

A TB vaccine for diabetics?

The century-old tuberculosis vaccine called BCG (Bacillus Calmette–Guérin) might lower blood sugar in diabetes patients several years after they get the shot, a small but path-breaking study, published in *npj Vaccines*, suggests.

In the study, “Long-term reduction in hyperglycemia in advanced type 1 diabetes”, three patients with type-1 diabetes received two jabs of the BCG vaccine. Three years later, another six patients received the same treatment. When the trial investigators, led by immunologist Denise L. Faustman from Massachusetts General Hospital in the U.S. followed these patients for five years after that, they found a sustained drop in a marker for high-blood sugar called HbA1c. Also, none of the patients experienced hypoglycaemia, or dangerously low blood sugar, a potentially life-threatening side-effect in patients taking insulin. Given the patent-free status of BCG, the study promises a safe and inexpensive treatment for type-1 diabetes, if replicated in larger clinical trials.

Even though the BCG vaccine doesn't work very well against childhood TB, it protects against leprosy, sepsis among babies, and leishmaniasis. It is also the first approved immunotherapy against bladder cancer. In a previous phase 1 trial, Faustman and her colleagues gave the BCG vaccine to three patients, finding that the patients produced more pancreatic insulin. Also, they had more of a type of immune cell called Regulatory T cells (Tregs), which protect against autoimmune diseases. Type-1 diabetes is an autoimmune illness in which insulin-secreting pancreatic cells are destroyed by the body's own immune system. But although BCG seemed to have regenerated the pancreas in the phase 1 trial, the team found little improvement in their patients' HbA1C levels.

This is why they continued the trial, hoping the vaccine would impact blood sugar over a longer period. The *npj Vaccine* study shows that the vaccine can lower blood sugar over a five- to eight-year period.

While the researchers don't know why the vaccine takes so long to impact HbA1c, they have an idea about how it does so. Using mice, the researchers showed that the vaccine changed how glucose was metabolised in the body, from a process called oxidative phosphorylation to another called aerobic glycolysis. Plus, BCG also increased the numbers of Tregs. While Tregs help type-1 patients a little, it is the switch to glycolysis which extracts more sugar from the bloodstream, which seems to be behind the improvement in HbA1c.

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