Anti-diabetic Therapy Ameliorates the Inflammageing-Based Cardiometabolic Risk Profile of People with Type 2 Diabetes Mellitus

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Abstract:

Aims: Inflammageing, the age-related increase of pro-inflammatory factors in the body, has been shown to be an important risk factor for the development of cardiometabolic disease. Previously, we have shown that diabetes mellitus type 2 aggravates inflammageing associated with the cytotoxic arm of the immune response. However, whether antidiabetic therapy can ameliorate this effect is unknown.

Methods: Blood collection for peripheral blood mononuclear cell isolation and anthropometric measurements were performed in patients with uncontrolled (HbA1c ≥7.5) type 2 diabetes (n=32) at time of admission and 6 months after treatment with metformin and SGLT2 inhibitors and/or incretin mimetics. The phenotype, proliferation capacity and cytokine production by cytotoxic lymphocytes were analysed using multiparametric flow cytometry at both time points.

Results: Oral anti-diabetic treatment resulted in a reduction of HbA1c levels (from 8.6% ±1.1 to 6.5% ±0.4, $p<0.001$) Significantly decreased production of tumor necrosis factor-α, Interferon γ and granzyme B from $CD8^+$ T cells and γδ T cells and Granzyme B by natural killer cells were observed in patients with type 2 diabetes mellitus six months after treatment compared to the time of admission. Further analysis indicated that the reduction in the pro-inflammatory profile of immune cells is associated with improved pancreatic β-cell function.

Conclusions: A reduction in blood glycemia is associated with a reduction in the pro-inflammatory profile of Th1-type cytotoxic immune cells in the blood of patients with Type 2 diabetes mellitus. More extensive studies are necessary to explore the potential benefits of diabetes medications in reducing the cardiometabolic complications of this disease.

Keywords:

Inflammageing, Cardiometabolic risk, Cytokines, Diabetes Mellitus, Type 2, Anti-diabetic therapy, Inflammation, Lymphocytes, Cytotoxic, Tumour Necrosis Factor-alpha, Interferon-gamma, Granzyme-B.