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Editorial

ROMANIAN JOURNAL OF DIABETES NUTRITION AND METABOLIC DISEASES - 20 YEARS AFTER

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Last year we celebrated 20 years since the publication of the first issue of the Romanian Journal of Diabetes, Nutrition and Metabolic Diseases. In fact, this event was well marked on the cover of the Journal. Last year marked also a number of important events in the field of diabetology, both related to science, current clinical practice and the life of the diabetologic community in our country. We shall try in the next couple of pages to comment the most important of these.

First, the number of people with diabetes continued to rise rapidly worldwide and everyone is now convinced about the reality of the diabetes epidemic phenomenon. Thus, the 2012 update to the Fifth Edition of the International Diabetes Federation (IDF) Atlas published in 2011 reports that currently 371 million people have diabetes. The same 2011 IDF Atlas [1] predicts that the number will rise to 552 million by 2030, meaning almost 10% of the world population. At least half of the people with diabetes are undiagnosed and 4.6 million deaths caused by diabetes were recorded in 2011. Finally, diabetes caused at least USD 465 billion dollars in healthcare expenditures in 2011 [1].

Facing this bleak reality, scientific community responded in 2012 by releasing a record number of guidelines/position statements regarding the diagnosis, screening and treatment of this condition. Thus, in April 2012 the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published their last common position statement regarding the treatment of type 2 diabetes (T2DM) [2]. According to the title itself of this position statement – "*A patient centered approach*" - the most important changes reflect the importance of the patient in the clinical decisions regarding the treatment of T2DM. The essence of this philosophy is "*...providing care that is respectful of and responsive to individual patient preferences, needs, and values – ensuring that patient values guide all clinical decisions*". The position statement is less proscriptive and less focused on numbers than previous guidelines, encouraging clinicians to work together with their patients in order to design an individualized treatment plan. Regarding the glycemic targets, the ADA/EASD guideline recommends a HbA1c < 7.0% (reflecting a mean blood glucose of

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~150-160 mg/dl) but emphasize on the importance of individualizing these targets. Thus, tighter targets (6.0 - 6.5%) should be aimed in younger and healthier patients, with a low duration of diabetes, and looser targets (7.5 - 8.0% or higher) in older patients, with long duration diabetes and established co-morbidities. A key point is avoidance of hypoglycemia [2]. The initial drug of choice in monotherapy remains metformin, indicated from the diagnosis of T2DM. If monotherapy fails to reach the HbA1c target over 3 months, next step would be dual agent therapy with the alternative to use a sulphonylurea, a thiazolidindione, a DPP-4 inhibitor, a GLP-1 receptor agonist or insulin. The higher the HbA1c, the more likely insulin will be required.

In the fall of 2012, IDF published a full updated guideline for the treatment of T2DM [3], including new studies and treatments which have emerged since its original guideline from 2005. The targets recommended by IDF are HbA1c < 7%, fasting plasma glucose < 115 mg% and postmeal plasma glucose < 160 mg%. A lower HbA1c target may be considered if it is easily and safely achieved. Conversely a higher HbA1c target may be considered for people with co-morbidities or when previous attempts to optimise control have been associated with unacceptable hypoglycemia. The IDF guideline suggests a step-wise approach to pharmacotherapy that commences with metformin unless there are contraindications. Sulfonylureas are the preferred second-line option. The main difference from the ADA/EASD guideline is represented by the inclusion of alpha-glucosidase-inhibitors [3].

Over the past decades, the prevalence of childhood obesity and subsequent T2DM has increased dramatically, especially in the USA and it is expected that this situation is going to exacerbate in the years ahead [4]. Very recently, the American Academy of Pediatrics published the first ever guideline devoted to the management of T2DM in children and adolescents [5]. According to this guideline, metformin is the only oral hypoglycemic drug approved for use in children. However, insulin remains the treatment of choice if ketosis is present, the distinction from type 1 diabetes (T1DM) is unclear, HbA1c > 9% or significant symptoms of hyperglycemia are present. The HbA1c target was fixed < 7% while the blood glucose goal in most children is 70-130 mg%. Targets for blood pressure and lipids were also established as well as treatment recommendations [5].

The American Diabetes Association (ADA) Standards of Medical Care from January 2012 [6] proposed a change in the prescription recommendations for anti-platelet therapy in diabetics. Thus, aspirin therapy should be considered as primary prevention treatment only in diabetic patients at increased cardiovascular risk (10-year risk higher than 10%) or as secondary prevention treatment in subjects with a history of cardiovascular (CVD) events but not in adults with low CVD risk. The 2013 ADA standards of care [7] brought new targets for blood pressure in diabetics, aiming for a systolic blood pressure <140 mmHg rather than <130 mmHg as previously recommended since accumulating evidence showed that treating patients' blood pressures more intensively is not beneficial, by and large, and is unnecessary. The diastolic target continues to be <80 mm Hg. The other recommendation that has changed is about self-monitoring of blood glucose levels in

patients (usually with T1DM) on intensified insulin treatment - multiple daily insulin injections or insulin pump. This year, the ADA recommends that these patients should test blood glucose at least prior to meals and snacks. In addition, testing is recommended postprandial, at bedtime, prior to exercise, after treating a low blood glucose level etc [7]. Obviously, the number of test strips required daily in this case can easily reach a two figure number, an aim difficult to reach in the presence of current economic conditions in most countries.

