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Jérôme Gay-Quéheillard, Jean Fioramonti, Rafael Garcia Villar, Xavier Emonds-Alt, Lionel Bueno

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INVOLVEMENT OF TACHYKININ RECEPTORS IN THE SENSITIZATION TO COW'S MILK PROTEINS IN GUINEA-PIGS

Gay J, Fioramonti J, Garcia-Villar R, Emonds-Alt X*, Buéno L.
INRA, Pharmacology and Toxicology Unit, Toulouse and *SANOFI Recherche, Montpellier, France.

Background: Previous studies have shown that capsaicin-sensitive afferent neurons are involved in food allergy, the sensitization rate to milk proteins being reduced by sensory denervation with capsaicin.

Aim: Since tachykinins are major mediators of intestinal afferent neurons, our aim was to determine whether NK1, NK2 and NK3 tachykinin receptors are involved in milk protein-induced sensitization.

Methods: Five groups of six Dunkin-Hartley guinea-pigs (250-300g) were used. Four groups were sensitized to milk proteins by giving them fresh pasteurised cow's milk to drink instead of water and a daily gavage of mixture of whey proteins enriched with β -lactoglobulin (β -LG; 100 mg/animal) for three weeks. During this period, three of the four groups of animals were treated daily with NK1 (SR 140333; 0.3mg/kg, ip), NK2 (SR 48968; 5mg/kg, ip) or NK3 (SR 142801; 5mg/kg, ip) receptors antagonists. The fourth group received daily vehicle of NK antagonists. The fifth group had water available instead of milk and was used as non sensitized control. Sensitization rates were evaluated by passive cutaneous anaphylaxis (PCA) test to determine anti β -LG antibody (IgE and IgG) titers, expressed as the log of the highest dilution giving local skin blueing. The number of mast cells was determined on transverse sections of jejunum stained with alcian blue-safranin O.

Results: IgE and IgG serum titers were significantly ($p < 0.01$) lower in sensitized animals treated with NK1 and NK3 receptor antagonists (1.14 ± 0.22 and 0.86 ± 0.08 , respectively) in comparison with vehicle-treated animals (1.84 ± 0.16), but were not significantly ($p > 0.05$) modified by the NK2 receptor antagonist (1.98 ± 0.15). No positive response to the PCA test was observed in non-sensitized animals. The number of mast cells was $113.3 \pm 9.2/\text{mm}^2$ in sensitized animals vs 78.1 ± 6.2 in non sensitized ($p < 0.05$). Treatment with the NK1 receptor antagonist abolished sensitization-induced increase in mast cell number (64.2 ± 6.7 mast cells/ mm^2) which was not modified by NK2 and NK3 receptor antagonists (120.7 ± 15.6 and 107.8 ± 12.8 mast cells/ mm^2 , respectively).

Conclusion: These results indicate that, in guinea-pigs, NK1 and NK3, but not NK2 receptors are involved in cow's milk sensitization assessed by IgE and IgG titers. However, NK1 but not NK3 receptor antagonist abolished food allergy hypermastocytosis, suggesting different roles for NK1 and NK3 receptors in the pathways of sensitization to β -lactoglobulin.