The need for comparison of oral food challenge outcome: the ALlergy Diagnosed by Open oR DOuble blind food challenge (ALDORADO) trial

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Ethical review	Approved WMO
Status	Completed
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON50961

Source
ToetsingOnline

Brief title
ALDORADO

Condition

- Allergic conditions

Synonym
Food allergy

Research involving
Human

Sponsors and support

Primary sponsor: Martini Ziekenhuis

Source(s) of monetary or material Support: Nutricia,Wetenschapsfonds Martini Ziekenhuis (sponsoring wordt aangevraagd)

Intervention

Keyword: Children, Diagnosis, Food Hypersensitivity, Oral Food Challenge

Outcome measures

Primary outcome

The primary outcome measure will be the difference in the proportion of positive outcomes of the DBPCFC and the open food challenge. Children who had a positive DBPCFC outcome but are not willing to perform the open food challenge will also be defined as a positive open food challenge.

Secondary outcome

The following secondary outcome measures will be analysed: eliciting dose (i.e. first dose that causes allergic symptoms) and stopping dose (i.e. cumulative total dose that has been eaten), occurrence of symptoms on all challenge days (objective, subjective and severity), percentage of false positive reactions (i.e. the occurrence of allergic symptoms on placebo day in case of DBPCFC) and percentage of successful introduction into diet (if OFC outcome is negative). Furthermore, we keep record of patients for whom an open food challenge might be indicated as first choice to investigate the added value of DBPCFC in these patients.

Study description

Background summary

It is of major importance to diagnose food allergy accurately. Current

guidelines support the use of oral food challenges to do so. The double-blind placebo controlled food challenge (DBPCFC) has been regarded as the *gold standard* for decades. However, DBPCFCs are costly, time- and resource intensive procedures. Structural implementation of less demanding open food challenges will only find support if research demonstrates that their outcome will be comparable to DBPCFC, yet this has been proven difficult to investigate. This non-inferiority study has been set up to address the research question to investigate if open food challenges are comparable to DBPCFC.

Study objective

We aim to compare the outcome of open and double-blind placebo controlled food challenges in children suspected of having food allergy. Within the first non-inferiority study, the ALDORADO trial, we hypothesise that the open food challenge is comparable to the *gold standard* DBPCFC in children suspected of having food allergy for cashew nut, hazelnut or peanut.

Study design

The ALDORADO trial is a single-centre non-inferiority study to compare the outcome of the DBPCFC and open food challenge in children who are suspected to be food allergic. Data will be collected prospectively and registered anonymously in the database. Informed consent will be obtained prior to inclusion.

Intervention

Participants will undergo both challenges for the specific potential food allergen. As patients and/or their parents might be reluctant to perform a second test if symptoms occurred during the first one, we chose not to perform the OFCs in random order but always start with the DBPCFC. Furthermore, the DBPCFC outcome will be kept blinded until the last challenge has been performed. Parents will be instructed not to introduce the food into their child*s diet until the last and final test has been performed. We defined unequivocal criteria to decide whether the OFC can be continued in case of (severe) symptoms. In case of an anaphylactic reaction, no further challenges will be planned. The interval between both challenges will be at least one week and no more than six weeks.

All challenges will be performed according to the European Academy of Allergy and Clinical Immunology (EAACI) guidelines. Symptoms are registered using the scoring system as proposed in a recent publication by Grabenhenrich et al. based on the EAACI guidelines. If mild symptoms (e.g. oral discomfort or abdominal pain) occur and do not aggravate in the next 30 minutes, patients will be encouraged to eat or drink the same dose again to determine OFC outcome. All OFCs will be conducted by specially pediatric trained nurses. At

least the second challenge of each patient will be performed by a different nurse and if possible there will be a different nurse each day. For this study, during the open food challenge the recipe for the verum day of DBPCFC will be used to exclude possible matrix differences. We chose to only use recipes in which the suspected food will be hidden in gingerbread, because these are validated in the Netherlands.

Study burden and risks

Within this study children are exposed to an extra food challenge with additional risk for the occurrence of severe symptoms. We will include as little children as possible needed to support our results and use defined unequivocal criteria to stop if clinically indicated. For this study, the previously mentioned scoring system by Grabenhenrich et al. will be used. Safety will be guaranteed to stop the specific OFC if one of the predefined symptoms occur and/or if clinically indicated. Following international guidelines anaphylaxis is defined as *a serious allergic reaction that is rapid in onset and may cause death*. Until now, it appeared difficult to refine this definition in such a way that it is suitable for a practical approach. Therefore, we decided to use the EAACI criteria to diagnose anaphylaxis. Further participation within our study will be ended if these criteria are met. During a weekly scheduled meeting the included patients will be discussed to decide whether it is safe to perform the second challenge or if participation should be ended. Paediatricians, paediatric dieticians and researchers will be present during this meeting.

During the design of this study, parents were interviewed to find out important aspects that should be taken into account. We included both parents whose child had already underwent at least one OFC as well as parents who were advised to perform their child*s first OFC. Parents were selected irrespectively whether it was an open food challenge or DBPCFC. We did not include children, because we aimed to collect information useful for our study design and estimated this would be too difficult for children to understand. In case parents of teenagers were interviewed, they were stimulated to discuss the topic with their child beforehand so their opinion could also be taken into account. All parents were convinced of the relevance of the study and were well aware of the necessity to perform an OFC to draw firm conclusion about a suspected food allergy. On the other hand, they mentioned that they may be more anxious as well as their child to perform a second OFC in case severe objective symptoms (e.g. dyspnoea) or discomfort occurs during the first OFC. Therefore, we decided to define clear stopping criteria.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Children from four till eighteen years old for whom it is recommended to perform an OFC for a suspected food allergy for cashew nut, hazelnut or peanut will be eligible for inclusion.

Exclusion criteria

Patients will be excluded if they use beta blockers and/or prednisolone, if they suffer from uncontrolled asthma, unstable angina pectoris, fever or if the patient reported to be pregnant. Patients should also be able to adequately report the occurrence of possible symptoms and will be excluded if they are not able to do so (e.g. mentally disabled or not native Dutch speaker).

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-11-2021
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO

Date:	26-05-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 27959
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL76237.000.21

Study results

Date completed: 27-02-2024

Results posted: 13-01-2025

First publication
13-01-2025