Hans Hartwig PGY6

EVMS EM Journal Club

NOV 2011

P: In infants greater than 6 wks with acute bronchiolits and no other cardiopulmonary complications

I Does racemic epinephrine and Dexamethasone

C compared to standard usual care

O Improve respiratory status and need for hospitalization?

Clinical scenario: 2AM at a local ED where a previously healthy 6 month old infant arrives in respiratory distress. Pt has had profuse rhinnorhea, cough, and now increased work of breathing. Mom has had some difficulty with feeding over the last 24 hrs but patient has maintained UOP. Temp 37.5, RR 55, HR 165 Sats 94% on RA. On exam pt has polyphonic wheezing with coarse breath sounds noted and belly breathing with mild to moderate retractions.

Search Strategy: Online (Pub med)search for recent interventions in care of bronchiolitis and admission rates

Citation: Plint,A, Epinephrine and Dexamethasone in Children with Brochiolitis NEJM, 2009. 360 2079-89 PERC

I: What is being studied:

Objective	To evaluate the effectiveness different interventions in bronchiolitis as they relate to hospital admission rates within 7 days of presentation to ED and evaluate the effectiveness on respiratory status in the ED.
Study Design	Multicenter RDBPCT in Peds ED 800 infants 6 wks – 12 months 4 different treatment groups 1) 2 epi + Dex 2) 2 epi + placebo 3) Placebo + Dex 4) Placebo + placebo
Inclusion Criteria	6 wks – 12 months with first episode of wheezing + URI sx + RSC season (Dec-April) 2004-2007 seen at PERC hospitals with RDAI scores of (4-15)
Exclusion Criteria	Infants with treatment prior to research nurse evaluation. Hx of steroid use in previous 2 wks, previous wheezing, asthma, cardiac or pulmonary disease, previous bronchodialator use, varicella exposure, infants <37 wks corrected age <6 wks at

	ED visit, Severe distress or no distress, Profound lethargy. Insurmountable barrier to communication
Intervention Compared	Computer Genreated Random Sequence determined treatment group: 2 nebulized treatments of 3 ml of generic epinephrine at 1:1000 given 30 min apart Oral Dexamethasone at 1mg/kg or placebo after first nebulized treatment. + 5 (0.6 mg /kg) daily doses of Dex or placebo with max of 10 mg/day. Parents taught how to administer. 90 min post intervention blinded physician determines the disposition
Outcome Evaluation	Primary: admission rates of the 4 groups by 7 days post ED presentation. Secondary: Respiratory status s/p intervention in ED RDAI Ssore, O2Sats, length and severity of symptoms

II. Are the results of the study valid?

Was the assignment of patient randomized?	Yes done using computer generated permuted blocks of 8 with identical packaging, solution characteristics. Patient caregiver, nurse, MD, pharmacy all blinded.
Have authors identified all important confounding factors?	Evaluated multiple confounding variables: Prematurity, hx of intubation, tobacco exposure, other clinically significant illness, hx of atopy, RSV status, duration of sx at presentation, age, sex, RDAI score. Previous treatments (Antibiotics, nebulizer treatement) Of note: RSV, hx of atopy, RDAI>6, pharmacy error did not effect the primary outcome studied.
Were all patients entered in study properly accounted for and attributed?	Yes. 800 randomized patients, 797 completed the study. Three lost to f/u were not included in the final data analysis.
Was follow up complete?	Yes. Patients families were contacted daily via telephone and a chart review of admission was done 22 days post ED visit. ONLY 3 patients lost to follow up total (not included in final analysis)
Were patients, health care workers, and study personnel blinded?	Yes, identical packaging, similar flavoring, follow up was blinded to intervention. Investigators, research staff, physicians, patients, data collectors, all blinded. Effects of EPI may have been difficult to mask
Were study groups similar at the start?	Yes, Median age 5 mo, similar sex dist. RDAI score

	median 8, HR 150 med, Ox Sats 97% med, Temp 37.6 med, RSV status all in mid 60%. Time of presentation all on day 3-4.
Aside from intervention were groups treated equally	Research Nursing interventions were consistent. "ill patients" were treated for underlying problems ie (hosp or surgery) on as needed basis. Treatment prior to enrollment was not described. Pharmacy error in group 1 and 3 with 0.8mg /kg of decadron in 23 pts. Additional bronchodialator treatments at 90 min ordered by physician in 20%. Similar numbers in each group terminated oral Dex (19,13,20,12) all due to phys prescribing oral prednisone. Pharmacist errors in 23 patients in group 1 and 23 patients in group 3

III. Results

How large was the treatment effect? Primary outcomes: Hospital admission rates were lower in the Epi/Dex compared to placebo. Relative risk of admission was 0.64 (CI 0.45-0.95) represents statistical significance HOWEVER when they adjusted for multiple comparisons, CI changed to include 1.0 or non-significant (0.37-1.15) So authors conclude there was a trend towards statistical significance	3556 screened, 1715 met criteria, 800 enrolled. of the 1841 inelligible 867 had prev wheezing or RAD, 90 had RDAI >15, 343 had RDAI <4. Of the 800 enrolled patients: by the 7th day: 1. 17% admitted 2. 23% 3. 25% 4. 26%

Absolute treatment effect?
In secondary outcomes, there was improvement in RDAI score and respiratory rate during the initial ED visit. The greatest effects in the Epi/Dex and EPI groups. There was a sig diff when compared to placebo

CER = control event rate (%) EER =

Admission	CER	EER	ARR, 95% CI	NNT, 95% CI
By Day 7	26.4	17.1	9 (1.25, 17.31)	11 (5.8, 79.7)
By Day 22	26.9	18.5	8 (0.10, 16.44)	12 (6.1, 986.9)

experimental event rate (%) ARR = absolute risk reduction (%) NNT = number needed to treat CI = confidence interval (%)

Relative risk for admission groups 1:4
Without adjustment:
0.65 with 95% CI of 0.45-0.95 P= 0.02
With adjusted values:
0.XX with 95% CI of XXX-XXX P = 0.07
11 infants need treatment to prevent one admission.
Relative risk for admission groups 2 or3:4
NO significant change in admission risk
Unadjusted p=0.87
Adjusted p= 0.52

The size of the confidence intervals suggests poor precision and that these estimates are not very precise. Closed the CI's the more precise the data.

IV

What are the clinically important outcomes?	NNT is 11 with group 1 vs placebo Racemic epi alone or with Dex significantly improved RDAI score at 1 hr status post treatment. Median time to D/C: 1. 4.6 hrs 2. 4.9 3. 5.1 4. 5.3 1:4 comparison is stat sig for time to d/c. Return to PCP or Medical provider? 1. 47% 2. 47 3. 53 4. 42 3:4 comparison is stat sig for return to MD Group 1 was only group to appear to be breathing close to quietly and feeding close to normal

Are the treatment outcomes worth the potential harms?	Uncommon adverse events Pallor: 76 Tremor: 15 Vomit: 14 One hosp infant had transient HTN in groups 2 and 3 with resolution.

Comments:

Seemed to exclude sicker patients so may have limited applicability

Seems to suggest a synergistic effect between epi and dex in less ill patients

Overall failed to show convincing evidence of benefit though there was a suggestion towards some benefit in the epi/dex group in patients who were mild-to-moderatly ill.