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A Randomized Prospective Double Blind Controlled Trial on Effects of Long-Term Consumption of Fermented Milk Containing *Lactobacillus casei* in Pre-School Children With Allergic Asthma and/or Rhinitis

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ABSTRACT: To examine whether long-term consumption of fermented milk containing a specific *Lactobacillus casei* may improve the health status of preschool children suffering from allergic asthma and/or rhinitis a randomized, prospective, double blind, controlled trial was conducted in 187 children 2–5 y of age. The children received for 12 mo either fermented milk (100 mL) containing *Lactobacillus casei* (10^8 cfu/mL) or placebo. The time free from and the number of episodes of asthma/rhinitis after starting intervention were the outcome measures. The number of fever or diarrhea episodes and the change in serum immunoglobulin were further assessed. No statistical difference between intervention and control group occurred in asthmatic children. In children with rhinitis, the annual number of rhinitis episodes was lower in the intervention group, mean difference (95% CI), −1.6 (−3.15 to −0.05); the mean duration of an episode of diarrhea was lower in the intervention group, mean difference −0.81 (−1.52 to −0.10) days. While long-term consumption of fermented milk containing *Lactobacillus casei* may improve the health status of children with allergic rhinitis no effect was found in asthmatic children. **(*Pediatr Res* 62: 215–220, 2007)**

The rates of allergic diseases in childhood are increasing worldwide, mainly in industrialized countries (1) possibly as the immune system does not receive adequate stimulation early in life (2). Allergic diseases cause disability among children (3), and can lead to an impairment of quality of life and reduce effectiveness at work of parents, with public consequences (4). Interventions aimed to improve allergic diseases condition could be of practical relevance, for both clinical and social implications.

Probiotic bacteria, improving the intestinal microbial balance, may facilitate modulation of immune response. Differences exist in the intestinal flora composition of allergic and nonallergic children (5). In particular, the occurrence of Clostridia in intestinal flora is higher in allergic subjects, while occurrence of bifidobacteria is lower (5–6). Moreover, current lifestyle has changed the gut microflora composition, with prevalence of enterobacteria on lactobacilli and bifidobacteria (6). Interfering in the gut flora throughout ingestion of live microbiota (Lactobacilli), could favor the correct maturation of the immune system (7), and reduce development of allergy in childhood (7–9). Randomized controlled trials hypothesized an effect of lactobacilli on atopic dermatitis in children (10–13) and suggested that the lactobacilli could be beneficial for the respiratory tract (14). Indeed, *Lactobacillus paracasei* might improve the quality of life of adolescents with perennial allergic rhinitis (15–16). Few studies examined the effect of probiotics on rhinitis and results are controversial (17–19). Randomized studies need to clarify the effects of probiotic bacteria on allergy-related disorders. *Lactobacillus casei* may be a promising strain as it survives through the gastrointestinal tract (20), be metabolically active during transit (21), and promote recovery from diarrhea in young children (22,23).

The aims of the current study were to investigate whether the long-term daily consumption of fermented milk containing a specific *Lactobacillus casei* may reduce the occurrence and duration of episodes of asthma and allergic rhinitis and modify the immunologic profile of preschool children with allergic asthma and/or rhinitis.

SUBJECTS AND METHODS

Population. This randomized, prospective, double-blind, placebo controlled study analyzed 187 children consecutively enrolled throughout a 12-month period in 8 care centers located in Milan and surroundings, Northern Italy. Enrolment was carried out between 01 April 2003 and 31 March 2004, and data collection ended on 31 March 2005. Inclusion criteria were: age 2–5 y inclusive; allergy proved by prick test; and diagnosis of allergic asthma and/or rhinitis. Exclusion criteria were: cow's milk allergy, lactose intolerance, severe food allergy or other severe chronic disease, perinatal respiratory problems, antibiotic use in the preceding 4 wk before starting intervention.

Skin prick tests were performed at enrolment and the end of the study in accordance with the Italian Society of Allergy and Clinical Immunology (24) and assessed pollens widespread in the examined area using standardized extracts (STALLERGÈNES France SA, Antony, France). As recommended

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Abbreviations: Cfu, colony forming units; **IQR,** interquartile range; **IgA,** Immunoglobulin A; **IgE,** Immunoglobulin E; **IgG,** Immunoglobulin G; **IgM,** Immunoglobulin M; **U,** arbitrary unit

by the Joint Council of Allergy, Asthma and Immunology (Palatine, IL), the prick test was considered positive when the wheal was at least 3 mm larger in diameter. Asthma was diagnosed and classified in accordance with the Global Initiative for Asthma (GINA) guidelines (25). Allergic rhinitis was diagnosed and classified in accordance with the Allergic Rhinitis and its Impact on Asthma (ARIA) (26).

