Abstract

Objectives: To assess the benefits and risks of antenatal corticosteroid therapy for fetal maturation.

Options: To administer antenatal corticosteroids or not to women at risk of preterm birth.

Outcomes: Perinatal morbidity, including: respiratory distress syndrome, intraventricular hemorrhage, infection, adrenal suppression, somatic and brain growth; perinatal mortality; and maternal morbidity, including infection and adrenal suppression.

Evidence: MEDLINE and PubMed searches 1996 to August 2002 for English-language articles related to antenatal corticosteroid therapy for fetal maturation, the Cochrane Library, and national statements including that of the National Institutes of Health (NIH), the American College of Obstetricians and Gynecologists, and the Royal College of Obstetricians and Gynaecologists.

Values: The evidence obtained was reviewed and evaluated by the Maternal-Fetal Medicine Committee of the Society of Obstetricians and Gynaecologists (SOGC) and recommendations were made according to guidelines developed by the Canadian Task Force on the Periodic Health Exam.

Benefits and Harms: A single course of corticosteroids reduces perinatal mortality, respiratory distress syndrome, and intraventricular hemorrhage. Information regarding repeat courses of corticosteroids is limited and conflicting, with many studies being retrospective and non-randomized. Some studies suggested a reduction in respiratory distress syndrome with repeat courses, but some found increased rates of neonatal and maternal infection; fetal, neonatal, and maternal adrenal suppression; decreased fetal or neonatal somatic and brain growth; and increased perinatal mortality.

Recommendations: The SOGC supports the recommendations of the NIH Consensus Development Panel:

1. All pregnant women between 24 and 34 weeks’ gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal treatment with a single course of corticosteroids. (I-A)

2. Treatment should consist of two 12 mg doses of betamethasone given IM 24 hours apart, or four 6 mg doses of dexamethasone given IM 12 hours apart (I-A). There is no proof of efficacy for any other regimen.

3. Because of insufficient scientific data from randomized clinical trials regarding efficacy and safety, repeat courses of corticosteroids should not be used routinely (II-2E) but be reserved for women participating in randomized controlled trials.

Validation: This Committee Opinion has been reviewed and approved by the Maternal-Fetal Medicine Committee of the SOGC and approved by SOGC Council.

Key Words
Corticosteroid, preterm birth, respiratory distress syndrome, perinatal morbidity and mortality


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INTRODUCTION

Preterm birth is a significant cause of perinatal morbidity and mortality, accounting for up to 85% of neonatal mortality not caused by lethal malformations. It is a major determinant of serious neonatal and infant morbidity including respiratory distress syndrome (RDS), necrotizing enterocolitis, intraventricular hemorrhage (IVH), and long-term neurodevelopmental handicap. In addition to its medical importance, preterm delivery has an important economic effect on both short- and long-term care of these preterm infants. The lifetime cost of a surviving preterm infant weighing less than 2500 g, including initial hospitalization, rehospitalization in the first years of life, and long-term morbidity with and without institutionalization, is over $600,000, with an annual cost in Canada of over eight billion dollars attributed to prematurity.

Despite improvements in perinatal care, the preterm birth rate in Canada has increased from 6.3% in 1981 to 6.8% in 1992 through 1994, a relative increase of 9%.

The quality of evidence reported in this document has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam (Table).

EVIDENCE AND OPINION

A meta-analysis of studies evaluating the use of corticosteroids in women at increased risk of preterm birth has concluded that a single course of corticosteroids reduced perinatal mortality (OR 0.60, 95% CI 0.48–0.75), respiratory distress syndrome (OR 0.53, 95% CI 0.44–0.63), and intraventricular hemorrhage (OR 0.48, 95% CI 0.32–0.72). In 1994, the National Institutes of Health (NIH) sponsored a Consensus Development Conference on the effect of corticosteroids for fetal lung maturation on perinatal outcomes, concluding that a single course of corticosteroids should be considered for women at risk of preterm delivery. It concluded that the optimal benefit of corticosteroids lasted for 7 days, and further research was needed to determine the possible benefit of repeat corticosteroid doses 7 days after the initial course. Despite this call for further research, repeat and “rescue” courses of corticosteroids have been increasingly used in clinical practice outside of clinical trials.

The NIH again convened a consensus panel in 2000 to address the issue of antenatal corticosteroid use for preterm women, reaffirming the benefit of a single course of corticosteroids, but concluding that current data did not support the routine use of repeat courses.

Previous studies in animal models have tried to evaluate the benefits and risks of repeat courses of corticosteroids. The findings include improved lung mechanics, gas exchange, and maturation, but also increased risk of reduced lung, brain, and overall body growth, delayed cerebral myelination, as well as deleterious effects on the hypothalamic-pituitary-adrenal axis.

Studies in humans of repeat corticosteroids use are limited, many being non-randomized and retrospective, and therefore subject to methodologic problems. Some studies suggested a reduction in the incidence and severity of RDS, increased...
rates of maternal and neonatal infection, maternal and fetal adrenal suppression, decreased fetal or neonatal somatic and brain growth, and increased perinatal mortality.

A randomized trial of single versus weekly courses of antenatal corticosteroids for women at risk of preterm delivery was stopped after an interim analysis found that weekly courses did not reduce composite neonatal morbidity (RR 0.80, 95% CI 0.59–1.10), but resulted in a trend toward more cases of severe IVH (9 vs 2 cases, \( p = 0.06 \)) and chorioamnionitis (24.1% vs 17.8%, \( p = 0.09 \)) in the weekly group. This study has been criticized for being terminated before its calculated sample size could have adequate power to find possible reduction in adverse perinatal outcome.

Both betamethasone and dexamethasone have been shown to have benefit for the fetus. A recent retrospective study comparing betamethasone and dexamethasone found that betamethasone, but not dexamethasone, reduced the risk of periventricular leukomalacia. This finding has not been reported by other investigators. The NIH consensus panel did not feel that there was enough evidence to recommend betamethasone over dexamethasone. Betamethasone use has been associated with transient reduction in fetal heart rate variability and fetal movement.

**RECOMMENDATIONS**

The SOGC Maternal-Fetal Medicine Committee, consistent with recommendations of the American College of Obstetricians and Gynecologists and the Royal College of Obstetricians and Gynaecologists, supports the recommendations of the NIH Consensus Development panel.

1. All pregnant women between 24 and 34 weeks’ gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal treatment with a single course of corticosteroids. (I-A)

2. Treatment should consist of two 12 mg doses of betamethasone given IM 24 hours apart, or four 6 mg doses of dexamethasone given IM 12 hours apart (I-A). There is no proof of efficacy for any other regimen.

3. Because of insufficient scientific data from randomized clinical trials regarding efficacy and safety, repeat courses of corticosteroids should not be used routinely (II-2E) but be reserved for women participating in randomized controlled trials.

**REFERENCES**


