Classics in Pediatric Hospital Medicine

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ABBREVIATIONS
CI: confidence interval
CRP: c-reactive protein
HS: hypertonic saline
LOS: length of stay
SBI: serious bacterial infection
s-TREM-1: soluble triggering receptor expressed on myeloid cells
UTI: urinary tract infection
VUR: vesicoureteral reflux

www.hospitalpediatrics.org
doi:10.1542/hpeds.2014-0219

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154 - 1663; Online, 2154 - 1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

FAILURE OF ANTIBIOTIC PROPHYLAXIS…AGAIN

We have decided to take a new look at 3 classics in hospital medicine. The first addresses the subject matter voted most likely to induce a Hospitalist versus Urologist thumb-wrestling match: antibiotic prophylaxis in urinary tract infection (UTI) with vesicoureteral reflux (VUR). Antibiotic prophylaxis has been prescribed for VUR for some time, and recent literature has sparked the debate.[1] *So, we thought this randomized double-blind placebo-controlled trial was worth investigating.*

The study.

This was a randomized double-blind placebo-controlled trial to examine the effect of antibiotic prophylaxis after UTI on recurrence and renal scarring in patients with VUR over 12 months. The primary outcome was number of UTIs. Secondary outcomes included asymptomatic bacteriuria, UTI with resistant bacteria, antibiotic administration for concomitant infections, and worsening of scarring.

The key findings.

The authors randomized 93 children (66.7% boys) aged 1 to 12 years with febrile UTI and VUR grades I to IV (73% grades III–IV). Ten of the 47 in the antibiotic group and 3 of 46 patients in the placebo group developed symptomatic UTIs (absolute risk increase of 14.8% [−28.0 to −1.0], $P = .03$). There was no difference in any other outcomes, including scarring. The trial was stopped early.

Why do we care?

A large trial designed to definitively answer the question of prophylaxis unfortunately raised more questions than it answered.[2] The trial by Hari et al is valuable because it contains a different population, boys, with more severe reflux than in the Randomized Intervention for Children with Vesicoureteral Reflux trial. The study was stopped early, so results have to be taken with a grain of urea, but given the increased risk, it likely represents a true finding. Unfortunately, infants <1 year of age were not included. In our eyes, this is another vote in favor of watchful waiting, and another reason to avoid prophylaxis in the absence of grade V reflux.

Hari P, Hari S, Sinha A, et al. Antibiotic prophylaxis in the management of vesicoureteric reflux: a randomized double-blind placebo-controlled trial [published online ahead of print August 31, 2014]. *Pediatr Nephrol*.

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FAILURE OF INFLAMMATORY MARKERS…AGAIN

The magic bullet in predicting infantile serious bacterial infection (SBI) has proven elusive. This time we are in Israel, where researchers investigated markers of inflammation in infants <90 days of life.

The study.

This was a prospective trial of infants 3 days to 3 months old presenting to the emergency department in Israel who underwent a full septic workup, including complete blood count; urinalysis; and blood, urine, and cerebrospinal fluid cultures. The infants had levels of procalcitonin, C-reactive protein, and soluble triggering receptor expressed on myeloid cells (s-TREM-1) assessed. Initial complaints included temperature >38°C or <35.7°C, emesis, apnea, lethargy, pathologic jaundice, decreased intake, and respiratory distress. Infants with underlying comorbidities, prematurity <37 weeks, and previous antibiotics were excluded. Infants with and without SBI were compared, and the markers were assessed for sensitivity, specificity, and area under the receiver operating curve.

The key findings.

A total of 112 infants were evaluated, with a total of 19 SBIs (17%). The mean age in the SBI group was 32 days (±27) and in the non-SBI group the mean age was 38 days (±19). The most common SBI was UTI (13/19), followed by meningitis and bacteremia. The sensitivity, specificity, and area under the receiver operating curve of C-reactive protein were 45%, 82%, and 0.60 (95% confidence interval [CI] 0.38–0.82); for procalcitonin, 55%, 75%, and 0.63 (95% CI 0.41–0.86); and for s-TREM-1, 82%, 48%, and 0.61 (95% CI 0.47–0.74).

Why do we care?

Although the rate of SBI was high (17%), the infants evaluated were from broad categories, reflecting a realistic approach. This study is small, but suggests a limited role for laboratories in predicting infantile SBI. A novel marker, s-TREM-1, has previously shown excellent sensitivity, but showed poor performance in the current trial.[1] A larger trial, replicating this "real-world" design, along with further study of s-TREM-1, may inform hospitalists on proper laboratory use. For the moment, it is prudent to ask if laboratory results should influence management.

Stein M, Schachter-Davidov A, Babai I, Tasher D, Somekh E. The accuracy of C-reactive protein, procalcitonin, and s-TREM-1 in the prediction of serious bacterial infection in neonates [published online ahead of print October 7, 2014]. *Clin Pediatr (Phila)*.

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FAILURE IN BRONCHIOLITIS… AGAIN

Finally, what self-respecting journal club would be complete without bronchiolitis. In light of the updated American Academy of Pediatrics guidelines,[1] we have scoured the globe for publications that may change practice. An Italian study reports on nebulized 7% hypertonic saline (HS) paired with hyaluronic acid.

The study.

This was a prospective randomized double-blind, controlled trial of nebulized 7% HS/0.1% hyaluronic acid versus normal saline inhaled twice daily in bronchiolitis. Infants <7 months of age with a first episode of bronchiolitis were randomized, with severity scoring with treatments. Infants <37 weeks and with previous wheezing and comorbidities were excluded. The primary outcomes were length of stay (LOS), safety, and clinical scores.

The key findings.

Of 42 infants, 39 completed the trial. Cough occurred in 4 with HS, compared with 2 with normal saline, and was not statistically significant. There was a trend toward reduced LOS in treatment versus placebo (4.1 vs 4.8 days, $P = .09$), but it did not reach significance. The clinical severity scores did not differ.

Why do we care?

This is a small trial that contains a novel treatment. The authors report their findings as a positive result, but by our interpretation, this was another negative trial. The LOS did not change, and was long at 4.1 to 4.8 days, and there was no change in clinical severity scores. It is small, so perhaps a larger trial with a different dosing mechanism may prove beneficial, but we suspect the axiom "First Do No Harm" is reinforced again.

Nenna R, Papoff P, Moretti C, et al. Seven percent hypertonic saline–0.1% hyaluronic acid in infants with mild-to-moderate bronchiolitis. *Pediatr Pulmonol*. 2014;49(9):919–925

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