients at the Tertiary Care Oncology Unit of Military Hospital, Rawalpindi.

Correspondence: Dr Anil Babar, Department of Oncology, Queen Elizabeth Hospital Birmingham England

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METHODOLOGY

The cross-sectional study was conducted at the Oncology Department, Combined Military Hospital Rawalpindi, from January 2020 to June 2020 after approval from the Ethical Review Board (letter number 104/08/20(44). The sample size was calculated by the WHO calculator taking 10% level of significance with population prevalence proportion of haematological response in CML patients with tyrosine kinase inhibitors as 11%.[11] An informed written consent was taken from patients participating. A non-probability sampling technique was used to gather the sample for this study.

Inclusion Criteria: Patients of either gender, aged 18 and above in the chronic phase of CML with a low-risk Sokal score were included.

Exclusion Criteria: All patients with a high Sokal score, in accelerated phase or blast crisis, and who refused to participate in the study were excluded.

All the patients were diagnosed based on clinical features, peripheral blood smear (PBS) findings, Bone marrow aspiration (BMA) findings, and real-time reverse transcriptase quantitative polymerase chain reaction (RT Q-PCR).

They were given a full briefing on the study procedure before enrollment. The consultant oncologist confirmed the diagnosis and decided to start the treatment after the consent of the patient. The dose of Imatinib administered was 400mg/day orally. All the patients were followed closely over three months using the following parameters: (1) monthly clinical examination, (2) 3-month CBC and peripheral blood smear examination. The patient was considered to have a complete haematological response if he/she achieved normal haemoglobin, leucocyte and platelet indices within three months of starting treatment with the said drug. The patient was free of all signs and symptoms and resolution of splenomegaly. Patients were interviewed and examined on all the follow-up visits for the presence of any adverse effects.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

A total of 46 patients of CML managed with Imatinib were included in the study. Of them, 33(71.7%) were male and 13(28.3%) were female. In our study, the age of patients ranges from 18-67 years, with a mean age of 47.2+10.6 years. There were 11(23.9%) patients in 18-40 years of age, 30(65.2%) were between the age of 41-60 years and only 5(10.9%) patients above 60 years. Results are demonstrated in Table-I.

In the current study, 42(91.3%) patients achieved complete haematological response to Imatinib at three months, while 4(8.7%) patients failed to show the required response within three months.

In terms of adverse drug reactions, the most frequent side effect shown by the patients was oedema in 18(39.1%), followed by a gastrointestinal disturbance in 12(26.1%), anaemia in 5(10.9%), and skin reactions in 3(6.5%) of individuals (Table-II).

Table-I: Basic Demographic Profile of Study Participants (n=46)

Study parameters	n(%)
Gender	
Male	33(71.3%)
Female	13(28.3%)
Mean Age	47.2+10.6 years
18-40 years	11(23.9%)
41-60 years	30(65.2%)
Above 60 years	5(10.9%)
Response to Imatinib at Three Months	
Complete remission	42(91.3%)
No remission	04(8.7%)

Table-II: Adverse reaction to Imatinib Seen in Study Participants (n=46)

Adverse effects	n (%)
Edema	18(39.1%)
GI disturbances	12(26.1%)
Anemia	05(10.9%)
Skin reaction	03(6.5%)
Others	01(2.1%)

DISCUSSION

The natural history of chronic myeloid leukaemia has changed in recent years, partly as a result of earlier diagnoses but mostly due to the availability of effective therapies.[12] CML is extensively studied in the West, but there needs to be more data available in the country. Chronic myeloid leukaemia (CML), being the commonest leukaemia in Asia, needed a

haematological profile and frequency of three phases of CML with early diagnosis and treatment among the Asian population to improve the survival rate in CML reported by Altekruse *et al*.[11] In this study, the mean age of presentation was 47.2+10.6 years, which is significantly lower than the mean ages in European (median age 55 years).[12] and American literature (median age 66 years).[13] While a few other studies showed a lower median age of presentation 34-35 years.[14]

CML is more common in males. This is evidenced by 33 males and thirteen females being diagnosed and treated in this study. In one study, among 335 patients with CML, the male-to-female ratio was 2:1, approximately similar to our study.[14] Usmani *et al*. 2019 published a study that showed analogous results with male dominated presentation of disease than females.[15]

Regarding complete haematological response, 91.3% of patients achieved it after three months of treatment with Imatinib, which is very close to the finding of the Aslam *et al*.[16] study in which the CHR is 92.5%. An even higher response (93.75%) is achieved in another study than in ours in 3 months of therapy. However, 8.7% failed to show a response in the specific period. The median time for CHR is one month. These figures strongly suggest that Imatinib is highly effective at the haematological level of response in the chronic phase of CML.

All the patients generally well tolerated the Imatinib therapy with some side effects. The most common side effect in our study was oedema. Regarding comparing other side effects with Aslam *et al*. study.[16] the gastrointestinal disturbance was observed in 26.1% rather than 33.3%, showing a significant 7% lower value. Following this, anaemia was observed in 10.9%, which is lower than the figures reported (19.2%) in Moura *et al*. study.[17] after long-term therapy with Imatinib in CP CML and skin toxicities in 6.5% of patients, and the figure is much lower than the one reported (36.5%) in Malhotra *et al*. study.[18]

The response in patients with CML who received Imatinib was good, and this drug is already in practice at various oncology centres. Most of the patients achieved complete remission at the cost of few and mild adverse effects, which highlights the effectiveness of this medication in haematological malignancies like CML.

LIMITATIONS OF STUDY

All the toxicities were grade 1/2 according to CTCEA v5.0; none required treatment interruption. Additionally, the complication rates and grades in this study were lower than the documented rates/grades in recent studies. They did not require any additional treatment for the anaemia or toxicities and hence did not affect the response rate to Imatinib.

CONCLUSION

This study concluded that Imatinib Mesylate is highly effective in treating chronic phase CML at the haematological level, so it should continue as the drug of first choice in CML. However, further study is intended to determine the molecular response of Imatinib.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

AB & RA: Conception, study design, drafting the manuscript, approval of the final version to be published.

AR & ZAA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MNP & AZ & II: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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