

CLINICAL PRACTICE GUIDELINES

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MANAGEMENT OF POSTNATAL CORTICOSTEROIDS FOR THE PREVENTION OF CHRONIC LUNG DISEASE IN PRETERM INFANTS



Ministry of Health Malaysia



Academy of Medicine, Malaysia

Statement of Intent

These guidelines are meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management options available locally.

Review of the Guidelines

These guidelines were issued in July 2003 and will be reviewed in July 2005 or sooner if new evidence becomes available.

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Postnatal Corticosteroids for the Prevention and Treatment of Chronic Lung Disease in Preterm Infants

Clinical trial evidence for the effectiveness of corticosteroids in the prevention of CLD is strong and the use of this treatment in the clinical setting has become popular. Follow up studies have started to appear in the literature and have suggested that there may be a danger in this practice¹⁻⁶. This clinical practice guideline attempts to provide some guidance to the practicing Paediatrician on the interpretation of this evidence in the clinical setting.

1. Terminology

The term bronchopulmonary dysplasia (BPD) was first used by Northway in 1967 to describe a condition characterized by chronic respiratory failure in neonates treated with mechanical ventilation for a primary lung disease.⁷ Today most neonates with chronic respiratory failure are preterms with a history of treatment by mechanical ventilation for respiratory distress syndrome. The disease tends to be less severe and does not follow the clinical and X-ray phases described by Northway.

There is no diagnostic marker for the condition so although the onset of the condition is known to occur very early in postnatal life, the diagnosis is made in infants who remain oxygen dependent and in whom other conditions have been excluded. BPD is commonly defined as oxygen dependency at 28 days of age.⁸⁻¹⁰ Some definitions also include X-ray evidence of BPD or a history of mechanical ventilation in the first week of life.¹¹⁻¹⁷ One of the weaknesses of this definition is that it is very common for very preterm infants below 28 weeks gestation to require oxygen for more than 28 days and most of these are normal. Chronic lung disease (CLD) generally refers to infants below 32 weeks who remain oxygen dependent at 36 weeks postmenstrual age. This definition has been found to be a more accurate predictor of long term outcome.¹⁸ In the clinical setting the terms are often used interchangeably. This guideline uses the term CLD and refers to either definition above: that is oxygen dependency at 28 days of life or at 36 weeks postmenstrual age.

However defined, chronic lung disease is an important problem. Severe cases have pulmonary hypertension and progress to cor pulmonale which is usually fatal. The treatment of CLD is costly. Most infants require a prolonged hospital stay and some continue with home oxygen therapy after discharge. Infants with CLD require more frequent hospital admission and have a higher risk of dying during the first year of life. Poor growth and abnormal neurological development are additional problems that these infants may face.

2. Incidence

The incidence of CLD depends on the definition. In the Malaysian Paediatric Association Very Low Birth Weight (VLBW) study, 4% of 962 VLBW infants born in 20 Malaysian hospitals were oxygen dependant at 28 days and had X-ray evidence of BPD while 28% died and 68% were normal.¹⁹ In developed countries where the mortality is lower BPD has reported in 11 to 57% of survivors.^{9,11-17,20,21} Survival of VLBW infants is rapidly improving in Malaysia and it is reasonable to assume that CLD will become more common.¹⁹

3. Corticosteroids

Inflammation plays an important role in the pathogenesis of CLD. This progresses to lung destruction and abnormal repair. Corticosteroids have been found to reduce the inflammatory response and decrease airways resistance.

There are 9 systematic reviews examining the evidence for systemic postnatal corticosteroids, mainly dexamethasone, in the prevention and treatment of chronic lung disease.²²⁻³⁰ In the 3 most complete of these, more than 35 randomised controlled trials are reviewed.²⁶⁻²⁸ These used courses of therapy ranging from 3 to 42 days. A 12 – 14 day course seems to be the most common.²⁶⁻²⁸ Early post natal steroids refers to corticosteroids begun within the first 96 hours after birth; moderately early, 7-14 days after birth; and delayed 3 or more weeks after birth.²²⁻²⁴

Corticosteroids have also been used in neonates for the prevention and treatment of post-extubation stridor and extubation failure and may have some benefit.²⁵

4. Early Postnatal Corticosteroids (<96 hours)

A Cochrane systematic review of 19 trials involving almost 2500 patients given early postnatal steroids or placebo found the following:

Benefits

Reduced oxygen dependency at 28 days and 36 weeks postmenstrual age, reduced overall incidence of death or chronic lung disease, reduced failure to extubate and reduced need for later steroids, reduced pulmonary air leak and patent ductus arteriosus.²² They did not show a reduction in overall mortality.

