

# Sensitization to turnip rape and oilseed rape in children with atopic dermatitis: a case-control study

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Turnip rape and oilseed rape 2S albumins are new allergens in children with atopic dermatitis suspected for food allergy. We recently found that 11% (206/1887) of these children had a positive skin prick test to seeds of oilseed rape (*Brassica napus*) and/or turnip rape (*Brassica rapa*). In the present case-control study we examined how the children with atopic dermatitis sensitized to turnip rape and oilseed rape had been breast-fed and whether they had some common sensitization pattern to certain foods or pollens. A total of 64 children with atopic dermatitis and a positive skin prick test to turnip rape and/or oilseed rape ( $\geq 5$  mm) were examined. Sixty-four age- and sex-matched children with atopic dermatitis but negative skin prick tests to turnip rape and oilseed rape served as case controls. The turnip rape and/or oilseed rape sensitized children with atopic dermatitis had significantly more often positive skin prick test reactions and IgE antibodies to various foods (cow's milk, egg, wheat, mustard;  $p < 0.01$ ) and pollens (birch, timothy, mugwort;  $p < 0.01$ ) than the control children. They had been exclusively breast-fed for a longer period (median 4 months;  $p < 0.05$ ) and had more often associated asthma (36%) and allergic rhinitis (44%). Children with atopic dermatitis sensitized to oilseed rape and turnip rape had high frequency of associated sensitizations to all foods and pollens tested showing that oilseed plant sensitization affects especially atopic children who have been sensitized to multiple allergens.

Sanna Poikonen<sup>1</sup>, Tuija J. Puumalainen<sup>2</sup>, Hannu Kautiainen<sup>3</sup>, Timo Palosuo<sup>2</sup>, Timo Reunala<sup>1</sup> and Kristiina Turjanmaa<sup>1</sup>

<sup>1</sup>Department of Dermatology, Tampere University Hospital and University of Tampere, Tampere, Finland, <sup>2</sup>National Public Health Institute, Laboratory of Immunobiology, Helsinki, Finland, <sup>3</sup>Rheumatism Foundation Hospital, Heinola, Finland

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Sanna Poikonen, Department of Dermatology, Tampere University Hospital, PO Box 2000, FI-33521 Tampere, Finland  
Tel.: +358 04 5256695  
Fax: +358 311 65654  
E-mail: sanna.poikonen@uta.fi

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Food allergy is common in young children with atopic dermatitis (AD) (1). The main allergenic foods in these children are cow's milk, egg, wheat, peanut, fish and soy (2, 3). When screening infants and young children with AD suspected for food allergy, we recently found that 11% of the 1887 children had positive skin prick test (SPT) reactions to seeds of oilseed rape (*Brassica napus* ssp. *oleifera*) and/or turnip rape (*Brassica rapa* ssp. *oleifera*) (4). The allergens in turnip rape and oilseed rape were identified as 2S albumins, also known as napins, and it was shown that about 80% of the SPT-positive

children had IgE to purified napins (5). In addition, positive labial or oral challenge reactions to seeds of turnip rape were seen in 89% of the 28 sensitized children, suggesting that oilseed plants are new important food allergens. They belong to the same *Brassicaceae* family as mustard (*Sinapis alba*) which has been reported to cause food allergy in children (6, 7). Oilseed rape and turnip rape are widely used in vegetable oil, such as canola oil, production and included, e.g., in margarine and baby foods, but whether these oils contain allergenic napins is at present not known.

Prolonged breast-feeding may affect the development of food allergies (8, 9). It is also evident that young children with AD are often allergic to multiple foods (2, 3). In the present case-control study we examined how the children with AD sensitized to turnip rape and oilseed rape had been breast-fed and whether they had some common sensitization pattern to certain foods or pollens.

## Methods

### Patients

Sixty-four children (43 boys and 21 girls) with AD sensitized to turnip rape and/or oilseed rape were included in the study. All children were examined at the Allergy Unit, Department of Dermatology, Tampere University Hospital, between May 2002 and September 2004. Their mean age was 2.5 yr (range 0.5–5.5 yr) and all 64 children had a positive SPT (mean wheal diameter  $\geq 5$  mm) to turnip rape and/or oilseed rape. Twenty-two children were challenged with seeds of turnip rape (4) and nineteen of them showed a positive labial or oral challenge reaction.

Sixty-four age- and sex-matched children with AD and negative SPTs to turnip rape and oilseed rape (mean wheal diameter  $\leq 2$  mm) were included as controls. These children were examined in the same period as the cases and were selected randomly from the files by matching the sex and age ( $\pm 6$  months).

