

ORIGINAL ARTICLES

Dietary recommendations for patients allergic to *Anisakis simplex*

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SUMMARY

Background: *Anisakis simplex*, a fish parasite, causes allergic urticaria, angioedema and anaphylactic shock through an IgE-mediated hypersensitivity mechanism. Consensus on the dietary recommendations that should be given to allergic patients is lacking. Our objective was to evaluate the usefulness of different types of diets in preventing further reactions in patients allergic to *A. simplex*.

Methods: Twenty-eight adult patients, who had suffered an allergic episode caused by *A. simplex* were asked to follow one of the following three diets for a mean period of 13.16 months: a fish-free diet (diet 1; n = 19), a diet including fish frozen for more than 48 hours (diet 2; n = 9) and a diet with fresh fish (diet 3; n = 12). In all patients raw fish was excluded. Relapse rates and changes in total serum IgE and specific IgE to *A. simplex* were studied during the follow up.

Results: During the 13-month follow-up none of the patients developed anaphylaxis. Urticaria symptoms were present in 5.8 %, 11.1 % (n.s) and 33.3 % (p = 0.016) of patients following diets 1, 2 and 3, respectively. Total IgE decreased by 64 % (p < 0.05), 48 % (p < 0.05) and 39.4 % (p < 0.05), respectively. Specific IgE to *A. simplex* decreased by 50.7 % (p < 0.05), 54.1 % (p < 0.05) and 23.6 % (p < 0.05) after diets 1, 2 and 3, respectively. No statistically significant differences were found among the groups in variations in total and specific IgE.

Conclusions: Patients allergic to *A. simplex* can eat fish that has been frozen at -20 °C for 48 hours without risk of a severe allergic reaction. Long term decreases in specific and total IgE may not be good markers of eventual contact with *A. simplex*.

Key words: *Anisakis simplex*. Dietary assessment. Food allergy. Parasites. Specific IgE. Total IgE.

INTRODUCTION

Anisakis simplex (fig. 1) is a helminth parasite included in the nematode class that parasitizes the stomach of marine mammals. The eggs of the adult worm are shed into the water in the mammals' feces where they develop into the infectious larval stage. The larvae are ingested by the first host, plankton crustaceans, which are then consumed by a fish or cephalopod, in which the larvae develop into their third stage. It is this stage that produces clinical manifestations in humans after accidental consumption of raw or partially cooked infested fish.

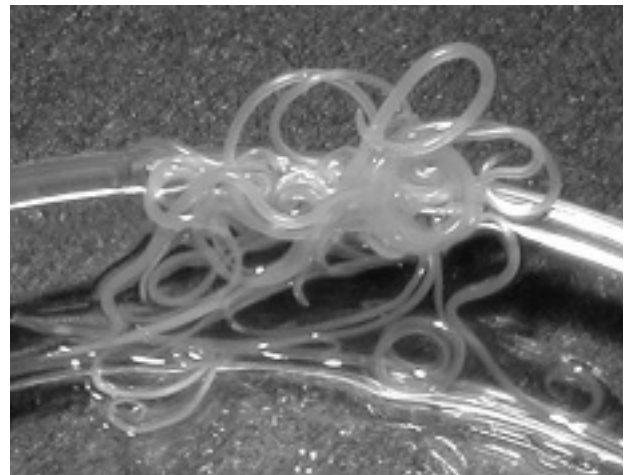


Figure 1.—*Anisakis simplex* larva.

A large proportion of fish from the northern Atlantic are infested by *A. simplex*. Many species of fish have been described as parasitized including anchovy, sardine, cod, salmon, bonito, hake, mackerel, ling, and squid, among others (1).

Since Kasuya described the first case of allergic reaction to this parasite in 1990, numerous cases have been reported in humans (2-4). These reactions present as symptoms of urticaria, angioedema or severe anaphylactic reactions related to the ingestion of fish, shellfish or cephalopods. Patients who have developed symptoms of allergy to *A. simplex* should take precautions when eating fish. The safest means of preventing new episodes is to stop eating sea fish in order to suppress any possible source of the parasite. However, this dietary restriction could create other problems related to inadequate nutrition, especially in high-risk patients with lipidic alterations. It is widely suspected that allergic symptoms are only induced by live parasites and that frozen fish (which contain only dead parasites) can be eaten by patients allergic to *A. simplex*. However, cases of asthma and conjunctivitis have been described after environmental exposure to the proteins of this parasite (5, 6) and some authors have suggested the presence of allergic symptomatology to *A. simplex* in patients who only ate frozen fish. It is, therefore, very important to establish a consensus on dietary recommendations for these patients.

