Gluten, enzymatic or acid hydrolysed gluten does not induce sensitisation by the oral route in contrast to i.p. dosing: a study in gluten-tolerant Brown Norway rats

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Aim: Hydrolysed wheat proteins have provoked IgE mediated symptoms after skin exposure or ingestion in subjects tolerant to wheat. Acid hydrolysed wheat protein in a facial soap has been described to break tolerance to wheat. We have previously investigated the sensitising capacity of wheat gluten (G), enzymatic hydrolysed (EHG) and acid hydrolysed gluten (AHG) in naive Brown Norway rats (Kroghsbo et al. 2014). The aim was to study the influence of wheat tolerance on the sensitising capacity of G, EHG and AHG.

Methods: Rats were bred for at least two generations on ordinary wheat-containing rat chow. After weaning the rats were kept on chow and then moved to a gluten free diet. Blood was drawn before dosing day 0 and a week after termination of dosing. Oral study: Rats were dosed by gavage with 20 mg G, EHG or AHG daily for 35 days. I.p. study: Rats were dosed with G, EHG or AHG 320 µg protein day 0, 14 and 28. Sera were analysed for specific IgG1 and IgE to the respective protein by ELISAs. Cross-reactivity was measured by inhibition ELISA’s and avidity by KSCN ELISA.

Results: At baseline >50% of the rats had low IgG1 titre to G, but no detectable IgE to G. Oral dosing with G, EHG or AHG did not induce significant changes in the level of specific IgG1 and IgE to either the product used for dosing or to G. I.p. dosing resulted in a significant increase in IgG1 antibodies to the respective proteins and in IgE to G and AHG. The G dosed rats had IgG1 with the highest avidity. IgG1 from AHG immunised rats showed a higher avidity to G than to the AHG. The inhibition ELISA’s showed a high level of similarity within and between the groups.

Discussion: In contrast to our study in naive rats, oral dosing in wheat tolerant rats could not induce a specific immune response above baseline. In the i.p. dosed animals the high level of cross-reactivity indicates a response dominated by antibodies to epitopes that are similar on all three products. The lower avidity to AHG (containing novel epitopes) compared to G in AHG dosed animals suggests a role for affinity maturation in the wheat tolerant animals.

Conclusion: Exposure by the oral route to EHG or AHG is very unlikely to break an already established tolerance to wheat and induce sensitisation. In the i.p. study prior affinity maturation to common epitopes on G and AHG makes it possible to induce a high avidity immune response to G by dosing with AHG. This may illustrate how AHG in a facial soap could break tolerance to wheat.