SIDE EFFECTS OF DRUGS

Hyperpigmentation associated with oxprenolol administration

Skin sensitivity reactions to beta-adrenergic receptor blocking drugs, usually psoriasis-like eruptions, have been widely reported.[1-5] We report here a patient who developed generalised hyperpigmentation of the skin during treatment with oxprenolol (Trasicor).

Case report

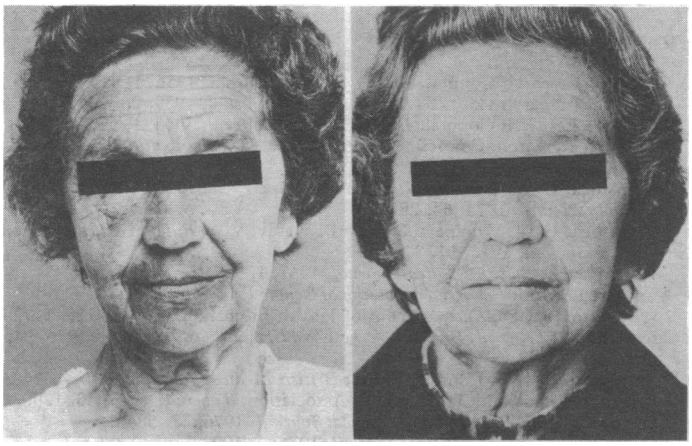
A 62-year-old housewife presented with a three-month history of increasing generalised skin pigmentation, which was particularly marked round the mouth, both sides of the neck, and the back of the hands. She had been found to be hypertensive five months earlier and was treated with oxprenolol 240 mg/day in addition to the digoxin and quinine sulphate which she had been taking for five years.

Physical examination confirmed the striking brown pigmentation, which was also present over the exposed areas of both legs as well as on the corset and brassière pressure areas. There was no buccal or notable periareolar pigmentation. Examination was otherwise satisfactory, her blood pressure being 180/90 mm Hg. Haematological values, blood urea and electrolytes, protein-bound iodine concentration, skull and chest radiographs, and electrocardiogram were all normal. Diurnal variation of plasma corticosteroids and urinary 17-hydroxycorticosteroid (17-OHCS) and 17-oxosteroid (17-OS) excretion were also normal. All drugs, including oxprenolol, were withdrawn and the pigmentation rapidly diminished, the blood pressure remaining normal. To determine whether the pigmentation was related to the oxprenolol treatment, and after full discussion with the patient, the drug was reintroduced in a dose of 160 mg daily in divided doses, and the patient was reviewed carefully each week. Details of plasma and urinary corticosteroids, plasma melanocyte-stimulating hormone (MSH), and plasma ACTH levels over this period are shown in the table. The pigmentation gradually reappeared (see figure), and the oxprenolol was withdrawn after four weeks' treatment.

Hormone and steroid assays before and during treatment with oxprenolol 40 mg four times a day

	Before treatment	On treatment			
		Week 1	Week 2	Week 3	Week 4
Pigmentation		−	+	+	+
Plasma corticosteroids (μmol/l)					
Morning	0·62		0·47	0·28	0·58
Evening	0·25				0·35
Urinary 17-OHCS and 17-OS (μmol/24 h)	40·3, 32·3 16·3, 13·9				63·3, 51·8 23·8, 20·7
Plasma MSH (ng/l)	13		32	35	60
Plasma ACTH (ng/l)	24	18	<34	<36	45

Conversion: SI to traditional units—Plasma corticosteroids: 1 μmol/l ≈ 0·036 mg/100 ml. Urinary 17-OHCS and OS: 1 μmol/24 h ≈ 0·29 mg/24 h.



Pigmentation during treatment with oxprenolol (left) which disappeared when treatment was withdrawn (right).

Comment

This patient developed pigmentation of her skin resembling that of Addison's disease during treatment with oxprenolol. The pigmentation regressed when the drug was withdrawn and recurred with further administration. Serum levels of MSH were not significantly raised during treatment when the pigmentation recurred. Plasma ACTH levels remained normal throughout the study. Plasma and urinary steroid levels remained unchanged.

The effect of oxprenolol in this patient may have been due to a local action of the drug on the skin, and it is most unlikely that MSH was implicated in the process. Photosensitisation is unlikely because of the generalised distribution of the pigment. The hyperpigmentation in this patient was therefore probably idiosyncratic in origin.

Beta-receptor blocking drugs, including oxprenolol, have been widely used for several years and it seems unlikely in the absence of other reports of hyperpigmentation with oxprenolol treatment that this effect is common. But in view of the delay that has sometimes occurred in recognising and reporting important side effects of drugs in widespread use, we have drawn attention to this association.

We thank Dr J J H Gilkes and Dr Lesley H Rees for performing the MSH assays and Dr J G Ratcliffe for performing the ACTH assays.

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(*Accepted 29 April 1977*)

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Hepatotoxicity of dextropropoxyphene

Distalgesic is a commonly used analgesic, each tablet of which contains 32·5 mg dextropropoxyphene and 325 mg paracetamol. Emmerson *et al* showed that daily doses of dextropropoxyphene 40 to 110 times the maximum clinical dose produced hepatic enlargement and fatty changes in the livers of rats.[1] So far only two cases of jaundice have been associated with the normal clinical use of dextropropoxyphene,[2 3] though paracetamol causes liver damage with jaundice in large doses but not in therapeutic doses. We report here two cases of hepatotoxicity induced by the dextropropoxyphene in Distalgesic.

Case 1

On 13 January 1977 a 56-year-old man was admitted for investigation of recurrent jaundice. He had first developed jaundice in 1944 and infective hepatitis was diagnosed. From 1971 to 1976 he had jaundice about twice a year. These episodes lasted two or three days, during which he passed dark urine. His usual analgesic at this time was codeine, but no convincing temporal relation could be established between the drug and the jaundice.

In July 1976 he was given Distalgesic to control low back pain. Ten days later he felt unwell and for a week noticed that his urine was dark, his motions pale, and his sclerae yellow. In October 1976 he again took Distalgesic and became jaundiced four days later. In December 1976 a third exposure to Distalgesic was followed by upper abdominal pain with jaundice beginning 24 hours later. He was not taking any other medication.

An intravenous cholangiogram was normal. A liver biopsy showed a minor degree of increase in fibrous tissue in the portal area with no liver cell necrosis and no bile stasis. After this biopsy he was given 130 mg dextro-