We performed a 13-month clinical and laboratory follow-up of 28 patients allergic to *A. simplex* who consumed one of three diets, each with different fish content.

MATERIAL AND METHODS

Twenty-eight patients, 20 women and eight men with a mean age of 52.53 ± 10.72 years, were studied. All had presented at least one episode of acute urticaria (six patients), anaphylaxis (11 patients) or anaphylactic shock (11 patients) due to sensitization

to *A. simplex* after eating fish or shellfish. All patients had a positive skin prick test and specific IgE to *A. simplex* and negative tests to the suspected fish or shellfish.

The mean latency period of symptoms after food intake was 2.3 ± 2.9 hours. The fish most frequently involved in the reactions were anchovies (33.33%), shellfish (26.19%), whiting (14.28%) and John Dory (9.5%). In 66.6% of patients the fish was cooked and in the remaining 33.3% it was marinated raw.

Patients followed one of three diets, in a crossover design, each for a mean duration of 13.16 months (range: 5-31 months). Diet 1 (n = 19) was fish-free, diet 2 (n = 9) included fish frozen for more than 48 hours and diet 3 (n = 12) included fresh fish. In all patients, raw fish was excluded. Relapse rates and changes in serum total IgE and specific IgE to *A. simplex* were studied before, during and after the diets.

For the statistical analysis, Fisher's test and the t-test for paired values were used. A value of $p < 0.05$ was considered statistically significant.

RESULTS

During the 13-month follow-up, none of the patients developed new anaphylactic episodes or anaphylactic shock.

Urticaria symptoms were present in 5.8% of the patients following diet 1 and in 11.1% (n.s) and 33.3% ($p = 0.016$) of those following diets 2 and 3 respectively (table 1). In diets 2 and 3, urticaria symptoms were temporally associated with fish intake.

Total IgE decreased by 64% ($p < 0.05$) after diet 1 and by 48% ($p < 0.05$) and 39.4% ($p < 0.05$) after diets 2 and 3, respectively. Specific IgE to *A. simplex* decreased by 50.7% ($p < 0.05$) after diet 1 and by 54.1% ($p < 0.05$) and 23.6% ($p < 0.05$) after diets 2 and 3, respectively. No statistically significant differences were found among groups in variations in total and specific IgE (table I).

Table I
Urticaria, total and specific IgE variations in patients following diet 1 (no fish), diet 2 (frozen fish) and diet 3 (fresh fish) for 13 months months

	Urticaria	Reduction in total IgE	Reduction in specific IgE
Diet 1 (n = 19)	5.8%	66% ($p < 0.05$)*	50.7% ($p < 0.05$)*
Diet 2 (n = 9)	11.1% (n.s)	47.6% ($p < 0.05$)*	54.1% ($p < 0.05$)*
Diet 3 (n = 12)	33.3% ($p = 0.016$)	39.4% ($p < 0.05$)*	23.6% ($p < 0.05$)*

* There were no statistical differences among the three diet groups.

DISCUSSION

The principal aim of this study was to clarify the dietary recommendations that should be given to patients who have suffered an episode of urticaria, anaphylaxis or anaphylactic shock due to sensitization to *Anisakis simplex*.

The parasitization rate of fish in Spain and probably in other European countries is high (from 40-80 % depending on the species) (1). Spaniards consume a large amount of fish (89 g/person/day) (7) and the treatment for *A. simplex* allergy is based on prophylaxis by avoiding contact with the live parasite. For this reason, raw fish, the main source of gastrointestinal anisakiasis, was not included in the three diets analyzed in this study. This restriction is easy to follow and does not cause significant nutritional problems in patients or their families since most raw fish in Spain is consumed in the form of appetizers before the main meal and does not form part of the meal itself.

Avoidance of raw fish is probably the main reason why the incidence of allergic reactions in the three groups was so low, or at least lower than expected. Omission of raw fish from the diet can prevent most severe allergic reactions to *A. simplex* and notably, in this study, anaphylactic symptoms were not observed with any of the diets recommended.

The only patient group that developed significant symptoms of urticaria related to fish during this period (33 % of patients) were those that followed the diet including fresh fish. Apparently, these patients came into contact with the parasite.

