Controlled specific immunotherapy of the nasal atopy

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SUMMARY

61 extrinsic nasal atopic patients (26 Grass-positive, 35 D.pt.-positive) underwent a longitudinal study of some clinical-diagnostic parameters in order to establish their usefulness for a specific controlled therapy.
The symptoms diary drawn up by the patient himself together with the research of the threshold and nasal responsiveness by the RRM provocation test and the evaluation on the same patient of the endo-point of the blocking antibodies result, at present time, the most suitable means to carry out in a satisfactory way a controlled specific therapy.

THE task of the allergist is to give a correct etiologic diagnosis in order to establish the right specific therapy. This one, in the case of the extrinsic atopy, is performed administrating intradermic growing quantities of the responsible allergens until achieving high total doses without undesirable side-effects for the patient.
Recent studies (Lichtenstein et al., 1968, 1969; Norman et al., 1971) have confirmed that the advantages of specific immunotherapy are linked to the induction in the organism of the patient of thermo-resistant antibodies of the IgG-class, G_1 and G_4 underlclasses, known as Cooke's blocking antibodies (BA). The BA, thanks to their peculiar affinity with the allergen and therefore to their competitiveness with the reagins, prevent the allergen-reagins union and than the liberation of chemical mediators involved in the allergic reaction.
Waiting for the availability of a radio-immunologic method for the BA (Lichtenstein et al., 1973), we wanted evaluate the suitability of some parameters routinely seeked in our patients, and of some tests more recently acquired for the specific therapy control.
This paper reports the results of the longitudinal study of these parameters carried out in the last two years in our Center on two selected groups of extrinsic nasal atopic patients, before and during the specific treatment.

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MATERIAL AND METHODS

Selection of patients. Two groups of never specifically treated nasal atopic patients selected on the basis of positivity 3-4 plus, 26 non in crisis periodic patients from Grass (G), and 35 perennial patients from Dermatophagoides pteronissimus (D. pt.) underwent our study. We controlled the following parameters, in every patient, after having achieved the full therapeutic dose 12, 40 and respectively 60.10^3 PNU:

Symptomatologic and objective data. We used the daily symptom diary, drawn up by the patient himself, statistically comparing the given scores for the necessary periods to reach the therapeutic indicated doses, with the score fixed to the following items before the beginning of the treatment:

a) weeks of crisis average (1 point a week) in the two-three years before the diagnosis;
b) sum of the points (from 1 to 3) given to the maximum intensity of the principal symptoms (sneezes, secretion, stenosis) suffered by the patients in the period(s) of crisis;
c) sum of the points given to extranasal associated symptoms (conjunctival and/or asmathic ones: from 1 to 3 points).

Moreover we gave a score to:

d) nasal mucosa lesions at the rhinoscopy (1, vasomotor; 2) oedematous-hypertrophic; 3, polypoid);
e) lesions found at the maxillar radiostratigraphy (1, concentric mucosa thickening; 2, limited polypoid lesion; 3, diffused polypoid lesion.

Skin tests. By using commercial diagnostic extracts we evaluated, before and at the fixed time, the end-point (E-P) of the skin response to the intradermic injection of 0.02 ml of concentration at fifth of the specific allergen (0.16-20 PNU/ml).

Muco-ciliary test (MC). The muco-ciliary clearance expressed in minutes, was evaluated following Tremble method (1948) for every nasal fossa, by using red phenol at 1% with calcium bibasic phosphate, and controlling the arrival of the colouring matter to the choanae at first in posterior rhinoscopy and now by optical fibre rhinopharingoscope.

Total protein levels, Ig and specific reagins of the nasal secretion. The nasal secretion was drawn following the technique suggested by us (Crifò, 1963), which has proved to be simple and advantageous in previous studies (Crifò, 1970). On the patterns, before-after the various therapy stages, we dosed the total proteins (micromethod of the biureto) the Ig G, A and M (Tri-partigen, low concentration, Behringwerke) and in few patients of the two groups, the specific reagins following the method of Wide and coll. on Munktell 00H paper disks (Wide et al., 1967, 1972).

Rhino-rheo-manometric nasal provocation test. We followed the technique recently reported (Crifò et al., 1975) which employes a RRM Cottle mod. 2001 (I.C.S. Ill., U.S.A.) to find a provocation threshold through the stimulation from 30 to 30 min. of a nasal fossa, at first with solvent only (basal value), than with following

doses, respectively of 10, 50 and 100 PNU of specific allergen in phosphate buffer 0.1 M pH 7.2, administrated per dosed spray (error ± 10%). The test was deemed positive when the nasal conductance (C) showed a 25% minimum drop of the basal value. The percent value of maximum drop of the C also was noted because it was considered as a sign of nasal responsiveness (Crifò et al., 1975).