Forty-six cases were allergic to cow's milk and fifty-one to wheat. Twenty-three of the controls had allergies to cow's milk and twenty-one to wheat as confirmed by open food challenges.

A structured questionnaire was used to collect data on breast-feeding, associated allergic rhinitis or asthma, allergies to pollen and food, and on family history of atopic disorders. The questionnaire was completed with the cases and controls visited the Allergy Unit. A diagnosis of asthma was confirmed from hospital records and only a diagnosis made by a pediatrician was accepted.

### Skin prick tests

Skin prick tests were performed with crushed seeds of turnip rape and oilseed rape moistened with physiological saline using a commercial one-peak lancet (ALK-Abelló A/S, Hørsholm, Denmark) and the prick-prick method as previously described (4). A panel of other SPTs examined included cow's milk, egg, crushed seeds of mustard (*S. alba*), wheat flour moistened with physiological saline and birch pollen. A wheal

diameter  $\geq 3$  mm was considered positive. Histamine dihydrochloride (10 mg/ml; ALK-Abelló A/S) was used as a positive and saline (Soluprick SQ; ALK-Abelló) as a negative control.

### IgE antibodies

IgE antibodies to oilseed rape, mustard, birch pollen, timothy and mugwort were measured using ImmunoCAP (Specific IgE, Phadia AB, Uppsala, Sweden). Sera were stored at  $-20^{\circ}\text{C}$  before testing. Values  $\geq 0.35$  kU/l were considered positive.

### Statistical analysis

The results were expressed as medians with interquartile ranges (IQR). The statistical comparison between cases and controls was made using the permutation test with the Monte Carlo p-value. We used also univariate and stepwise (forward selection) conditional logistic models with exact inference (Monte Carlo) to analyze the cases matched to the controls.

## Results

In univariate analysis the children with AD sensitized to oilseed rape and turnip rape showed statistically significant differences from the non-sensitized control children in all parameters except family history of atopy (Table 1). Exclusive breast-feeding had been significantly longer in the sensitized children compared to the case

Table 1. Univariate analysis of the 64 children with atopic dermatitis sensitized to oilseed rape and turnip rape (cases) and of the 64 age- and sex-matched non-sensitized children (controls)

|  | Cases<br>n (%) | Controls<br>n (%) | OR (95% CI)†      | p-value |
|--|----------------|-------------------|-------------------|---------|
| Atopy in family (parents and/or siblings affected) | 53 (83)        | 59 (92)           | 2.50 (0.72–11.11) | 0.18    |
| Exclusive breast-feeding $\geq 3$ months           | 50 (78)        | 39 (61)           | 2.22 (1.01–4.88)  | 0.047   |
| Asthma   | 23 (36)        | 6 (9)             | 6.67 (2.05–35.43) | <0.001  |
| Allergic rhinitis                                  | 28 (44)        | 14 (22)           | 4.50 (1.47–18.55) | 0.0034  |
| Sensitization to foods                             |                |                   |                   |         |
| Cow's milk   | 46 (72)        | 23 (36)           | 3.56 (1.66–8.49)  | <0.001  |
| Egg  | 59 (92)        | 24 (38)           | 36.00 (4.86–100)  | <0.001  |
| Wheat  | 51 (80)        | 21 (33)           | 6.00 (2.59–17.56) | <0.001  |
| Mustard  | 62 (97)        | 1 (2)             | 61.00 (10.73–100) | <0.001  |
| Sensitization to pollens                           |                |                   |                   |         |
| Birch  | 39 (61)        | 18 (28)           | 11.50 (3.06–100)  | 0.001   |
| Timothy  | 21 (33)        | 6 (9)             | 8.00 (2.01–72.21) | 0.0012  |
| Mugwort  | 18 (28)        | 4 (6)             | 7.50 (1.65–67.58) | 0.0026  |
| Total IgE $> 1000$ kU/l                            | 18 (28)        | 4 (6)             | 8.00 (2.01–72.21) | 0.0012  |

†Univariate conditional logistic model with exact inference (Monte Carlo).

