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Safety of a thickened extensive casein hydrolysate formula

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ABSTRACT

Objectives: Cow's milk allergy (CMA) is treated in formula-fed infants with an extensive protein hydrolysate. This study aimed to evaluate the nutritional safety of a non-thickened and thickened extensively casein hydrolyzed protein formula (NT- and T-eCHF) in infants with CMA.
Methods: Infants younger than 6 mo old with a positive cow milk challenge test, positive IgE, or skin prick test for cow milk were selected. Weight and length were followed during the 6 mo intervention with the NT-eCHF and T-eCHF.
Results: A challenge was performed in 50/71 infants with suspected CMA and was positive in 34/50. All children with confirmed CMA tolerated the eCHF. The T-eCHF leads to a significant improvement of the stool consistency in the whole population and in the subpopulation of infants with proven CMA. Height and weight evolution was satisfactory throughout the 6 mo study.
Conclusions: The eCHF fulfills the criteria of a hypoallergenic formula and the NT- and T-eCHF reduced CMA symptoms. Growth was within normal range.

Introduction

Cow's milk protein is a major food allergen in infants [1–4]. A food allergy is defined as an adverse health effect arising from a specific immune response that occurs after exposure to the responsible food allergen [5]. This immune reaction may be IgE or non-IgE mediated. Symptoms of cow's milk allergy (CMA) are not specific and most frequently involve the skin (e.g. atopic dermatitis), the gastrointestinal (GI) tract (regurgitation, vomiting, diarrhea, and constipation), the respiratory tract (wheezing or sneezing) or are more general (colic or anaphylaxis) [1]. To date, the diagnosis of CMA requires an elimination diet followed by a food challenge, which sometimes causes concern to (and is often refused) by the parents [6].

Correct diagnosis enables appropriate feeding of affected infants to sustain normal growth and development. Guidelines define a therapeutic hypoallergenic formula as one tolerated by

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Table 1
Formula composition (/100 g of powder)

For 100 g of powder	Unit	T-eCHF	NT-eCHF
Protein (casein) (n x 6.25)	g	12.1	12.0
Lipid	g	26.2	27.1
Carbohydrates	g	52.7	55.0
Starch	g	1.0	–
Fibres	g	3.6	–
Energy	kcal	510	512

NT-eCHF, non-thickened extensive casein hydrolysate formula; T-eCHF, thickened extensive casein hydrolysate formula; n, number of subjects

at least 90% of CMA infants with a 95% confidence interval [1,2,7]. These criteria are met by several extensively hydrolyzed protein formulas, based on whey or casein. The hypoallergenicity of this extensively hydrolyzed casein formula (eCHF) was published before [8]. This paper reports the anthropometric evolution over 6 mo feeding with the test formulas.

Materials and methods

Formula-fed infants were eligible for inclusion in this prospective, randomized, double-blind trial if they were less than 6 mo old with symptoms suggesting CMA, including frequent, troublesome regurgitation and/or vomiting at a frequency of more than 5 episodes a day [8]. Two formulas were compared: a non-thickened and a thickened casein extensive hydorlysate formula (NT- and a T-eCHF); the composition of the tested formulas is listed in Table 1. Infants already fed with an extensively hydrolyzed protein formula, or having experienced previous anaphylactic reactions, were not eligible for inclusion [8]. The trial was registered at ClinicalTrials.gov under Identifier NCT01985607, and the 1 mo results in 72 infants were published prior [8]. Criteria used to suspect CMA, inclusion, and exclusion criteria can be found in the first report (Supplement 1) [8].

The primary goal of this paper is present anthropometric data over a period of 6 mo in infants fed both versions of the eCHF. Anthropometric data (weight, length, and head-circumference), were collected at 1, 3, and 6 mo and the corresponding z-score were calculated according to the World Health Organization Child Growth Standards [9].

Secondary aims were to confirm the hypoallergenicity and the efficacy of two NT- and T-eCHF. The cow milk symptom score (CoMiSS) was used to assess the efficacy of each formula at the end of the 1 mo feeding period with the formula [10].

Before any statistical analyses, the normality of the quantitative variables were tested using the Shapiro-Wilk's test. In case of normality ($P > 0.05$) or number of patients >30 per group, continuous variables were tested using a Student *t* test. In case of non-normality and number of patients ≤30 per group, the non-parametric Mann-Whitney-Wilcoxon test were used instead. The categorical variables were tested using Chi^2 test (expected frequency >5), otherwise using Fisher exact test.

