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Oral desensitization in egg acute food protein-induced enterocolitis syndrome

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Abstract. – OBJECTIVE: Strict avoidance of trigger food is the primary management of food protein-induced enterocolitis syndrome (FPIES). No published data are available on active induction of tolerance with oral desensitization (OD) in FPIES.

CASE REPORT: We carried out an OD in a 9 and a half years old boy with persistent acute egg FPIES. OD was performed with increasing doses of raw egg every week, starting with an initial dose of 0.2 ml. The boy presented mild and transient gastrointestinal adverse reactions when the 4 ml dose was reached. He could tolerate a whole raw egg in less than 14 months.

CONCLUSIONS: Even though randomized controlled clinical trials on patients including various phenotypes of FPIES are needed, our experience is encouraging about the possible efficacy and safety of OD in this food allergy.

Key Words:
Food protein-induced enterocolitis syndrome, Oral desensitization, Oral food challenge.

Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a non-Immunoglobulin E (non-IgE) mediated food allergy (FA) characterized by repetitive, often projectile, vomiting within 1 to 4 hours of food ingestion, that may be associated with lethargy and pallor[1]. The International Consensus Guidelines for the diagnosis and management of FPIES[1] recommend using dietary elimination of the trigger food for the primary management of FPIES. However, the development of therapeutic approaches to accelerate FPIES resolution is also desirable[1], as is oral desensitization (OD) for some IgE-mediated FA[2]. This is among the biggest unmet needs in FPIES[3]. To date, no studies has been published on the OD in FPIES. Here we describe the first case of OD in a boy with long-lasting acute egg FPIES.

Case Report

We describe the case of a boy who was referred to our clinic when he was 15-month-old. Since he was 9 months of age, he had experienced, always 2 hours after ingestion of undercooked egg, 4 episodes of repetitive and projectile vomiting associated with severe pallor and lethargy. In occasion of the last 2 episodes, the child was admitted to the Emergency Department where he required intravenous fluid administration. We performed skin prick tests (SPT) with raw egg, egg yolk, and egg white extracts, all negative. Therefore, we made diagnosis of acute egg FPIES[4], suggesting an egg-free diet. Then, the child performed 6 oral food challenges (OFC) with egg, the first 4 with baked egg and the last 2 with raw egg, all failed with moderate severity of adverse reaction[1]. In occasion of the last 4 failed OFCs, intramuscular ondansetron was administered. Raw egg SPT performed before each OFC were always negative. Moreover, the boy was diagnosed with vernal keratoconjunctivitis at age of 7. He never suffered from any other illness. After the last failed OFC, when the boy was 8 and a half years old (therefore well over the average age of acquisition of tolerance to raw egg[5]), OD was proposed. The parents delayed for about a year before agreeing and refused to perform an OFC immediately before starting OD. In December 2019, when the boy was 9 and half, we started OD in hospital, with an initial dose of 0.2 ml of raw egg. The patient did not manifest side effects. The OD continued at home every other day with increasing doses every week (Figure 1). The boy ingested doses after meals and he avoided physical exertion for 2 hours after intake, as suggested for OD for IgE-mediated FA[4]. After 5 months, he became able to take a dose of 4 ml of raw egg, presenting, on one occasion only, abdominal pain about 2 hours after ingestion and lasting 3 hours. The

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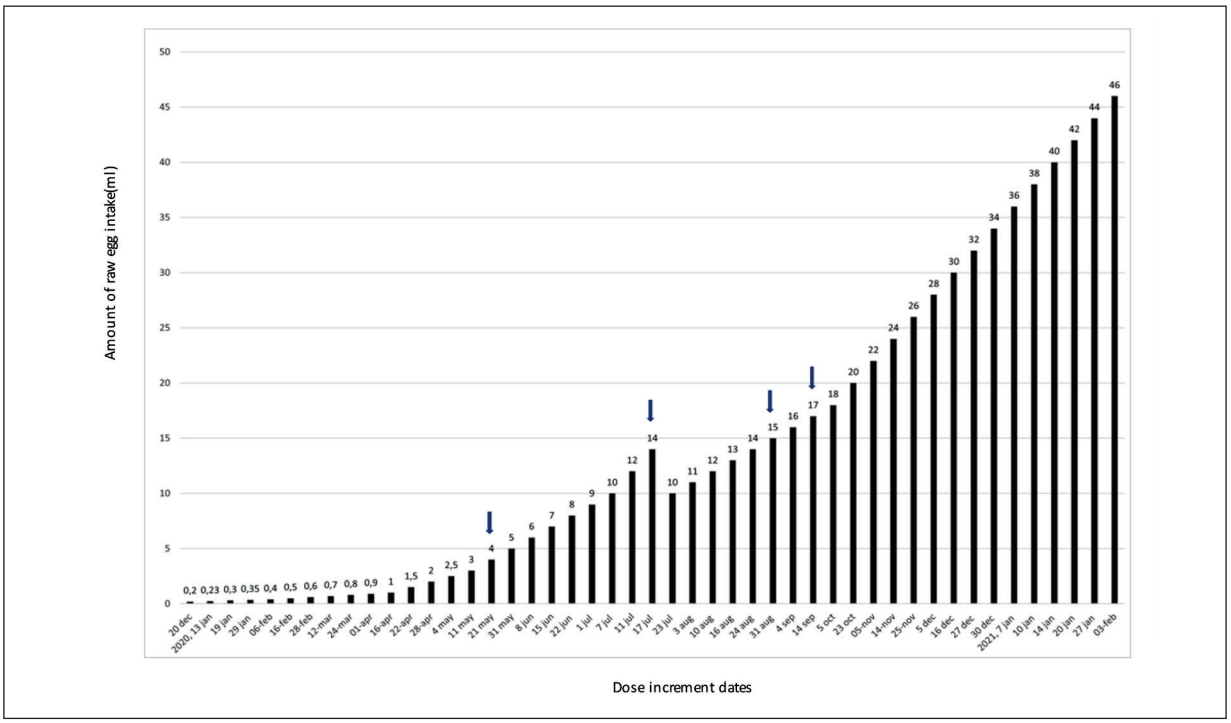

