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Publication date:
2019

Document Version
Publisher's PDF, also known as Version of record

The effect of amoxicillin-induced intestinal dysbiosis and cholera toxin on gut health and allergic sensitization to cow's milk – a study in Brown Norway rats

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INTRODUCTION

Cholera toxin (CT) is a mucosal adjuvant used in animal models of allergy. Some studies have shown that the commensal microbiota is critical for the adjuvant function of CT, but results are conflicting and the mechanism involved remain largely unknown. In the present study, we investigated how CT and dysbiosis induced by the antibiotic amoxicillin (AMX) affect gut health and sensitisation to cow's milk.

METHODS

Brown Norway rats (n=12/group) were gavaged daily with either AMX or water from 1 week before and 5 weeks during oral sensitisation with whey protein product with or without CT given by gavage 3 times per week. Elicitation was assessed by in vivo tests. Whey-specific IgG1 and IgE were quantified in serum, and total and specific IgA in faeces and serum by means of ELISAs. Intestinal microbiota composition was analysed by high-throughput 16S rRNA gene sequencing. Lymphocytes from intestinal tissues and blood were analysed by flow cytometry. Uptake of whey protein in intestinal tissues after oral challenge was assessed by ELISA. Jejunum and colon morphology was assessed by histological staining.

RESULTS

AMX-treatment did not affect sensitisation, but despite similar levels of whey-specific IgE serum levels, we found that allergic symptoms were slightly more sever in the AMX-group. Serum levels of specific IgG1 and IgA, and total IgA were higher in CT groups but unaffected by AMX, while faecal total IgA was significantly affected by AMX. We found that both AMX and CT affected intestinal whey protein uptake; higher concentrations were detected in epithelium in the CT-groups, and in Peyer's patches (PP) in the AMX groups. CT-treatment caused a massive increase in T- and B-lymphocytes in PP, while AMX caused a small reduction. In blood, CT and AMX resulted in additive upregulation of T- and B-lymphocytes. Eosinophils, goblet cells and mast cells were increased in jejunum of CT-treated rats, but AMX diminished the effects.

CONCLUSION

AMX-induced dysbiosis did not affect sensitisation, but did slightly increase severity of allergic symptoms. This could be related to differences in intestinal protein uptake, faecal IgA and circulating lymphocytes in the two groups. Local effects of CT on cell composition in small intestine tissue assessed by histology and flow cytometry were numerous, but all diminished by AMX.