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VASOMOTOR RHINITIS TREATED WITH LUNERIN® (DRACO), A NEW SYMPATHOMIMETIC ANTIHISTAMINIC PREPARATION

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Vasomotor rhinitis is here defined as non-infectious, non-seasonal, generally non-allergic nasal complaints, including nasal obstruction, increased secretion (rhinorrhea), sneezing, and impaired sense of smell.

In allergic rhinitis, the clinical investigation is usually simple. On the contrary in vasomotor rhinitis, the diagnosis is established by adopting excluding methods on the basis of anamnestic and clinical information. When the infectious and allergic cases have thus been excluded, there remain the patients with chronic nasal troubles for which they have generally consulted many doctors. Since the aetiology is manifold and basically unknown, treatment has often to be of a symptomatic and not causal character. A common pharmacological combination tried for these cases is the sympathomimetic and antihistaminic. The obscure aetiology and often individual varying responses to different preparations emphasize the need to find new and possibly improved combinations of pharmaceutical agents for the treatment of vasomotor rhinitis.

The present investigation reports the results of a clinical trial with a new preparation for the treatment of allergic and vasomotor rhinitis. It contains two components, one sympathomimetic and one antihistaminic. The aim of the present

investigation was to evaluate the effect of the preparation in a double-blind investigation on well-defined cases of vasomotor rhinitis.

Preparation

Lunerin® (Draco, Sweden*). Each tablet contains 50 mg phenylpropanolamine and 12 mg of bromfeniramine. The active substances are successively released from the tablet to obtain prolonged action.

The placebo tablet was identical in appearance and taste and consisted of the same constituents as Lunerin.

MATERIAL

Twenty-three well-known adult polyclinic patients with chronic nasal vasomotor troubles took part in the investigation.

To evaluate the effect of long-term treatment and to elucidate the optimum dosage, a further 27 patients with vasomotor or allergic rhinitis were the object of a subsequent uncontrolled study.

METHOD

Double-Blind Study

Detailed anamnestic information was obtained from each patient concerning the nasal symptoms, i.e. obstruction, secretion, itching, sneezing, and impaired sense of smell. Each patient was examined with respect to the relative and absolute number of eosinophilic blood corpuscles and by intradermal testing. Tablets, Lunerin and placebo, were given in randomised order with double-blind cross-over technique in a dosage of 1 tablet in the morning and 1 in the evening for two periods of 5 consecutive days, with a medication-free interval of three days. A detailed analysis of the nasal symptoms was made after each period, and side effects inquired for. After the second period, the patient was asked to state a preference for one of the periods. The investigation was carried out from November 1970 to March 1971 to exclude any influence of pollen allergens. The results were evaluated statistically according to Student's t-test.

Subsequent Study

The subsequent study of 27 patients included also patients with allergic rhinitis. Only active preparation was given. The initial dosage was one tablet

* Subsidiary to AB Astra, Sweden.

morning and evening. The effect was estimated after one week. Where the effect was good, the patient continued the treatment with one tablet morning and evening, 1 + 1. If the troublesome symptoms persisted, either the evening dose was doubled (1 + 2) or both morning and evening doses (2 + 2).

RESULTS

Double-Blind Study

Table 1 gives the results of the anamnestic information and laboratory tests. The findings confirm the diagnosis vasomotor rhinitis with a predominance of hypersensitivity to physical influences. The nasal discharge is predominantly thin and profuse, being most evident in the morning and during moist weather. Half of the patients with positive findings showed reactions to several different airborne and food allergens. Six patients showed positive intradermal reactions to pollen allergens in spite of chronic nasal complaints without fluctuation during different seasons. Provocation tests were not performed in the present investigation.

After the two test periods

- 15 patients preferred Lunerin to placebo,
- 5 patients preferred placebo to Lunerin,
- 3 patients indicated no preference.

Successive tabulation of these preferences in a sequence diagram (model Armitage) revealed that Lunerin was significantly ($2\alpha = 0.05$) better than placebo.

A detailed analysis of the effect on the nasal troubles itching, obstruction, and increased secretion established a statistical effect of Lunerin on obstruction ($p < 0.05$) and increased nasal secretion ($p < 0.001$). As far as itching is concerned no difference was established. As Table 2 shows, the frequency of nasal itching in this group of patients was low both before treatment and during the placebo period. A manifest effect of a preparation therefore is not to be expected on this parameter.

The detailed analysis of the effect of Lunerin on the sneezing frequency produced the following results:

TABLE 1

Present Material, 23 Patients With Chronic Vasomotor Rhinitis. Anamnestic and Clinical Findings

<i>Subjectively hypersensitive to:</i>	No. of patients
Pollen allergens	6
Other airborne allergens	12
Food allergens	3
Physical influences	13
<i>Nasal complaints:</i>	
Increased secretion	21
Sneezing	23
Obstruction	21
Impaired sense of smell	15
Nasal itching	14
Conjunctival itching	10
<i>Nasal secretion:</i>	
Thin	18
Thick	6
Viscid	1
Profuse	17
Sparse	5
Worst in the morning	17
Worst in daytime	1
Worst in the evening	4
Worst at night	2
Worst in moist weather	9
Worst in dry weather	5
<i>Laboratory examination:</i>	
Relative number of eosinophilic blood corpuscles, average 4.3 % (0.5-11.5).	
Absolute number of eosinophilic blood corpuscles, average 274/mm ³ (43-744).	
Intradermal testing negative in 12 patients.	
Intradermal testing positive in 11 patients.	
6	showed reactions to pollen allergens.
6	showed reactions to other airborne allergens.
3	showed reactions to food allergens.