The parents of eligible children received explanation about the aim of the study, and were requested to sign a consent form. The Ethics Committee of the coordinator center, the San Paolo Hospital, Milan, approved the study protocol.

Intervention. The study protocol scheduled daily oral supplementation of either an intervention "product", that is one pot (100 mL, 0.83 Kcal/g, 0.16% fat) of fermented milk containing two yoghourt cultures (*Lactobacillus bulgaricus,* 10^7 colony forming units [cfu]/mL, and *Streptococcus thermophilus*, 10^8 cfu/mL) and the probiotic strain *Lactobacillus casei* DN-114 001 (10^8 cfu/mL) or one pot (100 mL, 0.83 Kcal/g, 0.16% fat) of a non fermented milk (control), both providing the same dairy load. The intervention product was obtained mixing the yoghourt cultures and the probiotic strain plus the metabolites produced during fermentation. Milks, comparable in taste and texture, were bottled in identical opaque coded pots provided by Danone (Milan, Italy). All individuals involved in the trial were unaware of the milk supplied until codes were broken after the completion of the data analysis. Four trained health workers distributed milks twice monthly. At that time pots nonconsumed in the previous two weeks were got back. Administration of milks started 5 ± 1 d after enrolment. Consumption of other products containing probiotic bacteria was forbidden.

Baseline data collection and clinical examinations. Baseline data were collected at enrolment. Prospective data were recorded daily by the parents on a diary; a methodology used in literature (14), and included solicited questions (yes/no) about occurrence of symptoms of asthma (wheezing, chest tightness, cough, difficult breathing) or rhinitis (rhinorrea, nasal obstruction, nasal itching, sneezing). Occurrence of abdominal symptoms (diarrhea, nausea/vomiting, abdominal pain, constipation) was assessed by a sequence of questions (yes/no) adapted from the Abdominal Symptom Questionnaire (27). Questions were illustrated to the parents, who were instructed as to evaluate symptoms. The parents further recorded whether the child experienced fever and was given antibiotic treatments. Occurrence of an asthma episode was defined as the child experienced an episode or an attack of asthma (28). This definition has been used in recent studies (29,30) and by the National Center for Health Statistics (Hyattsville, M.D.). Occurrence of a rhinitis episode was defined as the child experienced two or more symptoms for longer than one-hour day (31). The family pediatrician confirmed diagnosis of an allergic episode on a physical examination (32). Ambiguous cases had to refer to the care center for testing (32). A new episode was identified as at least 2 d free from symptoms of asthma or rhinitis elapsed since the previous episode. The definition of diarrhea was 2 or more watery or unusually loose bowel motions in 24 h (33). A new episode of diarrhea was defined as the occurrence of diarrhea after a period of 3 or more symptom-free days (33). Fever was defined as the armpit temperature was above 37.2° for two consecutive measurements taken at 4 h interval. A new episode of fever was defined as the occurrence of fever for at least 24 consecutive hours after a period of 2 or more fever-free days.

Children were visited at the care centers within 3 ± 1 d (baseline) after enrolment, and at 3, 6, 9 and 12 mo after starting intervention, when data from diaries were collected and discussed with the parents by the same pediatrician (one for center).

Fecal samples were taken at baseline, and at 6 and 12 mo of intervention in a random subsample of 45 children, 30 in the intervention group and 15 in the control group. Presence of *Lactobacillus casei* was identified using DNA PCR analysis (34,35). The amount of *Lactobacillus casei* was not enumerated.

Immunologic blood assessment. Fasting blood samples were taken at 8.30 h ± 30 m at baseline and at 360 ± 5 d after starting intervention. Total serum immunoglobulins A (IgA), E (IgE), G (IgG) and M (IgM) were measured at the same clinical laboratory by an immunoturbidometric assay (Tina-Quant Roche Diagnostics SpA, Milan, Italy) on a Modular P800 analyzer (Roche Diagnostics).

