Acta Derm Venereol 2000; 80: 24–25

Antipruritic Action of Thalidomide

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The effect of thalidomide on itch was studied in 11 patients with chronic pruritus from psoriasis, eczema, nodular prurigo, senile pruritus and primary biliary cirrhosis. Itch, assessed subjectively by the patients on a 10 cm line and measured objectively as nocturnal scratch movement, was decreased by thalidomide 200 mg on the 2 nights it was given. There was no improvement in the underlying disorders and it is concluded that thalidomide is a primary antipruritic agent. The patients all became drowsy and it seems likely that, as with most other antipruritic agents, the antipruritic action of thalidomide results from a central depressant effect. The primary antipruritic effect of thalidomide should now be assessed therapeutically. ***Key words: pruritus; antipruritic drugs; thalidomide.***

(Accepted September 20, 1999.)

Acta Derm Venereol 2000; 80: 24–25.

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Now that thalidomide is coming back in therapeutic use (1), we report our 1983 study, carried out as part of a search for new antipruritic drugs, and a definition of their mode of action. We chose thalidomide because of its unexplained therapeutic effect, then recently noted, on nodular prurigo (2, 3), a condition which, as our own observations suggest, arises as an idiosyncratic response to scratch (4). We therefore considered the possibility that thalidomide acted primarily as an antipruritic, and tested this in patients with a variety of different pruritic disorders.

PATIENTS AND METHODS

We studied 5 male and 6 post-menopausal female patients, age range 20–75 years. All patients had persistent pruritus, and had been admitted to hospital (University Department of Dermatology, Newcastle upon Tyne) for investigation or treatment. In 9 of the patients the itch was due to psoriasis or various eczemas; of the 2 patients admitted for investigation of persistent itch with a normal skin, 1 was found to have chronic biliary cirrhosis and the other senile pruritus. None of the patients had been taking oral antipruritic or anti-inflammatory agents from at least 2 days before the study, and aqueous cream was the only topical preparation used during the study.

Itch was assessed subjectively by the patient marking on a 10 cm line each morning, and objectively as scratch measured by nocturnal limb movement meters (5). The meters were applied at 11.00 p.m. and removed at 06.00 a.m. for the whole study period of 6 consecutive nights. No treatment was given on the first 2 nights and the last 2 nights of the study, and thalidomide 200 mg was given at 22.00 p.m. on nights 3 and 4.

RESULTS

Before treatment a moderate degree of itch was recorded subjectively on the 10 cm line, and measured objectively as nocturnal scratch as recorded by limb meters (Fig. 1). During treatment there was a considerable and significant reduction in both itch ($p<0.05$) and scratch ($p<0.02$). Despite some discrepancies there was an overall correlation between subjectively assessed itch and itch objectively measured as scratch. There was nocturnal sedation in most of the patients taking thalidomide; some drowsiness persisted for a time during the day after thalidomide treatment, and 3 of the patients complained of this. After the treatment was stopped, itch and scratch returned to pre-treatment levels and there were no persistent effects of the drug. There was no change in the underlying condition during the study period.

DISCUSSION

We have shown that thalidomide decreases the itch of various disorders, both as assessed subjectively by the patients on a 10 cm line and as measured objectively as nocturnal scratch movement. The methodology used has been well validated in patients with a variety of pruritic diseases, and there is good

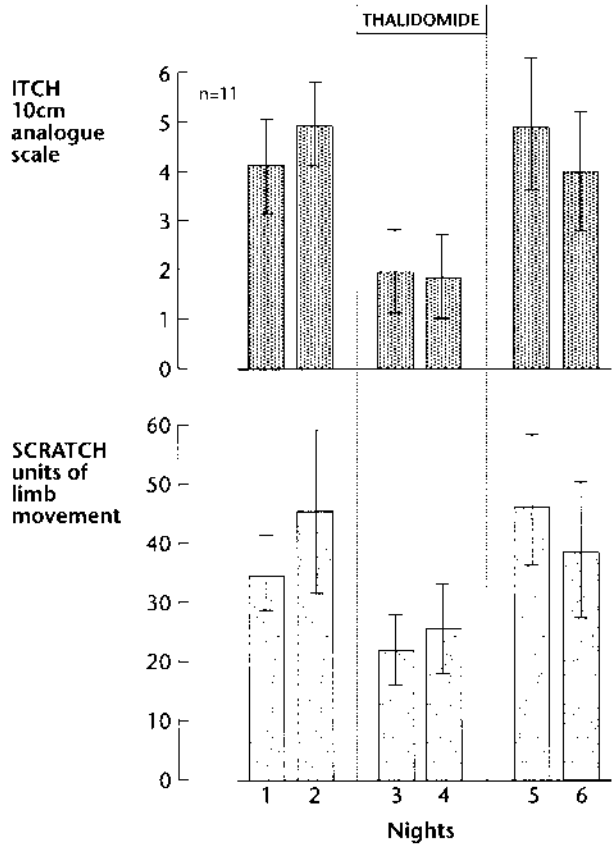

Fig. 1. The effect of thalidomide 200 mg, taken on nights 3 and 4, on subjective itch and scratch, measured as total limb movement (mean ± SEM).

