Oral β-agonists probably do not reduce the incidence of preterm delivery

Macones GA, Berlin M, Berlin JA. ***Efficacy of oral beta-agonist maintenance therapy in preterm labor: a meta-analysis.*** *Obstet Gynecol. 1995 Feb;85:313-7.*

Objective

To determine whether maintenance therapy with oral β-agonists reduces the incidence of preterm delivery (delivery between 20 and 37 weeks gestation) and to assess the complications of such therapy after successful resolution of acute preterm labour.

Data Sources

A MEDLINE search was done using the terms labor, premature, and the therapeutic use of beta-adrenergic receptor agonist; and the bibliographies of standard obstetrics textbooks were reviewed.

Study Selection

Randomised controlled trials were selected if they included an untreated or placebo group, if the intended duration of maintenance therapy was to at least 36 weeks of gestation, and if the analysis differentiated between patients with intact and ruptured membranes. Trials that compared different intravenous or intramuscular agents were excluded.

Data Extraction

Data on study quality and clinical characteristics for patients with intact membranes were used to calculate heterogeneity; the pooled odds ratio (OR) for the prevention of perinatal death, preterm birth, recurrent preterm labour, and respiratory distress syndrome; and the pooled difference in mean birth weight and interval between randomisation and delivery.

Main Results

6 studies were identified and 4 were eligible for inclusion (220 patients). 2 trials studied initial intravenous therapy with magnesium sulphate, 1 used ritodrine, and 1 used ethanol. Oral terbutaline and oral ritodrine were each used for maintenance therapy in 1 trial. Intention-to-treat analysis was used in 3 trials. The pooled OR for perinatal death was 1.04 (95% CI, 0.23 to 4.72); for prevention of preterm birth it was 1.09 (CI, 0.60 to 1.99), for recurrent preterm labour it was 1.05 (CI, 0.53 to 2.05), and for the respiratory distress syndrome it was 0.91 (CI, 0.29 to 2.91). The pooled difference in mean interval from randomisation to delivery was –0.22 days (CI, –2.5 to 1.99 days), and the pooled difference in mean birth weight was 43.3 g (CI, –13.3 to 99.0 g).

Conclusions

Oral β-agonists (terbutaline and ritodrine) used after successful treatment of acute premature labour do not decrease the risk for preterm delivery, recurrent labour, perinatal death, or the respiratory distress syndrome. They also do not increase the time to delivery or birth weight.

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Commentary

That tocolytic therapy can successfully, albeit temporarily, inhibit preterm labour has been well established. The delay achieved can be used to implement measures with directly useful effects, such as the administration of corticosteroids to promote fetal maturation or to transfer the mother to a centre with better facilities for neonatal care. Overall, however, the delay is insufficient to reduce the important adverse effects of preterm delivery: perinatal mortality and serious morbidity, such as that associated with the respiratory distress syndrome.

Even when preterm labour has been successfully inhibited, it frequently recurs before adequate fetal maturity is achieved. It was reasonable to hope that maintenance therapy with oral β-mimetics might successfully prevent recurrent preterm labour until the fetus was sufficiently mature. Unfortunately, as shown in this review, the published controlled trials have failed to support this hope: No benefits in terms of substantive delay of labour or improved fetal outcomes are shown.

The results of this review do not support the use of oral β-agonist maintenance therapy after a successfully treated episode of acute preterm labour. The clinical applications are clear: The routine use of this sometimes hazardous treatment cannot be justified. Because no benefit has been proved, the costs and potential risks of maintenance therapy must be seriously considered for each patient.

Nevertheless, the question about the role, if any, for oral maintenance therapy has not been answered. Preterm labour is a common and serious problem. Only 220 patients were enrolled in the 4 adequately controlled trials included in this meta-analysis. Although no statistically significant benefits were found, the wide confidence limits on the results included the possibility of clinically important benefits. Further controlled research to provide a clearer answer is required and would be justified.

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