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Significant pharmacokinetic interaction between dexamethasone and imatinib in a pediatric patient with acute lymphoblastic leukemia

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Introduction

Dexamethasone, a recognized substrate and inducer of CYP3A4, is susceptible to metabolic drug-drug interactions (DDIs). In a study investigating potential interactions with imatinib, dexamethasone emerged as the third most likely interacting drug. However, the clinical significance of this interaction remains unclear. This report presents a case study highlighting the pharmacokinetic interaction between imatinib and dexamethasone.

Case report

A 6-year-old female diagnosed with Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) was treated with dexamethasone and imatinib. Initially, her imatinib trough plasma level was 672.3 ng/mL while receiving 200 mg daily, which was subtherapeutic (reference range: 1000–3000 ng/mL), with a concentration-to-dose (C/D) ratio of 3.4.

Increasing the dose to 300 mg daily resulted in a plasma concentration of 1726.1 ng/mL and a C/D ratio 5.8. After discontinuing dexamethasone, the imatinib concentration rose sharply to 3771 ng/mL, with a C/D ratio of 12.6. Subsequently, reducing the imatinib dose back to 200 mg daily brought the concentration within the therapeutic range, reaching 2543 ng/mL with a C/D ratio of 12.7.

Discussion

This case study illustrates a marked increase in imatinib plasma concentrations upon the discontinuation of dexamethasone, suggesting that dexamethasone acts as an inducer of CYP3A4, leading to enhanced metabolism of imatinib. This finding corroborates previous research indicating that dexamethasone can significantly alter the pharmacokinetics of other drugs metabolized by CYP3A4 [1].

The subsequent rise in imatinib levels after stopping dexamethasone highlights the necessity for clinicians to be vigilant about potential interactions that may compromise treatment effectiveness [1]. Moreover, this case underscores the importance of individualized dosing strategies in pediatric oncology. As children metabolize drugs differently than adults, standard dosing regimens may not be appropriate. The significant fluctuations in drug levels observed in this patient emphasize the need for therapeutic drug monitoring (TDM) to optimize imatinib therapy and avoid toxicity [2].

Conclusion

This observation underscores the significant impact of dexamethasone on imatinib pharmacokinetics in a pediatric patient with Philadelphia chromosome-positive ALL. Given that dexamethasone likely induces the metabolism of imatinib via CYP3A4, it is essential to enhance monitoring and consider dose adjustments when co-administering these drugs. This approach helps optimize treatment outcomes while minimizing the risk of toxicities.

References

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