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RECENT THERAPEUTIC EVENTS: CIMETIDINE® AND PUVA

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After the paper of Hägermark et al., including the experimental aspects of Cimetidine® as well as the lack of effect on pruritus in their model, I will briefly relate my clinical experiences with that drug. With the usual moderate dose of 4–600 mg/day on a material of 40 atopic dermatitis (AD) patients the therapeutic results were in general favourable, though when compared with a reference group on the antihistamine dimethinden, the latter was found more beneficial (Table II). On the other hand, Cimetidine® has multiple and more and less serious side effects, according to a compilation of the literature (see Table I). In addition, cerebral toxicity was recently stressed even for children (2). The conclusion is that Cimetidine does not seem to have an important part to play in the antipruritic therapy of AD.

The theoretical basis for PUVA in AD is similar to that of psoriasis, i.e. a favourable effect of UV can be expected on the skin condition in most cases. It is, however, a more difficult problem to understand its mechanism (Table III). As regards the clinical results, although several workers use this method for AD, only one large material is mentioned (1) where favourable results were registered after a relatively long period of time (on average, 36 treatments) and maintenance therapy was also needed.

In my experience, in a very small but thoroughly followed group of AD patients, PUVA therapy was efficacious in some cases, especially against ecze-

Table I. *Side effects of Cimetidine*

Leucopenia/bone marrow toxicity
Headache/dizziness/bradycardia
Gastralgia/diarrhoea/vomitus
Mental confusion (mostly in elderly who were ill and had renal impairment, or due to overdose)
Fever
Stevens-Johnson syndrome
Gynecomastia in men/male sexual dysfunction (due to hyperprolactaemia—as galactorhea in woman observed—or to increased gonadotropins or to antiandrogenic effect?)
Interference with: anticoagulants
Interference with: parathyroid hormone secretion
Interference with: insulin release
Transient increase in alkaline phosphatase

Table II. *Clinical impressions of the effect of cimetidine® on itch in cases of severe atopic dermatitis*

	No. of cases
I. Pilot study ($N=20$)	
Good effect	4
Moderate effect	4
No effect	12
II. Single-blind ($N=20$)	
Cimetidine better than usual antihistamine	3
Cimetidine equal to usual antihistamine	6
Usual antihistamine better than cimetidine	11
Ages of patients: 18–40 (28 women, 12 men)	
Dose given I: 600 mg/day; II: 400 mg/day	
Other treatment given: hydrocortisone/indifferent cream	

Table III. *On effectivity of Puva treatment*

	Empirically	Possible mechanisms
In psoriasis		
Sunlight	Mostly beneficial	Inhibition of DNA synthesis by keratinocytes(+effect on dermal structures?)
Puva		
In atopic dermatitis		
Sunlight, IR	Deterioration	Increased sweating → increased itch?
Sunlight, UV (B+A)	Improvement	Desquamation removing pore closure of sweat duct ostium? (But subsequent thickening of corneum may promote plug formation at the ostium.) By promoting blood flow—increased absorption of dermal infiltrates? Antipruritic? (But initially reducing itch threshold)
Puva	Improvement	

Table IV. *Effect of Puva treatment in cases of extensive and lichenified lesions of atopic dermatitis*

Evaluation according to a score system.
Maintenance doses: every week – every 2 weeks

Mean total dose	Approx. clearing of lesions: Eczematous (%)	Approx. clearing of lesions: Lichenified (%)	Pigmentation at last treatment
50 J/cm²	50	25–50	Moderately brown
50–80 J/cm²	50–80	50	Moderately brown
>80 J/cm²	80	50–60	Moderately brown
After Puva therapy (in autumn–winter–spring)			
Maintenance given	30–50	25–50	
Without maintenance	0–25	0–25	

$N = 8$. Skin types: II and III.

matous or prurigo lesions but less so against lichenification. Maintenance therapy was absolutely necessary to combat recurrences (see Table IV). Thus, similarly to Morrison (1), I consider that PUVA may be a favourable therapy for the treatment of AD but an intense and prolonged effort is necessary to achieve these results. Consequently, strict indications should be considered. Among the contra-indications it may be debated whether children with AD should be treated by this method, but I feel one should wait with these cases until we have a clearer picture of possible long-term side effects. In addition, even the relative contra-indications should be considered and especially stressed that lubrication must be given against the drying effect and itching caused by PUVA therapy (Table V).

Table V. *Puva therapy for atopic dermatitis*

Indications:

Selected cases with particular resistance to conventional treatments and with extensive lesions, especially adults
Selected cases with particular resistance to conventional treatments and with extensive lesions, especially adults

Contra-indications:

Mild types of atopic dermatitis
Intolerance to light/taking of photoactive drugs
Eye disease
Liver/renal and other diseases.
Pregnncy
Childhood (?)

Relative contra-indications/special considerations:

Severely ichthyotic or extremely dry skin
Very low threshold of itch
Recent pyococcal superinfection

REFERENCES

1. Morrison, W. & Parrish, J. A., Fitzpatrick, T. B.: Oral photochemotherapy of atopic eczema. Br J Dermatol *98:* 25, 1978.
2. Thompson, J. & Lilly, J.: Cimetidine-induced cerebral toxicity in children. Lancet *i:* 725, 1979.

DISCUSSION

Soter (Boston). Q: When you administered Cimetidine, did you give it in divided doses and did you study delayed-type sensitivity reactions?

A: I gave divided doses and perhaps the doses given were not too high. I did not conduct delayed studies.

Q: Were the cancerogenic effects of PUVA considered?

A: Yes, we were very cautious and gave it only in "desperate" cases and never to children. I think PUVA cannot be used as a standard method in the therapy of atopic dermatitis.

Dobson (Buffalo): The main concern is that PUVA is capable of producing skin cancer developing from normal skin within a few years. If it is used only in the short term, as indicated, then it is impractical in a chronic disease.

Goldberg (Palm Beach): Most of the centers I contacted in the US do not use PUVA for atopic dermatitis. Perhaps we may use it to some very limited extent, but it should be remembered that it requires about 2 or 3 times the amount of treatment given for psoriatics.