VIEWPOINT

Guidelines for Management of Type 2 Diabetes 2012: Common Sense Prevails!

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Abstract
Recently, guidelines on the management of hyperglycemia in type 2 diabetes were released by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) as their formally adopted position statement. These guidelines are different from the previously published documents. They introduced a non-algorithmic patient-centered approach that stressed the principles of individualization of care based on several important patients' attributes. They affirmed the role of lifestyle modification as a basic requirement, metformin as the first line pharmacological therapy and individually-tailored basis for the choice of the second and third line drugs. In this paper, the authors reflect on these guidelines from the world-wide practicing physicians' view point.

Key words: Diabetes, Guidelines, Hyperglycaemia, Patient-centered care, American Diabetes Association, European Association for the Study of Diabetes.

Introduction

During the last 2 decades, a significant expansion has occurred in the number of medications being available for management hyperglycemia in type 2 diabetes (1). In addition to the increase in the classes and brands of new insulin analogues, a number of other medications became available too (2,3). These newer medications were based on improved pharmacokinetic properties (e.g. extended or modified release sulphonylureas), de novo manufacturing of new products targeting insulin resistance (such as Glitazones) (2), or newer agents based on physiological observations that were dormant for quite a while (such as incretin-based therapies, mainly Dipeptidyl peptidase-4 inhibitors (DDP4-I) and Glucagon-like peptide-1 agonists (GLP-1A) (3). The introduction of such agents created a very busy environment for the clinicians and stimulated vibrant discussions on how best to utilize these drugs to optimize glycemic control. In 2006, the "seven doctors" document was published as an opinion of experts from the

ADA and EASD (4). This document was widely referred to as the "ADA-EASD consensus" and was updated a couple of times under that perception (5,6). However, the ADA distanced itself from it and several internationally renowned physicians expressed their disagreement with some of its contents and how the original paper and its further modifications were conceived and perceived (7-10). In April of this year, guidelines were released (published online) by the two associations as their formally adopted position statement (11,12). These guidelines are different from the previously published document. They introduced a non-algorithmic arguments, patient-centered approach that stresses the principles of individualization of care based on several important patients' attributes (12). In this article, the authors reflect on these guidelines from the world-wide practicing physicians' view point. Initially, the history of clinical care guidelines is considered and later the salient features of the new ADA/EASD guidelines are discussed.

Evolution of Diabetes Care Guidelines

Clinical care guidelines are important quality tools. They aim to prevent unjustified variation in clinical practice and undue utilization of physicians' own individual interpretation of the literature and reliance on potentially misguided personal experiences. They are being increasingly utilized in many areas of clinical practice. Guidance documents may vary in their strength and evidence-based level from monograph, review articles, systematic reviews, "technical reviews", expert opinions and consensus statements. A body or more may throw their weight (singly or jointly) behind some of these guidelines by issuing them as "position statements" and "clinical care guidance". In diabetes, guidance of clinical practice evolved progressively. In the first instance, clinical practice was guided by expert opinions (reflecting practice in the centers of excellence as expressed in authoritative textbooks and articles published in general or specialized journals). Guidelines increased in size, detail and complexity over the years (13,14). Diabetes care has

Table 1. The key points in the Joint ADA-EASD Position Statement published on line in April 2012 and the authors' reflections and comments..

Key Points	Comments
Glycemic targets and glucose-lowering therapies must be individualized.	Hands on education to transfer skills of "know how" is needed.
Diet, exercise, and education remain the foundation of any type 2 diabetes treatment program.	Professional support and multidisciplinary care teams are needed to deliver this task.
Unless there are prevalent contraindications, metformin is the optimal first-line drug.	There is an overestimation of the contraindications of metformin by patients and professions.
After metformin, there are limited data to guide us. Combination therapy with an additional 1–2 oral or injectable agents is reasonable, aiming to minimize side effects where possible.	Cost is an issue in many parts of the world. Physicians should be aware of the cost implications on their patients.
Ultimately, many patients will require insulin therapy alone or in combination with other agents to maintain glucose control.	Clinical inertia should be fought by education of health care professions.
All treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, needs, and values.	Complacency should be avoided in cultures resistant to injections and where good control may be interpreted as absence of hyperglycemic symptoms.
Comprehensive cardiovascular risk reduction must be a major focus of therapy.	Asymptomatic risk factors are not viewed seriously by patients. Education is needed.

witnessed many examples of guidelines covering various aspects and specific groups (such as type 1 diabetes and the elderly) or circumstances (management of inpatients and during pregnancy) and even very ethnically-specific areas as management of diabetes during Ramadan fasting (15). Today, ADA-EASD guidelines, UK-based National Institute of Clinical and Health Care Excellence (NICE) guidelines and International Diabetes Federation (IDF) guidelines are amongst the most cited references in diabetes practice and education circles by physicians world-wide though not all were originally meant to be used as such. Therefore, local and regional key opinion leaders should adopt these guidelines carefully to suite their cultural, ethnic and socioeconomic circumstances.

