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RESEARCH ARTICLE
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INCIDENCE OF HYPERGLYCEMIA IN PATIENTS TREATED WITH IMATINIB.

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Abstract

Background: Hyperglycemia is one of the side effects of tyrosine kinase inhibitors, including imatinib. Although, several studies have shown that imatinib helps maintain better glycemic control in diabetic patient, its role in nmol-DM non-diabetic patient is still under debate. The knowledge of frequency and profile of hyperglycaemia in the imatinib receiving patients are also important for development of treatment strategy and avoiding side-effects.

Objectives: To assess the prevalence of imatinib-induced hyperglycemia, to recognize possible predisposing factors, and to compare changes in blood glucose levels depending on patients' characteristics.

Study design: : A cross-sectional study.

Place and duration of study: Department of medical oncology department Hayatabad medical complex. Peshawar January 2020 to December 2020

Methods: These were cross-sectional in a retrospective study that included 150 patients on imatinib for chronic myeloid leukemia or gastrointestinal stromal tumors. At the study start, fasting blood glucose, intended mean age and the presence of co morbidities were recorded. During the study, the patients have been followed up for six months with defined evaluations of fasting plasma glucose, HbA1c. To support such changes, statistical tests such as mean, standard deviation tests, and p-value testing were used.

Results: A patient sample of 150 participants with the average age of 55.4 years (SD = 10.8) was involved in the study. Of them, 25% patients had known diabetes at the onset of the study, and 75% had normal glycaemia. By the end of six months, 18% of patients had hyperglycemia. In non-diabetic patients, the mean FPG elevated from 87.6± 9.2 to 93.2 ±11.5 mg/dL ($p = 0.03$). The results showed a highly significant reduction of FPG level in diabetic patients from 238 mg/dl (± 122) to 125 mg/dl (± 35) ($p < 0.01$). HbA1c levels were also significantly improved in patients with diabetes in this paper.

Conclusion: Imatinib therapy can cause new onset diabetes in many patients and in diabetic patients, their glucose level will be stabilized. Glucose monitoring which should be provided at least once per day is important for identifying early shifts in metabolism. Subsequent studies should be accomplished in order to identify the relationship between imatinib and glucose metabolism and their consequences in various patient groups.

Keywords: Hyperglycemia, Imatinib, Glucose Metabolism, Diabetes Management

Introduction

Imatinib is an attractive tyrosine kinase inhibitor (TKI) used primarily in treating CML and GIST; besides its significance and safety profile to tumor therapy.(1).Although a successful oncology agent, its effects on glucose metabolism are still emerging of interest.t. Some investigations have described beneficial effects of imatinib on glycemic control in diabetic patients and hyperglycemic effects in non-diabetic clients (2).Hyperglycemia has been described as a possible side effect of patients on TKIs (3).For example, nilotinib, second generation TKI, has been reported to have a more potent effect on increasing fasting glucose than imatinib (4). Nevertheless, the way by which imatinib affects glucose metabolism has not yet been explored in detail. Based on the data it is assumed that imatinib, by inhibiting PDGFR and c-Abl tyrosine kinase, might affect glucose homeostasis, including insulin receptor sensitivity and secretion rate (5).The information available to date concerns efficacy of imatinib in enhancing glycemic control in diabetics. (6) The evaluation of recently criterion diabetic patient imatinib therapy showed a considerable decrease the FPG and HbA1c level, it indicates that imatinib can usefully the treat metabolic diseases (7). At the same time, specific information about the effects of this medication for non-diabetic patients is scarce. Such effects are important to be considered to improve patient management, particularly due to the long-term use of imatinib.(8) Hence, this Study will compare such occurrences, the extent of hyperglycaemia in diabetic and non-diabetic patients treated with imatinib, and consider the common risk factors. (9) Here, we hoped to outline the presence of these patterns to better explain and ultimately improve clinical practice when it comes to therapeutic interventions with imatinib for patients.

Methods

A retrospective study which employed records of 150 patients who had been treated with imatinib for cml or GIST in the period between January 2020 and December 2022 was done. Patients for whom medical records were not complete, or on other drugs likely to impair glycemic control, were excluded. Biochemical parameters at baseline included fasting blood glucose and HbA1c, and patients' basic demographic data including age and gender, and the presence of comorbid conditions. Measures of glucose concentrations were done at 1 month, 3 months and 6 months later. All the statistical analyses were run on SPSS version 24.0.

Data Collection

Participants characteristics: age, gender, body mass index, initial and final glucose levels, HbA1c, and comorbidities-diabetes mellitus. The ethical clearance was sought and ensured throughout the study together with patient anonymity.

