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Pharmacokinetic interaction between imatinib and rifampicin in a chronic myeloid leukemia patient dose adjustment challenges

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Introduction

The co-administration of CYP3A4 inducers like rifampicin with imatinib may significantly alter imatinib's pharmacokinetics, as CYP3A4 metabolizes imatinib. This clinical observation aimed to highlight a pharmacokinetic drug-drug interaction between imatinib and rifampicin.

Case report

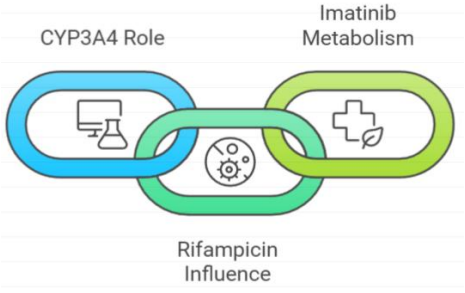
A 29-year-old male patient with chronic myeloid leukemia (CML) was being treated with imatinib 400mg daily. Three months into his treatment, rifampicin and isoniazid were introduced for tuberculosis prophylaxis, prompting the need for imatinib plasma concentration monitoring. The imatinib plasma concentration was found to be 305.3 ng/mL, which was subtherapeutic (reference range: 1000–3000 ng/mL), with a concentration-to-dose (C/D) ratio of 0.8.

After discontinuing rifampicin and switching to ethambutol, the imatinib plasma concentration increased significantly to 3838 ng/mL, which was supratherapeutic, with a C/D ratio of 9.6, despite maintaining the same 400 mg dosage. Consequently, the imatinib dose was reduced to 200 mg daily to bring the plasma concentration within the therapeutic range, achieving a level of 1466.2 ng/mL with a C/D ratio of 3.7.

Discussion

Imatinib's metabolism is primarily facilitated by CYP3A4, and the introduction of rifampicin, a potent CYP3A4 inducer, led to a marked reduction in imatinib plasma concentrations, underscores the necessity for monitoring plasma concentrations when initiating or modifying therapy with known enzyme inducers [1].

After discontinuation of rifampicin and switching to ethambutol, the imatinib concentration surged to 3838 ng/mL, indicating a rapid restoration of imatinib levels upon removal of the inducing agent. This scenario necessitated a dose adjustment to mitigate potential toxicity associated with elevated drug levels, demonstrating the delicate balance required in managing tyrosine kinase inhibitors therapies where drug interactions are possible [2].



Conclusion

This case highlights the importance of individualized treatment regimens and the role of therapeutic drug monitoring in optimizing therapeutic outcomes. As seen in this patient, maintaining imatinib plasma levels within the therapeutic range is crucial for achieving optimal clinical responses while minimizing adverse effects.
Moreover, healthcare providers should be aware of potential interactions between imatinib and other medications, particularly those that induce or inhibit CYP3A4.

References

1. Martins DH, Wagner SC, Dos Santos TV, Lizot Lde L, Antunes MV, Capra M, Linden R. Monitoring imatinib plasma concentrations in chronic myeloid leukemia. Rev Bras Hematol Hemoter. 2011;33(4):302-6.
2. Miura M. Therapeutic drug monitoring of imatinib, nilotinib, and dasatinib for patients with chronic myeloid leukemia. Biol Pharm Bull. 2015;38(5):645-54.