Pitfalls of 'inert' ingredients

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Sequence of events

DURING the 1999/2000 influenza outbreak, a 53-year-old man consulted because of a persistent productive cough that followed a flu-like illness. The patient was examined and prescribed erythromycin (Erymax® [Elan]) capsules. He made it very clear that he had a previous history of aspirin allergy and was reassured that there was no known cross-sensitivity between erythromycin and aspirin. Two days later, the patient's wife came to the surgery; she was angry and upset because, shortly after taking the erythromycin capsules, her husband had developed some tingling and swelling of his fingers and feet similar to the symptoms he had previously experienced with aspirin. They were both disturbed to find the following warning in the erythromycin patient information leaflet: '… capsules containing the colouring agent E110. This can cause allergic-type reactions including asthma. You are more likely to have a reaction if you are also allergic to aspirin.' Since the patient had highlighted his aspirin allergy, he and his wife were upset that he had been prescribed a preparation that could cause problems in patients with this history. Despite a home visit to review the patient and make a full apology, the patient's wife went on to make a formal complaint.

Discussion

This case raises a number of issues. Excipients are regarded as inert ingredients and, although most are well tolerated by patients, adverse effects have been described.[1-4] Obviously, it is not certain that this patient had an allergic reaction to substance E110. He may have had an allergic reaction to the active component, erythromycin. Should the patient be denied this useful antibiotic in the future? To avoid such confusion, a more rational approach would be to ban from medicines troublesome dyes, which have been associated with adverse events.[5,6]

This case also gives rise to concerns about an inconsistent level of content of drug information. The prescribing doctor in this instance was unaware both of the presence of E110 in erythromycin capsules and of the cross-sensitivity between E110 and aspirin.[7,8] There is no mention of this reaction in the British National Formulary, or in the Pharmaceutical Data Sheet Compendium, and there is no copy of the erythromycin patient information leaflet in the current Patient Information Leaflet Compendium. It seems paradoxical that there should be more information about this drug available to the patient than to the prescribing doctor.

Since 1994, and in line with European Community Directives, UK regulations have required drug companies to include a patient information sheet in all packs of newly introduced products or products requiring licence renewal. Details should be given of 'the excipients, knowledge of which is important for the safe and effective use of the medicinal product'.[9] For excipient E110 alone, the Medicines Control Agency advises that there are 195 licensed medicines that contain this ingredient. Of these, one-third do not require a prescription. At the time of writing, the Committee on Safety of Medicines (CSM) and the Medicines Control Agency have received 20 reports of adverse reactions which were suspected to be associated with the excipient E110 (CSM personal communication Dr Sarah Davis, 2001). At present, the level of dissemination of this type of information is variable. In some cases, troublesome excipients are present but no patient information sheet is provided. Other products include a list of excipients but no mention of previous reactions and some products list their excipients but only highlight some of the potential adverse reactions. The amount of information given appears to be incomplete. For example, the patient information sheet for erythromycin lists a potential problem with aspirin and excipient E110, as occurred in the above case. However, excipient E104 is another 'inactive ingredient' of erythromycin capsules. This dye has been banned in several countries because of a recognised association in causing urticarial reactions in atopic individuals.[10] No mention of this potential reaction is made in the erythromycin patient information leaflet.

This case raises concerns about the safety and toxicity of supposedly inert ingredients within our medicines and highlights loopholes in the amount of drug information available to both doctors and patients.

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