Rhinology, 22, 261-268, 1984

Specific local immunotherapy in the treatment of hay fever

F. Filiaci, S. Di Filippo, N. Lucarelli and G. Zambetti, Rome, Italy

SUMMARY

The authors refer results of a 3-year study carried out on ten patients suffering from hay fever, diagnosed by means of skin tests, specific nasal provocation and serum RAST who underwent specific local immunotherapy consisting of application of an aqueous allergenic extract, the initial level of which was based on threshold values resulting from the nasal provocation test.

The two-monthly check ups were based on the evaluation of mucociliary clearance, anterior rhinorheomanometry, specific nasal provocation and the test of Maunsell for blocking antibodies, as well as on the drawing up of a daily symptomatological diary for each single patient.

The results were extremely interesting: subsidence of symptoms during the pollinating season, an increase in the number of blocking serum antibodies and of threshold values relative to specific nasal provocation.

Conductance and mucociliary clearance, which were both decidedly pathological before beginning the local immunotherapy, slowly returned to the norm.

The authors, furthermore, refer that the use of disodium cromoglycate during the first months of specific local immunotherapy which allows them to reach doses 5-7 times greater than those obtainable with the above mentioned form of treatment, offers uncertain advantages as far as local and above all general immunity is concerned and this alone does not justify the use of nasal applications in the treatment of bronchial asthma of allergic origin.

INTRODUCTION

A study on the effectiveness of specific local immunotherapy in subjects affected by hay fever, was carried out in the allergology department of the 2nd ENT Division of Rome University. This type of treatment has already been tried out both for asthma (Harxheimer, 1951; Swineford, 1955; Melill, 1980) and for rhinitis (Taylor, 1972; Cook, 1974; Metha, 1977; Deushl, 1977), but the present study is not based only on the behaviour of certain clinical symptoms, but also on the findings of clinical tests such as nasal provocation etc.

We began to notice the potential of this sort of treatment after having analysed the data obtained, both for secretory and serum levels, after local nasal administra-

tion of anti-fluvaccine consisting of live virus attenuated/A Victoria 3/75 (Crifò et al., 1978; Vella et al., 1978; Crifò et al., 1980).
Our preliminary results (Crifò et al., 1979, 1980) encourage us to carry on with this line of study (Filiaci, 1981; Di Filippo et al., 1982) and in the present paper the authors refer data obtained up to January 1983.

MATERIALS AND METHODS

10 subjects, ranging from 16 to 43 years of age, of whom 4 males and 6 females, suffering specifically from hay fever diagnosed by means of skin tests, specific nasal provocation and serum RAST were taken into consideration in this study.
All subjects underwent the following tests both before and during treatment:
- nasal mucociliary clearance time, according to Tremble (Filiaci, 1981);
- evaluation of the level of serum blocking antibodies, according to Maunsell (Crifò et al., 1979);
- anterior rhinorheomanometry (Crifò et al., 1975);
- specific nasal provocation test (Crifò et al., 1975).

Furthermore, each patient was asked to draw up a daily symptomatological diary (Filiaci, 1981).
All subjects underwent local desensitizing therapy every other day, by means of instillation in each of the nasal fossa of two drops containing a mixture of pollens prepared in an aqueous solution. The dose level was determined before each application by means of the nasal provocation test; in fact, each single patient began therapy with a dose of total PNU, equal to that which provoked a positive reaction during the test: initially, however, this dose was limited to 10–50 PNU/ml. A complete check-up was carried out using all the above-mentioned tests every two months during therapy, so that each single dose of nasal vaccine could be increased on the grounds of the findings for such tests. Treatment was carried out for 36 months.

