

Treatment of Gestational Diabetes Mellitus

TO THE EDITOR: Crowther and colleagues (June 16 issue)¹ conclude that treatment of gestational diabetes mellitus reduces serious perinatal morbidity. However, we have some reservations.

For one, blood glucose monitoring and more attentive care of the subjects in the intervention group may have resulted in better outcomes, irrespective of insulin treatment. In addition, the incidence of postdate births was higher in the routine-care group; a postdate birth by itself carries a worse fetal prognosis than does delivery at 38 to 40 weeks of gestation.

Information on the degree of adherence of the intervention group to the study protocol (e.g., the percentage of the subjects who had reached the desired glucose levels) would provide critical support that the intervention itself caused the improved perinatal results.

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1. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005;353:2477-86.

TO THE EDITOR: Crowther et al. report the results of their randomized trial designed to assess the effects of the treatment of gestational diabetes on the incidence of serious perinatal complications (defined as death, shoulder dystocia, bone fracture, and nerve palsy). They report a significant reduction in these events; the number needed to treat to prevent a serious outcome was 34 (absolute risk reduction, 3 percent). However, most of these events (64 percent) involved shoulder dystocia, which cannot be considered a serious complication: it is a subjective appreciation of a technical difficulty.

Second, in addition to the number needed to treat, one should consider the number needed to screen to avoid one event, in order to evaluate the effect of the systematic screening of all pregnant women in the general population. The price of this attitude (i.e., over-medicalization of a physiological condition) is detectable in the study itself: more induction of labor and more admissions to a neonatal nursery.

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THE AUTHORS REPLY: Elchalal and Brzezinski raise the concern that factors other than glucose control may contribute to the better outcomes in the intervention group. Although this was not part of the protocol, women randomly assigned to the intervention group were more likely to have their labor induced, leading to an earlier gestational age at delivery. We interpret this as a “labeling effect,” whereby physicians, concerned about potential complications, were more likely to induce labor in women known to have glucose intolerance.

Women in the intervention group received individualized dietary advice from a dietitian, education on self-monitoring their blood glucose levels, physician support, and ongoing obstetric care. Insulin therapy, according to the protocol, was introduced when glucose levels failed to reach desired levels. Blood glucose control was achieved with diet alone, without insulin therapy, in 80 percent of the women.

Richard and colleagues emphasize that 64 percent of the serious perinatal implications were from shoulder dystocia and note concern that this reflects a subjective judgment. For each woman enrolled in the trial, the primary caregiver completed a checklist that included the presence or absence of shoulder dystocia and the measures used (categorized according to severity) to overcome any dystocia. Mild measures (episiotomy or moderate traction) were used in 5 cases (22 percent), whereas in 11 cases (48 percent) the women required moderate traction (suprapubic pressure or McRobert’s maneuver [flexion of the mother’s legs at all joints with abduction of the hips]), and in 7 cases (30 percent) more severe measures (rotation of the infant’s shoulders or delivery of the posterior shoulder) were required.

The Australian Carbohydrate Intolerance Study

in Pregnant Women (ACHOIS) trial was designed to assess whether treatment of gestational diabetes improved health outcomes; it was not designed as a screening trial. Populations vary as to the prevalence of pregnant women who will have gestational diabetes mellitus; hence the number needed to screen will need to be calculated for local populations.

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Treatment of HBeAg-Positive Hepatitis B with Peginterferon and Lamivudine

TO THE EDITOR: Lau et al. (June 30 issue)¹ studied pegylated interferon for the treatment of hepatitis B e antigen (HBeAg)-positive chronic hepatitis B. Overall, HBeAg seroconversion was highest among patients treated with pegylated interferon monotherapy, despite the more potent hepatitis B virus (HBV) DNA suppression with lamivudine at 48 weeks. Although viral suppression and HBeAg seroconversion are well correlated,² the degree of viral suppression needed for seroconversion to occur is not well defined. With regard to this study, it would be of interest to know what the degree of HBV DNA suppression was among patients in whom HBeAg or hepatitis B surface antigen seroconversion occurred, as a separate analysis. Knowledge of statistically significant predictors of seroconversion at 48 weeks and at 72 weeks would also be relevant. In addition, the characteristics of patients in whom seroreversion occurred between week 48 and week 72 would be important to know.

With regard to tolerance of pegylated interferon, nearly half the patients required dose modification. Since HBeAg seroconversion is known to occur with pegylated interferon at lower doses,³ it would be helpful if Lau et al. would comment on any effects of dose modification on seroconversion rates, HBV DNA levels, or both.

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1. Lau GK, Piratvisuth T, Luo KX, et al. Peginterferon alfa-2a, lamivudine, and the combination for HBeAg-positive chronic hepatitis B. *N Engl J Med* 2005;352:2682-95.

2. Mommeja-Marin H, Mondou E, Blum MR, Rousseau F. Serum HBV DNA as a marker of efficacy during therapy for chronic HBV infection: analysis and review of the literature. *Hepatology* 2003;37:1309-19.

3. Janssen HL, van Zonneveld M, Senturk H, et al. Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. *Lancet* 2005;365:123-9.

TO THE EDITOR: The comparison made by Lau et al. between peginterferon alfa-2a and lamivudine monotherapy administered for a fixed time period of 48 weeks, regardless of the occurrence and moment of seroconversion, does not make much sense. Current guidelines recommend administration of lamivudine for a minimum of one year and maintenance treatment for three to six months after HBeAg seroconversion is confirmed, on two occasions that are at least two months apart, in order to reduce the rates of relapse after treatment and potentially life-threatening flares.¹ The duration of treatment reported in this trial is therefore suboptimal for the majority of patients treated with lamivudine. It would have been more appropriate to continue lamivudine in patients who did not meet the criteria of current guidelines at week 48.

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1. Lok AS, McMahon BJ. Chronic hepatitis B: update of recommendations. *Hepatology* 2004;39:857-61.

THE AUTHOR REPLIES: As noted by Drs. Song and Rajvanshi, viral suppression has been correlated with HBeAg seroconversion. Among patients receiving peginterferon alfa-2a monotherapy in our study, the mean HBV DNA levels were reduced by 5.3 log copies between baseline and 24 weeks after treatment (week 72 overall) among patients with HBeAg seroconversion as compared with 0.8 log copies among patients without seroconversion. However,