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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 ELBW 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).

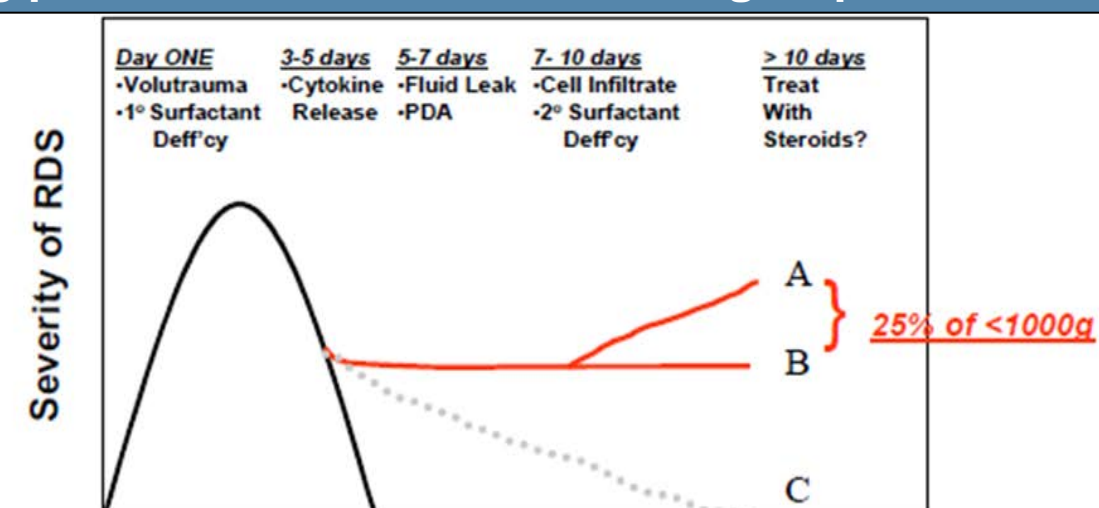
Why Betamethasone (BETA) ?

- 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 ELBW vs. receiving conventional care (SRX, no steroid controls).

Using postnatal steroids in selective group of ELBW



WHO WILL STEROIDS BENEFIT ?
 •Anatomically Normal Lung for Gestational Age
 •Chemically Normal Surfactant/steroids
 •Mechanically Normal "Optimal FRC"
 •Anti-inflammatory
 •Stabilize Membranes Fluid leaks/Cell integrity
 •Induce Surfactant
 •Other
 *Zia et. al., 2002