Figure 1. Progression of raw egg dose increments until a whole raw egg dose. Arrows indicate the dates of onset of adverse reactions presented by the boy during the desensitization procedure. More details are provided in the text.

boy did not present others side effects. At the dose of 14 ml, he manifested abdominal pain and diarrhea (bowel frequency up to 5 times a day) about 2 hours after ingestion. Symptoms continued for 5 days until a reduced dose (10 ml) was administrated twice a week. Although mild abdominal pain and increased number of soft stool evacuations persisted, weekly dose increments were resumed just over two weeks later. After another month, abdominal pain became less frequent (but did not disappear completely), soft stool evacuations were reduced to 3/day and the dose was increased by 1 ml/week.

Approximately 9 months after starting OD, the boy was able to take 22 ml of raw egg every other day with weekly increments of 2 ml. Abdominal pain became rare, stool consistency normal and evacuations were reduced to 2/day. On days when the raw egg dose was not taken, the boy ate some cookies containing egg. At about 11 months after starting OD, the boy became able to take 28 ml of raw egg every other day without any adverse reactions, except for occasional diarrhea. From the dose of 30 ml, the egg was taken one time in four as a scramble egg cooked in a pan for 1 minute, and three times in four as raw egg. At 13 months and 15 days after starting OD, the boy became able to take 46 ml (one whole egg) of raw egg without presenting any adverse reactions. He continued to ingest one whole raw egg 3 times a week for about 3 weeks, then he stopped taking it completely.

After one month of egg-free diet, SPT with raw egg resulted negative. Moreover, the boy performed an OFC ingesting a whole raw egg in single dose and he did not present any adverse reactions, demonstrating to have acquired tolerance (sustained unresponsiveness). During the next 4 months after the passed OFC, the patient often ate various-cooked eggs, and he never presented any adverse reactions.

Discussion

OD is an established dietary therapy for IgE-mediated FA[2]. It is suggested for children older than 5 years of age allergic to cow's milk, chicken egg, and peanut[2]. On the contrary, OD is not recommended for FPIES and there are no published experiences to date. However, actively inducing tolerance in children with long-lasting FPIES is considered an important need[3].

To our knowledge, this is the first case report on OD in FPIES. A peculiar aspect of our experience was the administration of increasing doses at home, contrary to what has been suggested for OD for IgE-mediated FA[2], with less discomfort for the patient and his family and savings in health care costs. This our choice because we wanted to proceed with very small dose increments, to ensure greater safety of the procedure. We performed 46 increments of the dose (and 1 decrease): if these increments had to be performed in day hospital, this would have implied a very long duration of the procedure because of the waiting lists. In addition, the boy would have missed many days of school and the parent would have lost many working days.

There are some weak points in our experience. Firstly, OD began a year after the last failed OFC. Moreover, our experience is based on just one case and the desensitization protocol lasted for 13.5 months. Then, it cannot be excluded the patient experienced a spontaneous acquisition of tolerance. Although there is this possibility, we consider it unlikely. In fact, our patient failed an OFC at the age of 8.5 years, well over the average age of acquiring spontaneous tolerance in acute egg FPIES[4]. This allows our patient to be included among those with long-lasting FPIES. Moreover, during the OD our patient presented symptoms (abdominal pain and diarrhea) compatible with a still active FPIES. The onset of symptoms probably coincided with the achievement of the trigger dose.

Conclusions

We report the first successful OD procedure performed in a boy with persistent acute egg FPIES. Our aim is to draw attention to the possibility of accelerating the acquisition of tolerance in this FA. Large, randomized, controlled trials including the various phenotypes of FPIES will be needed to verify the re al effectiveness of this therapy in the various possible scenarios.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Stefano Miceli Sopo: conceptualization (lead), writing - review and editing (equal), writing – original draft (lead); Dario Sinatti: writing – review and editing (equal), investigation (equal). Mariannita Gelsomino: writing – review and editing (equal), investigation (equal). All authors revised the article and given final approval of the version to be published.

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