Blocking antibodies (BA) level evaluation on the same patient. We used the technique suggested by K. Maunsell, easily practicable with the elsewhere reported examples (Crifò et al., 1974) and already proved to be advantageous in a recent study on the D pt. allergy (Crifò, et al., 1974). Being wellknown the allergometric EP, the EP of the BA before and during the treatment was evaluated as allergen concentration a fifth (from 0.16 to 100 PNU/ml) still positive in the intradermic tests carried out with 1 : 1 mixture of patient' serum and allergen, incubated at laboratory temperature for 16-24 hours.

RESULTS

Table 1 synthetizes the results obtained by the comparison between scores, and values of tests and dosages before every specific therapy and after that the patients

TABLE I

Longitudinal study of some clinical indices for a controlled immune-therapy in nasal atopy.

Indices	Grass-sensitive (26)			D.pt.-sensitive (35)		
	12	40	60	12	40	60
			10^3 PNU			
Clinical						
a) by diary	4/24	4/22	9/18(1)	5/29	16/28(1)	17/24(2)
b) by rhino-scopy and x-ray (3)	0/18	0/16	1/16	1/24	2/21	2/20
Skin-EP	3/24	4/22	6/21	2/34	6/32	8/22(1)
Nasal secretion:						
Total Prot.	n.s.(4) (12)	n.s. (12)	n.s. (12)	n.s. (24)	n.s. (21)	n.s. (22)
Ig G	n.s. (12)	n.s. (12)	n.s. (12)	n.s. (24)	n.s. (22)	n.s. (20)
A	n.s. (12)	n.s. (12)	n.s. (12)	n.s. (24)	n.s. (22)	n.s. (20)
M	n.s. (9)	n.s. (10)	n.s. (8)	n.s. (19)	n.s. (20)	n.s. (18)
Reagins (4)	n.s. (10)	n.s. (3)	n.s. (3)	n.s. (6)	n.s. (4)	n.s. (3)
M-C TEST (5)	0/24	0/22	2/21	0/33	2/24	2/21
RRM PROV. TEST						
a) Threshold	2/24	2/21	6/18(2)	4/26	9/19(2)	10/15(2)
b) responsivity (6)	1/24	5/21(2)	9/18(2)	14/26(2)	6/19(2)	3 15(2)
BA - EP	3/26	4/25	14/16	3/35	22/27	18/21

(1) P <0.05; (2) P 0.01; (3) 1-2th degree lesions; (4) non significative; (5) retour to normal values; (6) cases with immodified threshold.

had reached the total fixed therapeutic doses.

The diary method, even if faraginous, not always followed by the patient and someways critisable, has proved to be useful to evaluate the behaviour of the symptomatic effects of the specific therapy of the mono-allergen forms, and also as a psychologic link for the patient.

It has showed an improvement in the G-positive patients only after the full dose 60.10^3 PNU, and in the D. pt.-positive patients already after the full dose 40.10^3 PNU. Since after these doses the objective naso-sinusal lesions have showed an improvement only in few patients, the value of this index in control of therapy is modest. The same thing happens for the allergometric EP, for the clearance MC and for total proteins, IgG, A and M and specific reaginic levels of nasal secretion. It is to point out, with regard to these last, that it was proved an hight value of specific IgE antibodies before the therapy in the all 10 G-positive patients undergoing the longitudinal study, with levels even superior to those of the serum, while this was found — perhaps for the concomitant presence of BA — only in 6 of 10 D. pt.-positive patients studied.

The RRM nasal provocation test has showed an improvement rather correlated to the full dose reached when considering the achievement of a better threshold with a smaller percent drop of the C at not modified threshold as we could find in the G-positive patients (3/24, 7/21, 15/18) as well as in the D. pt.-positive patients (18/26, 15/19, 13/15). Such a result has been given by the study of EP of BA, evaluated by the test on the same patients, even if it has confirmed that such EP does not appear related to the possible symtomatologic improvement at least until the 40.10^3 PNU dose (12).

CONCLUSIONS

The longitudinal study of some clinical-diagnostic indexes usually researched in the nasal extrinsic atopic patient treated in our Center, has proved that the symptoms daily diary drawn up by the patient himself, the provocating RRM test, and the evaluation of the BA on the same patient following K. Maunsell, even if not much sensitive to a limited therapeutic dose, may be useful to control the advantages of the immunotherapy.

We deem that none of the three indexes by itself is sufficient to such control, but the combined three indexes may assure with good margin the menagement of a satisfactory specific immunotherapy of the extrinsic nasal atopy, at least before a suitable method of radio-immunologic dosage of BA is available.

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