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ANTIPRURITIC EFFECT OF UREA SOLUTIONS

An Experimental and Clinical Study

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Abstract. In a double-blind study on experimentally induced itch it has been shown that urea solutions have an antipruritic effect. Urea solutions have also been tried on a clinical material with pruritus. In most cases good effect on the pruritus was obtained. The anti-pruritic effect of urea is probably due to its local anaesthetic properties.

During the clinical trials with a 10% urea cream on different dermatoses, an antipruritic effect was noticed in several cases (4, 5). It was supposed that the antipruritic effect was due to urea, as the cream base did not contain any other component which could be suspected of having an antipruritic effect. Pruritus is a symptom which is often influenced by psychological and other factors and a more systematic study was necessary in order to state that urea has an antipruritic effect and that it is useful in the treatment of pruritus. The method for evaluation of the influence on experimental itch of topically applied drugs as developed by G. Rajka (3) seems to be suitable for such an investigation. In the present paper an experimental and a clinical study of the antipruritic effect of urea is reported.

MATERIAL AND METHODS

A. Experimental study

The following solutions were used:

I.	Urea	20 g
	Lactic acid	5 g
	Betain	5 g
	Tween 20	2.5 g
	Aqua dest. ad	100 ml
II.	Hydrocortisone	0.5 g
	Propylenglycol	10 g
	Tween 20	2.5 g
	Ethyl alcohol	10 g
	Urea	20 g
	Lactic acid	5 g
	Betain	5 g
	Sodium chloride	0.5 g
	Aqua dest. ad	100 ml

As placebo solutions the same solutions as I and II were used excluding urea. Lactic acid, betain and Tween 20 were added in order to make the solutions more suitable for clinical use. Tween 20 increases the penetration of urea into the horny layer. Lactic acid and betain make the horny layer more hygroscopic and bring down the pH of the solution to about three. In solution II propylenglycol and alcohol were added to get hydrocortisone dissolved according to a new method (2). The experimental itch duration test according to Rajka (3) was made on patients between 16 and 60 years of age suffering from itching dermatoses such as atopic dermatitis, various eczemas, itching psoriasis and pruritus. Solution I was tested on a group of 10 patients and solution II on 20 patients. Each patient was injected intradermally at two locations on the upper arms with 0.02–0.03 ml trypsin solution diluted 1: 10,000 and the duration of the itch was measured. Thereafter the test or placebo solution, double-blind, was applied to adjacent skin areas of size 4 times 4 cm. After 30 min new estimations of itch duration were made by a second pair of trypsin injections into the application areas. The criteria for antipruritic effect were that the measured itch duration had decreased by more than 20% after application of test substance compared with starting value and provided that this was not the case after placebo application. For further details see (3).

B. Clinical study

The clinical study was made on patients attending the out-patient department of the Dermatology Clinic in Uppsala for pruritus. During the time the investigation was going on 13 patients attended the clinic with pruritus as the main symptom. Among these patients one turned out to have urticaria and two had lichen planus. In the investigation 2 patients from the dermatology ward were also included. These patients had a suspected early mycosis fungoides with a seemingly therapy-resistent pruritus.

The patients were given solution I. They were asked to

drip the solution on a skin area that was itching. They were also asked not to put on the solution on the same place until the itch had started again. When they came to the clinic a week or two later they were asked about the duration of the antipruritic effect of one application. By not asking the patients in advance to register the time between application and itch return, we think that the results have not been essentially influenced by the investigation. Some of the patients have since received solution II also and found no significant difference between the two solutions. Since no systematic comparison has been made between solutions I and II with regard to antipruritic effect on a clinical material the results are not reported.

RESULTS

A. Experimental study

According to the above-mentioned criteria for antipruritic effect in the experimental study we found an antipruritic effect in 4 out of 10 patients with solution I. For solution II we found an antipruritic effect in 8 out of 20 patients. In one case equal antipruritic effect of solution II and of the placebo containing 0.5 % hydrocortisone as well as ethyl alcohol was registered, whereas in a further case an increase of itch threshold occurred to both these substances. No case was observed in this series, where placebo was superior to that of urea solutions. The results are summarized in Table I.

