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A Clinical Screening Tool Identifies Autoimmune Diabetes in Adults

Response to Furlanos et al.

Fourlanos et al. (1) report on a screening instrument designed to facilitate management of latent autoimmune diabetes of adults (LADA). They assert that in poorly controlled type 2 patients exhibiting two or more of five features (age <50 years, hyperglycemic symptoms, BMI <25.0 kg/m², and personal and family history of autoimmunity), the “logical” next step is confirmatory islet antibody testing (1).

Although the effect of routine use of the instrument on outcomes such as HbA_{1c} is unknown, the article raises important questions relating to the manage-

ment of clinically diagnosed type 2 diabetes. The authors state that LADA patients can require rapid escalation of oral therapy or early commencement of insulin (1). However, patients with severely deficient β -cell function but insufficient LADA features still need insulin therapy. In addition, some LADA patients achieve reasonable initial glycemic control with oral agents (2), with insulin available should this strategy fail.

We have concerns that the LADA instrument fails to meet the necessary criteria for a valid screening tool (3). In their small study, Furlanos et al. report a sensitivity of 90% and specificity of 71%. However, the positive predictive value is 21%, indicating that the probability of correctly diagnosing LADA is low. This, and the high false-positive rate (28%), suggest a limited ability to identify patients most in need of early insulin therapy.

The authors' apparent intention is to promote the instrument as part of usual care. Because of this, and since the American Diabetes Association does not recommend islet antibody testing in type 2 diabetes (4), why do the authors recommend serological confirmation (1)? Even in the case of children, in whom education, dietary counsel, and treatment differ markedly by diabetes type, autoantigens may be present in a substantial number with otherwise straightforward type 2 diabetes (4). One reason for antibody testing may be to characterize LADA patients fully for intervention studies (1), but this would only be appropriate in specialist centers.

We contend that the management of poorly controlled type 2 diabetes in adults should be based on detailed clinical assessment (including the LADA instrument components), review of glycemic control, implementation of strategies (including educator and dietitian input) that might improve adherence to self-management, a discussion of available therapies (including insulin), and adequate monitoring and support. The use of the LADA instrument and/or autoantibody testing appears redundant in this setting.

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A Clinical Screening Tool Identifies Autoimmune Diabetes in Adults

Response to Davis et al.

We thank Davis et al. (1) for their comments regarding the recent publication of a clinical screening tool for latent autoimmune diabetes in adults (LADA) (2). It is appreciated that the authors' routine management of “poorly controlled adult type 2 diabetes” incorporates the “LADA instrument components.” However, our observations of the management of such patients by internists and diabetes nurse practitioners in the community are often contrary to the practice of the authors. Adults with suboptimal glycemic control due to declining β -cell function (often secondary to autoimmune disease) are underrecognized, leading to delays in commencing insulin therapy. The clinical screening tool was developed to aid primary care physicians and diabetes nurse practitioners to consider the pathophysiological process of autoimmune β -cell destruction. The authors cite that the positive predictive value of the clinical screening tool is low

at 21% but do not mention that the negative predictive value of the tool is 99%; hence, the tool is highly reliable at excluding LADA and has a sensitivity of 90%, meaning that most LADA patients can be identified with the assistance of this noninvasive and cost-free clinical screening tool.

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Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes: The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN)

Response to Knopp

We read with interest the results of the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN)

(1). The composite primary end point rate (10 mg/day atorvastatin versus placebo) showed a hazard ratio of 0.90 (95% CI 0.73–1.12, $P = 0.34$) after 4 years. Knopp et al. (1) highlight some of the differences between ASPEN and previous atorvastatin trials (Collaborative Atorvastatin Diabetes Study and Anglo-Scandinavian Cardiac Outcomes Trial) also involving diabetic individuals without established coronary heart disease (2,3).

Other differences may also be relevant. In ASPEN, 78.3% of those on atorvastatin and 76.4% of those in the placebo group were included in the analysis. This represents a substantial “drop-out” rate. Furthermore, by the end of the study, medication was taken by 67.5% of those in the atorvastatin group and 57.6% of those in the placebo group. The “drop-in” rate in ASPEN was also high; 26.9% of those on placebo and 15.4% of those in the atorvastatin group took concomitant hypolipidemic agents. Nevertheless, LDL cholesterol was reduced by 29% with atorvastatin relative to placebo. Is it possible that among the patients on atorvastatin, some took a second statin? If so, how many of the placebo-treated patients were taking a statin and for how long?

In the ASPEN study (1), blood pressure was well controlled (mean 133/77 mmHg). The blood pressure in the Collaborative Atorvastatin Diabetes Study and the Anglo-Scandinavian Cardiac Outcomes Trial was ~138/78 and 143/80 mmHg, respectively (2,3). This difference may influence any benefit accruing from lipid lowering in ASPEN. There was also a change in protocol during the ASPEN study. Did this lead to a difference in the duration of follow-up in the primary and secondary prevention groups?

The differences outlined above, together with those mentioned by the ASPEN authors (1), may have contributed to the nonsignificant reduction in events reported in this trial.

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Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes: The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN)

Response to Gazi and Mikhailidis

We appreciate the interest of Gazi and Mikhailidis (1) in the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN) and their proposed reasons for the nonsignificant results (2).

We mention in our article the high rates of treatment “drop in” and “drop