Study shows gut microbe composition different in young children with and without type 1 diabetes

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New research published in *Diabetologia* (the journal of the European Association for the Study of Diabetes) shows that children diagnosed with type 1 diabetes have a less balanced composition of gut bacteria compared with children of the same age without diabetes. The research is by Dr Marcus de Goffau and Dr Hermie Harmsen, University Medical Center Groningen, the Netherlands, and colleagues.

The incidence of type 1 diabetes is increasing worldwide, showing a particularly sharp increase among children under the age of 5 years. Recent studies indicate that adverse changes in gut microbiota are associated with the development of type 1 diabetes, but little is known about the microbiota in children who have diabetes at an early age. Thus

in this new study the microbiota of children aged 1 years with new-onset type 1 diabetes was compared with the microbiota of age-matched healthy controls.

A deep global analysis of the gut microbiota composition was done by phylogenetic microarray analysis using a Human Intestinal Tract Chip (HITChip), an analytical device designed specifically for studying gut bacteria.

Patients were recruited into two research projects – the DIPP (Finnish Type 1 Diabetes Prediction and Prevention) study in Finland and the international VirDiab (Viruses in Diabetes) study, which included cases and control children from seven European countries.

Faecal samples were collected from children newly diagnosed with type 1 diabetes and controls. DNA was successfully isolated from 28 diabetic children: four from France, one from Greece, three from Estonia, two from Lithuania and 18 from Finland. The diabetic children were matched with control children according to age; DNA was isolated successfully from 27 control children. One of the control children was from Lithuania and the rest were from Finland. The samples were collected from the diabetic children within 4 weeks of the diagnosis of diabetes and were coupled with samples from age-matched controls. Samples were collected by the parents at home and shipped by mail at ambient temperature to the laboratory, where they were subsequently stored at -75°C.

The researchers found that in children younger than three years, the combined abundance of the class Bacilli (notably streptococci) and the phylum Bacteroidetes were higher in diabetic children, whereas the combined abundance of the important (usually beneficial) Clostridium clusters IV and XIVa was higher in the healthy controls.

Controls aged three years and older were characterised by a higher fraction of butyrate-producing species within Clostridium clusters IV and XIVa than was seen in the corresponding diabetic children or in children from the younger age groups, while the diabetic children older than three years could be differentiated by having an unusually high microbial diversity. An increased diversity is often associated with unstable or with unusual bacterial networks; in children with coeliac disease or adults with colorectal cancer an abnormally high microbial diversity is found.*

The authors discuss that the ideal scenario for the gut is to have the right balance of bacteria to produce the fermentation product butyrate, which is readily absorbed by the human gut and turned into energy. Production of sufficient butyrate by bacteria in the gut leads to optimal gut function and prevents/minimises inflammation and other metabolic problems. The authors explain that, as the gut microbiota of very young children (1-3 years) is still developing very rapidly**, the proper kind of balance to produce butyrate is not yet exactly the same as it is when children are older than 3 years.

The authors also recalculated their results without the non-Finnish children to adjust for any geographical differences, and their main findings remained unchanged.

They say: "The results from both age groups suggest that non-diabetic children have a more balanced microbiota in which butyrate-producing species appear to hold a pivotal position. Although distinct differences have been found in each age category between the healthy and diabetic children, the main differences with regard to Clostridium clusters IV and XIVa appear to represent two sides of the same coin, as they together emphasise the importance of developing balanced bacterial cross-feeding complexes that have sufficient potential for butyrate formation."

They add: "Dietary interventions aimed at achieving or maintaining optimal butyrate production levels might measurably reduce the risk of developing type 1 diabetes, especially in children with genetic risk for developing type 1 diabetes."

The authors say more work needs to be done on establishing exactly what foods are best for promoting ideal gut conditions, however they conclude: "We think a diet high in fruits and vegetables is best as these are rich in fibre/complex carbohydrates, which are important because butyrate-producing species are dependent upon them indirectly via cross-feeding relations with fibre degraders. Simple sugars, on the other hand, cause an overabundance of species which are very proficient in quickly utilising sugars—Streptococci for example—thus outcompeting or limiting the amount of species which are beneficial for human health. Excessive protein and animal fat consumption might similarly indirectly negatively affect butyrate production as they stimulate non-butyrate-producing species which are very good in utilising this type of food source (such as Bacteroides)."***

More information: Notes:

*As always in gut microbiota analysis, too much of a good thing is usually not good, but never having 'bad' bacteria is also not ideal. Bifidobacteria are, for example, normally found in the human gut, but if an adult has +50% Bifidobacteria, something is definitely wrong, whereas 50% or more Bifidobacteria in babies is normal. E. coli numbers in excess of 1% in adults is usually considered unhealthy, yet in babies having numbers in between 1 and 10% is just perfectly fine (in fact beneficial). A proper microbial balance in the gut is dependent upon age and can be achieved in many different ways; as long as the combined microbial composition leads to the right balance of (metabolic) processes).

**This article from *Nature* also demonstrates that the microbial development of the human gut is especially rapid during the first 3 years of life, and then stabilises. www.nature.com/nature/journal/ … abs/nature11053.html

***The authors refer to the following publication from *Science* www.ncbi.nlm.nih.gov/pmc/articles/PMC3368382/

Provided by Diabetologia