UPDATE ON TREATMENT OF TYPE 2 DIABETES MELLITUS

JORGEN RUNGBY

Bispebjerg University Hospital, Copenhagen, Denmark

Type 2 diabetes is a heterogeneous disease and therefore it may be complicated to treat hyperglycaemia. Treatment is ideally based on pathophysiological knowledge about the causes of hyperglycaemia in the individual patient:

«The right pill in the right mouth».

The lecture will focus on anti-hyperglycaemic treatment, including an introduction to recently introduced drugs and a discussion of recently published outcome trials.

KEYWORDS: diabetes mellitus, treatment, drugs.

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LIPODYSTROPHY AND DIABETES

Ekaterina Sorkina

Endocrinology Research Centere, Moscow, Russia

Lipodystrophy syndromes form a heterogeneous group of rare disorders of deficient body fat associated with potentially serious metabolic complications, including diabetes, hypertriglyceridemia, and steatohepatitis. Lipodystrophies can be categorized based on their etiology (genetic or acquired) and the degree of fat loss: affecting the entire body (generalized), some regions of the body (partial) or localized lipodystrophy (eg, from injectable drugs). It has been shown in the last 20 years that the cause of the majority of inherited forms of lipodystrophy is the mutation in one of the genes involved in adipogenesis. Acquired lipodystrophies are often associated with autoimmune diseases, although the most common form is HIV-associated lipodystrophy. Major causes of mortality in lipodystrophic patients include heart disease, liver disease, kidney failure, acute pancreatitis and sepsis. Diabetes is common in patients with congenital forms of generalized and partial lipodystrophy as well as in acquired generalized lipodystrophy and is known as a special type of diabetes — lipoatrophic diabetes. Major characteristic of the lipoatrophic diabetes is marked insulin resistance, usually associated with acanthosis nigricans, hypertriglyceridemia, liver disease and arterial hypertension in young patients with no signs of obesity. Due to the rarity of lipodystrophy syndromes, many clinicians are unfamiliar with their diagnosis and management, and lipoatrophic diabetes is usually misdiagnosed as diabetes mellitus type 2 or type 1. This lecture summarizes the diagnosis and management of lipodystrophy syndromes and lipoatrophic diabetes in particular, based on the International practice guideline and local experience of studying different forms of lipodystrophies in Russia.

KEYWORDS: diabetes mellitus; lipodystrophy; lipoatrophic diabetes.

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DIABETES AND CANCER

Itamar Raz

Hadassah Hebrew University Ein Kerem Hospital, Jerusalem, Israel

To date, the medical literature has indicated that diabetic patients experience an increase in the incidence of cancer. The main organs that are involved are liver, pancreas, lungs, ovaries and breast. The risk for early mortality also seems to be increased when compared to non-diabetic patients. Better glucose control has not been shown to necessarily influence mortality. There is also a strong link between obesity and cancer. It is estimated that $^{1}/_{3}$ of breast cancer can be prevented by adopting a healthy lifestyle. Intentional weight loss was shown to reduce the incidence of cancer. Both diabetes and obesity are the cause and result of insulin resistance, resulting hyperinsulinemia and increase in free IGF1, enhanced cell replication and growth. In both obesity and diabetes there is an increase in cytokines that enhance/promote cell growth. In women with breast cancer, recurrence of the tumor was strongly related to high insulin levels. Observational studies have demonstrated an increased risk to develop cancer in patients treated with insulin or sulphonylurea. Exogenous hyperinsulinemia can directly enhance cell growth. However, the ORIGIN study which followed 12,000 patients under insulin therapy over a period of 6 years did not show any increase in the risk to develop cancer. The thiazolidinedione family of drugs was expected to reduce the risk to develop cancer by reducing insulin resistance and deleterious cytokines and also by having a direct inhibitory effect on cell growth. Metaanalyses of various studies with rosiglitazone suggest that this drug may indeed reduce the risk for cancer. On the other hand, some studies have suggested that pioglitazones may increase the risk of bladder cancer. In mice treated with high doses of metformin (equivalent to 18 gm/per day in humans) the free recurrence time from breast carcinoma was increased. Observational studies have demonstrated a reduction in the incidence of liver, lung and GI cancer under metformin therapy. Metformin inhibits the progression of breast carcinoma cell line and seems to improve survival in patients with lung cancer. Metformin affects carcinoma cells by increasing AMP-Kinase which inhibits mTOR and enhances tumor suppressors, thereby preventing cell proliferation. At the end of 2014 there were 213 studies registered in the NIH dealing with metformin to prevent cancer development and progression. In my lecture I will discuss new data on the relationship of anti-diabetic drugs to cancer development and progression.

KEYWORDS: diabetes mellitus, cancer, metformin.

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