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UPDATES IN CLINICAL MEDICINE

Update in Diabetology

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Several important developments in the diagnosis and treatment of diabetes mellitus occurred during the last year. First of all, continuing its initiative from 2010, in January 2011, the American Association of Diabetes (ADA) included in its annual clinical practice guideline the use of glycated haemoglobin (HbA1c) as a diagnostic criterion for diabetes mellitus (1). Thus, HbA1c ≥6.5% is diagnostic for diabetes. HbA1c between 5.7%-6.4% is considered to define one of the categories of increased risk for diabetes (prediabetes): IFG and IGT, while a HbA1c < 5.7% is considered to be normal. In order to be valid, the diagnostic test should be performed using a method that is standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. The use of HbA1cwas proposed also by the EASD (European Association for the Study of Diabetes) but it is up to the national diabetes associations to include it in their local clinical practice guidelines.

In respect to the current clinical practice, following the results of the major trials of cardiovascular prevention in type 2 diabetes (ACCORD, ADVANCE, VADT an UKPDS 10 year follow up analysis), it was established that intensive glycemic control leads to a decrease of the microvascular diabetic complications but it does not decrease the frequency of cardiovascular events, at least not during the active period of the trial (2). The positive effect becomes however evident after 10 years of follow-up ("metabolic memory" effect), highlighting the importance of a tight glycemic control at the diagnosis of T2DM (2). The practical conclusion is that therapeutic targets in T2DM should be individualized to each patient. Thus, in older and more vulnerable patients, with concomitant CVD and limited life expectancy, who don't tolerate hypoglycaemia the HbA1c target should be ~7.5%-8%. Contrariwise, in younger patients without CVD, a HbA1c < 7% should be targeted, even <6.5% if this can be achieved without hypoglycaemia.

There were a number of reports and reviews about diabetes and cancer. The key take-home message of the last 12 months is that T2DM patients are at increased risk for cancer and they should be periodically screened for specific malignancies. On the positive side, metformin was reconfirmed to reduce the risk of cancer in T2DM and may also reduce mortality (3). This strengthens the position of metformin as the first step in the treatment of T2DM.

Another major topic was represented by drugs used for T2DM treatment. The last year brought the dawn of Thiazolidindiones. Thus, on 23 September 2010, EMEA recommended

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a ban on drugs containing Rosiglitazone (Avandia, Avandamet and Avaglim). In the same time, the FDA restricted drastically its use in the USA – it cannot be prescribed as a first line drug but only when other therapies failed. The main reason was the increasing evidence confirming the initial report of Niessen from 2007 regarding an increased risk of MI in patients using Rosiglitazone. In addition, the RECORD study (sponsored by GlaxoSmithKline) failed to show any benefit of this drug in CVD prevention (4). Also during the last year, data was published (5) regarding the increased risk of bladder cancer in T2DM patients treated with Pioglitazone (Actos). The risk is higher in those patients exposed to the highest cumulative doses of Pioglitazone, especially the elderly. Following these reports France and Germany suspended the use of Pioglitazone while the FDA recommended a labelling update for Pioglitazone regarding this risk. A single European position regarding this issue is still waited from EMEA.

The hopes for the launch of a new class of oral antidiabetic drugs – inhibitors of the sodium glucose cotransporter-2 (SGLT-2) in the proximal renal tubules were also set back. Thus, in July 2011, the FDA voted against the approval of dapagliflozin (Bristol-Myers Squibb and AstraZeneca), largely because of fears that the product may cause breast and bladder cancer. Additional concern was related to the lack of absence of hard pharmacokinetic data regarding this drug.

To finish on a brighter side this up-to-date in diabetology, two new drugs from the class of GLP-1 receptor agonists were approved for clinical practice last year. These are Liraglutide (Victoza from Novo Nordisk) that was approved by the FDA for use in the USA (it was already used in Europe for a couple of years) and the once-weekly exenatide (Bydureon from Eli Lilly and Amylin Pharmaceuticals) that was approved by EMEA for use in the UE.

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