20th ESE Postgraduate Training Course on Endocrinology Diabetes and Metabolism

Abstracts and clinical cases

FROM INSULIN PUMP TO BIONIC PANCREAS: THE STEP FORWARD IN PUMP THERAPY

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Insulin pumps will soon celebrate their 40th anniversary. They lower HbA1c in people with type 1 diabetes, especially in motivated people with high baseline HbA_{1c} values. Similarly, their use reduces severe hypoglycaemia, especially in those who encounter severe hypoglycaemia frequently. Some 15 years after its introduction in clinical practice, Continuous Glucose Monitoring has become an established treatment modality. There is sound evidence that patients can lower their HbA_{1c} when using this technology, and spend less time in hypoglycaemia. Evidence supports the notion that CGM can also decrease the incidence of severe hypoglycemia. The added value of CGM during pregnancy is unclear, but larger trials are under way. Insulin pumps and Continuous Glucose Monitoring combined with a control algorithm constitute an artificial pancreas or closed-loop. In several trials with a duration up to three months, time in target increased through a decrease in both time above target and time below target. In parallel to several pivotal trials, a first product will come to the market in 2017. Bihormonal closed-loop, employing both insulin to lower glucose and glucagon to increase glucose, may show further benefits.

KEYWORDS: diabetes mellitus, CGM, insulin pumps.

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GLUCOSE CLAMP TECHNIQUE IN ENDOCRINOLOGY

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Mathematical models of glucose homeostasis (HOMA-IR, Matsuda etc.) are usually used in clinical practice for quantitative assessment of insulin resistance. However those methods are not accurate enough (high variability of glucose and insulin levels) and have a number of limitations. That is why hyperinsulinemic euglycemic clamp test is the gold standard of quantitative assessment of insulin resistance. Glucose clamp technique is being used to measure insulin resistance since late 1970s. Hyperinsulinemic euglycemic clamp test is based on peripheral glucose disposal assessment in conditions of inhibited endogenous insulin secretion and gluconeogenesis. To achieve these conditions acute increase of insulin concentration in blood (100 mU/ml at average) is created by its constant intravenous infusion with the rate 1 mU/kg/min and simultaneous intravenous infusion of glucose in order to maintain euglycemia (around 5 mmol/l). To calculate the amount of the infused glucose fast and multiple venous blood glucose measurements are needed (every 5 min during several hours). When the rate of glucose infusion is equal to the rate of its peripheral disposal, euglycemic steady state is achieved. M-value is calculated: it is the rate of whole body glucose metabolism at a single level of hyperinsulinemia during steady state conditions of glucose during clamp test. In order to achieve a maximal possible suppression of endogenous insulin, glucagon and growth hormone release during hyperinsulinemic clamp tests, a concomitant infusion of somatostatin can be applied. There are other types of clamp tests, each of them can be used to study a particular problem. For example, hyperglycemic clamp technique is a method for the quantification of beta-cell sensitivity to glucose. In this case the stimulation of endogenous insulin secretion takes place, which can be used to study functional activity of pancreatic beta-cells, insulin secretion phases, and pharmacokinetic properties of some antidiabetic drugs. Hyperinsulinemic hypoglycemic clamp technique is used for assessment of counterregulation and other metabolic parameters during hypoglycemia. For assessment of hepatic glucose production glucose clamp with tracers is used. Euglycemic insulin clamp technique is also used to study time-action profiles (pharmacokinetics and pharmacodynamics) of insulin preparations (including biosimilars). In this case glycemic level lowering is expected in some period of time after subcutaneous injection of the study drug and is corrected back to euglycemic level by increasing the glucose infusion rate. The increase of glucose infusion rate will reflect most precisely the beginning, peak and end of action of the study insulin, i.e. it will characterize its biological activity profile. It is preferable to study rapid- and short-acting insulins on healthy volunteers, as they usually demonstrate less intraindividual variability. Patients with type 1 diabetes are more suitable for the studies to determine the time-action profile of long-acting insulins. Thus, clamp test is the most reliable and accurate diagnostic method for both evaluation of the properties of insulin resistance and studying pharmacodynamic and pharmacokinetic characteristics of antidiabetic drugs. Its infrequent use in clinical practice is due to considerable manpower input of this method, which requires additional technical equipment and specially trained staff.

KEYWORDS: glucose clamp, diabetes mellitus, insulin resistance.

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