Sample size and randomization. The sample size was calculated to detect a reduction of 40% or more in the mean number of episodes of asthma and/or rhinitis occurring during the 12-mo intervention period. Recursive calculation was performed through the recruitment period. Admitting a two-tailed type I error level of 5% with a power of 80%, and assuming an expected annual number of episodes in controls equal to the one reported in the last year before intervention in children already recruited, 6o children with asthma and 66 with rhinitis needed in each group. Children were randomly assigned to the intervention or control group based on a computer generated, blocked randomization list by each center. A block size of four was used, stratified according to gender, age ($<$ or $\geq$3 y) and diagnosis of asthma and/or rhinitis. For fecal analysis, 15 blocks were randomly (same chance) selected. Within each of these blocks the two children assigned to intervention group and one (same chance) of the two controls were considered.

Outcome measures. The primary outcome measures were the time (number of days) free from episodes of asthma and/or rhinitis after starting intervention, and the cumulative number and duration (number of days) of episodes. Secondary outcome measures were the number and duration of episodes of diarrhea or fever and the change in immunologic profile.

Statistical analysis. Log transformation was used for the cumulative number of episodes of asthma and/or rhinitis, duration of episodes, and immunoglobulin, as these variables were not normally distributed. Univariate comparison between groups was performed by the *t* test or the Mann-Whitney test, the χ^2 test and ANOVA for repeated measures. Kaplan-Meier survival curves for the time free from episodes were constructed and compared by the log-rank test. Adjustment for potential confounders (age, severity of asthma and rhinitis at baseline) was performed using a Cox regression analysis. Logistic regression analysis was used to assess the effect of intervention on incidence of asthma and/or rhinitis, and estimate the corresponding odds ratio (OR). Analyses were performed on the intention to treat population. A significance level of 0.05 was used and the statistical tests are two-tailed. The SPSS software, version 12.0 (SPSS Inc., Chicago, IL), was used for the statistical analysis.

RESULTS

Of the 196 children randomized, 187 started the study receiving either fermented milk containing *Lactobacillus casei* ($n = 92$) or nonfermented milk ($n = 95$). Figure 1 details

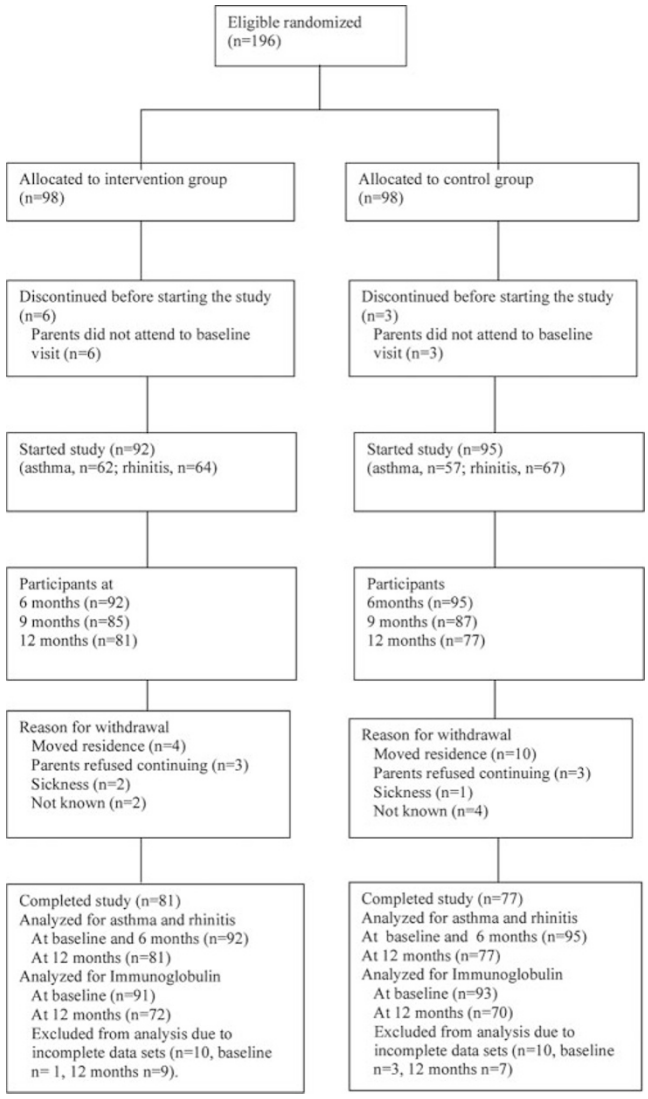

Figure 1. Flow diagram of participants' progress.

