The gut microbiome and type 2 diabetes: Current evidence and future directions

Diabetes is a chronic metabolic condition and a significant public health concern. Disruptions to or imbalances in the gut microbiome have been associated with the development and progression of the condition. In this commentary, the authors discuss the current evidence for the role of the gut microbiome in type 2 diabetes, as well as the emerging interventions aimed at improving glycaemia via microbiome-dependent pathways. In particular, given the wide range of nutrients that appear to affect both the microbiome and other chronic conditions that are commonly comorbid with type 2 diabetes, the promotion of healthy eating patterns in this population is discussed.

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Living symbiotically within the gastrointestinal tract are as many bacteria as we have cells in our body; these are referred to as the gut microbiota (Gilbert et al, 2018). Advances in sequencing technologies have implicated the gut microbiota as an important factor for the maintenance of health. However, disruptions to or imbalances in this biological system have been associated with the development and progression of disease (Marchesi et al, 2016).

Recent research implicates the gut microbiota as a potential candidate driving the inflammatory response associated with type 2 diabetes. Disruptions to the tight junctions of the gut epithelium, prompted by high-fat diets, result in an increased permeability of the gut (Moreira et al, 2012). Molecules that are specific to bacteria are then able to leak out of the gut into the circulation, promoting systemic inflammation; this is often referred to as "leaky gut" (de Groot et al, 2017). This inflammation results in altered metabolism and influences energy balance, glucose metabolism and body weight (Cani et al, 2012). New research suggests that high blood glucose may also promote leaky gut (Thaiss et al, 2018).

Compositional changes to the microbiome that are seen in people with type 2 diabetes are associated with plasma glucose concentrations (Larsen et al, 2010). People with type 2 diabetes appear to have gut microbial dysbiosis and a decreased abundance of bacteria that produce butyrate, a short-chain fatty acid that appears to have a beneficial effect on insulin sensitivity (Qin et al, 2012). In fact, faecal microbiota transplants that increase levels of butyrate-producing bacteria have been shown to improve insulin sensitivity in humans (Vrieze et al, 2012). Furthermore, metagenomic techniques can differentiate microbiome signatures between people with type 2 diabetes or impaired glucose sensitivity and those with normal glucose sensitivity, suggesting the potential for monitoring and identifying individuals at risk of type 2 diabetes using such strategies (Qin et al, 2012).

In addition, emerging evidence has implicated the microbiome as a pathway mediating the therapeutic and adverse effects of metformin, a common medical intervention used to treat type 2 diabetes (Forslund et al, 2015). Moreover, a small intervention study reported metformin-induced changes in gut-related pathways, including microbiome composition and glucagon-like peptide-1 secretion (Napolitano et al, 2014).

Future therapies and practical implications

Due to the potentially central effects of the microbiome on type 2 diabetes and other chronic diseases, a range of microbiome-targeted therapies are currently being explored. These include

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probiotic interventions, which deliver specific strains of beneficial bacteria, and prebiotic interventions, which use various fibres to promote the growth of beneficial bacteria. A recent meta-analysis reported a significant reduction in fasting blood glucose from probiotic interventions (Samah et al, 2016). While probiotic supplements are widely available to the consumer, further research is needed to confirm these results in larger populations, and to identify the optimal dose and strain requirements, before these products can be recommended. There is also significant research interest in using microbiota transplants to treat chronic diseases that may be modulated by the gut microbiome, including type 2 diabetes. The first such study reported that a faecal microbiota transplant resulted in improvements in insulin sensitivity and was associated with increases in beneficial bacteria (Vrieze et al, 2012).

While there are limited studies in populations with type 2 diabetes that have used dietary interventions to specifically target the microbiome, dietary interventions may be key to improving outcomes. As well as other beneficial compounds, vegetables and fruit are a rich source of fibre and polyphenols, both of which appear to be critical for optimal gut health and functioning. The incorporation of fermented foods (e.g. yoghurt, sauerkraut, kimchi) in a habitual diet may also provide benefits due to their high probiotic content, as well as microbial metabolites such as short-chain fatty acids, that drive health effects. Furthermore, mono- and polyunsaturated fats have a beneficial impact on gut microbiome composition and gut health, while saturated fats seem problematic (Alcock and Lin, 2015; Menni et al, 2017).

Conclusion

Current evidence suggests that people with type 2 diabetes have an altered gut microbiome compared with healthy individuals and that this may have a mechanistic role in the disease state. Several promising therapies that target the microbiome have been proposed; however, evidence to date is preliminary. A diet rich in fibre, mono- and polyunsaturated fats, polyphenols and fermented foods may benefit the microbiome and improve management of type 2 diabetes and related chronic conditions. Focusing advice on the gut microbiome may help patients to make necessary changes to their diets. ■

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