RESULTS

Now we shall discuss the results obtained during the last two years of treatment. The first year of therapy showed no significant change in comparison with pre-treatment values, except for the symptomatologic score which brought to light a noticeable improvement even after 4–5 months, during the period of full pollination (Figure 7).
As far as the test of mucociliary transport is concerned, we noticed a wide range of reaction up to the end of the first six months of the second year of treatment (Figure 1), with 50% pathological reactions such as a slowing down (15′–30′) or even a block (30′) of mucociliary clearance. This phenomenon, due to the local stimulus, tended to go back to normal levels towards the end of the second year and even more during the third year of treatment. At the end of these three years

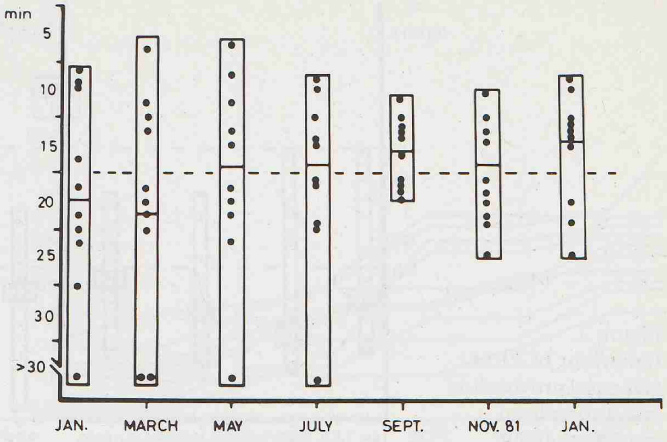

Figure 1.
Behaviour of MCT in specific local immunotherapy.

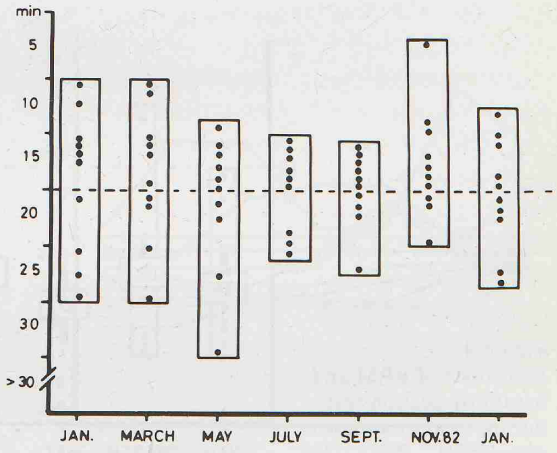

Figure 2.
Behaviour of MCT in specific local immunotherapy.

we observed no block of mucociliary transport and only a slight slowing down of this process.

As far as anterior rhinorheomanometry is concerned, we were able to observe how the continuous allergenic stimulus caused various degrees of nasal obstruction even out of the critical spring period in most of the patients, during almost all the first year of treatment; from the second year onwards there was a slight, slow return to the norm for the average values of conductance (Figure 3) which became stable during the third year (Figure 4).

We also observed an increase of average threshold values for the specific nasal provoction test (Figures 3 and 4); in fact, from a basic level of 70 PNU/ml to be

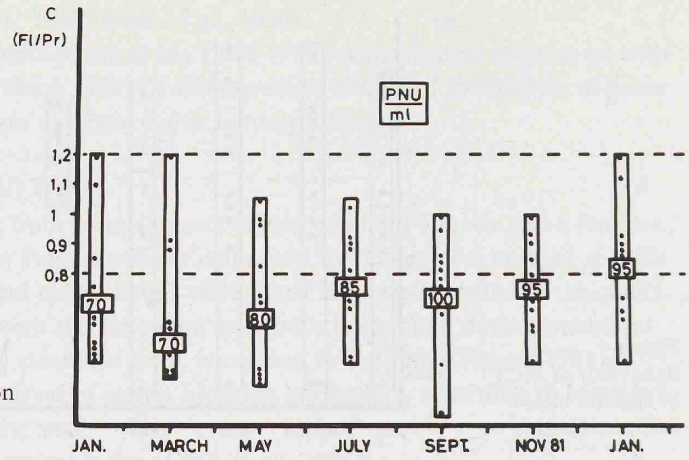

Figure 3.
Behaviour of RRM and nasal provocation test during local immunotherapy.

