CLINICAL EVALUATION OF A SUSTAINED REALISE ANTIHISTAMINE, AVIL RETARD

By

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Over the last 30 years, antihistamines have found a firm place in the treatment of allergic disorders. Most of the antihistamines require frequent administration, often resulting in a missed dose. Cost consideration and side effects in certain individuals have led to the advent of sustained release preparations Avil Retard is one such formulation containing 75 mg. of Pheniramine maleate To test its retard action we have compared Avil Retard given once daily with Avil '25' administered 8 hourly.

Material and Methods: 100 patients of chronic allergic dermatoses with itching as the predominent symptom, attending the Dermatology outpatient Department of G. M. & Associated Hospital, Lucknow, formed the clinical material Patients engaged in a vocation requiring constant alertness were excluded from the study. The patients were instructed not to use any other medicine or any indigenous preparations, systemic or local, during the trial period.

It was a crossover study in which every patient received both the treatments in a random order. Evaluation period for each treatment was one week. Avil '25' was given as one tablet three times a day after meals Avil '75' was given as a single tablet administered daily after the evening meal The patients who responded inadequately to both the treatments were given double the dose of Avil Retard '75', as one tablet twice a day.

The efficacy was evaluated at the end of one week's therapy with each treatment. The degree of relief from itching during the day time and the undisturbed sleep at night were employed as criteria to assess the efficcacy. With respect to itching. the response was classified as follows :

Excellent – complete relief through the waking period.
Good – Partial relief through the waking period.
Fair – Complete or Partial relief, but not through the waking period.
Poor – No relief or worsening of the condition.

The type, severity and duration of side effects volunteered by the patients were meticulously recorded at the time of evaluating efficacy.

Results: Out of the 100 cases, 14 did not turn up even for the first follow-up. Hence, data from only 86 cases is available for analysis.

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61.6% were males and 38.4% were females (Table 1). As the cases were taken by random sampling. this ratio of 1.606 represents the usual ratio of male to female patients attending the skin OPD of G M. & Associated Hospitals, Lucknow.

TABLE No. 1

Showing age and sex of patients

Age group	Males	Females	Total
Upto 20 years	11	1	12
21 to 40 years	24	23	47
41 to 60 years	17	9	26
60 years	1	0	1
Total	53(61.6%)	33(38.4%)	86

Though the clinical material came from a wide variety of skin diseases, it can be seen from Table 2 that most of the cases of allergic etiology.

TABLE No. 2

Showing Diagnosis

Diagnosis	No. of patients
Allergic dermatitis	32
Urticaria	8
Contact Eczema	8
Contact dermatitis	7
Atopic dermatitis	6
Neurodermatitis	6
Allergic eczema	3
Allergic contact dermatitis	3
Chronic urticaria	3
Generalised itching	2
Dermatitis Herpetiformis	2
H. S. Purpura	1
Epidermatophytosis	1
Pityriasis Rosea	1
Lupus Erythematosus	1
Lichen Planus	1
Pruritus Ani	1
	86

TABLE No. 3

Number and percentage of patients showing the degree of relief from itching

Response	Severity of itching					
	Very Severe		Severe		Moderate	
	Avil	Avil R	Avil	Avil R	Avil	Avil R
	'25'	'75'	'25'	'75'	'25'	'75'
	(28)	(28)	(52)	(51)*	(6)	(6)
Excellent	8	9	8	7	2	1
Good	16	14	32	35	3	3
Fair	1	3	10	4	1	2
Total	25	26	50	46	6	6
	82.2%	92.9%	96.2%	90.2%	100%	100%

( ) Number of patients in each group

* One patient did not come for follow-up

Table 3 shows the degree of relief from itching. Out of 86 cases studied, to start with, 28 cases (32.6%) complained of very severe itching, 52 cases (60.5%) complained of severe itching, and only 6 cases (6.9%) complained of moderate itching. It can be seen that excellent to fair response to both the treatment in all the three groups was comparable.

TABLE No. 4

Showing degree of relief from itching

Response	Avil '25'	Avil Retard '75'
Excellent	18 (20.0%)	17 (30.0%)
Good	51 (59.3%)	52 (61.2%)
Fair	12 (13.9%)	9 (10.6%)
Total	81. (94.2%)	78 (91.8%)

Table 4 shows excellent to good response of itching to both the treatments, irrespective of the pretreatment severity of itching. No difference between the treatments could be appreciated.

TABLE No. 5

Showing order of administration and relief from itching

Response	Avil'25' 1st drug (39)	Avil R '75 1st drug (47)	Avil'25' 2nd drug (47)	Avil R '75, 2nd drug (38)
Excellent	10	6	8	11
Good	21	30	30	22
Fair	5	7	7	2
Total	36 (92.3%)	43 (91.5%)	45 (95.7%)	35 (92.1%)

* One patient did not come for evaluation

Out of 86 cases, 39 received Avil '25' as first treatment, and Avil Retard '75' was the first treatment in 47. Table 5 indicates that the order of treatment has not affected the response appreciably.

