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Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy: A Consensus Statement From the American Diabetes Association and the European Association for the Study of Diabetes

Response to Nathan et al.

We applaud the efforts of those who developed the American Diabetes Association/European Association for the Study of Diabetes algorithm for managing type 2 diabetes (1). Although the algorithm provides a comprehensive assessment of the clinical utility of various medications, the authors' strong focus on A1C as a measure of glycemic control may lead to inadequate management of glycemia because it fails to consider important issues relevant to diabetes pathophysiology and outcomes.

First, the algorithm assumes that patients have only recently developed type 2 diabetes and that the A1C is only slightly elevated. The majority of type 2 diabetes is diagnosed 9–12 years after it develops (2). Further, the algorithm suggests that individuals should first be started on lifestyle modification and metformin and then evaluated at 3 months regardless of current A1C. This initial therapy is inappropriate for patients with an A1C >10% because the average lowering capacity of metformin at a 2,000-mg dose is ~2%. In addition, not all patients are responders or candidates for that specific therapy (as with most medications). Early and aggressive intervention improves outcomes; however, the algorithm neither promotes nor supports early, aggressive management.

Second, although the authors focus on an A1C <7% as the goal, the contribution of postprandial glucose (PPG) to A1C is ignored. Monnier et al. (3) showed that PPG is the primary contributor to glycemia when A1C levels are <7.3% and very similar to fasting at levels of 8.4%. Earlier studies (4,5) showed fasting plasma glucose to be an inexact measure of glycemic control relative to A1C. Why, then, should we recommend that clinicians and patients rely on fasting plasma glucose measures to guide daily diabetes management?

Third, there is a strong link between postchallenge/PPG excursions and macrovascular disease independent of A1C levels (6,7). Monnier et al. (8) showed that glucose fluctuations during postprandial periods exhibited a more specific triggering effect on oxidative stress than chronic sustained hyperglycemia. Further, reducing glycemic excursions is causally associated with carotid intima-media thickness, a validated surrogate cardiovascular end point (7).

Assessing the benefit of a given therapy cannot be based solely on cost and efficacy in lowering glucose. The STOP-NIDDM (9) study showed a clear association between treatment with acarbose and a significant reduction in cardiovascular disease and hypertension. Use of rapid insulin reduces hypoglycemia (10). Newer medications, such as pramlintide and exenatide, have demonstrated improved PPG control and significant weight loss (11,12).

The mission of the American Diabetes Association is "to prevent and cure diabetes and to improve the lives of all people affected by diabetes" (13). Is it prudent to ignore or diminish the value and clinical utility of these medications simply because they do not meet subjective criteria regarding cost versus A1C-lowering effects? Exenatide, in combination with metformin, could be used earlier to get more patients to target and avoid costly long-term complications. We must remember that the highest cost in diabetes is not the medications; rather, it is the complications that result from not achieving good diabetes control.

The algorithm is substantially incomplete in communicating the necessity for early, aggressive management using treatment modalities that address all glycemic abnormalities. We strongly urge the authors to reevaluate their focus on A1C and expand the algorithm to include strategies to manage postprandial hyperglycemia, which is clearly required to achieve normal metabolic control.

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Response to Nathan et al.

Although stating that lifestyle interventions "should [. . .] be included as part of diabetes management," the American Diabetes Association/European Association for the Study of Diabetes consensus (1) on managing hyperglycemia in type 2 diabetes dismisses lifestyle interventions because of their "limited long-term success"; hence, the recommendation to immediately start newly diagnosed patients on lifestyle intervention plus metformin. The consensus even suggests that increased physical activity may lead to "potential problems associated with neuropathy, such as foot trauma and ulcers" (a statement not supported by a reference) and that "the most convincing long-term data that weight loss effectively lowers glycemia have been generated in [. . .] type 2 diabetic patients who have had bariatric surgery," which is hardly a model of lifestyle intervention.

A growing body of literature shows that lifestyle intervention is both feasible and effective in achieving and reinforcing the goals sought by pharmacological means (2–4). It cannot, however, be prescribed. Health operators, who are mainly trained to treat acute conditions, should stop thinking of their chronically ill patients as pill-popping automata who are "noncompliant" when they fail to ingest 10–15 tablets, walk 30 min, and perform other tedious tasks everyday. Adults learn and apply new concepts if they perceive them as reasonable, useful, and related to personal experience. Realistic self-management plans can only stem from alliances between patients and operators within reorganized working practices.

Some recent *Cochrane Database System Review* studies suggest that lifestyle intervention in type 2 diabetes is especially effective when implemented by interactive group education (2–4). Group education is far superior to the individual approach because of peer-to-peer relationships, dynamics, and other positive aspects of group education that are impossible to elicit in traditional one-to-one, usually top-down consultations. Group education also generates higher satisfaction in patients and operators. In our experience, substituting individual visits with group visits in routine care of type 2 diabetic patients achieved long-term (5 years) sustained weight loss, stabilization of A1C, and amelioration of cardiovascular risk factors while reducing prescribed medication (5). Over the first 4 years, group care cost an additional 56.7 U.S. dollars per patient to keep A1C one percentage point lower and 2.12 U.S. dollars per point gained in the quality-of-life score.

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Response to Nathan et al.

Recently, a joint consensus statement by the American Diabetes Association/European Association for the Study of Diabetes (1) recommended starting insulin therapy for type 2 diabetes with basal insulin and increasing doses until a fasting glucose <130 mg/dl was