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Postnatal Betamethasone Decreases Respiratory Index in Ventilated Extremely Low Birth Weight Neonates Compared to Conventional Care

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Background

Bronchopulmonary dysplasia (BPD) is a major complication of ventilatory care and affects up to 50% of ELBW neonates. A 2010 AAP Policy indicated that glucocorticoids may be considered for ELBWs on mechanical ventilation > 7 day postnatal age to abate progression of BPD. For > 16 years, we used postnatal BETA in lieu of dexamethasone or hydrocortisone to decrease ventilator support in high risk neonates because of its better safety profile (DeCastro, et al J Perinatol 29:297, 2009).

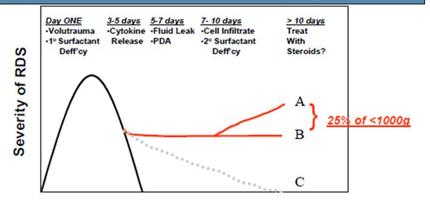
Why Betamethasone (BETA) ?

- Antenatal BETA has been associated with a decreased risk of cystic periventricular leukomalacia (PVL) when compared to dexamethasone or the absence of glucocorticoid therapy (Baud O et al., N Engl J Med 1999; 341: 1190–1196)
- Betamethasone has been used in pregnancy for over 20 years with an unprecedented high level of safety and efficacy.
- The CNS penetration of BETA is lower compared to dexamethasone because of lower lipid solubility and higher binding to serum proteins. (Trenque T et al., Fundam Clin Pharmacol 1994; 8: 430–436)
- Single subcutaneous dose of 0.1 mg of BETA is 2- to 3- fold more potent than dexamethasone in accelerating fetal lung maturity without impairing fetal survival or weight gain and achieves lower peak than IV dose. (Christensen HD et al, . J Soc Gynecol Invest 1997; 4: 130–134)

Objective

To determine whether low dose (0.125mg/kg IM), short course (every 24 hours for 3 days) BETA between 7-30 days postnatal age would reduce the respiratory index in ELBWs vs. receiving conventional care (SRX, no steroid controls).

Using postnatal steroids in selective group of ELBWs



•Anatomically Normal
Lung for Gestational Age
•Chemically Normal
Surfactant/steroids
•Mechanically Normal
"Optimal FRC"

WHO WILL STEROIDS BENEFIT ?
•Anti-inflammatory
•Stabilize Membranes
Fluid leaks/Cell integrity
•Induce Surfactant
•Other

*Zia et. al., 2002

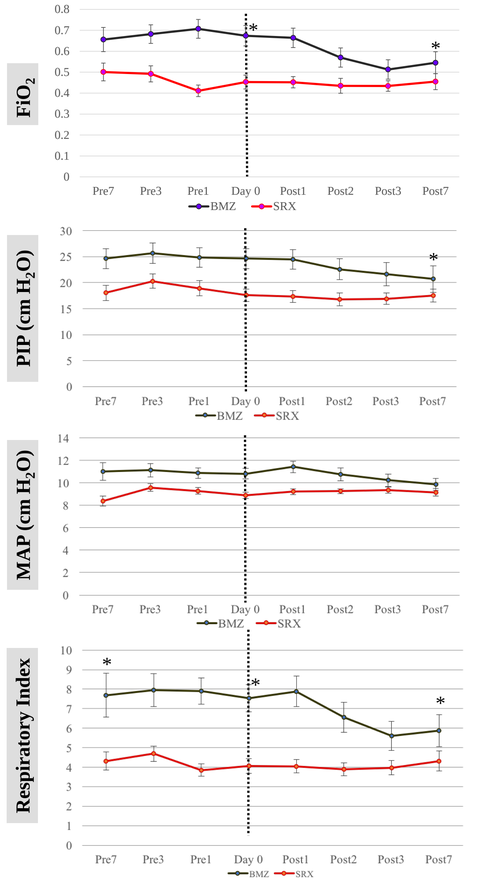
Demographics of ELBWs

	Betamethasone (Mean±SD, n = 25)	Control (Mean±SD, n = 26)
Birth Weight (grams)	698.2 ± 167.7	717.7 ± 145.2
Gestation (wks)	24.5 ± 1.2	25.3 ± 1.5
Male	56%(14/25)	54%(14/26)
BETA (DOL)	19.7 ± 6.3	none
Apgars <6 at 5 mins	60% (15/25)	42% (11/26)
Antenatal steroid	80% (20/25)	77% (20/26)
IUGR	12% (3/25)	8% (2/26)

Secondary Outcomes

		Betamethasone (Mean±SD, n = 25)	Control (Mean±SD, n = 26)
Weight Gain	Pre-BETA (gm/kg/d)	17.5 ± 12.8	17.0 ± 11.9
	Post-BETA (gm/kg/d)	12.5 ± 12.8	15.6 ± 13.5
Bld Glucose (max)	Pre-1week	157.4 ± 45.7	179.7 ± 48.3
	Post-1week	148.2 ± 45.5	118.9 ± 37.0
BPD		88% (21/24)	77% (20/26)
Ventilator days		59 ± 42	53 ± 48
EUGR at disposition		16% (4/25)	31% (8/26)

FiO_2, PIP, MAP and Respiratory Index at various time points between 7 days pre- & post- BETA (day of administration: 0) in BMZ and SRX groups.



Methods

- This is a IRB approved, retrospective chart review from Jan 2013 – Dec 2015 of ELBWs who were intubated, ventilated and required FiO_2 > 0.35 between 7-30 day postnatal age. Patients who received low dose BETA (0.125mg/kg IM Q24hr) for short duration (3d) were compared to a cohort who fulfilled entry criteria without BETA.
- FiO_2 and respiratory index (mean airway pressure x FiO_2) were calculated at -7,-3,-1, 0,+1,+2,+3 and +7d after initiation of BETA along with demographics, respiratory variables and co-morbidities.
- 2-way repeated measures ANOVA was used for statistical analysis.

Results

- Over the 3 year period of 247 ELBWs admitted, data analyzed include 25 pts who received BETA and 26 controls.
- From -7d to 0d, average FiO_2 was unchanged in both groups.
- At initiation of BETA, FiO_2 was 0.67±0.24 & 0.45±0.16 ($p<0.001$) and RI was 7.5±3.5 & 4.1±1.9 ($p=0.001$) for BETA vs. control.
- PIP, Respiratory Index (RI) and FiO_2 decreased at +7d compared to 0d in BETA group ($p=0.008$ for PIP; $p=0.02$ for RI, $p=0.03$ for FiO_2), but no change in the control group.
- No significant difference in weight gain, hyperglycemia, uremia, iNO use, infection, or NEC between the groups.
- Total number of ventilator days were 59±42d & 53±48d respectively and rate of BPD (O_2 requirement at 36 weeks) were 88% (21/24) vs. 77% (20/26); p=ns.

Conclusion

- There's a clinician selection bias to use BETA for sicker ELBWs.
- There's a significant short-term benefit of BETA in reducing the RI and FiO_2 without increasing co-morbid complications.
- There's no decrease in ventilator days or BPD with administration of BETA. Long term neurodevelopmental evaluations are in progress.
- We speculate that our clinicians selected patients with higher RI and FiO_2 who may be too sick to lower BPD.
- A prospective RCT is in progress. We seek to determine if low-dose betamethasone is a suitable alternative corticosteroid treatment for evolving BPD.