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Current Antihyperglycemic Treatment Guidelines and Algorithms for Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Type 2 diabetes mellitus and obesity are associated with increased cardiovascular risk. While lifestyle interventions such as medical nutrition therapy and appropriately prescribed physical activity remain cornerstones of disease prevention and treatment, most patients with type 2 diabetes will eventually require pharmacotherapy for glycemic control. Fortunately, many of these patients are able to achieve desired glycemic targets with the use of currently available antihyperglycemic agents. Both not-for-profit disease-specific organizations and healthcare specialty societies have provided guidance about the appropriate selection of these therapies. Type 2 diabetes treatment guidelines and algorithms have been developed, taking into account a combination of evidence-based information and expert opinions, with various groups offering diverse glucose goals and approaches to hyperglycemia management. Virtually all recognize that type 2 diabetes is a multifaceted disease, necessitating an integrated yet individualized approach to patient care.
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KEYWORDS: Algorithm; Hemoglobin A_{1c}; Treatment guidelines; Type 2 diabetes mellitus

Type 2 diabetes mellitus, along with obesity, has reached epidemic proportions in the United States.[1,2] Between 80% and 90% of patients with type 2 diabetes are overweight or obese, and many also have cardiovascular disease (CVD).[3] A recent population-based observational study showed that overweight and obese people in Sweden had a higher risk of coronary heart disease (hazard ratios, 1.27 and 1.49) than normal-weight patients with type 2 diabetes.[4]

Although comorbidities, including overweight and obesity, are common factors in type 2 diabetes, patients have varied initial clinical presentations, different courses of disease progression, and different responses to antihyperglycemic medications. Lifestyle interventions, including appropriately prescribed physical activity and medical nutrition therapy, are cornerstones of antihyperglycemic treatment. However, most patients with type 2 diabetes will also require pharmacotherapy.

This review provides an overview of some current guidelines and algorithms for the treatment of patients with type 2 diabetes. It focuses on the importance of improving plasma glucose to optimize patient outcomes, and includes a discussion on target goals for people with elevated glucose, blood pressure, and lipids. The treatment guidelines and algorithms recognize the importance of individualized therapy for patients with type 2 diabetes.

FOCAL POINTS OF ANTIHYPERGLYCEMIC TREATMENT GUIDELINES FOR TYPE 2 DIABETES

A number of medical organizations have developed guidelines and algorithms for the treatment of patients with type 2 diabetes. Most recent recommendations are derived from evidence-based information and expert opinion. They include the 2007 American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) Diabetes Clinical Practice Guidelines,[5] the 2007 Texas Diabetes Council Glycemic Control Algorithm,[6] the 2008 AACE/ACE Road Map,[7] the 2009 AACE/ACE treatment algorithm,[8] the 2008 Canadian Diabetes Association (CDA) Clinical Practice Recommendations for T2DM,[9] the 2010 American Diabetes Association (ADA) Standards of Medical Care,[10] and the 2009 ADA/European Association for the Study of Diabetes (EASD) writing group consensus statement and algorithm on the medical management of hyperglycemia in type 2 diabetes.[11]

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To determine whether glycemic control was improving in patients with diabetes, 3 phases of the National Health and Nutrition Examination Survey (NHANES), conducted between 1999 and 2004, were reviewed for trends in hemoglobin A_{1c} (HbA_{1c}) concentrations.[12] Data showed that mean HbA_{1c} for the entire NHANES population cohort declined from 7.82% in 1999 to 7.18% in 2004, at which time 55.7% of study patients achieved HbA_{1c} <7.0%, the goal recommended for most diabetes patients by the ADA. These findings suggest that the care of patients with diabetes, including those with type 2 diabetes, has improved but further improvement is possible.

