

Research Media Watch:

Kamale V, Thamke R.

1) Association Between Hypertonic Saline and Hospital Length of Stay in Acute Viral Bronchiolitis A Reanalysis of 2 Meta-analyses

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Importance

Two previous meta-analyses of nebulized hypertonic saline (HS) on hospital length of stay (LOS) in acute viral bronchiolitis have suggested benefit. Neither study fully addressed the issue of excessive heterogeneity in the cohort of studies, indicating that it may be inappropriate to combine such dissimilar studies to estimate a common treatment effect.

Objective

To reanalyze the existing data set for sources of heterogeneity to delineate the population most likely to benefit from HS.

Data Sources

They used the previously analyzed cohort of randomized trials from 2 published meta-analyses comparing HS with normal saline (or, in 1 case, with standard of care) in infants hospitalized for bronchiolitis. We also repeated the search strategy used by the most recent Cochrane Review in the Medline database through September 2015.

Study Selection

Eighteen randomized clinical trials of HS in infants with bronchiolitis reporting LOS as an outcome measure were included.

Data Extraction and Synthesis

The guidelines used for abstracting data included LOS, study year, setting, sample size, type

of control, admission/discharge criteria, adjunct medications, treatment frequency, mean day of illness at study enrollment, mean severity of illness scores, and mean age.

Main Outcomes and Measures

Weighted mean difference in LOS and study heterogeneity as measured by the I² statistic.

Results

There were 18 studies included of 2063 infants (63% male), with a mean age of 4.2 months. The mean LOS was 3.6 days. Two main sources of heterogeneity were identified. First, the effect of HS on LOS was entirely sensitive to the removal of one study population, noted to have a widely divergent definition of the primary outcome. Second, there was a baseline imbalance in mean day of illness at presentation between treatment groups. Controlling for either of these factors resolved the heterogeneity (I² = reduced from 78% to 45% and 0%, respectively) and produced summary estimates in support of the null hypothesis (that HS does not affect LOS). There was a weighted mean difference in LOS of -0.21 days (95% CI, -0.43 to +0.02) for the sensitivity analysis and +0.02 days (95% CI, -0.14 to +0.17) for studies without unbalanced treatment groups on presentation.

Conclusions and Relevance :

Prior analyses were driven by an outlier

population and unbalanced treatment groups in positive trials. Once heterogeneity was accounted for, the data did not support the use of HS to decrease LOS in infants hospitalized with bronchiolitis.

Comment:

The mainstay of treatment for acute bronchiolitis remains supportive. Nebulized HS is a safe and potentially effective treatment of infants

with acute bronchiolitis. From the above data the two main source of heterogeneity were identified firstly the widely divergent definition of the primary outcome and secondly imbalance in mean days of illness at presentation between the treatment groups. It has been seen that HS did not change the length of hospital stay but still it is the treatment of choice todate. However further studies are required to make the necessary changes.

2) Association Between Laboratory Calibration of a Serum Bilirubin Assay, Neonatal Bilirubin Levels, and Phototherapy Use

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Importance

The American Academy of Pediatrics treatment recommendations for neonatal jaundice are based on age-specific total serum bilirubin (TSB) levels. In May 2012, Ortho Clinical Diagnostics adjusted the calibrator values for Vitros Chemistry Products BuBc Slides (Ortho Clinical Diagnostics), a widely used method to quantify TSB, after concerns of positively biased results.

Objective

To investigate the association between recalibration of a reflectance spectrophotometry serum bilirubin assay and TSB levels and phototherapy use among newborns.

Design, Setting, and Participants

Descriptive study comparing TSB levels and phototherapy use before and after recalibration at Kaiser Permanente Northern California, a large, integrated health care delivery system. The study

evaluated live births at or after 35 weeks' gestation at 12 facilities that used universal serum bilirubin screening before (January 1, 2010, through April 30, 2012; n = 61 677) and after (July 1, 2012, through December 31, 2013; n = 42 571) recalibration. The analysis took place in December 2015.

Intervention Recalibration of bilirubin testing instruments.

Main Outcomes and Measures

Proportions of newborns with (1) at least 1 TSB value at or above 15 mg/dL; (2) at least 1 TSB level exceeding the American Academy of Pediatrics phototherapy threshold; (3) phototherapy during the birth hospitalization; and (4) at least 1 readmission for phototherapy.

