INSULIN FOR TYPE1 & TYPE 2 DIABETES MELLITUS: PATHOPHYSIOLOGY, COMPLICATIONS & TREATMENT

GUEST EDITOR

Prof. Dr. Georgios Panoutsopoulos

Department of Nutrition and Health Sciences

University of Peloponnese

Tripoli, Greece

DESCRIPTION

According to the World Health Organization (WHO) diabetes is the direct cause of 1.5 million deaths and 48% of all deaths due to diabetes occurred before the age of 70. Another 460,000 kidney disease deaths are caused by diabetes and raised blood glucose is found to cause around 20% of cardiovascular deaths. Moreover, there is a 3% increase in age-standardized mortality rates from diabetes in 2023. In lower–middle-income countries, the mortality rate due to diabetes increased by 13%. By contrast, the probability of dying from any one of the four main noncommunicable diseases (cardiovascular diseases, cancer, chronic respiratory diseases, or diabetes) between the ages of 30 and 70 increased by 22% globally.

Diabetes mellitus represents a group of physiological dysfunctions characterized by hyperglycemia resulting directly from insulin resistance (in type 2 diabetes mellitus—T2DM), inadequate insulin secretion/production, or excessive glucagon secretion (in type 1 diabetes mellitus—T1DM). Type 1 diabetes is a chronically progressive autoimmune disease that affects approximately 1% of the population in the developed world. This adverse immune response is induced and promoted by the interaction of both genetic and environmental factors. In contrast, in type 2 diabetes, insulin resistance coupled with reduced insulin output appears to be the major cause of hyperglycemia (affecting approximately 8.5% of the adult population). Microvascular complications of diabetes include retinal, renal, and possibly neuropathic disease. Macrovascular complications include coronary artery and peripheral vascular disease. Diabetic neuropathy affects autonomic and peripheral nerves.

Type 2 diabetes mellitus consists of an array of dysfunctions characterized by hyperglycemia and resulting from the combination of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion. Poorly controlled type 2 diabetes is associated with an array of microvascular, macrovascular, and neuropathic complications. However, many patients with type 2 diabetes are ultimately treated with insulin. Because they retain the ability to secrete some endogenous insulin, they are considered to require insulin but not to depend on insulin. Nevertheless, given the potential for confusion due to classification based on treatment rather than etiology, the older terms have been abandoned. Another older term for type 2 diabetes mellitus was adult-onset diabetes. Currently, because of the epidemic of obesity and inactivity in children, type 2

diabetes mellitus is occurring at younger and younger ages. Although type 2 diabetes mellitus typically affects individuals older than 40 years, it has been diagnosed in children as young as 2 years of age who have a family history of diabetes. In many communities, type 2 diabetes now outnumbers type 1 among children with newly diagnosed diabetes.

Unlike patients with type 1 diabetes mellitus, patients with type 2 are not dependent on insulin for life. This distinction was the basis for the older terms for types 1 and 2, insulin-dependent and non–insulin-dependent diabetes. Although the etiology of diabetes may differ from T1DM to T2DM, common features may occur during the progression of the disease. In the case of T2DM (insulin resistance), pancreatic β-cell failure may occur in the long term, while in T1DM (pancreatic β-cell death/insulin deficiency) insulin resistance can be induced as the condition progresses. Thus, similarly to both types of diabetes, particularly in the long term, insulin resistance and β-cell dysfunction/death may be present, impairing several tissues and cell function and metabolism. Individuals with T1DM and T2DM share several cardiometabolic complications, such as endothelial dysfunction, changes in glomerular filtration/kidney function, low-grade inflammation, oxidative stress, blood coagulation, mitochondrial dysfunction, cardiac dysfunction, anabolic resistance, metabolic inflexibility, and gut microbiota dysbiosis. The treatment of these conditions and the management of glucose balance may require pharmacological, surgical or particularly, lifestyle-related interventions such as exercise and nutritional changes. Exercise is the most effective non-pharmacological tool to prevent and treat cardiometabolic diseases related to both types of diabetes. As recently demonstrated, the combination of acute resistance and aerobic exercise can improve glycaemia control, metabolism, oxidative stress, inflammation, and skeletal muscle anabolic adaptations in people with T1DM. Similarly, people with T2DM also improve their metabolic and molecular profile in response to exercise training. The combination of exercise with dietary interventions has also been extensively studied and found to result in additional positive cardiometabolic adaptations. The potential nutritional strategies to improve cardiometabolic health in diabetic people include protein supplementation, amino acids, probiotics/symbiotics, nitric oxide/nitrate donors, heat-shock response activators, antioxidants, polyunsaturated fatty acids (omega 3/6), and vitamins.

