

Positive family history of allergy in children with hypersensitivity to cow's milk

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SUMMARY

Background: Allergy belongs to the most frequent chronic diseases in developed countries. Its manifestation and development are determined by genetic predisposition as well as specific and non-specific environmental factors. The aim of this paper was to evaluate the type and incidence of allergic/atopic diseases among family members (1st and 2nd degree of kinship) of children with the diagnosis of hypersensitivity to cow's milk.

Material and methods: Positive family history of atopic and allergic diseases among the closest relatives was analysed in a group of 180 children with the diagnosis of hypersensitivity to cow's milk.

Results: Allergoses were found in 163 (91.1%) families, affecting 55.5%, 36% and 50% mothers, fathers and siblings of the patients, respectively. The disease of the same type as in children was present in 37.2% siblings and in 11.7% parents. Forty-five per cent of patients were from high-risk families, where 2, 3 or 4 relatives were affected by the disease (in 37.8%, 6.7% and 0.56% cases, respectively).

Conclusions: Clinical manifestation of allergoses differed between various generations of the same family. The systems most often affected by the allergic process were skin, gastrointestinal tract and respiratory system.

BACKGROUND

Allergy belongs to the most frequent chronic diseases in developed countries. Its manifestation and development are determined by genetic predisposition as well as specific and non-specific environmental factors [1,2].

The mechanism involved in the inheritance of allergic diseases has not been fully understood. Detailed analysis of family history in atopic patients showed that hereditary background was found in 50–75% patients [3–6]. Based on the incidence of atopic diseases among family members, Kjellman and Businco estimated empirical risk of developing allergy by the children of affected subjects. Its mean value was 19.8% (20–40%) when allergosis affected one parent only and 43% (40–60%) when both parents suffered from different types of allergy. This value

nearly doubles (72.2%; range 70–80%) when mother and father demonstrate the same type of allergy, and it is approx. 32.3% (25–35%) when atopy is diagnosed in siblings [7,8]. Nevertheless, it is a fact that allergosis inheritance is based not only on the concept of simple dominance or recessiveness, but also on the phenomenon of gene penetrance (ability to exhibit a trait), expressivity (quantitative difference in developing the inherited trait) and specificity (qualitative difference in trait expression) [9]. These conditions might partly explain the occurrence of a variety of clinical forms of allergic disease through various generations of a given family.

In accordance with contemporary theories of inheriting atopic diseases, based on the achievements of molecular biology, it is believed that genes control different stages of immune response [10–14]. Genetic control involves the following:

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- 1) genetic response specificity (6-HLA chromosome, 14-TcR α chromosome);
- 2) the level of IgE antibodies (11q-FcE RI α chromosome, 5q31-q33-II 3, 4, 5, 9, 13 chromosome, 7 and 16 chromosome);
- 3) proinflammatory cytokine synthesis (genes for TNF, HSP, TAP);
- 4) response threshold of shock organs (bronchial hyperactivity – 5q31-q31 chromosome and 7, 11 chromosome).

The aim of this paper was to evaluate the type and incidence of allergic/atopic diseases among family members (1st and 2nd degree of kinship) of children with the diagnosis of hypersensitivity to cow's milk.

MATERIAL AND METHODS

Detailed analysis of family history of atopic and allergic diseases among the closest relatives was performed in a group of 180 children (114 boys – 63.3% and 66 girls – 36.7%) with the diagnosis of hypersensitivity to cow's milk. The diagnosis of was based on the positive result of elimination and challenge test, positive skin tests and the presence of specific IgE antibodies in blood serum). The study was carried out with the participation of the closest family members including parents, grandparents and siblings of affected children – 360, 375 and 180 people, respectively.

Family history of atopic diseases (atopic dermatitis, prurigo, extrinsic asthma, seasonal or perennial rhinitis, urticaria, Quincke's oedema, anaphylactic shock) or allergy (contact dermatitis, urticaria, hypersensitivity to the venom of insects, topical or generalised drug-induced reactions, intrinsic asthma etc.) among family members of 1st and 2nd degree of kinship were obtained from patients' mothers during the initial 2 visits in Outpatients Clinic for Patients with Food Allergy. The mothers were also asked about possible intolerance/food allergy and the type of food allergens among the closest relatives of their children.

Statistical analysis

The results obtained were analysed statistically. Mean value and standard deviation were calculated for measurable traits, while structure index – for qualitative traits. In the case of qualitative traits, fraction significance test and compatibility test for 2 empirical distributions were used for the statistical assessment of differences, with $p < 0.05$.

