

REFERENCES

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Conflict of interest: Professor Seale has served on the advisory groups of several pharmaceutical companies which produce respiratory drugs, including GlaxoSmithKline and Boehringer Ingelheim.

Self-test questions

The following statements are either true or false (answers on page 47)

3. Anticholinergic bronchodilators are more effective than beta agonists.
4. Anticholinergic bronchodilators do not prevent the decline of lung function in patients with chronic obstructive pulmonary disease.

Medicinal mishap

Topical drug with systemic risk

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Case

A 75-year-old woman with hypertension and diabetes was prescribed warfarin for atrial fibrillation. During three and a half years of treatment her INR was 2.3–2.5.

When her INR rose to 14.1 on 27 February I thought it was a laboratory error (she displayed no bleeding) but told her to stop the warfarin. On 2 March the INR was 12.0, but she had developed huge bruises on all limbs and carpal tunnel pain. By 6 March the INR was 6.2, but the woman had bigger thigh and cheek haematomas. On 10 March the ecchymoses were subsiding and warfarin was resumed when the INR fell to 1.7.

Comment

The cause of this patient's problems was probably an interaction with an antifungal drug. Her dentist had prescribed amphotericin lozenges and miconazole oral gel on 9 February. She asked me on 13 February if these products might affect her warfarin, but as they were topical preparations I ignorantly reassured her.

Her dentist was also unaware of the potential interaction when the patient asked him about her warfarin. He may have been alerted had she been a surgical case rather than someone having her dentures fixed. The hospital pharmacy computer was not linked to her community pharmacist so there was no warning of the interaction between warfarin and miconazole.

Warfarin interacts with several antifungals including itraconazole, fluconazole and ketoconazole. The interaction may be mediated through the cytochrome P450 system.¹ Miconazole can inhibit the metabolism of drugs by cytochrome

P450 3A and 2C9 and this is probably how it increases the effect of warfarin.

Although miconazole oral gel has a low bioavailability some is absorbed into the systemic circulation. This may be sufficient to cause a significant interaction with warfarin. Several reported cases involved bleeding.^{2,3} As the consequences of bleeding can be catastrophic, high INR may require more intense treatment than this patient received.⁴

The interaction can also occur with other formulations of miconazole but may not be mentioned in the product information. There have been reports with topical cream⁵ and vaginal pessaries.⁶

Conclusion

Topical medications can have systemic effects including drug interactions. As miconazole oral gel is available without a prescription, the public as well as health professionals need to be warned about the potential interaction with warfarin.

The case also serves as a reminder not to dismiss patients' concerns too quickly. A check of the product information would have alerted me to the interaction between miconazole oral gel and warfarin.

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