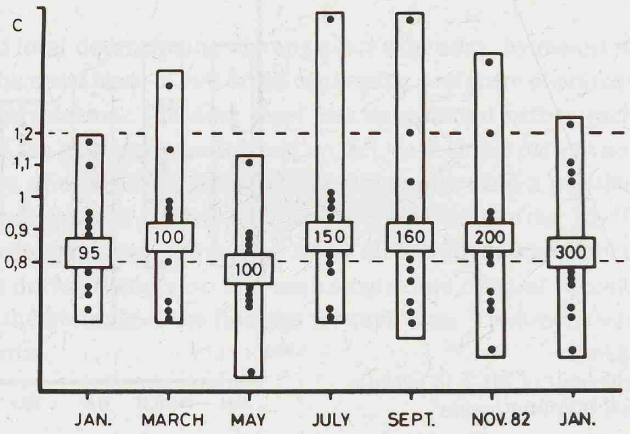

Figure 4.
Behaviour of RRM and nasal provocation test during local immunotherapy.

found at the end of the first year, we reach values such as 300 PNU/ml by the end of three years of treatment. This would seem to indicate a good level of nasal desensitization, if we consider that initial values ranged from 10–50 PNU/ml. Finally, we also found a reaction in the serum antibodies. The serum blocking power was tested in each subject in order to bring to light the increase of the specific blocking antibodies. At the end of the first year of treatment, these antibodies were still very few, but from that moment onwards, there is a progressive and noticeable increase (Figures 5 and 6). In fact by the end of the cycle of treatment, all subjects had reached a minimum level of 100 PNU/ml.

The data referred, relative to the above-mentioned clinical procedures, were inte-

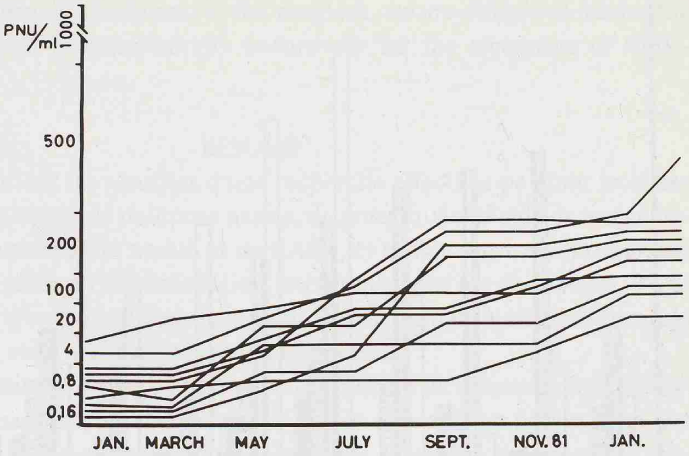

Figure 5.
Behaviour of the blocking antibodies during specific local immunotherapy.

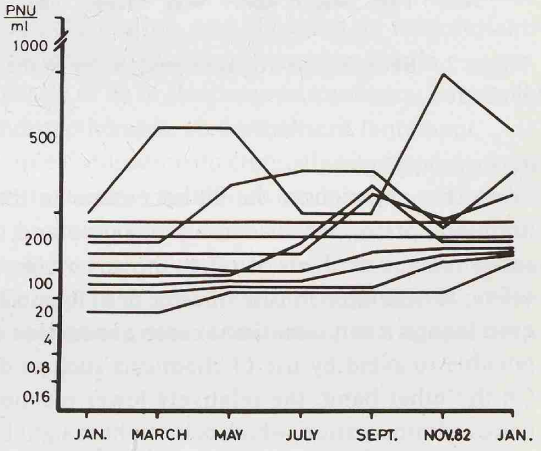

Figure 6.
Behaviour of the blocking antibodies during specific local immunotherapy.

grated with those obtained by means of the symptom diary drawn up by each single patient.

The monthly behaviour pattern of the symptoms (Figure 7) shows that after an initial regression due to local therapy, one can notice a progressive reduction of symptoms (tickling, sneezing, discharge, obstruction, lacrimation) which were evident particularly during the first spring period from the beginning of local therapy. The attenuation of symptoms was very significant during the second year of treatment and they had disappeared completely by the time therapy was completed.

