Annual Saudi Hematology Congress
ASHC 2023

Title

Adverse effects of Imatinib in patients with chronic myeloid leukemia

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Introduction

Tyrosine kinase inhibitors were invented in the early 2000s and are now considered to be one of the most effective anti-cancer agents. They are used to treat multiple malignancies such as chronic myeloid leukemia, hepatocellular carcinoma, and non-small cell lung cancer. Their discovery revolutionized the treatment and prognosis of chronic myeloid leukemia. Imatinib was the first tyrosine kinase inhibitor used in CML. It produces very good responses, but many side effects have been reported. In this study, we aim to evaluate the adverse effects of Imatinib in our population.

Methodolgy

a retrospective study, descriptive and analytical, about 171 patients with chronic myeloid leukemia, followed up in an internal and onco-hematology department between January 2012 and December 2022.

Results

Our study included 171 patients, with a mean age of 47.57 years [17-90], consisting of 75 men and 96 women, with an F/M sex ratio of 1.28. The median diagnostic delay was 4.5 months. Splenomegaly was found in 88.8% of our patients, and 28.48% had a perfomans status of III or IV. The complete blood count (CBC) revealed anemia in 117 patients (68.42%), leukocytosis with myelemia on blood smear in all our patients, with major hyperleukocytosis (greater than 100,000/mm^3) in 53.21% of our patients. Tumor lysis syndrome was observed in 60 patients (35%).

The myelogram classified the disease into a chronic phase in 135 patients (78.94%) and an accelerated phase in 36 patients. Karyotype revealed the Philadephia chromosome in 148 patients (86.5%) reflecting translocation t(9;22). The resulting transcript BCR-ABL was detected in all patients. Ninety-seven patients (56.72%) were treated with Hydroxyurea before initiation of tyrosine kinase inhibitors. All our patients were put on Imatinib as first-line therapy.

Adverse effects of Imatinib were observed in 43 patients (25.14%). They consisted of hematological side effects in 39 patients: Thrombocytopenia in 20 patients, Neutropenia in 11, Anemia in 5, and 1 case of eosinophilia. Pancytopenia was observed in two patients. The management of hematological complications consisted of the suspension of treatment in 5 patients with platelets count ≤50 000/mm^3, and in two patients with Neutrophils ≤500/mm^3, and the reduction of dosage in 10 patients, this resulted in the resolution of the disorder in all patients, with the restoration of treatment at a dose of 400 mg/day in 35 patients. Only 4 patients required a long-term dose of 300 mg/day to prevent adverse effects.

Dermatologically, 3 patients developed mild and transient itching on initiation of treatment, and two developed toxidermia, requiring the switch to another class of tyrosine kinase inhibitors: Nilotinib in one patient and Dasatinib in another.

A disturbance in liver function was observed in 6 patients, consisting of a slight increase in the transaminases within the two first weeks of the start of the treatment. This effect resolved after a brief cessation of treatment, with no further occurrence. Only one patient developed gynecomastia.

There was no significant association between the occurrence of an adverse event and response to Imatinib in our study (p=0.260).

Conclusion

Our study shows that it is not rare for adverse events to occur upon initiation of Imatinib. However, these events are often benign and can be resolved by adapting or temporarily interrupting treatment, or simply by monitoring the patient closely and observing the improvement in their condition. Serious incidents are not the rule, and there are always other options for continuing to treat the patient without these risks. Another bright spot is that the presence of these effects does not impair the patient's response to treatment.