Newborn Critical Care Center (NCCC) Clinical Guidelines

Vitamin A Therapy

Bronchopulmonary dysplasia (BPD) is the most common pulmonary morbidity in premature infants. It manifests with decreased oxygenation/ventilation, increased work of breathing, and susceptibility to infection. The pathogenesis of BPD is multifactorial. From a purely pathological perspective, it is a developmental disruption in lung growth and maturation that can be seen on microscopy. From a clinical perspective, it includes injury to an immature lung (volutrauma, barotrauma, oxygen toxicity, infection) and factors inhibiting lung healing. The lung healing can also be influenced by many factors including nutrients, antioxidants and inflammatory cells.

Many trials have been conducted to evaluate treatments aimed at reducing the incidence of BPD with minimal success. Vitamin A (Aquasol A) is one of the only treatments proven to reduce the incidence of death or BPD at 36 weeks' postmenstrual age in premature infants. In animal models involving oxidative lung injury, Vitamin A supplementation has been shown to increase mean alveolar area, improve alveolar regeneration, decrease pulmonary fibrosis, and prevent damage to the diaphragm[1]. One of the largest, landmark studies establishing the use of Vitamin A supplementation as an intervention to decrease the risk of BPD in extremely-low-birth-weight infants was an RCT by Tyson et al. (1999) which included 807 infants and demonstrated an NNT of 14-15 infants[2]. A Cochrane Review published in 2016 (10 trials; 1460 randomized patients) concluded that Vitamin A therapy is associated with a small reduction in death or oxygen requirement at one month of age and a marginal reduction in oxygen use at 36 weeks' postmenstrual age for very low birth weight infants.[3] There may also be a reduction in the incidence of retinopathy of prematurity and nosocomial sepsis with Vitamin A use.[3]

More recently, multiple systematic review and meta-analyses support early supplementation of Vitamin A in premature infants and conclude it to be "worthy of clinical application" and a safe and efficacious intervention for the prevention and treatment of BPD[4-6]. One of these analyses (Huang et al.), also suggests Vitamin A may also improve the survival rate of these infants but this is not universally supported by the other studies.[4-6] Another meta-analysis published in 2022 concluded that the small reduction in oxygen requirement at 36 weeks postmenstrual age was not statistically significant but reductions in periventricular leukomalacia and any grade of ROP were significant.[7] In addition, a review on oxidative stress and BPD highlights the antioxidant and anti-inflammatory properties of vitamin A and the authors conclude it "should be prescribed" as a proven therapeutic strategy. There are ongoing studies to evaluate alternative routes of administration (endotracheal/inhalation) which have shown promise in animal models.

CRITERIA FOR ADMINISTRATION

1. All infants < 28 weeks gestation (as recommended in the NCCC ELBW Guidelines)
2. Infants ≥ 28 weeks gestation meeting the following criteria:
   A. Birth weight < 1000 grams

      AND

   B. Need for mechanical ventilation or supplemental oxygen ***at 24 hours of life***

      Example: *CPAP, FiO2 0.21 would* ***NOT*** *qualify*
3. Qualifying out born infants as long as the first dose is given by 96 hours of life

DRUG INFORMATION FOR VITAMIN A (AQUASOL A)

- *Dose & Interval:* Aquasol A 5000 IU IM every Monday, Wednesday, Friday
- *Length of treatment:* 4 weeks or 12 doses
- *Administration:* Light-shielded via 30-gauge needle

CONSIDERATIONS

- First dose given after 24 hours of life but by 96 hours of life
- First dose would be the first Monday, Wednesday, or Friday after 24 hours of life

References

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