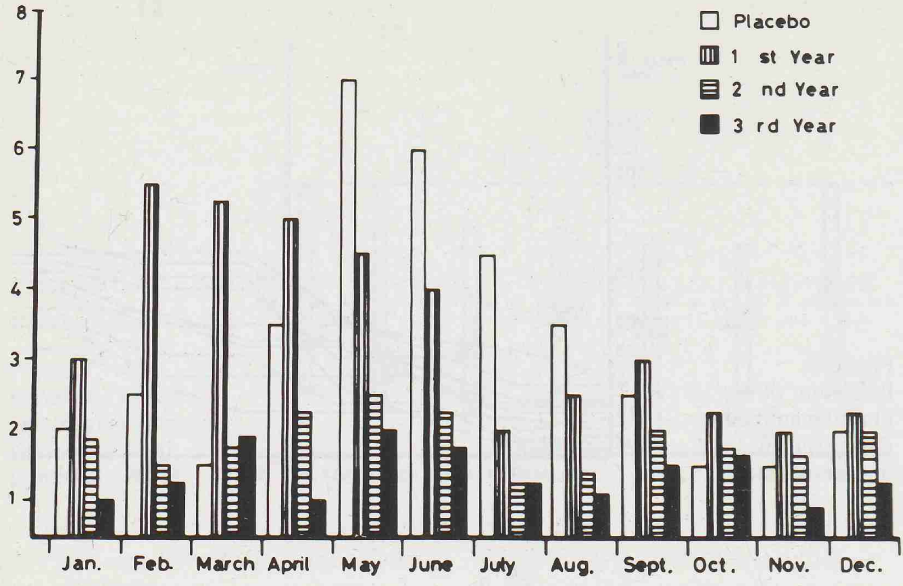

Figure 7. Behaviour of average weekly score in the symptomatologic diary during local therapy.

CONCLUSIONS

From this experience, the authors come to the conclusion that specific local immunotherapy is considerably effective and, in comparison with traditional subcutaneous methods, it offers the advantage of greater tolerance and greater safety (for example in case of error or of hypersensitive reaction to the vaccine), even though it can sometimes cause a reduction of nasal conductance (which it is possible to avoid by use of chemicals such as disodium cromoglycate).

On the other hand, the relatively lower reaction in comparison with subcutaneous administration, which is brought to light by a smaller increase in the blocking antibodies, makes this method of application advisable only in those subjects with local allergic manifestations, since it cannot offer adequate protection to conjunctival and bronchial mucosa, or so at least our data seem to indicate.

However, on the grounds of more recent studies that our group has carried out on perennial rhinopathy caused by dermatophagoides pteronissimus and parietaria officinalis, we believe that local application of disodium cromoglycate - compound which manages to stabilize the target cells but does not reduce the antigen charge of each single dose - enables us to apply a much more rapid increase of the dose level (sometimes up to 5-7 times greater than that given to positive graminacee subjects) which results in a greater increase both of local immunity and, above all, of the number of serum blocking antibodies.

It is not possible to confirm this supposition until our patients have carried out a sufficiently long term of treatment; at the moment, we are obliged to advise the use of specific local immunotherapy exclusively for the treatment of rhinopathics.

RÉSUMÉ

Les auteurs rapportent les résultats d'une recherche effectuée pendant trois ans chez dix patients atteints de pollinose nasale, diagnostiquée à l'aide de tests cutanés, de tests de provocation nasale et de RAST, et traitée par immunothérapie spécifique locale grâce à l'administration intranasale tous les deux jours, d'une solution aqueuse d'extrait allergénique dont la dose initiale a été établie sur la base de la valeur seuil du test de provocation nasale.

Les explorations bimestrielles comportent une mesure de clearance mucociliaire, une rhinoréomanométrie antérieure, un test de provocation nasale et un test de Maunsell pour le dosage des anticorps bloquants. La symptomatologie est évaluée à l'aide d'une fiche médicale rédigée quotidiennement par chaque patient.

Les résultats obtenus démontrent une réduction graduelle de la symptomatologie nasale durant la période de pollinisation, une élévation du taux des anticorps bloquants et du seuil de réponse au test de provocation nasale.

