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Résumé

Nous avons contrôlé le niveau d'efficacité et de tolérance d'une nouvelle immunothérapie intitulée E.P.D. (Enzyme Potentiated Desensibilisation) ; elle consiste en une injection intradermique d'un mélange composé d'une solution allergénique en doses extrêmement basses et d'un enzyme, le bêta-glycoronidase. Le traitement prévoit une injection par an de pointes polliniques pour les allergiques saisonniers et deux injections par an, l'une en février et l'autre en novembre, pour les enfants souffrant d'allergie apériodique (dermatophagoïdes).

L'étude a été menée sous forme « double-blind » sur un groupe de 35 patients pédiatriques, dont 8 étaient atteints d'allergie aux pollens de graminées et 27, d'allergie aux acariens (dermatophagoïdes pteronyssinus et farinae).

Analysés de façon statistique d'après un score symptomatologique, les résultats présentent un bon niveau d'efficacité clinique, tant chez les sujets souffrant d'allergie saisonnière qu'apériodique.

S'alliant à la commodité d'administration et à l'excellent niveau de tolérance de l'immunothérapie, cette efficacité rend l' E.P.D. particulièrement indiquée pour le traitement ou pour la réduction de la symptomatologie allergique chez les enfants souffrant d'allergie.

Mots-clés : E.P.D., Immunothérapie, Acariens, Graminées.

Summary

A double blind study was made on a group of 35 children, 8 of whom were allergic to Grass and 27 allergic to Pteronyssinus and Farinae Dermatophagoids.

We verified the efficacy and tolerability of a new immunotherapy called E.P.D. (Enzyme Potentiated Desensibilization). This particular immunotherapy consists in an intradermal injection of a mix made up of an allergic solution at extremely low doses and an enzyme, beta-glycuronidase. The vaccine is administered once a year, two weeks before pollen peaks for children with seasonal allergies and two times a year,in February and November, for children with non-seasonal allergies (Dermatophagoids).

The results, statistically analyzed on the basis of a symptoms score, showed good clinical efficacy in patients affected by both seasonal and non-seasonal allergies.

Due to the clinical effectiveness, easy administration and excellent tolerability of the immunotherapy, E.P.D. is particularly suited for treating or reducing allergic symptoms in allergic children.

Key-words: E.P.D., immunotherapy, Dermatophagoides, Grasses.

INTRODUCTION

Immunotherapy with E.P.D. (Enzyme Potentiated Desensibilization) vaccine is a relatively new method for treating IgE-mediated allergies, asthma, conjunctivitis, and oculo-rhinitis (1).

The vaccine is formed by two components that are prepared extemporaneously and injected intradermally. One component is made up of small quantities of several inhalatory allergens and includes the most common pollens, dust mites, several molds, and dandruff.

The second component is an enzyme-beta-glycuronidase- which has been purified, pre-treated and activated to work as an adjuvant to the immune system.

The adjuvant action of this enzyme is based on its ability to enhance the antigen when presented by macrophages to T lymphocyte cells, thereby creating clonal anergy. As a result, only 1 or 2 doses are needed to obtain clinical improvement.

This method of treatment differs from traditional specific desensibilization immunotherapy (SIT) whose vaccines are injected subcutaneous (2, 3, 4, 5) or administered orally (6, 7) or intranasally. In fact, S.I.T. uses extracts with much higher doses of allergens that are gradually increased to induce tolerance to the allergen (8).

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Early studies of desensibilization therapy with E.P.D. were carried out by McEwen's group in the Pharmacology Department of St. Mary's Hospital of London (McEwen et al, 1967). The group first used the inoculation technique with epidermal window. Afterwards, the group used the pre-treated beta-glycuronidase (9, 10, 11) to prepare the E.P.D. extract that could be administered intradermally (12, 12, 13, 14).

Many works have been published on the clinical efficacy of this therapy (15) and on an evaluation of laboratory parameters that aim to monitor the efficacy of this extract (16).

