Extensively hydrolyzed casein formula containing lactobacillus rhamnosus GG prevents the occurrence of other allergic manifestations in subjects with cow’s milk allergy: 3-year randomised controlled trial

Rita Nocerino, Linda Cosenza, Antonio Amoroso, Margherita Di Costanzo, Carmen Di Scala, Giorgio Bedogni, Roberto Berni Canani

University of Naples "Federico II", Italy

Aims: Children with cow’s milk allergy (CMA) have an increased risk to develop other allergic manifestations. We performed a randomized controlled trial (RCT) to test whether the early administration of an extensively hydrolyzed casein formula (EHCF) containing *L. rhamnosus* GG (LGG) can reduce the 3-year incidence of other allergic manifestations in these patients.

Methods: A parallel-arm RCT was performed in children aged 1 to 12 months with IgE-mediated CMA. Patients were allocated to one of two groups of dietary interventions: EHCF (Nutramigen®, Mead Johnson, Evansville, IN, USA) and EHCF+LGG (Nutramigen LGG®, Mead Johnson, Evansville, IN, USA). All subjects were evaluated during a 36 months follow-up. Other allergic manifestations (atopic eczema, allergic urticaria, asthma and oculorhinitis) were diagnosed using standard criteria by pediatricians blinded to group assignment. Tolerance acquisition was evaluated every 12 month by the result of oral challenge.

Results: 220 subjects (147 male, 67%) with a mean (SD) age of 5.7 (3) months were randomized, 110 to EHCF and 110 to EHCF+LGG. Binomial regression using intention-to-treat analysis revealed that the absolute risk difference (ARD) for the occurrence of at least one allergic manifestation over 36 months was -0.22 (95%CI: -0.35% to -9%, *p*<0.001) for EHCF+LGG vs. EHCF. The ARD for the occurrence of atopic eczema was -0.13 (95%CI: -0.25% to -1%, *p*<0.05), -0.14 (95%CI: -0.25% to -2%, *p*<0.001) for allergic urticaria, -0.11 (95%CI: -0.22% to 0%, *p*<0.05) for asthma, and -0.17 (95%CI: -0.29% to -6%, *p*<0.01) for oculorhinitis in EHCF+LGG vs. EHCF group. Binomial regression for repeated measures using per-protocol-analysis with Bonferroni’s correction for 3 comparisons (contrasts) revealed that the ARD for the acquisition of cow’s milk tolerance was 0.20 (95%CI 0.05 to 0.35, *p*<0.01) at 12 months, 0.24 (95%CI 0.08 to 0.41, *p*<0.01 at 24 months and 0.27 at 36 months (95%CI 0.11 to 0.43, *p*<0.001) for the EHCF+LGG vs. the EHCF group.

Discussion/Conclusion: Compared to EHCF, EHCF+LGG reduces the incidence of other allergic manifestations in children with IgE-mediated CMA. Moreover, the use of this hypoallergenic formula increases the rate of tolerance acquisition at 12, 24 and 36 months.