Table 1. *Baseline characteristics of children**

	Intervention group (n= 92)	Control group (n= 95)
Boys	60 (65.2)	60 (63.1)
Age at enrollment (y)		
2	6 (6.5)	4 (4.2)
3	22 (23.9)	31 (32.6)
4	29 (31.5)	29 (30.5)
5	34 (32.9)	31 (32.7)
Allergic disease at enrollment		
Asthma†	62 (67.4)	57 (60.0)
Intermittent	43 (69.4)	44 (77.2)
Mild persistent	16 (25.8)	13 (22.8)
Moderate persistent	3 (4.8)	–
Rhinitis‡	64 (69.5)	67 (70.5)
Mild intermittent	31 (48.4)	35 (52.2)
Moderate/severe intermittent	19 (29.7)	16 (23.9)
Mild persistent	10 (15.6)	14 (20.9)
Moderate/severe persistent	4 (6.3)	2 (3.0)
Asthma and rhinitis	34 (36.7)	29 (30.5)
Siblings (yes)	59 (64.1)	67 (70.5)
Breastfeeding (yes)	83 (90.2)	79 (83.2)
Duration of breastfeeding (months)§	7.2 (6.1)	6.2 (4.8)
Smokers in household	30 (32.6)	41 (43.2)
Health in past 12 months:		
Episodes of asthma		
0	34 (37.0)	39 (41.1)
1–3	39 (42.4)	38 (40.0)
≥4	19 (20.7)	18 (18.9)
Episodes of rhinitis		
0	35 (38.0)	32 (33.7)
1–3	31 (33.7)	27 (28.4)
≥4	26 (28.3)	36 (37.9)
Admission to hospital (yes)	15 (16.3)	11 (11.6)
Episodes of fever		
0	12 (13.0)	11 (11.6)
1–2	36 (39.1)	39 (41.1)
3–4	26 (28.3)	37 (38.9)
≥4	18 (19.6)	8 (8.4)

Values are means (standard deviation) or numbers (percentage) of children.

* No significant difference between groups.

† According to GINA (25). Percentage calculated among children with asthma.

‡ According to ARIA (26). Percentage calculated among children with rhinitis.

§ In breastfed children.

the progress of participants throughout the study. Table 1 reports baseline characteristics of the children. The block randomization resulted in a similar distribution of age, allergic disease and severity in the intervention and control groups. At the baseline, among children with allergic rhinitis (n = 131) the disease was, respectively, perennial or seasonal in 42/64 (65.6%) and 22/64 (34.4%) of children in the intervention group *versus* 37/67 (55.2%)and 30/67 (44.8%) in the control group (p = 0.224). No between groups difference at 12 mo was found in the skin prick tests (intervention group, positive 81/89 *versus* 89/93, control group). Before intervention, 37/62 (59.7%) and 33/57 (57.9%) of asthmatic children used asthma medications in the intervention and control group, respectively, while 40/64 (62.5%) and 40/67 (59.7%) children with rhinitis used allergic medications. No significant change in using medications occurred during the study period in intervention or control group.

Asthma and rhinitis episodes. The time free from episodes of asthma/rhinitis was longer in the intervention group compared with the control group (mean [95% CI] 3.5 [2.7 to 4.3] *versus* 2.1 [1.5 to 2.7] months, p = 0.027) with an adjusted intervention:control ratio of 0.76 (0.56 to 1.03) (p = 0.082). In children with asthma, mean (95% CI) time free from episodes was 4.1 (3.1 to 5.0) months in the intervention group *versus* 3.3 (2.4 to 4.3) months in the control group (unadjusted p = 0.231; adjusted p = 0.405) (Fig. 2). In children with rhinitis the corresponding values were 6.2 (5.0 to 7.4) and 5.1 (4.0 to 6.3) (unadjusted p = 0.937; adjusted p = 0.937) (Fig. 2).