 ISSN 0001-5555

correlation between itch and scratch before treatment (5–8). We did not use an inert control because the sedative effect of thalidomide cannot be concealed, and a sedative control would likewise be vitiated by the associated antipruritic effect. However, while patient expectation inevitably has an effect on subjective assessments of response, for which the crude tool of 'inert', or worse 'placebo', control, is generally used, patient expectation can have little if any effect on scratch movement during sleep.

The antipruritic effect we observed with thalidomide was rapid in onset and offset, and there was no change in the underlying condition in any of the patients during the study. Thus, the antipruritic action of thalidomide is a primary effect of the drug, and not secondary to improvement of the disease. Furthermore, the antipruritic response was found in patients with unrelated disorders, from eczema and psoriasis with different abnormalities in the skin, to senile pruritus and biliary cirrhosis with a normal skin. One of the patients had nodular prurigo and the antipruritic response to thalidomide was no different from that found in the others. The lesions of nodular prurigo appear as an idiosyncratic response to scratch (4) and regress with its frustration, for example by encasing an affected limb in a cast. Since the itch improved rapidly without any improvement in the underlying disorder, the beneficial effect of thalidomide on nodular prurigo is the consequence of its antipruritic action rather than of improvement of the disease, e.g. by an undefined immune mechanism, as in lepromatous reactions (3).

Our findings also suggest an explanation of the antipruritic effect of thalidomide. Antipruritic drugs are primary or secondary; the former ameliorate the sensation and the latter the underlying disease, as do corticosteroids in eczema and psoriasis and pure H1 receptor antagonists in urticaria (5–8). Our observations clearly exclude this secondary mode of action, and we therefore conclude that thalidomide is a primary antipruritic drug. Primary antipruritic drugs have not been well defined but, apart from the poorly understood response to drugs acting on peripheral sensation and opiate receptor related transmission, we have shown that the common property of all primary antipruritic drugs is a central depressant, sedative-anxiolytic effect. Thus a primary antipruritic effect is seen with the benzodiazapines and the older, 'sedative' H1 antihistamines, but not with the newer 'non-sedative' H1 antihistamines (5–8). Thalidomide is a powerful central depressant and a sedative or related property is the likely explanation of its action as a primary antipruritic drug.

In conclusion, our findings suggest that thalidomide has a non-specific, primary antipruritic effect by virtue of its central depressive action. This probably explains the drug's antipruritic action, which was recently found in patients with chronic renal failure (9). Comparison of the magnitude of this antipruritic action with other centrally depressive antipruritics, such as benzodiazipines, anxiolytics and the older, sedative H1 receptor antagonists, is now required in different diseases to establish the place of thalidomide as an antipruritic therapy.

ACKNOWLEDGEMENT

We are grateful to Grunenthal GMBH for providing the thalidomide (in 1983).

REFERENCES

1. Powell RJ. New roles for thalidomide. Br Med J 1996; 313: 377.
2. van den Broek H. Treatment of prurigo nodularis with thalidomide. Arch Dermatol 1980; 116: 571–572.
3. Barnhill RL, McDougall AC. Thalidomide; use and possible mode of action in reactional lepromatous leprosy and in various other conditions. J Am Acad Dermatol 1982; 7: 317–323.
4. Shuster S. Dermatology in internal medicine. Oxford: Oxford University Press, 1979: 39.
5. Felix RH, Shuster S. A new method for the measurement of itch and the response to treatment. Br J Dermatol 1975; 93: 303–312.
6. Muston H, Felix R, Shuster S. Differential effect of hypnotics and anxiolytics on itch and scratch. J Invest Dermatol 1979; 72: 283.
7. Shuster S. Reason and the rash. Proc Roy Inst GB 1981; 53: 136–163.
8. Krause LB, Shuster S. The mechanism of action of antipruritic drugs. Br Med J 1983; 187: 1199–1200.
9. Silva RBS, Viana PCF, Lugon NV, Hoette M, Ruzany F, Lugon JR. Thalidomide for the treatment of uraemic pruritus: a crossover randomised double-blind trial. Nephron 1994; 67: 270–273.