Evaluation of the outcome of clinical or home introduction of milk in children with Non-IgE-mediated cow*s Milk Allergy (ENIGMA trial)*

Published: 07-06-2023
Last updated: 07-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Food intolerance syndromes
Study type	Interventional

Summary

ID

NL-OMON53347

Source
ToetsingOnline

Brief title
Clinical versus home introduction in non-IgE mediated milk allergy

Condition

- Food intolerance syndromes

Synonym
cow milk allergy, food allergy

Research involving
Human

Sponsors and support

Primary sponsor: Martini Ziekenhuis

Source(s) of monetary or material Support: Het Martini Wetenschapsfonds wordt gevraagd voor financiële ondersteuning van salariskosten voor de invoer van data en de abonnementskosten van de database

Intervention

Keyword: cow's milk allergy, food challenge test, home introduction, tolerance

Outcome measures

Primary outcome

The primary endpoint is the number of participants who are tolerant (negative

outcome of the test) or intolerant (positive outcome of the test) for milk.

The outcome is determined 1 week after the start of the test

Secondary outcome

Secondary endpoints of this study are:

•Percentage of patients with regular milk consumption). Milk consumption is

based on normal daily intake for age

Determined 6 weeks after completion of the test

•Percentage and type of reported symptoms

Reported symptoms are classified according to predefined criteria

Determined 6 weeks after completion of the test.

•Healthcare utilisation during the study period

Healthcare utilisation is determined by evaluation of the number of physical

and telephone consultations, and correspondence by mail.

Determined 6 weeks after completion of the test

Study description

Background summary

Cow*s milk allergy (CMA) is the most common food allergy among infants. CMA can be divided into immunoglobin E (IgE) and non-IgE-mediated allergy. In case of IgE-mediated allergy, symptoms occur within two hours after ingestion, and are potentially life-threatening. In patients without sensitisation, symptoms may occur up to 48 hours after ingestion and predominantly affect the gastrointestinal tract and skin. The gold standard to diagnose a cow*s milk allergy is to perform a double-blind placebo controlled food challenge (DBPCFC). Determination of DBPCFC outcome for non-IgE-mediated allergy can be challenging due to delayed presentation of symptoms after the DBPCFC has been performed. Furthermore, in the majority of infants with non-IgE-mediated cow*s milk allergy, symptoms are mild and therefore introduction under medical supervision is superfluous. To date, there is no validated diagnostic to confirm a diagnosis of non-IgE-mediated cow*s milk allergy and potential over diagnosis is due to the overlap of symptoms with other common diseases in infants.

Study objective

The aim of this study is to compare the outcome of a clinical challenge test and home introduction of cow*s milk for children with a suspected non-IgE-mediated cow*s milk allergy. We want to evaluate the ability of both tests to determine the tolerance for cow's milk and subsequently if regular daily consumption of milk is comparable in these patients.

Study design

Patients with a suspected non IgE mediated cow*s milk allergy will be randomized to a clinical challenge test or home introduction of cow*s milk. The outcome of both introduction methods is based on predefined criteria. For patients with a negative outcome of the test (=tolerant for milk) unrestricted exposure to cow*s milk is recommended. In case of a positive outcome (=intolerant for milk), parents are recommended to gradually increase the amount of cow*s milk in their child*s diet by means of the *milk ladder*. During regular follow-up visits we will inquire whether regular consumption of an age appropriate portion of cow*s milk is successful. If needed, parents will be motivated to continue further introduction and/or the schedule of the "milk ladder" wil l be adjusted. Number of all consultations will be registered.

Intervention

An adjusted DBPCFC or standardised home introduction schedule for cow*s milk.

Study burden and risks

Most food allergies present at young age, because the majority of food products are introduced at that time. This especially accounts for cow*s milk. A relatively low number of IgE mediated cow*s milk allergies present with severe reactions. On the contrary, the risk of severe reactions is negligible in non-IgE-mediated cow*s milk allergy especially if FPIES is excluded. Furthermore, many children who lack sensitisation, overgrow cow*s milk allergy before the age of one year.1 Therefore, we aim to optimise the diagnostic process in order to prevent unnecessary elimination. There is no additional risk for participants. Both introduction methods are part of routine care in our allergy centre. The dosing schedules are adjusted but the cumulative dose does not exceed the dose recommended in the (inter) national guidelines.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

-maximum age of eighteen months;
-suspected to be allergic for cow*s milk

Exclusion criteria

- children older than the age of eighteen months;
- sensitised for cow*s milk (i.e. SPT >3mm (in combination with positive control >=3mm) or specific IgE >0.35 kU/L)
- patient suffers from acute (i.e. within one hour after cow*s milk had been eaten) and moderate-severe IgE-mediated symptoms after ingestion of cow*s milk (see Appendix, table A1);
- patient suffers from symptoms according to the FPIES criteria after ingestion of cow*s milk (see table 2);
- patient uses beta blockers and/or prednisolone;
- patient suffers from uncontrolled respiratory symptoms or severe eczema or a chronic condition because of which the patients cannot be included as judged by the treating physician;
- parents are unable to adequately report the occurrence of possible symptoms (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:	Pending
Start date (anticipated):	01-04-2023
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO Date:	07-06-2023
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

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT05785299
CCMO	NL83741.000.23