We have so far been made to believe that the previous guidelines on diabetes have been written by the evidence –based rulings. In reality, evidence-based practice is defined by 3 criteria 1) lessons learned from clinical trials 2) investigators or clinicians' expertise and 3) patients perceptions and acceptance of the disease process. Up till now the clinical guidelines have ignored the patients' perspective and mainly concentrated on lessons from clinical trials. The new guidelines, for the first time, incorporated the three elements and thus can truly claim being evidence-based guidelines (16).

The New ADA/EASD Guidelines 2012

Rationale

In the new guidelines, a discussion of the size of the problem and pathogenesis and the rationale of the management approach to follow was presented. The five mega trials (UKPDS, DCCT, ADVANCE, VADT and ACCORD) were summarized (17-21). It was concluded that microvascular complications were reduced fairly readily in most of the studies whereas the reduction in macrovascular complications was not easily demonstrable (i.e. *not statistically significant*) or needed longer time to become statistically significant (*UKPDS early reports versus extended observation period*). Perhaps the most worrying was the increased mortality seen in ACCORD's intensive glycemic arm. The differences in the outcomes were partly explained by many authorities on the basis of the differences in the patients' characteristics (age, duration of diabetes, presence of cardiovascular complications) and the degree of glycemic control (gentle, versus aggressive as measured by the target HbA1c of < 7.0% versus HbA1c < 6.0%) (11). Based on these differences, the theme of "individualization of targets" was introduced in varying levels of details by the Canadian and Australian Diabetes Associations (20,21). Although this concept was proposed in previous ADA guidelines, this is the first time that it was formally adopted in full detail as the central theme of the

Table 2. ADA Guidelines for Glycemic, Blood Pressure and Lipid Control. *Refer (11).*

Variables	American Diabetes Association Goals
HbA1c	< 7.0% *(individualization)*
Preprandial glucose	70-130 mg/dL (3.9-7.2 mmol/l)
Postprandial glucose	< 180 mg/dL (<10.0 mmol/l)*
Blood pressure	< 130/80 mmHg
Lipids	LDL: < 100 mg/dL (2.6 mmol/l) < 70 mg/dL (1.8 mmol/l) (with overt CVD) HDL: > 40 mg/dL (1.0 mmol/l) > 50 mg/dL (1.3 mmol/l) TG: < 150 mg/dL (1.7 mmol/l)

*HDL = high-density lipoprotein; LDL = low-density lipoprotein; PG = plasma glucose; TG = triglycerides; CVD= Cardiovascular disease. * Different from IDF*