In the pooled data the cumulative number of asthma and rhinitis episodes was lower in the intervention than in the control group (median, inter quartile range [IQR], 5 [2 to 9] *versus* 7 [4 to 11], unadjusted p = 0.036; adjusted p = 0.073). In children with asthma no difference between groups was found (Fig. 3). In children with rhinitis difference between groups was significant (unadjusted p = 0.040; adjusted p = 0.053) with a mean number of episodes of respectively 3.2 (2.4 to 4.1) *versus* 4.8 (3.5 to 6.1), that is a mean difference of 1.6 episodes/y (Fig. 3). In the 3–6 mo of intervention occurrence of episodes of rhinitis in the period was lower in the intervention group ($p < 0.01$) with an adjusted odds ratio (95% CI) of 0.39 (0.19 to 0.82, $p < 0.01$). No significant difference between intervention and control group was found in the mean duration of an episode of asthma (mean difference [95% CI] −0.47 [−1.47 to 0.53] days) or rhinitis (mean [95% CI] 1.02 [−0.27 to 2.32] days).

Abdominal symptoms, diarrhea and fever episodes. Abdominal symptoms were reported in 56.5% *versus* 64.2% of children in intervention and control groups, respectively (p = 0.282). In particular, 40 (43.5%) and 49 (51.6%) children, respectively, experienced diarrhea (p = 0.267). The corresponding number of children who reported episodes of fever was, respectively, 79 (85.9%) and 74 (77.9%) (p = 0.157). Antibiotics were administered to 66 (71.7%) and 65 (68.4%) children, respectively in intervention and control groups. Ta-

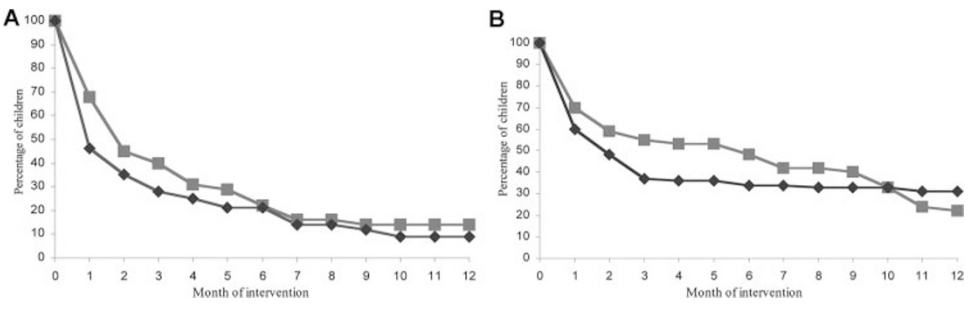

Figure 2. Children free from episodes of asthma (A) or rhinitis (B) in children with asthma (A) or rhinitis (B) at enrolment. Intervention Group (■); Control Group (♦).

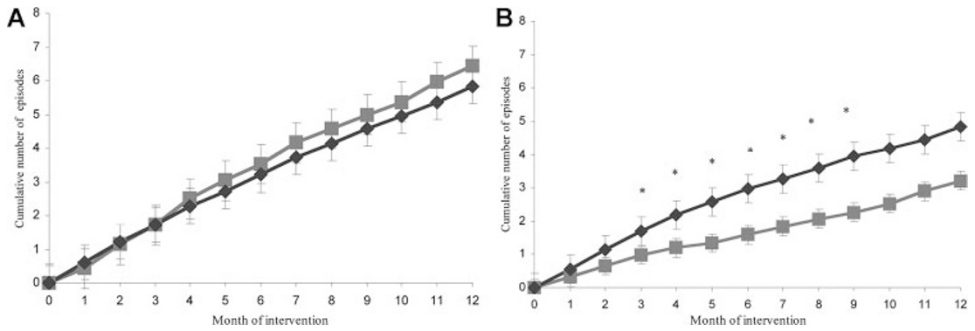

Figure 3. Mean (SEM) of the cumulative number of episodes of asthma (A) or rhinitis (B) in children with asthma (A) or rhinitis (B) at enrolment. Intervention Group (■); Control Group (◆). (* = Significant difference at the specified time: $p < 0.05$).

