ABSTRACT

Objectives

The objectives of the study were to compare the atrophogenic potential of up to 6 weeks use of calcipotriol ointment, 50 µg/g, betamethasone 17-valerate ointment, 1 mg/g, mometasone furoate ointment, 1 mg/g and the vehicle of calcipotriol ointment, in healthy volunteers.

Study Design

The study was a single-centre, prospective, randomised, double-blind, within-subject comparative study of the atrophogenic potential of:
1) Calcipotriol ointment (50 µg/g), BID
2) Betamethasone 17-valerate ointment (1 mg/g), BID
3) Mometasone furoate ointment (1 mg/g), OD and vehicle ointment OD,
4) Vehicle of calcipotriol ointment BID

in healthy volunteers.

Methodology

Included were healthy volunteers of either sex and aged 18 years or older. Subjects must have given written informed consent, and females must have demonstrated not to be pregnant at the time of recruitment, and agreed not to become pregnant during the study. Excluded from the study were subjects with pre-existing atrophy, hypersensitivity to any of the investigational products or other skin diseases in the target areas of the abdomen.

At the first visit, the subjects were assessed for eligibility with respect to the inclusion and exclusion criteria. Female subjects had a urine pregnancy test at this visit. Eligible subjects were enrolled in the double-blind "treatment" phase, lasting 6 weeks. Subjects attended visits at 2, 4, and 6 weeks after being randomised. During the study, subjects...
applied each of the four randomised treatments to one of four 4 cm x 4 cm areas of the abdomen. The treatment tubes were identically labelled, except that each indicated a different abdominal treatment area to which that particular treatment was applied and there were separate tubes marked for the morning and evening application. All treatments were applied twice daily, except in the mometasone furoate arm, wherein mometasone furoate was applied once daily plus vehicle ointment was applied once daily.

At baseline and after 2, 4 and 6 weeks, the presence of atrophy was determined by means of ultrasound examination, unaided visual examination and magnified visual examination. Reports of adverse events were elicited with a non-leading question at all on-treatment visits.

The Primary Response Criterion was the change in skin thickness, as measured by ultrasound, induced by each of the four treatments in the four treated areas of the body.

Results
The mean change in skin thickness from baseline to subsequent visits was not the same for all treatments (P=0.017). The mometasone treated sites had a far larger degree of skin thinning compared to the other treated sites. The mean change in skin thickness from baseline to each subsequent visit was similar for sites treated with betamethasone, calcipotriol and the vehicle of calcipotriol ointment. There was no statistically significant effect of time (P=0.85) and no evidence of any treatment by time interaction (P=0.91).

The skin thickness for the untreated site decreased with each subsequent visit, and had the greatest decrease in thickness of any site.
Adverse events judged possibly or probably due to use of study medication were reported by a total of 2 subjects, including:

1 subject given Betamethasone 17-valerate ointment (1 mg/g) BID
1 subject given Mometasone furoate ointment (1 mg/g) OD and vehicle ointment OD

"Folliculitis" was reported by 1 subject on a total of 1 treatment location, and "Rash erythematous" was reported by 3 subjects on a total of 2 treatment locations.

No withdrawals due to adverse events which were judged possibly/probably related to use of the study drugs occurred. One subject was withdrawn following an appendectomy at week 3. This subject was replaced.

Conclusion
The application of corticosteroid ointments induced a thinning of the skin that was either significantly greater than that of calcipotriol (mometasone furoate applied once daily), or showed a trend to exceed the effect of calcipotriol (betamethasone valerate applied twice daily). However because of the difficulties in interpreting the data from the 'control (untreated) site' the results of the study cannot be considered reliable.