RESULTS

Detailed analysis of the family history showed that the majority of patients – 163 (91.1%) came from the families with positive history of atopy and/or allergy. The relatives of those children were allergic to inhalatory, contact and food allergens. The closest relatives of analysed patients (their parents,

Table 1. Allergic diseases and/or food intolerance in patients' relatives (anamnesic analysis).

Relatives	Allergic diseases										
	Allergic rhinitis (seasonal or perennial)	Bronchial asthma	Contact dermatitis	Urticaria	Food allergy – gastrointestinal form	Atopic dermatitis	Anaphylactic shock	Hypersensitivity to venom of Hymenoptera	Quincke's oedema	Recurrent otitis	Drug-induced allergy
Mother	20	13	18	6	19	4	3	3	4	-	5
Father	16	5	3	3	11	6	1	3	1	-	1
Siblings	15	20	-	2	13	57	-	3	1	3	9
Grandparents	10	37	5	2	6	1	-	4	1	-	1
Other relatives	6	7	3	-	-	3	3	2	1	-	1

Table 2. Food intolerance in patients' relatives.

Degree of kinship	Type of non-tolerated food									
	milk	egg	citrus fruit	beef	colouring agents	bananas	soya	parsnip	fish	Total N (%)
Mother	24	2	3	1	2	-	-	-	-	32 (17.8%)
Father	15	2	2	-	1	-	-	-	-	20 (11.1%)
Siblings	64	3	2	11	7	6	5	3	2	103 (57.2%)
Grandparents	3	3	1	-	-	-	-	-	-	7 (1.9%)

Table 3. Clinical symptoms in patients and family history data.

Study group N %	Clinical symptoms				
	skin	respiratory system	other organs and systems	gastrointestinal tract	cumulative forms
Analysed children*	133 (73.9%)	100 (55.6%)	87 (48.3%)	60 (33.3%)	-
Mother	13 (7.2%)	8 (4.5%)	22 (12.2%)	11 (6.1%)	54 (30%)
Father	29 (16.1%)	17 (9.5%)	49 (27.2%)	19 (10.6%)	114 (63.3%)
Siblings	45 (25%)	22 (12.2%)	34 (18.9%)	13 (7.2%)	114 (63.3%)
Grandparents	18 (10%)	16 (8.9%)	48 (26.7%)	6 (3.3%)	88 (48.9%)
Other relatives	8 (4.5%)	3 (1.7%)	14 (7.8%)	2 (1.1%)	27 (15%)

* combination of at least 2 isolated symptoms

Table 4. Allergy and/or food intolerance in patients' relatives.

Relatives	Type of clinical symptoms N %				Total N %	
	one parent	both parents	the same disease type	different disease type	with atopy	without atopy
Mother	56 (31.2%)	43 (23.8%)	12 (6.7%)	87 (48.3%)	99 (55.0%)	81 (45.0%)
Father	22 (12.2%)		9 (5.0%)	56 (31.1%)	65 (36.0%)	115 (64.0%)
Siblings	90 (50%)		67 (37.2%)	23 (12.7%)	90 (70.9%)	37 (29.1%)

grandparents or siblings) were found to suffer from asthma, allergic rhinitis and conjunctivitis, allergic dermatosis as well as other diseases with likely allergic background (psoriasis, gastric and duodenal ulcer, ulcerative colitis, migraine) (table 1).

Food intolerance was usually observed in the siblings of analysed children and the main factor triggering undesirable effects was cow's milk and its products. The list of food allergens responsible for somatic symptoms in family members of these patients has been presented in table 2. In the majority of cases, allergic process involved skin as well as respiratory system and gastrointestinal tract. Comparative evaluation of somatic symptoms observed in analysed patients proved that in 65 mothers (36.2%), 32 fathers (17.8%), 80 siblings (44.5%) and 40 grandparents (22.2%) the same systems were affected by the allergic process (table 3).

Among relatives of 1st degree of kinship, 99 (55.5%) mothers and 65 (36%) fathers as well as 90 (50%) siblings) of the patients complained of clinical symptoms of allergy and/or food intolerance during the first visit of the child in the outpatient clinic or earlier in the past. The same disease type which was manifested by the children was observed in 21 (11.7%) cases in mother and father, while 67 (37.2%) siblings displayed identical symptoms as analysed patients (table 4).

Eighty-one patients (45%) came from high-risk families: in 68 (37.8%) cases 2 family members (mo-

Table 5. Accumulated incidence of allergy in relatives of patients with hypersensitivity to cow's milk.