Complications

There was an increased risk of hyperglycaemia, hypertension and hypertrophic cardiomyopathy, increased growth failure, increase gastro-intestinal bleeding and intestinal perforation. There was no evidence of increased IVH, PVL, ROP, NEC, pulmonary haemorrhage or infection.

Long Term Outcome

The reviewers were able to locate two follow up studies.^{1,6} Important long term complications were found and these included: increased risk of abnormal neurological examination, increased cerebral palsy and developmental delay and increased death or development delay.

Conclusion

The reviewers of the review recommend further follow up studies but in the mean time conclude that the benefits of early postnatal steroids may not outweigh the risks. Early postnatal steroids are precluded as the treatment should only be considered in infants who cannot be weaned from mechanical ventilation. A further multicentre study is underway.

5. Moderately Early Postnatal Corticosteroids (7-14 days)

There are 2 full systematic reviews addressing this question^{27,29}. The most complete, a cochrane systematic review of 7 trials involving almost 600 patients found the following:

Benefits

There was reduced mortality at 28 days, reduced CLD at both 28 days and 36 weeks postmenstrual age, reduced aggregated death or CLD at 36 weeks, reduced failure to extubate.²⁷

Complications

The following complications were found: increased hyperglycaemia, hypertension, and hypertrophic cardiomyopathy, increased gastrointestinal bleeding, and increased infection rate. There was no increase in IVH, NEC, and ROP.

Long Term Outcome

The reviewers found only one long term study on 36 infants followed up for 15 months.³² This study was unable to show any increase in abnormal neurological examination and combined death or abnormal neurological examination.

Conclusion

The reviewers concluded that there were both benefits and adverse effects and that there was no reliable evidence concerning the long term effects of postnatal corticosteroids. Clinicians must weigh up each individual case.

6. Delayed Postnatal Corticosteroids (> 3 weeks)

There are 9 trials involving over 550 subjects.

Benefits

A Cochrane systematic review found that there was reduced failure to extubate, need for further late steroids, and need for home oxygen.²⁸ Mortality was not affected but there was a decrease in aggregated mortality and CLD.

Complications

Hypertension was increased but hyperglycaemia was not. Gastrointestinal complications and infection were not increased.

Long Term Outcome

Long term follow up was reported in one study.^{4,5} This showed an increase in abnormal neurological examination both overall and in survivors. There was no significant increase in cerebral palsy or death and cerebral palsy.

Conclusion

The authors concluded that the use of delayed steroids should be reserved for ventilator dependant infants in whom it is felt that steroids are essential to facilitate extubation.

Summary

In summary postnatal steroids do show benefits in weaning from mechanical ventilation and reducing CLD and possibly also mortality. However the adverse effects are considerable and these include abnormal neurological findings and cerebral palsy on follow up. Adverse effects may outweigh the benefits.

7. Recommendations

1. The benefits and risks of postnatal corticosteroid use in oxygen dependant preterm infants should be weighed up in each individual case. (Grade A)
2. Postnatal corticosteroids should be reserved for situations where there is evidence of chronic lung disease such as failure of the X-ray to clear and continued high ventilator settings after 7 days and it is apparent that weaning may not be possible without steroids. (Grade A)

3. Postnatal corticosteroids for the purpose of preventing or treating CLD should not be given to infants below 7 days of age.
(Grade A)
4. A suggested regime would be a starting dose of 0.5mg/kg/day tapering after 3 days, keeping the duration of treatment to a minimum.
(Grade A)
5. These recommendations should be revised when data becomes available from ongoing trials (DART Study, Doyle 2000).
(Grade A)
6. Each Paediatric department should develop its own written policy on the indications of postnatal steroids.
7. Antenatal corticosteroids remain proven and beneficial in reducing RDS and their use should not be influenced by these new recommendations on the use of postnatal steroids.
(Grade A).

*Grading of Recommendations based on AHCPR 1994.

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