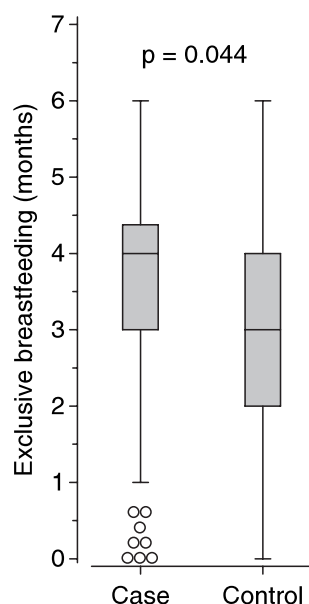


Fig. 1. Box-and-whiskers plot of exclusive breast-feeding in 64 cases and controls. Box shows median and inter-quartile range, and whiskers indicate highest and lowest value excluding outliers (circles).

controls (Fig. 1). In the cases the median exclusive breast-feeding time was 4 months (IQR 3.0–4.4 months) and in the controls 3 months (IQR 2–4 months;  $p = 0.044$ ).

Atopic dermatitis appeared at a mean age of 3 months (range 2 wk–9 months) in the cases and 7.5 months (range 2 wk–36 months) in the controls. Associated asthma ( $p < 0.001$ ) and allergic rhinitis ( $p < 0.01$ ) were more common in the sensitized children than in the controls (Table 1).

Almost all the children sensitized to oilseed rape and turnip rape were sensitized to mustard (97%) and egg (92%) which gave odds ratios of 61 and 36, respectively (Table 1). In agreement with this, the forward stepwise model showed that only these two foods entered into the model. The median total IgE level was significantly higher in the sensitized children (318 kU/l; IQR 90–1115 kU/l) than in the controls (35 kU/l; IQR 8–137 kU/l;  $p = 0.0036$ ).

## Discussion

We reported recently that the rate of sensitization to oilseed rape and turnip rape was as high as 11% in the young children with AD suspected for food allergy (4). Most of the sensitized children challenged with the seeds of turnip rape had positive labial or oral reactions showing that these oilseed plants have an obvious potential for food allergy (5). Because the seeds of these

oilseed plants are not eaten in ways similar to sesame or other seeds causing food allergy (10–12), we examined how the sensitized children had been breast-fed and whether they had some common sensitization pattern to other foods or pollens. This was, however, not the case because these children were sensitized significantly more frequently than the control children to all pollens and foods tested.

The highest sensitization rate (97%) to mustard in the present children was not unexpected, because the seeds of mustard contain 2S albumins highly homologous with oilseed rape and turnip rape (5). Mustard has been reported to cause food allergy in children and adults in France (6, 7). Its consumption is, however, negligible in young children or their lactating mothers in Finland and therefore it is highly unlikely that mustard is the primary cause of the frequent sensitization to oilseed rape and turnip rape in the present children. A significant (97%) association between mustard hypersensitivity and sensitization to mugwort pollen was recently reported from Spain (13). In contrast, only 28% of the present children were sensitized to mugwort and to our knowledge, there is no evidence that mugwort pollen contains 2S albumins. As birch pollen, oilseed rape pollen contains profilin which may rarely cause airway symptoms (14, 15).

In addition to mustard, oilseed rape and turnip rape sensitization was strongly (OR 36) associated with a positive SPT reaction and IgE antibodies to egg. This finding cannot be explained by any molecular cross-reactivity, but it is noteworthy that IgE antibodies to egg in infancy predict later development of atopic disease (16, 17). In agreement with this, the egg and oilseed plant sensitized children had associated asthma and allergic rhinitis significantly more often than the control children.

Prolonged exclusive breast-feeding may increase sensitization to cow's milk (8, 9) and have an effect on the appearance of AD (18, 19). Though allergy to cow's milk showed only a weak association (OR 3.6) to oilseed plant sensitization, the present children had been breast-fed exclusively significantly longer time than the control children. The median breast-feeding times were 4 and 3 months but because the present data was collected retrospectively it may contain some sampling bias. However, we can not exclude the possibility that the present children were sensitized to oilseed plant allergens in the mothers' milk. Supporting this, a few of the sensitized infants were exclusively breast-fed. Consumption of vegetable oils from oilseed

plants such as canola oil rich in alpha-linolenic acid has recently increased significantly in the US and elsewhere (20). At present, these oils are consumed by adults including lactating mothers and they are added also to baby and other foods due to their nutritional value (21). Whether these oils contain allergenic proteins, such as 2S albumins in amounts sufficient to cause the frequent sensitization observed in the present children, needs to be elucidated in further studies.

In conclusion, the present study showed that the AD children sensitized to oilseed rape and turnip rape had associated asthma, allergic rhinitis and sensitizations to foods and pollens significantly more often than the non-sensitized control children. Significantly longer exclusive breast-feeding suggests that in addition to food also mothers' milk could be the source for the frequent sensitization to oilseed plants.

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