Les valeurs de la conductance nasale et de la clearance mucociliaire, nettement pathologiques au début de l'immunothérapie, se normalisent lentement.

En outre, les auteurs rapportent que l'utilisation du cromoglycate disodique pendant les premiers mois de l'immunothérapie spécifique locale, permet d'administrer des doses d'antigènes cinq à sept fois supérieures à celles administrées dans la présente étude. Ces doses plus élevées entrainent une amélioration de l'immunité locale et surtout générale. Cette dernière s'avère insuffisante dans la présente étude pour l'utilisation de la voie nasale dans le traitement de l'asthme bronchique d'origine allergique.

REFERENCES

1. Cook N. Pre-seasonal local nasal desensitization in hay fever. J Laryngol Otol 1974; 88:1169.
2. Crifò S, Filiaci F. Il test diretto di Maunsell per gli anticorpi bloccanti nella pratica allergologica. Folia Allerg Immunol Clin 1974; 21:151.
3. Crifò S, Saponara M, Cittadini S, De Seta E, D'Ascanio GF. Rinoreomanometria clinica: i valori del normale. Boll Soc Ital Biol Sper 1975; 51:420.
4. Crifò S, Filiaci F, Cittadini S, De Seta E. RRM nasal provocation test. Rhinology 1975; 13:135–9.
5. Crifò S, Filiaci F, Pelosio A, Rocchi G. Risposta secretoria e sierica dopo vaccinazione antiinfluenzale per via nasale con virus vivo attennato A/Victoria/3/75. Boll Soc Ital Biol Sper 1978; 54:1021–6.
6. Crifò S, Di Filippo S, Filiaci F, Lucarelli N, Masieri S, De Seta E. Immunoterapia specifica locale nell'etopico. Folia Allerg Immunol Clin 1979; 26:373.

7. Crifò S, Vella S, Filiaci F, Resta S, Rocchi G. Secretory immune response after nasal vaccination with live attenuated influenza viruses. Rhinology 1980; 18:87–92.
8. Crifò S, De Seta E, Lucarelli N, Masieri S. Specific local immunotherapy in nasal allergy. Allerg Immunol 1980; 7:1.
9. Deushl H, Johansson SG. Hyposensitization of patients with allergic rhinitis by intranasal administration of chemically modified grass pollen allergens. Acta Allerg 1977; 32:248.
10. Di Filippo S, Lucarelli N, Mancini CMA, Filiaci F. La desensibilizzazione locale della rinite allergica vantaggi e limiti. Med. Moderna 1982; 6:313.
11. Filiaci F. A comparative study of subcutaneous and local administration of specific immunotherapy in allergic rhinopathics. Rhinology 1981; Suppl. 1:219–25.
12. Harxheimer H. Bronchial hypersensitization and hyposensitization in man. Int Archs Allergy Appl Immun 1951; 20:40.
13. Melillo G, Cocco G, D'Amato G. Local hyposensitization by inhalation in allergic asthma. Respiratory Allergy, Masson Italia Editori, Milano, 1980.
14. Metha SB, Morrison-Smith J. Nasal hyposensitization in hay fever. Clin Allergy 1977; 5:279.
15. Swineford O jr, Cumbia JW, Berger KW, Lucws DC. Treatment of pollen hay fever and asthma with aerosols of pollen extract. J Allergy 1955; 26:305.
16. Taylor G, Shivalkar PR. Local nasal desensitization in allergic rhinitis. Clin Allergy 1972; 2:125.
17. Vella S, Filiaci F, Marcelli M, Resta S, Volpi A. Reazione di citatonicità cellulo mediata anticorpo - dipendente per l'evidenziazione di anticorpi nel secreto nasale. Giornale di Malattie Inf e Parassitarie 1978; 1:8.

Research carried out within CNR project No 810004204: national work group on cardio-respiratory dysfunction.

Franco Filiaci, M.D.
Associate Professor of Pediatric ENT
'La Sapienza', Rome University
Viale del Policlinico
00161 Rome - Italy