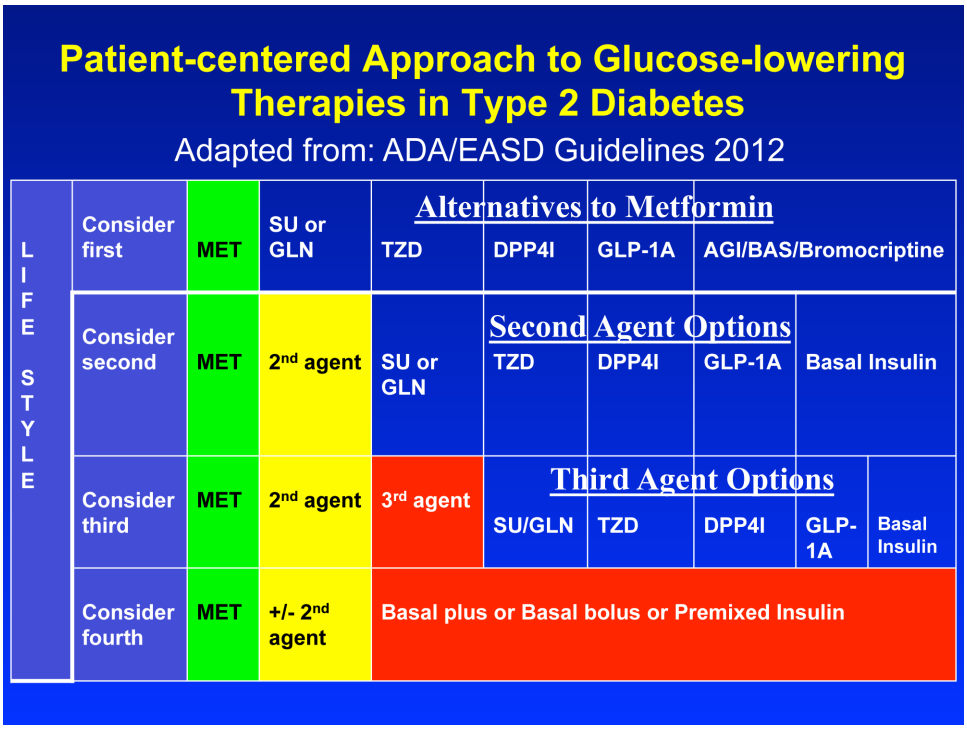

Figure 1. Schematic representation of the ADA-EASD 2012 guidelines. Life style modifications are the platform upon which the first, second, third and fourth lines are launched progressively on individual basis. (ref 11). This scheme is produced by HF Saadi.

MET denotes metformin; SU, sulphonylurea; GLN, glinide; TZD, thiazolidendione; DPP4-I, dipeptylpeptidase 4 inhibitor; GLP-1A, glucagon like peptide 1 "Agonist"; AGI, alpha glucosidase inhibitor; BAS, bile acid sequestrant; Basal plus denotes administration of basal insulin once or twice plus a pre-prandial rapid insulin with one or two meals; Basal bolus is the intensive "physiological" replacement regimen using basal insulin once or twice together with preprandial insulin with each meal.

guidance (12)

Key Points

The key points in the current guidelines are presented in Table 1. It was emphasized that glycemic targets and glucose-lowering therapies must be individualized. Diet, exercise, and education remain the foundation of any type 2 diabetes treatment program. However, many physicians still support the notion that initiation of metformin at diagnosis is still their preferred option (if there is no contraindication). The guidelines point out that there are limited comparative data to guide the choice of medication after metformin. Combination therapy with an additional one to two oral or injectable agents should follow and ultimately, many patients will require insulin therapy. The guidelines stress the fact that all treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, and needs. Although the main focus in this document was hyperglycemia, the opportunity was not lost to state that comprehensive cardiovascular risk reduction must be a major target of therapy. Physicians' inertia should be avoided and insulinization be considered early in the disease process essentially in the presence of significant hyperglycemia in order to prevent the deleterious effects of glucose toxicity (22,23).

Targets

The new guidelines continue to recommend HbA1c goal of 7% as the general target for most people with diabetes. However in the elderly, those with history of severe hypoglycemia and those with short life expectancy, a looser target of 7.5% was recommended. In contrast, more stringent HbA1c targets (e.g., 6.0–6.5%) might be considered in selected patients (with short disease duration, long life expectancy, no significant cardiovascular disease) if this can be achieved without significant hypoglycemia or other adverse effects of treatment. This hopefully will

prevent or delay diabetic vascular complications over time. The document stressed the multiple interventional approach by reiteration of the targets of blood glucose, lipids and hypertension (Table 2).

Tools

The anti-diabetic therapy tools can be summarized as three modalities. The guidelines continue to emphasize lifestyle as the first line, but perhaps 6 months is too long without medication. The IDF-style approach seems more appropriate particularly in areas where lifestyle modification cannot be supported readily due to the inadequate access to educators and dieticians in resource-poor regions. Non-insulin medications include metformin as first line (with alternatives if not tolerated or contraindicated), followed by the addition of a second agent if targets were not met, moving on to adding a third agent or adding insulin/ intensifying insulin therapy (Figure 1).

Strategy

A general scheme is given as outlined above. However, additional options are provided in "supplementary material" published on "Diabetes Care" website and in the "Lecture Resource Slide Deck" with modifications aiming to 1. avoid hypoglycemia 2. reduce or avoid weight gain and 3. contain cost. The individualization criteria need to be applied at first phase after metformin and at later phases with further additional therapy. The patient's own needs and personal preferences should guide this process. Initiation of insulin is by basal insulin as the default choice or alternatively by conventional premixed twice daily insulin. Intensifications can be brought about by basal bolus regimen or by addition of rapid insulin as the third dose with premixed used twice. The text and accompanying illustrations are very well written and fairly focused and concise.

Conclusions

The latest diabetes care guidelines released as a joint position statement from the ADA and EASD represents a qualitatively different approach to diabetes care. It has moved from the authoritative prescriptive dictation to guidance that will facilitate a joint decision between the physician and patient based on multivariant-based individualization of targets, tools and strategies with prevailing common sense and clinical judgement.

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