Diabetes, a complex multisystem metabolic disorder characterized by hyperglycemia, leads to complications that reduce quality of life and increase mortality. Diabetes pathophysiology includes dysfunction of beta cells, adipose tissue, skeletal muscle, and liver. Type 1 diabetes (T1D) results from immune-mediated beta cell destruction. The more prevalent type 2 diabetes (T2D) is a heterogeneous disorder characterized by varying degrees of beta cell dysfunction in concert with insulin resistance. The strong association between obesity and T2D involves pathways regulated by the central nervous system governing food intake and energy expenditure, integrating inputs from peripheral organs and the environment. The risk of developing diabetes or its complications represents interactions between genetic susceptibility and environmental factors, including the availability of nutritious food and other social determinants of health.

The area of type 2 diabetes is rapidly changing due to recent treatment approaches with pleiotropic effects, which also target several diabetes complications (cardiovascular, renal, retinal, etc.) and the incorporation of “non-classical” complications such as diabetic livers, diabetic lungs, cognitive impairment, etc. To try and reverse this dramatic trend, actions capable of increasing an early

diagnosis of diabetes and its complications, together with innovative treatment for ameliorating glycemic control and the prognosis of chronic diabetic complications, are needed.

The discovery of insulin in 1921 represented a milestone in the treatment of diabetes. In 1923, the Nobel Prize for Medicine was awarded for its discovery, and it was one of the most important discoveries in the history of medical science because it affected hundreds of millions of people worldwide. Thousands of lives have been saved and the life expectancy of people with diabetes has been significantly extended. Since its discovery, insulin has been continuously improved through pharmacological development and optimized for therapeutic purposes, including the development of intermediate- and long-acting insulins, the ability to produce human insulin, and finally, the development of insulin analogs with improved properties using recombinant DNA technology. Despite increasing awareness, diabetes is still one of the most challenging health problems in the 21st century. In the last 15 years, the number of people diagnosed with type 1 diabetes increased by 45%, and those diagnosed with type 2 diabetes increased by 95%. Although, recently, the focus in the treatment of diabetes has been directed to new therapeutic options, insulin is still one of the most potent therapeutic options for patients with type 2 diabetes, and the only one for patients with type 1 diabetes.

OBJECTIVE

DM is a complex metabolic disorder that affects multiple organ systems and leads to various complications, including kidney disease, cardiovascular disease, immune dysfunction, retinopathy, and neuropathy. The knowledge of the underlying mechanisms and pathways involved in these complications needs in-depth discussion for future perspectives and potential treatments to inhibit the burden of diabetes and its complications. enhance diagnosis, prevent chronic complications, and identify potential therapeutic targets for the management of diabetes mellitus and its associated dysfunctions. Considering this context, this Special Issue will focus on the roles of insulin and insulin action in a broad sense. The information provided in this special issue will be of value to researchers and clinicians who strive to incorporate recent advances in diabetes treatment into their research and practices.

CALL FOR PAPERS

This Special Issue welcomes articles either highlighting recent developments in or providing new experimental (in vitro or animal model) or clinical (human) data related to pathogenesis of Type 1 & Type 2 diabetes and its complications. We would appreciate it if the authors provided a brief section in their manuscript indicating the novelty of their findings or, in the case of review articles, provided personal views on a particular topic. Topics include but not limited to;

- type 1 diabetes mellitus
- type 2 diabetes
- Insulin
- diagnosis
- cardiovascular risk
- metabolic syndrome
- continuous glucose monitoring
- atherosclerosis

- biomarkers
- diabetic foot ulcer
- autoantibodies
- insulin resistance
- microvascular complications
- glycemic control
- Pathophysiology
- Gene therapy
- Oral hypoglycemic agents
- Stem cells
- β-cells regeneration
- inflammation
- treatment