As pediatric surveys are very limited (13, 14, 15), we felt it would be useful to evalutate the clinical efficacy and reliability of the E.P.D. vaccine on a much larger survey group, because its easy administration and lack of side effects make it particularly suited for desensitization therapy in allergic children (4).

MATERIALS AND METHODS

POPULATION AND AIM OF THE SURVEY

Thirty-five patients (19 m, 16 f) between 4 and 16 years of age (average age : 7 years and 4/12months) were involved in the study. Eight children suffered from rhinoconjuctivitis, 7 had asthma, and 20 suffered from both rhinoconjunctivitis and asthma. These children were compared with a similar number of children in a control group who suffered from the same problems and were not currently undergoing treatment with vaccines.

Eight children were allergic to Grasses and 27 were allergic to Dermatophagoid mix. Some (15) were also allergic (but to a lesser extent) to other allergens (Pellitory, Ragweed, Food Allergies). The allergy diagnosis was made on the basis of the children's medical history, prick tests with 3rd and 4th class positivity according to the standard presented by the Italian Society of Clinical Immunology and Allergology, and the dosage of IgE-specific serum.

■ The children were divided into two groups :

• Group 1 was made up of 8 children allergic to Grasses. Four had rhinoconjunctivitis and the other four suffered from both rhinoconjunctivitis and asthma.

The children were clinically examined in a pre-run that took place in Spring and Summer of 1993 (April-September). Symptoms were recorded at that time. The same patients were given the E.P.D. vaccine in March 1994 and March 1995. The symptoms occurring in the Spring and Summer of 1994 and 1995 were later compared.

• Group 2 was made up of 27 children allergic to dust mites. Seven had asthma and 20 suffered from rhinoconjunctivitis and asthma. The first dose of E.P.D. was administered in November 1994, and the second was given in February 1995. These patients were monitored through clinical pharmacological scores in November 1994, March 1995, and November 1995.

IMMUNOTHERAPY

An extemporaneous mix of 0.05 ml of E.P.D. (S.A.R.M. - Guidonia - Rome, Italy) composed of 0.01ml of a beta-glycuronidase solution (corresponding to 40 Fishman Units) and 0.04 ml of allergenic solution (corresponding to 0.02 B.U. of each allergen) was administered during active therapy. A solution containing no active ingredients was administrated in the placebo treatment to the control group. The vaccine was injected intradermally.

■ Clinical Diary Card

Patients were requested to keep a daily record of the presence and grade of symptoms (nasal blocking, sneezing, rhinorrhea, conjunctivitis, asthma, and cough) following a zero to 2 scoring system (0 = absent, 1 = mild, 2 = severe). The daily intake of drugs (antihistamines) was recorded on the same diary card.

■ Statistical analysis

Was performed on global (group 1 April/September ; group 2 every six mounths) symptoms/drug intake scores employing the Wilcoxon test. Probabilities <0.05 were considered significant.

RESULTS

The following results emerged from an analysis of the clinical data :

• Comparing scores from March 1994 and March 1995, there was a reduction in the clinical score of Group 1 patients allergic to Grasses. A significant reduction occurred in patients whith rhinoconjunctivitis and those suffering from both asthma and rhinoconjunctivitis (Figure 1).

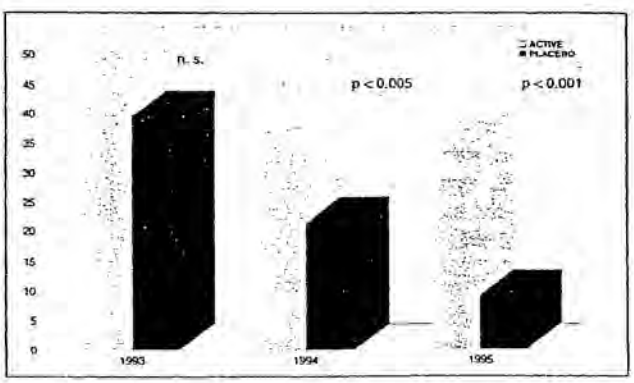

Figure 1 : Weekly symptoms/medications scores in the actively treated and placebo group before (1993) and after treatment in grass pollen allergic children