TABLE 2
The Effect of Lunerin®, Draco, on Nasal Complaints.

	Nasal secretion			Nasal obstruction			Nasal itching		
	Before	During Placebo	During Lunerin	Before	During Placebo	During Lunerin	Before	During Placebo	During Lunerin
Constantly	6	4	0	6	7	4	0	0	0
Often	7	8	3	11	6	4	5	1	1
Occasionally	8	8	12	4	8	7	9	9	7
Never	0	1	6	0	0	6	0	4	6
Total number of patients	21	21	21	21	21	21	14	14	14
Statistical, Student's t-test, difference between the period of placebo and Lunerin	$p < 0.001$			$p < 0.05$			no difference		

	During Placebo	During Lunerin
Number of patients without sneezing attacks	0	3
Number of patients with 1-5 sneezing attacks per week	7	9
Number of patients with 6-10 sneezing attacks per week	4	4
Number of patients with ≥ 11 sneezing attacks per week	12	7
Mean number of sneezing attacks per week	26.0	9.9

The analysis demonstrates that Lunerin has a statistically significant influence on the mean sneezing frequency ($p < 0.05$). Further, comparing the sneezing frequency during the two periods, 19 of the 23 patients had less sneezing complaints during Lunerin than during placebo. Three had an equal frequency during the two periods. One had more sneezing attacks during the period with Lunerin.

Table 3 shows the side effects. There are no apparent differences between the Lunerin and the placebo period. The frequency of side effects is low. Only few patients complained of drowsiness during the Lunerin intake.

Subsequent Study

The mean treatment period was 36 ± 2 days. At control after one week, 18 patients had obtained a good improve-

TABLE 3
Side Effects.

	During Lunerin	During Placebo
Drowsiness	4	1
Eye smarting	1	
Cough		1
Thirst	1	
Constipation	1	
Number of patients with side effects during Lunerin		6
Number of patients with side effects during Placebo		1
Number of patients with side effects during Lunerin and placebo		1
Number of patients without side effects		15

ment of the symptoms with the normal dosage 1 + 1. Compared with the subjective troubles before the study, a highly significant improvement of the symptoms was noted during daytime as well as in the morning before the first tablet intake. A further slight improvement was shown during the next month, and no signs of tachyphylaxis was noted.

After one week of therapy, 9 patients had still some remaining symptoms and were therefore given a higher dose, 1 + 2 for 3 patients and 2 + 2 for 6 patients. The increased dose produced a marked improvement in the symptoms without any obvious increase in the frequency of side effects.

As in the controlled study, the side effects were usually moderate and often disappeared in the continued treatment. One female patient became very tired; another discontinued the treatment after some days because of tremor.

DISCUSSION

The aetiology of vasomotor rhinitis is far from elucidated. In general, it is thought to depend on an imbalance between the sympathetic and the parasympathetic nervous system in the nasal mucosa elicited by a number of quite different factors, e.g., physical influences, endocrine and psychogenic causes, etc. The disease seems to be increasing in frequency, which might be due to environmental changes such as bad functioning air conditioning systems, electrical heating, the frequent use of synthetic carpets and the massive exposure to new chemical preparations.

The use of sympathomimetic agents in the treatment of the disease seems logical against the background of the nasal pathophysiology with vasodilation, swelling of the erectile nasal tissues, oedema, and increased nasal secretion. Because the vasomotor troubles also can be elicited by undiagnosed allergens, the use of antihistaminics is justified particularly as these preparations are also credited with an anticholinergic influence.

Each of the components in the tested preparation has

previously been demonstrated to have an effect on allergic and vasomotor troubles, both in uncontrolled (*Boyer 1938, Murphy 1939, Fuchs & Maurer 1959*) and controlled studies (*Schiller et al. 1959, MacLaren 1959*).

In clinical trials on diseases with definite psychosomatic components, it is particularly important that the investigation be carried out in a proper manner with no objections to the method. Therefore the main part of the present investigation was performed with double-blind cross-over technique: neither the patient nor the doctor knowing when active preparation and placebo were given. In vasomotor rhinitis, there are few possibilities of objectively evaluating the treatment. To obtain numerical results, an analysis was made of the sneezing frequency, the patients noting each sneezing attack during the investigation.

The material in the present controlled investigation is small, 23 patients. This is because it was done as a cumulative sequence analysis and could be completed as soon as a statistically significant effect was demonstrated. The statistically significant effect was apparent not only concerning the patient's preferences for active substance over placebo but also concerning the effect of the preparation on the nasal symptoms, such as increased secretion, nasal obstruction, and sneezing.

The subsequent study of the optimum dosage demonstrated that in most cases a single morning and evening dose was sufficient, and that no tachyphylaxis was observed at long-term treatment. Where this normal dosage was insufficient, a marked therapeutical effect was achieved with a higher dosage, 1 + 2 or 2 + 2.

A particular advantage of the present preparation is the sustained release form, giving a very long-acting effect without such fluctuations in the serum concentration as can be seen after plain tablets. (*Lindberg & Persson 1972, Persson & Ekman 1972*).

CONCLUSION

Lunerin® (Draco, Sweden) had a statistically significant effect on all nasal troubles in a controlled double-blind investigation on patients with vasomotor rhinitis. In most cases, the optimum dosage was one tablet in the morning and one in the evening. At long-term treatment, no tachyphylaxis was noted.

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