Table 2. *Median (interquartile range) cumulative number of episodes of diarrhea and fever throughout the study. Number of valid observations within square brackets*

	3 months			6 months			12 months		
	Intervention Group	Control Group	*p**	Intervention Group	Control group	*p**	Intervention Group	Control group	*p**
Diarrhea									
All children	0 (0;0) [*n*=92]	0 (0;0) [*n*=95]	0.277	0 (0;1) [*n*=92]	0 (0;1) [*n*=95]	0.098	1 (1;2.5) [*n*=81]	1 (0;3) [*n*=77]	0.745
Children with asthma	0 (0;0) [*n*=62]	0 (0;0) [*n*=57]	0.421	0 (0;1) [*n*=62]	0 (0;1) [*n*=57]	0.213	1 (1;3) [*n*=54]	1 (0;3) [*n*=47]	0.653
Children with rhinitis	0 (0;0) [*n*=64]	0 (0;0) [*n*=67]	0.895	0 (0;0.75) [*n*=64]	0 (0;1) [*n*=67]	0.361	1 (1;2.5) [*n*=57]	1 (0;2) [*n*=54]	0.437
Fever									
All children	0 (0;1) [*n*=92]	1 (0;1) [*n*=95]	0.106	1 (0;2) [*n*=92]	1 (0;2) [*n*=95]	0.971	2 (1;4) [*n*=81]	2 (1;4) [*n*=77]	0.728
Children with asthma	0 (0;1) [*n*=62]	1 (0;1) [*n*=57]	0.184	1 (0;2) [*n*=62]	1 (0;2) [*n*=57]	0.882	3 (1;4) [*n*=54]	3 (1;4) [*n*=47]	0.762
Children with rhinitis	0 (0;1) [*n*=64]	1 (0;1) [*n*=67]	0.275	1 (0;2) [*n*=64]	1 (0;2) [*n*=67]	0.950	2 (1;4) [*n*=57]	2 (1;4) [*n*=54]	0.544

*Significance of difference between groups.

Table 3. *Immunological profile of children. Values are geometric mean (95% CI), adjusted for age. Number of valid observations within brackets*

	Baseline			12 months of intervention		
	Intervention Group	Control	*p**	Intervention Group	Control	*p**
All children	(*n*=91)	(*n*=92)		(*n*=72)	(*n*=70)	
IgA (mg/dl)	90.9 (81.6;101.2)	98.0 (89.1;107.8)	0.466	105.5 (96.5;115.3)	100.7 (79.4;125.9)	0.660
IgG(mg/dl)	890.5 (845.8;937.5)	905.2 (863.5;948.8)	0.988	952.1 (905.5;1001.5)	934.7 (794.3;955.0)	0.643
IgM (mg/dl)	98.0 (90.5;106.1)	92.3 (85.4;99.8)	0.272	98.3 (90.6;106.7)	93.0 (83.1;102.3)	0.323
IgE (U/ml)	217.3 (172.1;274.4)	205.9 (163.1;259.9)	0.620	248.5 (190.2;324.5)	275.9 (218.7;467.7)	0.560
Children with asthma	(*n*=61)	(*n*=54)		(*n*=51)	(*n*=42)	
IgA (mg/dl)	93.0 (82.5;104.9)	95.3 (84.1;107.9)	0.855	102.8 (92.7;114.0)	96.5 (83.6;111.3)	0.507
IgG (mg/dl)	892.2 (838.7;949.9)	890.2 (838.6;944.9)	0.786	945.1 (892.4;1000.9)	923.6 (871.1;979.0)	0.533
IgM (mg/dl)	103.8 (94.3;114.3)	93.8 (84.5;104.2)	0.102	98.8 (89.8;108.8)	95.8 (87.3;105.1)	0.695
IgE (U/ml)	250.9 (190.7;385.4)	200.2 (145.2;275.9)	0.188	255.0 (181.8;357.7)	252.9 (176.5;362.6)	0.913
Children with rhinitis	(*n*=63)	(*n*=53)		(*n*=49)	(*n*=50)	
IgA (mg/dl)	88.9 (76.9;102.8)	104.3 (93.3;116.6)	0.148	105.1 (93.0;118.9)	104.0 (89.1;121.5)	0.763
IgG (mg/dl)	896.7 (839.2;958.0)	902.1 (852.3;954.7)	0.819	954.5 (894.7;1018.1)	917.8 (868.5;969.8)	0.351
IgM (mg/dl)	94.6 (85.9;104.0)	90.4 (82.3;99.4)	0.740	98.5 (89.1;108.9)	90.9 (84.4;97.9)	0.233
IgE (U/ml)	200.3 (152.5;263.2)	226.7 (173.3;296.4)	0.625	244.3 (175.9;339.2)	318.4 (232.1;436.8)	0.199

* Significance of difference between groups.

ble 2 details the cumulative number of diarrhea and fever episodes throughout the study. In children with rhinitis, the mean duration of a single episode of diarrhea was lower in the intervention group compared with the control group (mean [95% CI] 1.04 [0.55 to 1.53] *versus* 1.85 [1.32 to 2.38] days) with an adjusted intervention:control ratio of 0.80 (0.63 to 0.99; $p = 0.048$).