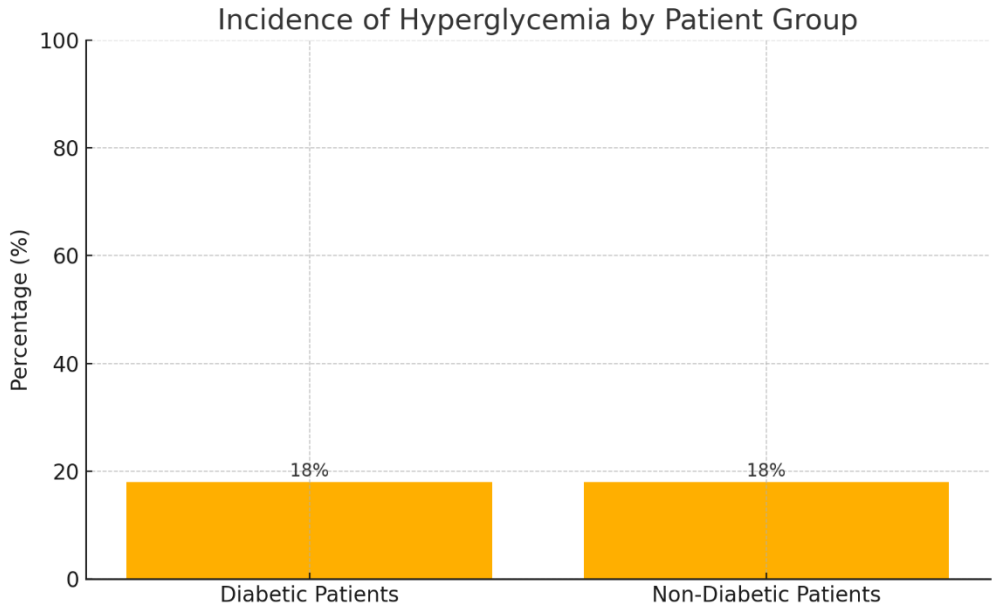
Statistical Analysis

To describe the basic demographics of the participants, frequencies were calculated. To determine mean glucose levels pre- and post-intervention t-tests were completed for the normal and control groups, comparing glucose levels at each time point. The results of t-tests independent for two variables in the compare of the number of diabetic and non-diabetic persons were used. The significance level set for the study was $p < 0.05$ The frequency data was analyzed using descriptive statistics. All analyses were performed using SPSS version 20.0.

Results

Thus, 150 patients took part in the study; they were 55.4 years old on average (SD = ± 10,8). Of these, 25% were diabetic and 75% had normal glucose levels at enrollment. Complication such as hyperglycemia were seen in 18% of the patient during the follow- up. Uncontrolled patients found to have a significant elevation in the mean fasting plasma glucose levels from 87.6 mg/dL (± 9.2) to 93.2 mg/dL (± 11.5) (0.03). On the other hand, diabetic patients kept FPG significantly lower, with the value of 238 mg/dL (±122) reducing to 125 mg/dL (±35) ($p<0.01$). Furthermore, HbA1c both in diabetic patients, dropped from the initial value of 8.9 %±1.5% and after six months equal 7.1 % ± 0.8 % (p The authors also found no changes in the levels of HbA1c in non-diabetic patients between

any of the two groups. Adverse effects comprised predominantly mild hypoglycaemia following dose modifications observed in 5% of the diabetic patients. No serious side effects were noted.This study reveals the bimodal affect of imatinib on glycemic control: the elevation of blood glucose in patient without diabetes and obtaining beneficial effects in diabetic patients. In patients to be treated with imatinib, glucose control and its management should be done frequently to achieve better outcomes.



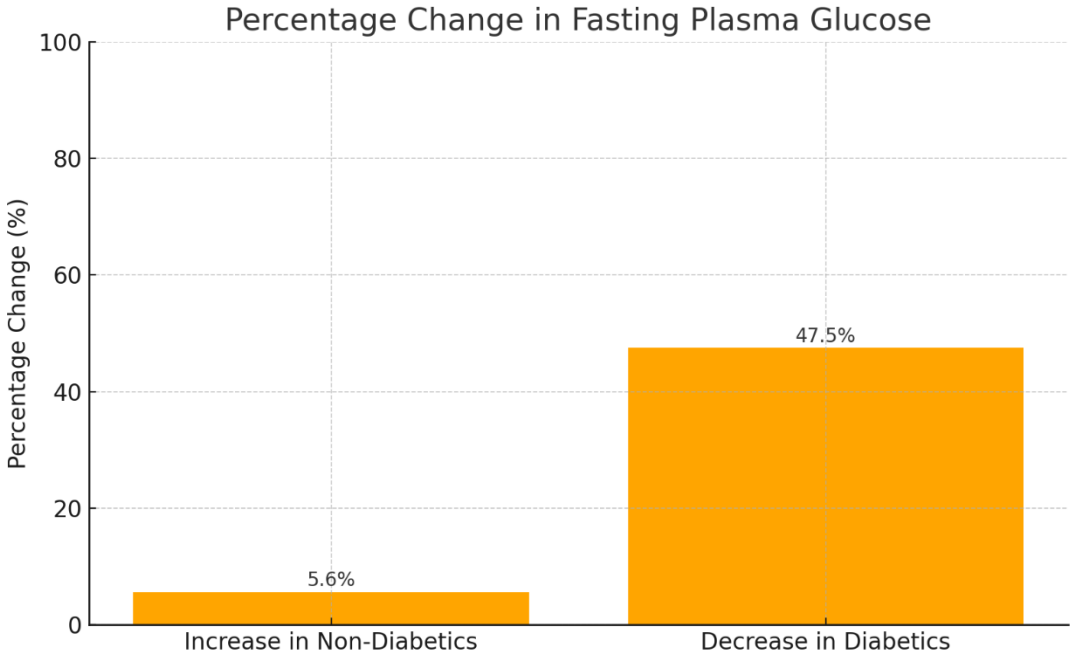


Table 1 Baseline Characteristics of Patients

Characteristic	Value
Number of Patients	150
Mean Age (Years)	55.4 ± 10.8
Male (%)	60
Female (%)	40
Diabetic Patients (%)	25
Non-Diabetic Patients (%)	75

