Pharmacologic Prevention and Treatment of BPD

East Bay Newborn Specialists Guideline

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Background:

Bronchopulmonary dysplasia (BPD) is defined as the need for oxygen at 36 weeks corrected age in infants born at less than 32 weeks of age who required oxygen in the first month of life. Prior to the use of surfactant and modern ventilator strategies ("old BPD"), BPD was characterized by significant airway disease. Most of the babies with BPD in the modern era ("new BPD") have disease which is characterized by alveolar simplification, rather than severe airway disease.

Treatment strategies for the "old BPD" emphasized use of diuretics for decreasing interstitial and airway edema, and bronchodilators for preventing and/or reversing bronchospasm. However, these approaches have little relevance to most babies with "new BPD".

Both Vitamin A and Caffeine have been shown to decrease the incidence of BPD in patients at risk for "new BPD".

The following are guidelines for use of medications for the prevention and treatment of infants at risk for, or with, BPD.

Vitamin A:

- Vitamin A plays multiple key roles in lung protection and healing, and has been shown to decrease the rate of BPD.
- Vitamin A for the prevention of BPD should be used as follows:
    - Infants with birth weight $\leq$ 1000 g
    - On (or expected to be on) oxygen and/or positive pressure for longer than 24 hrs
    - Started within the first 4 days of life
    - Dose 5000 Units IM 3 times/week
    - Duration of therapy 4 weeks
- As of January, 2012, there is a national shortage of injectable Vitamin A. There are no alternative preparations of Vitamin A for use in this population.

Caffeine:

- Caffeine has been shown to decrease the rate of BPD, and improve short-term neurologic outcome.
- Caffeine for the prevention of BPD should be used:
    - Infants with birth weight $\leq$ 1250 g
    - At risk of apnea and/or BPD
    - Started within first 10 days of age
    - Dose 20 mg/kg loading dose, followed by 5 mg/kg/day (note that higher doses are usually well tolerated)
    - Duration of therapy until off positive pressure for at least 5 days
- Most babies are off caffeine by 34 weeks
- Babies should be off caffeine for at least 7 days before they are discharge home, unless they are going to be discharged on caffeine.

Diuretics:

- Diuretics have a role in the management of infants with acute fluid overload and/or oliguria.
- Diuretics have been shown to improve pulmonary function in post-term infants with "old BPD", at least in the short term.
- Chronic or long-term diuretic therapy was frequently used for the management of patients with "old BP". However, there is neither a physiologic basis nor clinical trial data to suggest that chronic or long-term diuretics have any role in the management of babies with "new BPD". Whether there is any role for chronic diuretic therapy in the unusual baby with severe BPD that "looks like old BPD" is unclear.
- Chronic diuretic therapy for BPD is not indicated for infants less than 36 weeks corrected age.
- Some VLBW infants > 36 weeks corrected age with severe "old BPD" *may* benefit from diuretics. Rather than starting these infants on chronic diuretics, give them a brief (3-5 day) trial of diuretics, then discontinue the diuretics. If they improve on diuretics, and deteriorate when they are off diuretics, consider intermittent short courses of diuretics or chronic diuretics.
- Remember that for some parents, home O2 is easier than home diuretic therapy. Prolonged O2 therapy may also be less toxic than prolonged diuretic therapy.
- Diuretic options for chronic treatment include:
    - Chlorthiazide 20-40 mg/kg/day plus Spironolactone 2-4 mg/kg/day
    - Furosemide 1-2 mg/kg/day plus Spironolactone 2-4 mg/kg/day

Inhaled Bronchodilators:

- Airway disease, including increased baseline airway resistance and increased airway reactivity, were common features of "old BPD" in infants who were > 40 weeks corrected age.
- A significant number of infants with "new BPD" will develop airway reactivity in early childhood
- There is neither a physiologic basis nor clinical trial data to support the use of inhaled bronchodilators in preterm infants with "new BPD" at less than 40 weeks corrected age
- A trial of inhaled bronchodilators might be indicated in babies with severe "old BPD" who are greater than 40 weeks corrected age.
- If an infant with severe BPD at > 40 weeks corrected age shows significant clinical improvement with inhaled bronchodilators, consider ongoing PRN or routine treatment. Whether routine treatment of these babies is superior to PRN treatment is unknown.

Inhaled Steroids:

- There is no evidence to support the use of inhaled steroids for prevention or treatment of BPD in infants at less than 40 weeks corrected age.
- There is evidence that inhaled steroids are effective in management of older children with reactive airway disease.
- There may be rare instances where infants with severe BPD at greater than 40 weeks corrected age might benefit from inhaled steroids. Coordinate the treatment of these infants with Pulmonology.

Surfactant:

- Surfactant for the prevention and treatment of RDS is not included in this Guideline.
- Surfactant for the prevention and treatment of BPD (or evolving BPD) is still experimental, and should only be done as part of a controlled trial.

Systemic Steroids:

- The use of systemic steroids for the prevention or treatment of BPD (or evolving BPD) is covered in a separate Guideline.

Inhaled Nitric Oxide:

- One large clinical trial showed that inhaled Nitric Oxide significantly decreases the rate of BPD in high risk infants. However, there is a recent NIH consensus statement which states that there is insufficient evidence to consider inhaled Nitric Oxide standard of care for prevention of BPD. We do not currently use inhaled Nitric Oxide for the prevention of BPD.
- Preterm infants with severe pulmonary hypertension, and infants with late BPD complicated by severe pulmonary hypertension may benefit from the use of inhaled Nitric Oxide. The use of iNO in these situations is covered in separate Guidelines.

References:

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