Frozen fish, however, does not seem to pose a high risk for patients allergic to *A. simplex*. Only 11 % reported symptoms of urticaria, which was not significantly different from the first group, who avoided fish altogether. However, despite the lack of significance, some of the cases of urticaria that developed in patients following diet 2 could have been due to reactions to the parasite. Some home freezing methods may not have been sufficiently effective to kill it (the larvae requires temperatures of -20 °C for 48 hours) or a small group of patients may have ingested a large amount of parasite proteins capable of producing reactions.

When this problem was first seriously addressed in Spain in 1994, the most common advice given to patients was to completely eliminate all fish from the diet. However, because of the serious drawbacks of this dietary restriction and the negative results of later oral provocation studies with dead, frozen (8) or lyophilized larvae (9) and with parasite excretion-secretion antigens (10), these recommendations are now being reconsidered. Today, most allergists advise freezing fish well before cooking. The clinical findings of our study do not repudiate this recommendation.

Although the symptoms presented by the patients in the third group were not severe, we believe that patients should be advised not to eat fresh fish. An exception could be made in locations where the fish are known not to be infested by *A. simplex*.

The laboratory data, however, were less easy to interpret. As expected, the patients who included no fish in their diet showed the greatest reduction both in total and specific IgE. This reduction was smaller in the group that ate frozen fish during this period and was smallest in the third group. These data appear to correlate with the clinical data. However, the difference among the three groups was not statistically significant. The kinetics of these immunoglobulins, after contact with the parasite, complicate this type of study. After a clinical or subclinical reaction total and specific IgE usually increase approximately 1 month later (11) and then drop to previous levels. Therefore, single determinations of these immunoglobulin levels over a certain period may not be sufficient to correctly reflect their fluctuations.

The clinical data obtained in this study appear to support the previously-mentioned theory that reactions occur only to live parasites and, in most cases, that their secretions must pass through the intestinal wall. Possibly, gastric acid components break down *A. simplex* allergens (12). In other words, for an allergic reaction to occur there must be a concomitant infestation of anisakiasis.

In brief, we can conclude that patients allergic to the parasite *A. simplex* can eat fish that has been frozen at -20 °C for 48 hours without being at risk of suffering a severe allergic reaction.

RESUMEN

Antecedentes: *Anisakis simplex*, un parásito del pescado, causa urticaria alérgica, angioedema y choque anafiláctico a través de un mecanismo de hipersensibilidad mediado por IgE. No se ha llegado a un consenso claro sobre las recomendaciones dietéticas que se deben dar a los pacientes alérgicos. Nuestro objetivo fue evaluar la utilidad de distintos tipos de dietas para prevenir nuevas reacciones en pacientes alérgicos a *A. simplex*.

Métodos: Se pidió a 28 pacientes adultos, que habían sufrido un episodio alérgico causado por *A. simplex*, que siguiesen una de tres dietas durante un promedio de 13,16 meses: dieta sin pescado (dieta 1; n = 19), dieta con pescado congelado durante más de 48 h (dieta 2; n = 9) y dieta con pescado fresco (dieta 3; n = 12), pero evitando el pescado crudo en todos los casos. Durante el período de seguimiento

se estudiaron las tasa de recaídas y las variaciones de la IgE total sérica y la IgE específica de *A. simplex*.

Resultados: Durante los 13 meses de seguimiento ninguno de los pacientes experimentó anafilaxia. Se produjeron síntomas de urticaria en el 5,8, 11,1 (n.s.) y 33,3% ($p = 0,016$) de los pacientes tras llevar a cabo las dietas 1, 2 y 3, respectivamente. La IgE total disminuyó un 64% ($p < 0,05$), 48% ($p < 0,05$) y 39,5 ($p < 0,05$), respectivamente. La IgE específica de *A. simplex* descendió un 50,7% ($p < 0,05$), 54,1% ($p < 0,05$) y 23,6% ($p < 0,05$) tras las dietas 1, 2 y 3, respectivamente. No hubo diferencias estadísticas en las variaciones de la IgE total y específica entre los grupos.

Conclusiones: Los pacientes alérgicos al parásito *A. simplex* pueden comer pescado que haya sido congelado a -20°C durante 48 h sin riesgo de sufrir una reacción alérgica importante. Puede que las disminuciones a largo plazo de la IgE total y específica no sean buenos indicadores de posibles contactos con *A. simplex*.

Palabras clave: *Anisakis simplex*. Evaluación dietética. Alergia alimentaria. Parásitos. IgE específica. IgE total.

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