The AACE/ACE guidelines that were published in 2007[5] and the ADA Standards of Medical Care updated in 2010 (Table 1)[10] emphasize the importance of educating patients on the potential short- and long-term complications of type 2 diabetes, teaching self-management skills, psychosocial adjustments, and lifestyle interventions (Figure 1).[13,14]

As even modest weight loss has been shown to reduce insulin resistance,[10] the AACE/ACE and ADA guidelines specifically address medical nutrition therapy and appropriately prescribed physical activity. A healthy nutritional diet is considered an essential component of any comprehensive diabetes program.[15] Diets should be individualized, based on weight, lipid profiles, medications, and lifestyle. Total carbohydrates should represent 45% to 65% of daily energy intake. Fiber intake of up to 50 g/day is encouraged, and fat consumption should be limited to <30% of total calories.[5] At least 150 min/wk of physical activity is encouraged.

The ADA Standards of Medical Care recommend weight loss for overweight or obese individuals who have or are at risk for diabetes and indicate that "for weight loss, either low-carbohydrate or low-fat, calorie-restricted diets may be effective in the short-term (up to 1 year)." Patients on low-carbohydrate diets should have their lipid profiles, renal function, and protein intake (in those with nephropathy) monitored and their antihyperglycemic therapy adjusted as needed. Saturated fat intake should be <7% of total calories; intake of trans fat should be minimized. Monitoring carbohydrate intake is essential to achieving glycemic control.[10] Similar to the AACE/ACE guidelines, the ADA recommends ≥150 min/wk of moderate-intensity aerobic physical activity performed at 50% to 70% of maximum heart rate, plus resistance training ≥3 times/wk in the absence of contraindications.[10]

Reinforcing the Need for Individualized Treatment Goals

Guidelines for treating patients with type 2 diabetes emphasize the need for individualized treatment targets to facilitate attaining and maintaining glycemic goals while minimizing the potential for adverse events. The ADA guidelines consider several factors in goal setting, including the patient's age, time since diagnosis, presence of comorbidities, and pregnancy status.[10] This is in agreement with the scientific statement by the ADA, the American College of Cardiology (ACC) Foundation, and the American Heart Association (AHA) regarding intensive glycemic control and the prevention of cardiovascular events based on findings from recent large-scale type 2 diabetes trials (Table 2).[16] The ADA/ACC/AHA scientific statement indicates that the data from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release and Controlled Evaluation (ADVANCE) trial, and Veterans Affairs Diabetes Trial (VADT) do not warrant major adjustment to already established HbA_{1c} targets, but rather emphasize the need for clarification of appropriate goals in certain populations.[16-19] The scientific statement agreed that HbA_{1c} should be <7.0% in most nonpregnant adults, but also recognized that HbA_{1c} targets should be less stringent in certain individuals, including those prone to hypoglycemia, advanced vascular complications, and/or extensive comorbidities, and those individuals with long-standing diabetes in whom lower HbA_{1c} goals have been difficult to attain despite diabetes self-management education, glucose monitoring that is appropriate for the patient, and the use of

Table 1 Comparison of treatment targets for the management of patients with type 2 diabetes mellitus

Target Treatment Goals	AACE/ACE 2007[5]	ADA 2010[10]
HbA_{1c}	≤6.5%	<7.0%
Fasting glucose*	Fasting plasma glucose: <110 mg/dL	Preprandial capillary plasma glucose: 70-130 mg/dL
Postprandial glucose*	2-hr postprandial glucose: <140 mg/dL	Peak postprandial capillary plasma glucose: <180 mg/dL
Blood pressure	<130/80 mm Hg	<130/80 mm Hg
Cholesterol (lipids)†	LDL-C <100 mg/dL (<70 mg/dL for patients with diabetes and coronary artery disease) HDL-C >40 mg/dL in men, >50 mg/dL in women Triglycerides <150 mg/dL	LDL-C <100 mg/dL‡ HDL-C >40 mg/dL in men, >50 mg/dL in women Triglycerides <150 mg/dL

AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; ADA = American Diabetes Association; HbA_{1c} = hemoglobin A_{1c}, HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

*For glucose, 1 mg/dL = 0.5551 mmol/L.

†For cholesterol, 1 mg/dL = 0.0259 mmol/L; for triglycerides, 1 mg/dL = 0.0113 mmol/L.

‡In individuals with overt cardiovascular disease, a lower LDL-C goal of <70 mg/dL (1.8 mmol/L), using a high-dose of a statin, is an option.

Adapted from *Endocr Pract*.[5] and *Diabetes Care*.[10]