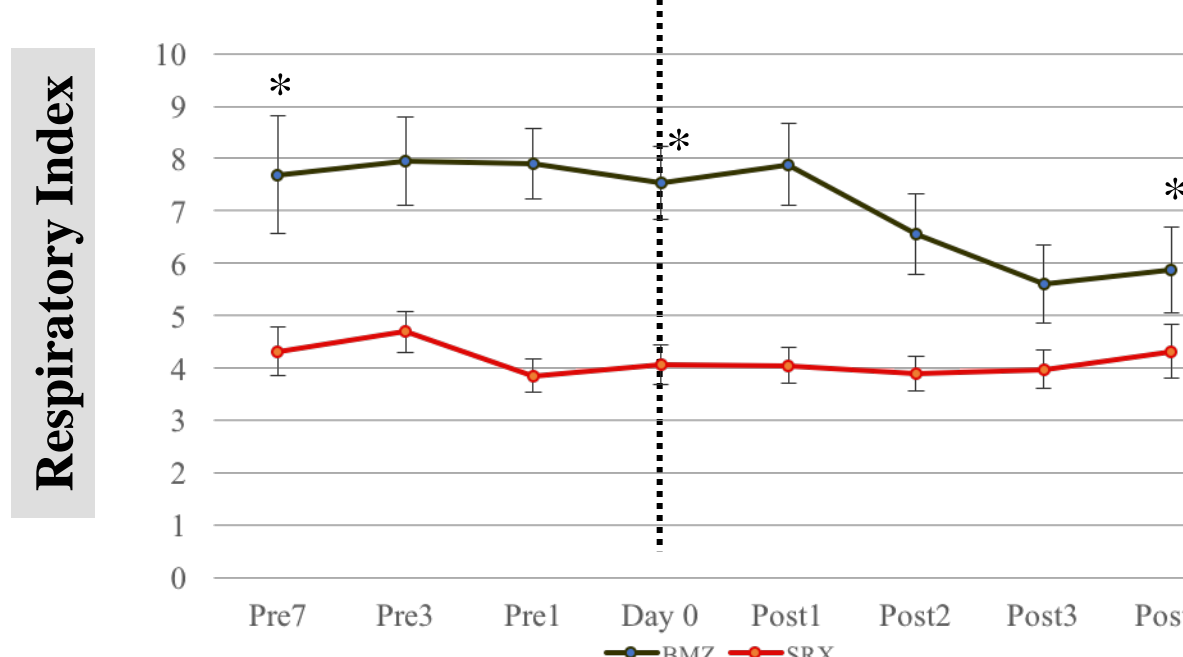
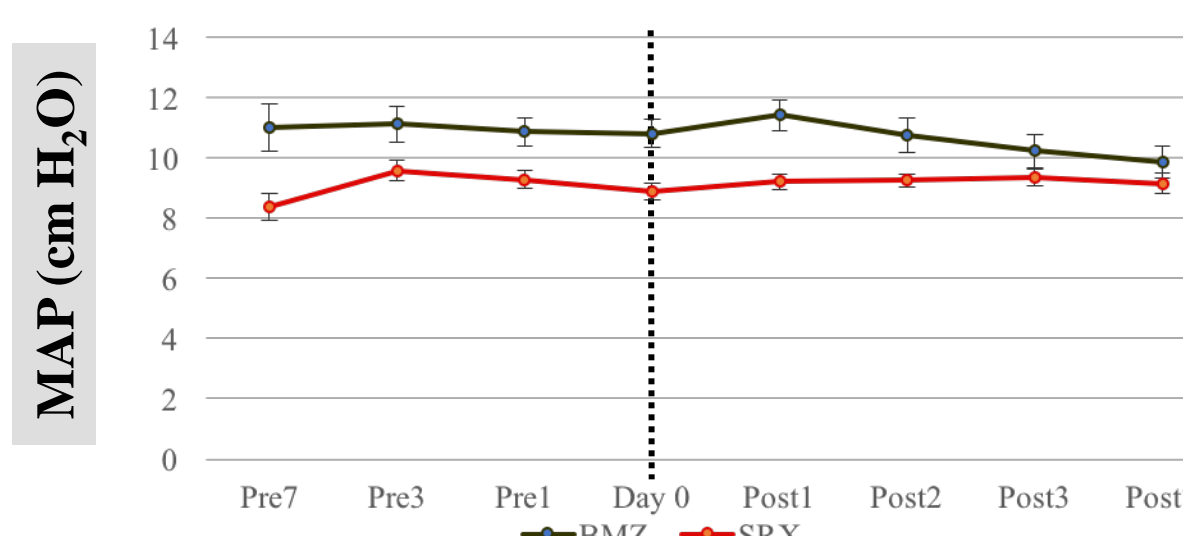
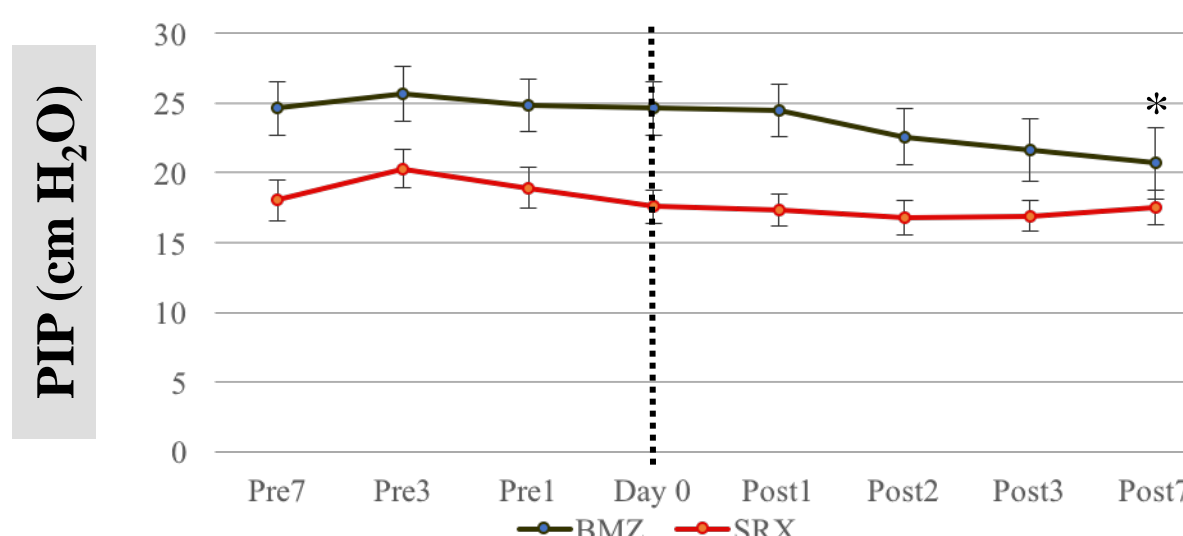
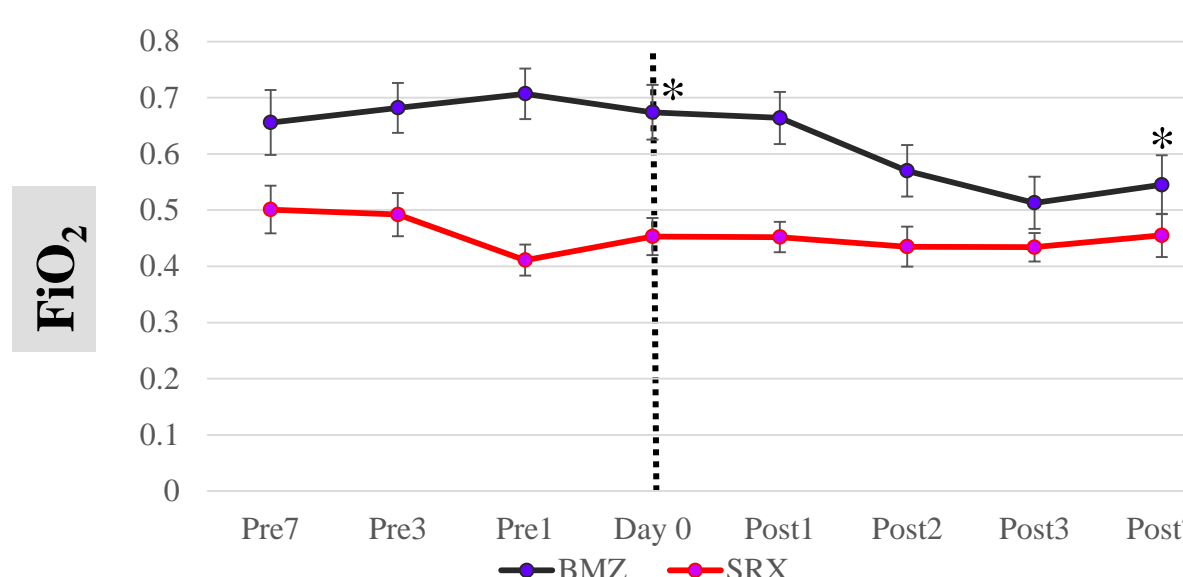
Demographics of ELBW

	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
Appgars <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 (gm/kg/d)	Pre-BETA	17.5 ± 12.8	17.0 ± 11.9
	Post-BETA	12.5 ± 12.8	15.6 ± 13.5
Bld Glucose (max) (mg/dl)	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)	

FiO₂, 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 ELBW who were intubated, ventilated and required FiO₂ > 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.
- FiO₂ and respiratory index (mean airway pressure x FiO₂) 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 ELBW admitted, data analyzed include 25 pts who received BETA and 26 controls.
- From -7d to 0d, average FiO₂ was unchanged in both groups.
- At initiation of BETA, FiO₂ 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 FiO₂ decreased at +7d compared to 0d in BETA group (p=0.008 for PIP; p=0.02 for RI, p=0.03 for FiO₂), 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 (O₂ 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 ELBW.
- There's a significant short-term benefit of BETA in reducing the RI and FiO₂ 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 FiO₂ 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.