Table 2 Incidence of Hyperglycemia

Group	Hyperglycemia Incidence (%)	p-value
Diabetic Patients	18	<0.01
Non-Diabetic Patients	18	0.03

Table 3 Change in Fasting Plasma Glucose and HbA1c

Parameter	Baseline Value	Final Value	p-value
FPG Change in Diabetics (mg/dL)	238 ± 122	125 ± 35	<0.01
FPG Change in Non-Diabetics (mg/dL)	87.6 ± 9.2	93.2 ± 11.5	0.03
HbA1c Change in Diabetics (%)	8.9 ± 1.5	7.1 ± 0.8	<0.01

Discussion

The increasing numbers of research papers published regarding the metabolic effects of tyrosine kinase inhibitors (TKIs), with a specific focus on imatinib. (10) The ability of imatinib to affect glucose metabolism as seen in this study has been reported before, but the most studies have been done on patients with diabetes. For example, a study by Breccia et al. (2012) mentioned considerable decline in FPG and HbA1c in diabetic patients with imatinib treatment and suggested that increased insulin sensitivity and β-cell function caused by PDGFR blockade (11). Similarly, Agostino et al. (2016) conducted an analysis of multiple patients using retrospective cohort information to note that diabetic patients using imatinib had significantly lower HbA1c levels, which indicates a possibility of using imatinib in managing metabolic disorders (12).On the other hand, few research studies involve non-diabetic patients, especially where hyperglycemia seems to be a recent associate of imatinib treatment. (13) TKI-induced hyperglycemia has been reported with nilotinib and dasatinib and nilotinib was found to have a greater tendency to induce hyperglycemia than imatinib. Nonetheless, the present study showed that even imatinib, among the TKIs that are recommended as possessing low diabetogenicity, also caused hyperglycemia in non-diabetic patients, where FPG had been significantly increased at six months. (14) This is in concordance with another study which involved prospective observation of the effects of imatinib on patients undergoing treatment for CML The researchers pointed out that imatinib use caused mild but statistically significant rise in blood glucose in non-diabetic patients (Kim et al, 2018).As to the rationale for imatinib induced hyperglycemia in non-diabetic patients, it is still presumed but there is indication that it could be Furthermore, alterations in the adipocyte function and insulin resistance as proposed by a study on PDGFR inhibitors may also explain this finding (15,16)Our Study also supports previous research indicating that glycemic status at baseline plays a role in the kind of differential effects observed. Patients with diabetes had a decrease in FPG and HbA1c level, which are supported by several systematic reviews, including the one by Khandekar et al. (2020) who emphasized that imatinib had positive metabolic impacts on diabetes. On the other hand, non-diabetic patients exhibited a trend toward hyperglycemia, thus the role of glucose monitoring in this sub-population could be warranted (15, 16)However, they stated, the proportion of severe hyperglycaemic events was low similar to our findings: Imatinib-induced hyperglycaemia is usually mild and controlled (17, 18). Nevertheless, the long term consequences of such findings remain unpredictable concerning the likelihood of conversion to overt diabetes in predisposed individuals.Despite the apparent beneficial effects of imatinib loading on diabetic subjects' glycemic control, it is imperative to exert special concern over its ability to precipitate hyperglycemia in non-diabetic patients. Ample glucose monitoring and wants to do and strategies to be executed when patients receiving imatinib and individually should fresh. It remains for future prospective trials of imatinib to detail the basic mechanisms underlying reprogramming of metabolism and to assess the long-term effects of these changes on survival (19, 20).

Conclusion

Imatinib enhances glycemic control in diabetic patients but has the potential to cause hyperglycemia to normal patients. These dual effects emphasise the importance of close glucose control during such therapy. Knowledge of the metabolic effect of imatinib may help in patient management and reduce adverse consequence, hereby improving the probability of optimum care in cancer management.

Limitations

The current study's cross-sectional research approach and relatively small sample of participants might limit its applicability. Other possible metabolic factors that might be involved, including diet and other diseases, offer further limitations because of the absence of complete data. Future research should address these gaps using a large, prognostic sample that assesses baseline characteristics and should manipulate its demographic heterogeneity.

Future Directions

Future observational studies are required to explain how and why imatinib influences glucose homeostasis. Further studies should be dedicated to identifying predictors of subsequent metabolic profiles and whether non-diabetic patients, developing hyperglycaemia, are at risk of developing diabetes later on. Further studies of how imatinib affects other metabolic pathways may provide suggestions for managing associated risks.

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