Do Antibiotics Raise Diabetes Risk via Gut Microbiota?

Liam Davenport | |April 01, 2015

People who take multiple courses of antibiotics may face an increased risk of developing both type 1 and type 2 diabetes, potentially through alterations in gut microbiota, conclude US researchers.

The team, led by Ben Boursi, MD, a postdoctoral researcher in the department of gastroenterology at the University of Pennsylvania, Philadelphia, found that the risk of diabetes was increased by up to 37%, depending on the type of antibiotic and the number of courses prescribed.

"Overprescription of antibiotics is already a problem around the world as bacteria become increasingly resistant to their effects," commented Dr Boursi in a statement.

"Our findings are important, not only for understanding how diabetes may develop, but as a warning to reduce unnecessary antibiotic treatments that might do more harm than good."

The study was published online ahead of print March 24 in the *European Journal of Endocrinology*.

The More Courses of Antibiotics, the Greater the Risk

Dr Boursi explained that studies both in animal models and humans have shown an association between changes in gut microbiota in response to antibiotic exposure and obesity, insulin resistance, and diabetes.

Speaking to *Medscape Medical News*, he noted: "In mice, we know that germ-free mice are lean and, by fecal transplantation, we can transmit obesity to them. We also know that low dose of penicillin may induce obesity in mice models."

He added that there have been several studies in humans indicating that exposure to antibiotics in early childhood is associated with an increased risk of obesity in later life, while other investigations have reported differences in gut microbiota between people with and without diabetes.

To investigate further, Dr Boursi and colleagues conducted a nested case-control study using data from the Health Improvement Network (THIN), a UK population-based database, from which they identified 1,804,170 patients with acceptable medical records.

As diabetes is associated with an increased risk of infection, the team wanted to exclude all cases with prediabetes or undiagnosed diabetes. To do that, they removed all patients diagnosed with diabetes within 183 days of starting follow-up and included only patients with exposure to antibiotics more than 1 year prior to the index date.

From the original cohort, they were able to select 208,002 diabetes patients and 815,576 controls matched for age, sex, general practice site, and duration of follow-up before the index date.

Conditional logistic regression analysis revealed that exposure to a single antibiotic prescription was not associated with an increased risk of diabetes, adjusted for body mass index (BMI), smoking, last blood glucose level, and the number of infections before the index date, alongside a history of coronary artery disease and hyperlipidemia.

However, treatment with two to five courses of antibiotics was linked to an increased risk of diabetes with penicillin, cephalosporins, macrolides, and quinolones, at adjusted odds ratios (ORs) ranging from 1.08 for penicillin to 1.15 for quinolones.

The highest risk for diabetes was seen among people who received more than five courses of quinolones, at an adjusted OR of 1.37. An increased risk of diabetes was also seen in patients who took more than five courses of tetracyclines, at an adjusted OR of 1.21.

Interestingly, the researchers were unable to find an association between diabetes risk and treatment with imidazole, antiviral drugs, and antifungals, regardless of the number of courses.

To account for further possible confounding factors, the researchers repeated the analysis only in individuals without skin or urinary-tract infections, which are more common among diabetes patients. This had no impact on the results.

Next Steps

When the analysis was restricted to type 1 diabetes, the risk was increased only following exposure to more than five courses of penicillin or two to five courses of cephalosporin, at odds ratios of 1.41 and 1.63, respectively.

Commenting on the findings, study coauthor Yu-Xiao Yang, MD, assistant professor of medicine and epidemiology, University of Pennsylvania, pointed out their investigation was observational in nature.

"We are not able to establish cause and effect necessarily, but it is actually pretty consistent with the experimental data, which is more definitive in terms of the animal data than in humans."

Dr Yang said that the next step for the team will be to expand their focus, as the antibiotics data "provide indirect evidence suggesting the importance of gut microbiota on metabolic outcomes, including diabetes."

Describing their findings as "important evidence," he concluded: "Based on this indirect evidence and existing data in animals, we are planning to more directly investigate the effect of altered microbe environments in humans."

The work was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences at the National Institutes of Health. The authors have reported no relevant financial relationships.

Eur J Endocrinol. 2015. Published online March 24, 2015. Abstract