Immunologic profile. No overall statistical difference was found at baseline or at 12 mo of intervention between intervention and control groups for any examined immunologic variable, neither significant difference occurred when children with asthma and rhinitis were considered separately (Table 3).

Compliance. Compliance estimated on the basis of nonconsumed pots was 70% and 74% in intervention and control

groups, respectively. Compliance was higher in the first semester (80% in both groups), then declined to 59.9% and 68.0%, respectively. Fecal analysis showed that no child carried *Lactobacillus casei* at baseline. In the intervention group the rate of recovery of *Lactobacillus* casei was 78.6% and 77.8% at 6 and 12 mo, respectively. No control child showed presence of *Lactobacillus casei* in the fecal sample at 6 or 12 mo.

DISCUSSION

This study evaluated whether long-term consumption of a fermented milk containing a specific *Lactobacillus casei* (DN 114 001) may induce benefits on preschool children with allergic asthma and/or rhinitis. Compliance to treatment was good enough. However, based on nonconsumed pots, it was approximately 14% reduced during the second semester of intervention as compared with the first semester. This may be a limitation of the study that could have been prevented to find significant differences between groups. A methodological limitation is that the control used was a nonfermented milk. A better control would be fermented milk without the addition of the *Lactobacillus casei* or a sterilized fermented milk. Indeed, a control group similar to the one used in the present study was used in other studies (19). Only recently it was generally agreed that this control would be not acceptable (*e.g.*, The First International DIA Workshop: "Developing Probiotics as Foods and Drugs – Scientific and Regulatory Challenges" Oct 16–17, 2006, Adelphi, M.D.; http://www.isapp.net/IS_news.htm). However, it should be noted that the present trial started in 2003, when appropriateness of the control group was controversial. The study demonstrated the effect of fermented milk containing a specific *Lactobacillus casei* strain, but it is not possible to conclude about the effect of *Lactobacillus casei per se*. Indeed, articles state that plain yoghurt may have impact on rhinitis and asthma (18). Due to these shortcomings caution should be exercised in drawing definitive conclusions.

The analysis of pooled data revealed that children receiving fermented milk containing *Lactobacillus casei* had 33% lower occurrence of rhinitis episodes/y as compared with the control group. No significant difference between groups was found in children with asthma for any outcome measure. In children with rhinitis number of annual episodes was lower in the intervention group, with an occurrence of episodes twice lower during the second quarter of intervention. The nonsignificance during the first quarter may suggest that improvement of balance and metabolic profile of intestinal microflora and modulation of immune response is not immediate. Indeed, Guerin-Danan *et al.* (36) found that after one month of consumption more than 50% of healthy infants consuming *Lactobacillus casei* exhibited significant increase in the fecal population of *Lactobacillus*, but it may not excluded that longer time needs in non healthy children. The vanishing effect during the second semester might be due, at least in part, to the reduced compliance.

Studies reported positive immunostimulatory effect of bacteria in preventing recurrent infections in children (*e.g.*, 37). In the present study the fermented milk containing *Lactobacillus* did not exercise a significant effect on fever. It can be not excluded that this is due to the relatively low dose ingested daily (100 mL). Hatakka *et al.* hypothesized that the immunostimulatory effect of *Lactobacillus* may be dose dependent (14).

It has been suggested that assumption of *Lactobacillus casei* may reduce incidence and duration of diarrhea in infants and young children (22,23,38). In this study the annual incidence of diarrhea did not differ between the intervention and control groups but duration of an episode was lower in children receiving *Lactobacillus* (1.0 *versus* 1.7 d). Comparable results have been found in smaller studies (39).

In conclusion, within the limitations of the present study, one can infer that long-term consumption of fermented milk containing a specific *Lactobacillus casei* may improve the health status of children with allergic rhinitis but appear to do not exercise significant effect in children with asthma.

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