Raised serum protein-bound iodine after topical clioquinol

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RAISED serum levels of protein-bound iodine (PBI) in patients with normal thyroid function have been observed on many occasions after oral treatment with 5-chloro-7-iodo-8-hydroxyquinoline (iodochlorhydroxyquinoline, clioquinol, Enterovioform) (Thoren, 1960; Levin, Josephson & Grünewald, 1966; Sonksen et al., 1968). It is less well appreciated that clioquinol administered topically can be absorbed in sufficient quantities to influence the PBI and the uptake of radio-active iodine by the thyroid gland.

Case reports

Case 1
Mrs G. F., aged 26, complained to her general practitioner (A. C. U.) of anxiety. There were some other clinical features suggesting thyrotoxicosis and the serum PBI was found to be 17.0 μg/100 ml (normal, 3.5-8 μg/100 ml). She was referred to a physician (H. J. B. G.) in whose opinion she was euthyroid. A second PBI estimation was again raised at 11.0 μg/100 ml. It was then appreciated that for the previous 4½ months the patient had been applying Vioform-hydrocortisone cream to her hands as treatment for an exacerbation of chronic cheiropompholyx. This application was stopped and 14 days later the PBI was 6.8 μg/100 ml.

Three months later, after cessation of the local application, the PBI was 5.0 μg/100 ml. Vioform-hydrocortisone treatment was again applied for 12 days although the cheiropompholyx was quiescent and the skin was intact. The PBI 9 days after restarting the application had risen to 8.4 μg/100 ml.

Case 2
Four months after Mrs S. H., aged 36, developed varicose dermatitis she started using Vioform-hydrocortisone cream, and continued to do so for 17 weeks until her first out-patient visit to the skin department (B. S.). Apart from her varicose condition she complained of constant nervousness. Further examination revealed some signs of thyrotoxicosis. The PBI was 22 μg/100 ml. She stopped using the cream, and 3 weeks later her PBI was 5.2 μg/100 ml. She agreed to use the cream again, and after 3 weeks, during which time she had used nearly three 20 g tubes, her PBI was 13.4 μg/100 ml. She then stopped using the cream and her PBI had returned to 5.0 μg/100 ml a month later.

Comment
Vioform-hydrocortisone cream contains 3% clioquinol and 1% hydrocortisone in a water-soluble base composed of sodium lauryl sulphate, cetearyl alcohol, spermaceti, glycerin, yellow soft paraffin, and water. The patients were using approximately 1.7 and 1.2 g of the ointment respectively daily, thus each day about 35-50 mg of clioquinol was applied to the skin. Sonksen et al. (1968) gave 500 mg clioquinol orally daily for 2 weeks to eight healthy subjects and found a mean PBI level at the end of this period of 118 μg/100 ml. The elevation of the PBI may be influenced by the length of treatment as well as the dose and it may be important that our patients had each been applying the drug for over 4 months.

Corticosteroids applied to the skin are absorbed to a varying extent depending on the concentration, the total dose, the anatomical site of the application, the pathological state of the skin, the solubility of the particular steroid used, the character of the vehicle, and the age of the patient (Scoggins & Kliman, 1965; Sarkany & Hadgraft, 1969; Feiwel, 1969). Using large doses (1200 mg daily) of 1% hydrocortisone with an occlusive dressing, Scoggins & Kliman (1965) found that 'less than 10% of the dose was absorbed'. It seems probable from the findings...
in our two patients that a much higher proportion of the dose of clioquinol is absorbed.

Haskins, Luttermoser & Brady (1950) investigated the absorption and distribution of iodine after the oral administration of clioquinol to rabbits and suggested that this drug was absorbed, and eliminated, without degradation and without the liberation of inorganic iodine having occurred to any great degree. In human studies using clioquinol labelled with radio-active iodine, Liewendahl & Lamberg (1967) confirmed that a high proportion of the dose was absorbed from the gut. These workers also showed that, in rats, much of the drug was taken up by the thyroid gland in the unchanged form (Lamberg & Liewendahl, 1967). Iodine derived from the clioquinol was rapidly incorporated into the iodo-tyrosine precursors of thyroid hormone. This latter observation may explain why, although clioquinol interferes with the thyroidal uptake of iodine (Henderson Smith, 1964), no case of hypothyroidism attributed to clioquinol therapy has been recorded. Another possible risk of treatment with this drug is retinal damage (Lancet, 1968). The present cases suggest that very long-term application of clioquinol to extensive skin lesions should be embarked upon with caution.

The high levels of PBI found after clioquinol treatment are due in part to protein-binding of the drug as well as to contamination of the serum by inorganic iodine (Liewendahl & Lamberg, 1968). Although normal PBI levels were regained by our patients within 3 weeks of the cessation of treatment, the work of Thorén (1960), Levin et al. (1966), and Sonksen et al. (1968) suggests that this estimation is probably valueless as a test of thyroid function for at least 2 months after oral administration of clioquinol.

References

Metabolic alkalosis treated with intravenous hydrochloric acid

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In clinical practice, a severe metabolic alkalosis is found less frequently than a severe metabolic acidosis. In both disturbances the treatment consists of removing the cause and correcting the deficits or excesses in the body fluids. The severe metabolic acidosis of diabetic coma or that which follows cardiac arrest often needs urgent correction by giving sodium bicarbonate intravenously. In contrast, a metabolic alkalosis very rarely causes an immediate threat to life. In two patients recently admitted to this unit, the metabolic alkalosis required specific treatment with intravenous hydrochloric acid.

Laboratory methods
pH was determined electrometrically using a capillary electrode (Siggaard-Andersen et al., 1960). The electrode was calibrated with two phosphate buffers of pH 7.416 and 6.839 at 38° (Semple, Mattock & Uncles, 1962). The normal range was taken as 7.35–7.45.
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