No. of relatives	Degree of kinship	N	%	Total
2	father-mother	35	19.4	68 (37.8%)
	mother-siblings	21	11.6	
	father-siblings	9	5.0	
	two siblings	3	1.7	
3	mother-father-siblings	8	4.4	12 (6.7%)
	mother-two siblings	2	1.2	
	father-two siblings	2	1.2	
4	mother-father-two siblings	1	0.56	1 (0.56%)
1	mother	33	18.3	63 (35%)
	siblings	20	11.1	
	father	10	5.6	
	other relatives	17	9.5	17 (9.5%)

ther, father or siblings) were affected by the allergic disease, in 12 (6.7%) – atopy was diagnosed in 3 relatives and in the case of 1 child (0.56%) allergic diseases were observed in 4 members of the family (table 5).

DISCUSSION

Numerous reports in literature provide evidence for the variety of allergosis forms through different generations of the same family burdened with atopic disease [1–6]. In our study, the incidence and type of allergy were traced on the basis of family history of the closest relatives of 180 children with diagno-

sed hypersensitivity to cow's milk. It was established that in as many as 163 cases (91.1%), children's families were affected by allergic diseases such as asthma, allergic rhinitis, skin allergosis, food allergy and intolerance or the disorders with likely allergic background (gastric and duodenal ulcer, psoriasis, migraine, colitis ulcerosa); such diseases were not detected only in 17 (8.9%) children.

This high percentage of children whose closest relatives presented clinical symptoms of allergy corresponds to the findings of other authors. Cantani confirms familial background of food hypersensitivity/intolerance in approx. 66.6% of Italian children [15]. Dannaeus found that hereditary factor in the case of food allergy is involved in 60% with early and 21% with delayed symptoms of the disease [16]. Moneret-Vautrin traced atopic background in 90% children and 63% adults with the symptoms of food allergy [17]. Perrin claims that hypersensitivity to various foods is one of the first stigmas of atopic constitution [18], and Jakobsson and Lindberg found familial atopy in 70% of children with hypersensitivity to cow's milk [19]. Sampson proved that allergic diseases were present in 96% of the families of atopic children [20]. For the sake of comparison, the study on the familial occurrence of food allergy in Polish children published in 1982 by Kaczmarek showed that the percentage of relatives affected by the intolerance to cow's milk was 34% [21].

In our study, nearly half of patients (81 – 45%) came from high-risk families: 2–4 closest relatives complained about or manifested the symptoms of allergy during the first visit of the child in outpatients clinic or earlier in the past, while 63 (35%) children had at least 1 relative affected by this kind of diseases.

It was also established that 21 (11.7%) parents and 67 (37.2%) siblings suffered from the identical disease type as that observed in analysed patient, and clinical symptoms involved the same organ. This concurrence was most often observed for skin – 87 (48.3%), then for respiratory system – 47 (21.1%) and gastrointestinal tract – 43 (23.9%).

Businco and Kjellman quoted earlier [7,8] showed that positive family history of atopy may be also of prognostic value for the development of allergic diseases in the progeny. According to Kjellman, familial anamnesis is characterised by low specificity which follows from the fact that only half of the

children with positive family history develop the symptoms of allergy before 11 years of age [22].

Predictive value of family history as simple screening in the prognosis of the development of allergic diseases in children is estimated by other authors at 11–45% [23,24]. Many authors claim that the correlation between family anamnesis and selected cord blood parameters (elevated IgE, increased lymphoblastic transformation index for food allergens, disturbed IFN- γ and IL-4 and IL-6 ratio, reduced CD25+ and CD4+CD45RO+, increased CD4+CD45RA+), considering particularly low sensitivity and specificity of those indices when used on their own, allows for best possible prognosis of atopic diseases in the offspring. On the basis of these data, it is possible to identify 85% children threatened with the development of allergy [8,22,23,25].

To conclude, it should be emphasised that both our study and the findings of other investigators confirm the role of constitutional factor in children with the symptoms of hypersensitivity to cow's milk. The knowledge of this problem should convince paediatricians to implement widely-accepted preventive measures in children from high-risk families (breast-feeding, hypoallergenic maternal diet during lactation, HA formula milk, delayed introduction of solid foods, avoiding exposure to tobacco smoke and animal epithelium).

CONCLUSIONS

1. The analysis of family history of the patients with diagnosed allergy to cow's milk confirmed the participation of constitutional factor in 91.1% of cases.
2. Various or identical clinical manifestations of allergic diseases were observed among closest relatives of analysed patients.
3. Due to familial occurrence of allergy which was proved in our study, it is advisable to implement generally accepted preventive measures in the children from high-risk families.

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