Table I

	Antipruritic effect on experimental itch
Solution I	In 4 out of 10 patients
Solution II	In 8 out of 20 patients

B. Clinical study

The patients who have taken part in the clinical investigation are listed in Table II. The age of the patient, initials and sex are given. Most of the patients have earlier had some treatment for their pruritus, but not being satisfied with its effect. In their case, the earlier "ineffective" treatment is also given in Table II.

In all cases except the patient with chronic urticaria the pruritus disappeared a few minutes after the application of the urea solution I. The

Table II

Age	Initials	Sex	Earlier treatment	Duration of antipruritic effect after applying urea solution I	Remarks
60	C. A.	♀	—	5 h	—
57	G. B.	♀	Antihistamines	12 h	—
57	H. L.	♀	Zinc lotion[a]	24 h	The patient was excoriated
40	K. G.	♂	Alum lotion[b] Antihistamines	24 h	—
21	L. M.	♀	—	A few days	Pruritus only on the legs
79	M. G.	♂	—	24 h	—
24	N. G.	♀	—	48 h	Onset of itch after partus
78	S. J.	♂	Avlosulfon Alum lotion	12 h	The patient was excoriated
26	Ö. M.	♀	Steroid ointment	A few days	Used oral contraceptives Pruritus regio pubis
93	E. H.	♂	Antihistamines Alum lotion	A few days	—
43	J. N.	♂	Antihistamines	0 h	Urticaria chron
55	S. E.	♀	Steroid ointments	2 h	Lichen planus
56	S. H.	♀	Steroid ointments	3 h	Lichen planus
87	B. A.	♂	Steroid ointments Alum lotion Antihistamines	A few days	Early mycosis fungoides?
58	P. E.	♂	Steroid ointments Alum lotion Antihistamines	24 h	Early mycosis fungoides?

[a] Zinc oxide, 12.5 g; Talcum, 12.5 g; Glycerol, 12.5 g; Ethyl alcohol, 10 g; Aqua dest., ad 100 ml.
[b] Aluminiumacetotartrate, 1 g; Ethyl alcohol, 10 g; Aqua dest., ad 100 ml.

duration of the antipruritic effect was rather short in the 2 cases with lichen planus. All patients except the one with chronic urticaria and the two with lichen planus expressed their satisfaction with the antipruritic effect of the urea solution I and wanted to continue the same therapy. An astonishingly good effect was noticed in the 2 patients with early mycosis fungoides where all other treatment against their pruritus had failed.

DISCUSSION

Similarly as in earlier studies with local therapeutics (ointments), an influence on the trypsin-induced itch was found for the urea-containing solutions but not for the placebo solutions. The composition of the placebo solutions was identical to the test solutions except for the absence of urea. We therefore conclude that urea has an antipruritic effect. The antipruritic effect of 20% urea in solution is considerably greater than 0.5% hydrocortisone when used as in the present investigation. The placebo solution to urea solution II contained 0.5% hydrocortisone and had no antipruritic effect in this investigation. We regard the antipruritic effect of urea as good but do not want to compare with other antipruritic substances without simultaneously testing them against urea in the same group of patients. The aim of the present experimental investigation has only been to find out in a double-blind study if urea has an antipruritic effect and not the degree of that effect. To get an idea about the clinical usefulness of urea solutions against pruritus the clinical study was performed. The general impression is that urea solutions are useful in the treatment of pruritus. The effect on the patients with early mycosis fungoides was extremely good compared with all other topical preparations that had been tried. The effect on the pruritus of the patient with urticaria seemed to be non-existent. At present we feel that urea solution is an alternative in the treatment of pruritus but that further studies are needed in order to make possible a comparison with other antipruritic substances.

The mechanism of the antipruritic effect of urea is not known. It is possible, however, that it is the local anesthetic effect of urea (1) which is of importance.

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