Toxigenic and non-toxigenic Clostridium difficile: determinants of intestinal colonisation and role in childhood atopic manifestations

Citation for published version (APA):


Document status and date:
Published: 01/01/2008

DOI:
10.1136/gut.2007.143214

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

Document license:
Taverne

Please check the document version of this publication:

• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:
www.umlib.nl/taverne-license

Take down policy
If you believe that this document breaches copyright please contact us at:
repository@maastrichtuniversity.nl
providing details and we will investigate your claim.

Download date: 14 Sep. 2023
and INR. MELD scores can range from 6 to 40 (MELD scores greater than 40 are all grouped together and receive a score of 40)".

Despite the fact that it should be impossible to achieve a MELD score of >40, many of the online calculators do indeed generate numbers greater than this ceiling value. This is dependent upon numbers entered for the international normalised ratio (INR), bilirubin and creatinine. We would therefore caution all clinicians when using these or similar calculators to analyse retrospective data. MELD scores can easily and incorrectly be generated with values >40.

Calculation of the median score (with interquartile ranges) would not highlight this problem, but sample mean and SD may do. These values may skew the data—for example, the 5-month survival probability with a MELD score of 40 should actually be lower than depicted on the graph, and the mean MELD score in table 1 should be <18.

This has potential ramifications for all large multicentre trials and systematic reviews utilising published MELD scores collected in this way.

We would also like to add comment to sodium not meeting the fourth criterion of “stability” in a scoring system for organ stability in a scoring system for organ allocation. Sodium levels, like creatinine, can be manipulated through overzealous usage. We would therefore caution all clinicians when using these or similar calculators to analyse retrospective data. MELD scores can easily and incorrectly be generated with values >40.

The aim of this study was to examine which factors influence (non-)toxicogenic C. difficile colonisation and to examine the role of C. difficile toxigenicity on the development of atopic manifestations.

Faecal samples of 957 one-month-old infants, participating in the KOALA study, were available for analysis (for a detailed description of methods see Penders et al). The samples have been subjected to real-time PCRs for the detection of C difficile and its toxins A and B, according to the assays as described in Penders et al, Belanger et al and van den Berg et al, respectively.

Information on potential determinants of (non-)toxicogenic C difficile colonisation, atopic symptoms and potential confounders was retrieved through repeated questionnaires. Specific immunoglobulin E (IgE) was measured in blood samples collected at the infant’s age of 1 and 2 years. A clinical diagnosis of eczema was made at 2 years.

A total of 200 infants (20.9%) were colonised with non-toxicogenic (A B), 36 (3.58%) with toxicogenic A B and 4 (0.4%) with toxicogenic A B C difficile. Hospital delivery (especially caesarean section) and hospital admission following birth were associated with higher colonisation rates of both toxicogenic and non-toxicogenic C difficile. Exclusively breastfed infants were less often colonised with (non-)toxicogenic strains compared with their formula-fed counterparts. Boys were at increased risk of being colonised with toxigenic strains (fig 1). Maternal education, maternal organic and/or vegetarian diet, maternal probiotic and antibiotic use during pregnancy, birth season, number of siblings, fever in the first month of life and the presence of furry pets were not associated with colonisation by either non-toxicogenic or toxigenic C difficile.

Colonisation of infants with non-toxicogenic, but not with toxicogenic, C difficile increased the risk of developing (parentally reported and clinically diagnosed) eczema and sensitisation to food allergens (tables 1 and 2). This implies that toxins A and B are not responsible for the increased risk of eczema and sensitisation among carriers of C difficile. The different reference categories are shown in figure 1.
associations of non-toxigenic and toxigenic C. difficile with these atopic outcomes suggest that other bacterial components or properties, differing between toxin-positive and toxin-negative strains, may play a role. In contrast to eczema and sensitisation to food allergens, recurrent wheeze was positively associated with toxin-positive C. difficile (table 1). This could indicate different biological mechanisms underlying the aetiology of wheeze compared with eczema and sensitisation.

In conclusion, the present study showed that although both non-toxigenic and toxigenic C. difficile strains share the same environmental origin, they are differently associated with atopic manifestations. In contradiction of our hypothesis, the association between C. difficile and eczema and sensitisation cannot be explained by disruption of the epithelial barrier function by toxins A and B. The different associations between non-toxigenic and toxigenic C. difficile with atopic manifestations, however, demonstrate the importance of studying the effect of gut bacteria in health and disease beyond the genus and species level. Further investigations are necessary to understand better the role of non-toxigenic C. difficile strains in disease development.

J Penders,1,2 E E Stobberingh,3 P A van den Brandt,3 R van Ree,4 C Thijssen5,6

1 Department of Epidemiology, Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Maastricht University, Maastricht, The Netherlands; 2 Department of Medical Microbiology, University Hospital of Maastricht, Maastricht, The Netherlands; 3 Department of Epidemiology, Care and Public Health Research Institute (Capphi), Maastricht University, Maastricht, The Netherlands; 4 Department of Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands

REFERENCES


Upper gastrointestinal symptoms and asthma: a manifestation of allergy?

We welcomed the systematic review by Havemann et al (Gut 2007;56:1654) further highlighting the significance of the association between gastro-oesophageal reflux disease (GORD) and asthma. The importance of this association is underlined by the magnitude of published studies concerning this subject (731 studies evaluated in Havemann’s review). The reviewers conceded that the direction of causality and the underlying mechanism responsible for this association remain undetermined. Mechanisms postulated include hyperexpansion of the asthmatic chest leading to failure of the gastro-oesophageal junction (GOJ) with attendant reflux symptoms, or shared stimulation of vagus nerve-mediated reflex arcs resulting in both bronchial smooth muscle constriction (causing asthma) and GOJ relaxation (causing GORD). Causality has also been speculated to occur in the reverse direction, with aspiration of gastric fluid into the bronchial tree of patients with GORD leading to symptomatic bronchial irritability and asthma.

An alternative explanation also merits consideration. Asthma is characterised by increased numbers of eosinophils in the bronchial mucosa, airways lumen and circulating blood, in numbers that correlate with asthma severity. It appears that in patients with allergic diseases such as asthma and allergic rhinitis, the migration...