The Effect of Topical Capsaicin on Substance P Immunoreactivity: A Clinical Trial and Immunohistochemical Analysis

Sir,

We read with interest the report by Kantor & Resnik (1), demonstrating the poor response of capsaicin cream in the treatment of lichen simplex chronicus. We have performed a double-blind study comparing 0.025% capsaicin cream with 0.075% capsaicin cream in nodular prurigo. Clinical response in terms of itch sensation was assessed using a visual analogue scale. In addition, immunohistochemical analysis was performed to assess substance P levels in pre- and post-treatment skin biopsies. Thirty-six per cent of patients reported complete symptomatic relief from capsaicin, and we therefore feel that capsaicin cream does have a role to play in the treatment of nodular prurigo.

METHODS

Fourteen patients with nodular prurigo unresponsive to previous therapy were recruited from outpatients clinics at both hospitals. Informed consent was obtained and patients were counselled regarding the use of capsaicin and its side-effects. Patients were asked to treat an affected area with cream A (capsaicin 0.075%, Axsain, Euroderma Ltd) and another preferably on a symmetrical site with cream B (capsaicin 0.025%, Zostrix, Genderm Corp.), in a double-blind fashion. Patients acted as their own control in that a pre-treatment skin biopsy was taken. Patients were asked to apply the cream 3 times daily for 2 weeks. A lesion of nodular prurigo was then biopsied from both treatment sites for immunohistochemical analysis. Tissue was fixed in Zamboni's fluid for 6 h at room temperature and then transferred to 0.1 M phosphate-buffered saline, 15% sucrose and 0.1% azide. Frozen sections were cut, dried for 1 h and then stained by indirect immunofluorescence with antisera to substance P. Staining was assessed semi-quantitatively with a fluorescence microscope. During the study patients were asked to complete a daily symptom questionnaire with visual analogue scales ranging from 0–10.

RESULTS

Fourteen patients with histologically proven nodular prurigo were recruited. Of these, 5 (36%) reported complete symptomatic relief from capsaicin after 2 weeks, scoring 0–1 on the visual analogue scale. This compares to a mean score of 6 pre-treatment (range 4–9). There was also a noticeable clinical change in these patients, with flattening of their lesions. From the visual response curves there was no difference between 0.025% and 0.075% capsaicin creams. We were unable to demonstrate any difference in substance P immunoreactivity between pre- and post-treatment biopsies after 2 weeks of treatment with either concentration of capsaicin.

DISCUSSION

Nodular prurigo is a chronic skin condition associated with intractable pruritus, in which a proliferation of substance P-containing nerve fibres has previously been documented (2). Capsaicin is a naturally occurring alkaloid which depletes substance P, the neurotransmitter thought to be important for transmission of pain and itch sensation in unmyelinated C fibres. Several authors have reported successful use of topical capsaicin in the treatment of chronic pruritic conditions such as nodular prurigo, chronic prurigo and neurodermatitis circumscripta (3), psoriasis (4), haemodialysis pruritis (5), brachioradial pruritis (6) and aquagenic pruritis (7), but its role in treatment of these conditions is still not widely accepted. We therefore conducted this trial to compare two strengths of 0.025% and 0.075% cream and to assess the effects on substance P immunoreactivity in lesions of nodular prurigo. We were unable to detect any difference in terms of clinical response between 0.025% and 0.075% capsaicin creams, but 36% of patients responded to treatment overall. Although this figure is not high, nodular prurigo is well recognised as an extremely difficult condition to treat. All patients had previously been unresponsive to topical steroid therapy and we were therefore encouraged by this response rate. In our study there was no control group treated with placebo or comparison therapy, as in our experience topical capsaicin causes erythema and burning and it would have been difficult to blind the study. We therefore cannot exclude a placebo effect. However, in all patients the antipruritic effect was gradual and increased over 7 days until all symptoms had resolved, as one would expect from the mechanism of action of capsaicin. We would expect a placebo response to be maximal initially and then gradually decline. Although we were not able to demonstrate depletion of substance P in skin of patients following treatment with capsaicin, it is possible that immunohistochemistry is not sufficiently sensitive to detect small differences in substance P levels. In addition, whilst capsaicin is known to deplete substance P from sensory C fibres (8) and these fibres have been shown to proliferate in nodular prurigo (2), it has not been proven that substance P release per se is responsible for the pruritus in this condition. Our study was limited in terms of only 2 weeks' treatment; further studies are needed to assess whether capsaicin depletes substance P immunoreactivity and is clinically effective over a longer period. Although we are aware of the limitations of this pilot study, our study does corroborate with previous author's findings (3) and suggests, on clinical grounds, that capsaicin has a useful role in the treatment of nodular prurigo.

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