In 10.5% (9/86) cases Avil '25' was found to be better than Avil Retard '75', whereas Avil Retard '75' was better than Avil '25' in 8.2% (7/85) cases.

Out of 86 cases in the study, 63 complained of disturbed night sleep to start with. 32 of these 63 cases received Avil '25' as first treatment and 31 received Avil Retard '75' as the first treatment.

TABLE No. 6

Showing effect on night sleep in 63 patients who complained of disturbed night sleep

Order of treatment	No. of pts with undisturbed night sleep	
	Avil '25'	Avil Retard '75'
As 1st drug	26/32	30/31
As 2nd drug	26/31	30/31*
	52/63 (82.5%)	60/62 96 8%)

* One patient did not come for evaluation

As seen from Table 6, Avil Retard '75' could correct the sleep disturbances in 96 8% of the cases, whereas Avil '25' could do the same in only 82 5% of the cases. The difference was found to be statistically significant ($p < 0.02$)

In 10 cases Avil Retard '75' in the dose of one tablet twice daily at an interval of 12 hours was also tried. These cases were selected from amongst those who failed to respond favourably to both the treatments. 8 of these had also complained of disturbed night sleep in the pretreatment period. It can be seen from table 7 that excellent to fair response was achieved in all the 10 cases and it was possible to correct sleep disturbances in 100% of the cases.

TABLE No. 7

Showing efficacy of Avil Retard '75' one tablet twice a day on itching and night sleep

Response	No of patients	
	Relief from itchihg	Undisturbed night sleep
Excellent	1/10 (10%)	8/8
Good	6/10 (60%)	
Fair	3/10 (30%)	
	10/10 (100%)	8/8 (100%)

TABLE No. 8

Showing side effects with all the three treatments

	Number of complaints		
	Avils '25'	Avil R '75' one O.D.	Avil R '75' one B.D.
No. of pts complaining	8/86 (9 3%)	4/85 (4.7%)	7/10 (70%)
Complaints			
(a) Drowsiness (variously described)	6	2	4
(b) Dryness of mouth	2	–	2
(c) Nausea, vomiting	–	1	1
(d) Giddiness	–	–	1
(e) Loss of appetite	–	1	–
(f) Constipation	–	1	–
(g) Feeling of warmth	–	–	1
(h) Numbness and tingling	–	–	1
(i) Irrelevant talk	–	–	1
	8	5	11

8 patients in Avil '25' group, 4 in Avil Retard '75' once a day group, and 7 patients in Avil Retard '75' twice a day group complained of side effects (Table 8). Avil Retard '75' twice a day produced significantly higher incidence of side effects. The difference between Avil '25' and Avil Retard '75' once a day, however, was not significant. The side effects in all the three treatment groups were mild in intensity and required no treatment or discontinuation of drug therapy.

DISCUSSION

The results from this trial indicate that Avil Retard '75' once a day is as good as Avil '25' three times a day with respect to relief from itching in chronic allergic dermatoses. When undisturbed night sleep is employed as a criterion of assessment, Avil Retard '75' definitely scores over Avil '25'.

By using histamine scratch test in normal volunteers, Sethi, et al[1] (1970) and Gerbig[2] (1967) have reported that the effect of single dose of Avil Retard '75' was similar to that of Avil '25' given three times a day. Maddison, et al[3] (1969) compared Avil Retard '75' (1–2 tablets/day) with Avil '50' (3–4 tablets/day) in the treatment of Hay fever. They reported that the retard preparation was the

preferred dosage form. In our study, though the same degree of improvement was observed with Avil Retard '75' O. D. and Avil '25' t. i. d., a good number of patients preferred the long acting form, perhaps, mainly because of the convenience of taking only one tablet. On the other hand, 2 patients appeared dissatisfied with only one tablet per day. In fact, they complained of the reduction in tablets when they were switched over to Avil Retard '75' therapy. Since their response to both the treatments was same their dissatisfaction could be attributed to psychological factors.

With respect to side effects, there was nothing to choose between Avil Retard '75' and Avil '25'. The incidence of side effects in both the groups was comparable and low.

When the patients who had failed to respond favourably to Avil Retard'75' O.D. or Avil '25' t. i. d. were put on Avil Retard '75' b. i. d., excellent to fair response was seen in all of them. But the incidence of side effects with this dose was much higher. However, the side effects were still mild in intensity and required no treatment or discontinuation of drug therapy.

SUMMARY

Avil Retard '75' in a single dose was compared with Avil '25' given three times a day in 86 patients of chronic allergic dermatoses. Dose of Avil Retard '75' was doubled in 10 patients who showed inadequate response to the first two treatments

With respect to relief from itching, single dose of Avil Retard '75' was comparable to three doses of Avil '25'. But the long acting preparation was definitely better in correcting the disturbed night sleep.

Avil Retard '75' twice a day was the most effective of the three treatments, but also produced the highest side effects. However, the side effects were still mild in intensity, requiring no treatment or discontinuation of drug therapy.

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