The year 2012 brought also some important scientific developments in the field of diabetes. Maybe the most exciting was the long awaited publication of the ORIGIN study results [8]. The study included 12.537 patients with cardiovascular risk factors and altered glucose metabolism (either prediabetes or T2DM) assigned to receive treatment with insulin glargine or standard diabetes care, respectively omega-3 fatty acids or placebo in order to assess the effect of these interventions on the risk of CV events. After a median follow-up of 6.2 years, the rates of CV events were similar in the insulin-glargine and control groups. The disappointment for this negative result was counter-balanced by the positive news, mainly the safety and efficacy of this treatment. Thus, long term treatment with insulin glargine was associated with a low risk of severe hypoglycemia (1 event per 100 person-years) and a minor weight gain (a mean of 1.6 kg), maintaining a HbA1c lower than 6.5% throughout the 7 years of the study in this group of patients. Most important, the ORIGIN study proved beyond doubt that treatment with insulin glargine is not associated with increased risk for cancer, bringing the end to an old debate [8]. No cardiovascular benefits were seen either with the use of omega-3 fatty acids treatment [9]. Unfortunately another study provided negative results regarding the impact of therapeutic intervention on CV risk decrease in T2DM patients. Thus, the Look AHEAD trial, designed to determine the effect of intensive lifestyle changes (diet and exercise) on the rate of CV events in T2DM, was stopped when it became clear that the primary outcome of the study was not being met [10].

On the bright side, two randomized controlled trials regarding the effects of bariatric surgery in T2DM patients showed that this kind of therapy is associated with better metabolic control and often with diabetes remission when compared with the conventional/standard [11] or intensive [12] medical treatment of T2DM, even with the trend for reduced cardiovascular risk. In addition, a new analysis of the JUPITER study data [13] showed that the benefits of statin therapy for the primary prevention of myocardial infarction, stroke or cardiovascular death exceed by far the risk for diabetes reported recently for this class of drugs. Finally, the results from the long-awaited FREEDOM study showed that patients with diabetes and severe coronary heart disease have a better prognosis after coronary artery bypass grafting (CABG) in comparison with the percutaneous coronary interventions (PTCI) [14].

Regarding the therapy of diabetes and metabolic disorders, the last 12 months brought the confirmation of the increased risk for bladder cancer in pioglitazone treated patients [15,16], the risk increasing with the time of exposure and age. The thresholds of

24 months and 65 years, respectively were identified as the time thresholds above which the risk becomes relevant, especially in the presence of other risk factors for bladder carcinogenesis as smoking for example. The list of DPP-4 inhibitors and GLP-1 agonists receiving approval by FDA or EMA became longer but everyone is waiting for the incretin therapies to provide the expected benefits on the long term – improvement of the beta cell function and decrease of the CV risk. Important progresses were made in the armamentarium of obesity treatment. Thus, FDA approved lorcaserin (Belviq, Arena Pharmaceuticals) and phentermine-topiramate (Qsymia, formerly Qnexa; Vivus) for the treatment of obesity [17]. A third obesity drug – the combination of naltrexone SR/bupropion SR (Contrave) - may come to market in the next year.

As for our Journal, the second half of 2012 brought a "guard change" in the editorial staff of the *Rom J Diabetes Nutr Metab Dis*. Prof. Maria Moţa became the Editor-in-Chief of the Journal, after a hard work as Managing Editor during the previous three years. The results of her activity are evident, including the quality of the science published and the visibility of the Journal which is now internationally indexed by Index Copernicus, getCITED, SCOPUS, Scirus, etc. For all her contributions Prof. Maria Moţa deserves our deep gratitude. The same is valid for Prof. Constantin Ionescu-Tîrgovişte, the Honorary Editor of our Journal. Now the Managing Editing activity was taken over by a team from Bucharest.

Starting with this issue, we have changed the editorial structure, with much greater responsibilities (and obviously a lot more work!) devolved to our Assistant Editors. Our main aim in the following three years will be to publish a Journal that people will enjoy to read. This implies that we welcome not only basic clinical and experimental diabetes research, but also commentaries, debates and good quality reviews that will be accessible to a wider audience. As science knows no boundaries, we welcome papers from around the world and we are happy that in the last two issues from 2012, four international articles were published, one from Pakistan, Asia. The second aim for the end of our mandate is to accomplish the dream of having our Journal indexed in ISI Thomson Master Journal List.

In order to succeed, we are dependent on you, both diabetologists and physicians with an interest in the field of diabetes and metabolism, to send us your scientific work, even if sometimes this implies sacrificing data that could be published in other better positioned journals. Personally I think this will be a sacrifice that could bring great rewards on the long term, contributing to the development of our specialty and the perspectives of the future generations of diabetologists. As for ourselves, the managing team, we shall be happy to help and assist in order to improve the quality of all materials submitted for publication.

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