• Patients in Group 2 allergic to dust mites showed a general improvement already 6 months after E.P.D. therapy began (first administered in 1994). This improvement was visible in both patients with asthma and children with rhinoconjunctivitis (Figure 2). This improvement grew, especially after the second dose of E.P.D. Patients with both rhinoconjunctivitis and asthma improved more slowly compared to patients only suffering from asthma.

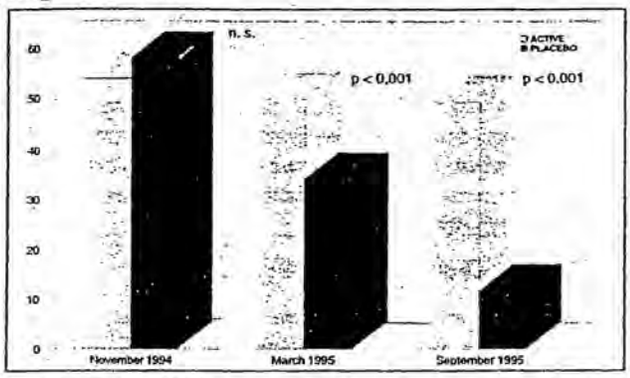

Figure 2 : Weekly symptoms/medications scores in the actively treated and placebo group at different times in Dermatophagoides allergic children

CONCLUSIONS

Several Authors have shown overall clinical effectiveness of th E.P.D. treatment (1, 6), and we believe our study confirms these results.

Considering pollen peaks in Italy, one administration per year (in March, as recommended by the producer) has shown to be sufficient in obtaining good clinical improvement in patients allergic to Grass. Even though our survey on patients allergic to Grass is limited (8 cases), these children were monitored regularly for three years and showed evident clinical improvement (Figure 1).

Nevertheless, after one year of E.P.D. therapy, improvement was not complete in patients with rhinoconjunctivitis and also in those children suffering from asthma and rhinoconjunctivitis.

Two administrations per year, in February and October, are recommended for dust mite allergies. E.P.D. was more effective in patients with asthma than in children with rhinoconjunctivitis. All, however, showed improvement in 12 months.

Symptoms totally disappeared in all our patients with asthma who were treated for an appropriate period of time. While symptoms did not totally disappear in patients with rhinoconjunctivitis, their clinical conditions improved.

Clinical improvement therefore appeared greater in asthmatic patients than in children suffering from rhinitis or rhinoconjunctivitis. Children allergic to dust mites who were monitored for 18 months (the largest group) showed clear improvement in the frequency and severity of the symptoms. Positivity to more than one allergen does not seem to influence the final efficacy of the E.P.D. treatment.

For these reasons, E.P.D. therapy is a particularly interesting method, especially for children where easy administration (1 or 2 administrations per year) and the lack of significant side effects (only 3 patients in our study showed a slight, brief asthma attack 15-30 minutes after administration) make the risk/benefit ratio particularly favorable.

E.P.D. treatment is particularly useful for children allergic to Grasses or dust mites. Moreover, this treatment appears just as advantageous (even though we intend to study the problem more at length) in children allergic to differents pollens (Grasses, Pellitory, Ragweed, Alternaria) or in children allergic to pollens and dust mites. In fact, besides containing several pollen extracts, this vaccine also contains several other antigens.

However, other studies on larger groups are needed to evaluate the clinical effectiveness over time. Moreover, an evaluation of laboratory parameters (Interleukin 6 and 10) (16) is required to monitor and better regulate the effectiveness of the E.P.D. treatment and to study the exact mechanism that triggers the action of this new immunotherapy.

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