The main criterion (changes in score of regurgitation between D30 and D0) was compared between groups using an analysis of covariance (ANCOVA), including the baseline value as covariate if the conditions of normality were respected, otherwise using a Wilcoxon test or an ANCOVA based on ranks. This criterion was also analyzed within each group with a paired *t* test if the conditions of normality were respected, otherwise using a Wilcoxon matched-pairs signed ranks test. The secondary criteria were analyzed in the same way. Results are presented as mean +/− standard deviation and/or median (quartile 1–quartile 3).

Full–analysis set (FAS) population was defined as all infants from the safety population having an evaluation of the main criteria.

Moreover, "CMA+" population was defined as all infants from the FAS having a CMA confirmed by either a positive food challenge or positive skin prick test (i.e., a papula to cow's milk at least 3 mm bigger than the negative control) or positive specific IgE (i.e., >0.35 kU/l). Infants with a negative food challenge and infants who did not undergo the food challenge constituted the "CMA?" group.

The study was approved by the Ethical Committee of the UZ Brussels as the primary center and by each participating hospital. Physicians from nine centers in five different countries were selected because of their qualifications and interest in participating in this trial. Informed consent was obtained from parents before randomization.

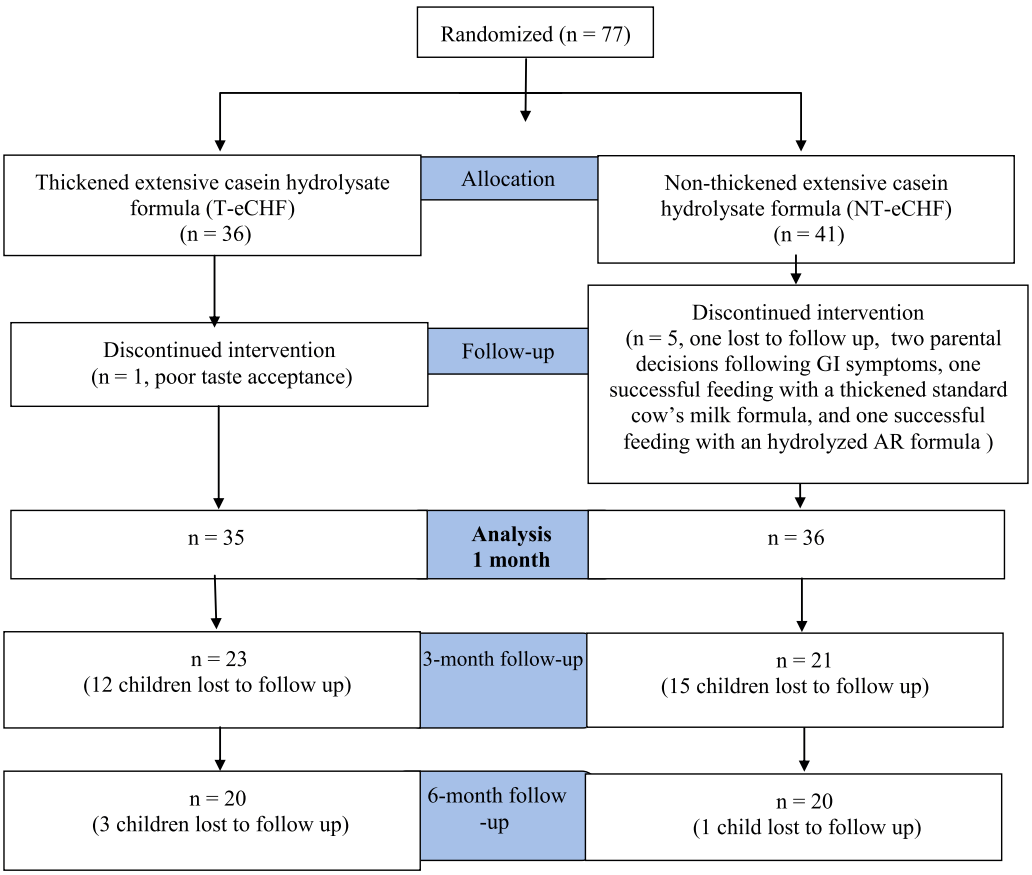

Fig. 1. Flow diagram. n, number of subjects; PPR, per protocol data set for regurgitations; PPA, per protocol data set for allergy; GI, gastrointestinal; AR, antiregurgitation.