Results

In 104 420 infants (61 677 in the prerecalibration period and 42 511 in the

postrecalibration period), a TSB was obtained in 99.2% of infants during birth and in 99.5% of infants within the first 30 days after birth. The postrecalibration period was associated with a 1.25 mg/dL (95% CI, 1.19-1.31; $P < .001$) decrease in mean maximum TSB, which led to a 39% relative reduction (from 20.4% to 12.4%) in infants with a TSB level of 15 mg/dL or more and a 51% relative reduction (from 9.3% to 4.5%) in infants with a TSB level that was at or above the American Academy of Pediatrics phototherapy threshold. Phototherapy during birth hospitalizations was reduced by 59% (absolute risk reduction, 5.5%; 95% CI, 4.7%-6.1%) and readmissions for phototherapy by 53% (absolute risk reduction, 1.8%; 95% CI, 1.4%-2.3%).

Conclusions and Relevance

Modest recalibration-induced reductions in mean TSB concentrations was associated with a significant reduction in the percentage of infants with clinically significant hyperbilirubinemia. Current laboratory accuracy standards are insufficient to detect biases that can have significant clinical effect. These data underline the need for increased integration of laboratory expertise into clinical guidelines and to support international initiatives to standardize laboratory measurements.

Comment:

Clinical impact of the BuBc Slide Recalib Ortho Clinical Diagnostics' method of measuring

bilirubin is unique when compared to other commonly used methods. The difference between the methods is the way different bilirubin fractions are measured or calculated. Total bilirubin is measured with the TBIL slide that measures both conjugated (including delta bilirubin covalently bound to albumin) and unconjugated bilirubin species. Most other methods calculate the concentration of unconjugated bilirubin by subtracting the direct reacting fraction containing the conjugated species from the total value of bilirubin. Ortho platforms use a separate slide, BuBc, that directly measures both conjugated (excluding delta bilirubin) and unconjugated fractions. The BuBc slide also has an ultrafiltration layer that excludes large molecules, such as hemoglobin, minimizing interference from hemolysis. The ultrafiltration layer also excludes albumin, which is why the BuBc slide does not measure delta bilirubin, but it allows the calculation of delta bilirubin (TBIL-BuBc).

Since bilirubin concentrations can be measured using both the TBIL and BuBc slides, there are different options for how values are reported. To match with other bilirubin methods, the total bilirubin value reported from the TBIL slide, the unconjugated bilirubin value from the BuBc slide, and a calculated conjugated value derived from subtracting the unconjugated value from the total (measured Tbil-measured Bu= Bc (calculated).) This allows any delta bilirubin that may be present in the patient to be accounted for in the conjugated value.

3) Sequential Therapy is Superior to Triple Therapy for *Helicobacter pylori* Infection in Children: A Meta-Analysis

Huang, Y. & Zhan, X. *Ind J Pediatr* (2016) 83: 307. doi:10.1007/s12098-015-1878-0

Objectives

To assess the efficacy and safety of 10-d sequential therapy compared to 5 to 14-d triple therapy for treating *Helicobacter pylori* infections in children according to the eradication rates.

Methods

The Cochrane Library, MEDLINE, EMBASE, China National Knowledge Infrastructure databases, and other sources were searched in November 2014 without language restrictions. Randomized controlled trials (RCTs) that compared sequential therapy with triple therapy for *H. pylori* eradication in children were included. Dichotomous data were pooled to obtain the relative risk (RR) of the eradication rate with a 95 % confidence interval (CI).

Results

Fourteen RCTs with 1698 participants (718 and 980 for sequential and triple therapy, respectively) were included. The intention-to-treat eradication rates were 73 % (95 % CI: 70–76) and 66 % (95 % CI: 64–70) for sequential and triple therapy, respectively. The pooled RR was 1.16 (95 % CI: 1.09–1.23), resulting in a number needed to treat of 16 (95 % CI: 10–48), favoring sequential therapy. Sequential therapy was superior to 7- and 10-d triple therapy. Sequential and triple therapy did not differ significantly in the overall risk of adverse effects.

Conclusions

In children, sequential therapy appears to be superior to triple therapy for *H. pylori* eradication, although the eradication rates remain lower than the expected goal with both treatments. Factors-associated with a higher risk of eradication failure, such as compliance and antimicrobial resistance, remain insufficiently investigated. Therefore, further high-quality RCTs are needed to compare these different eradication treatment approaches.

Comment:

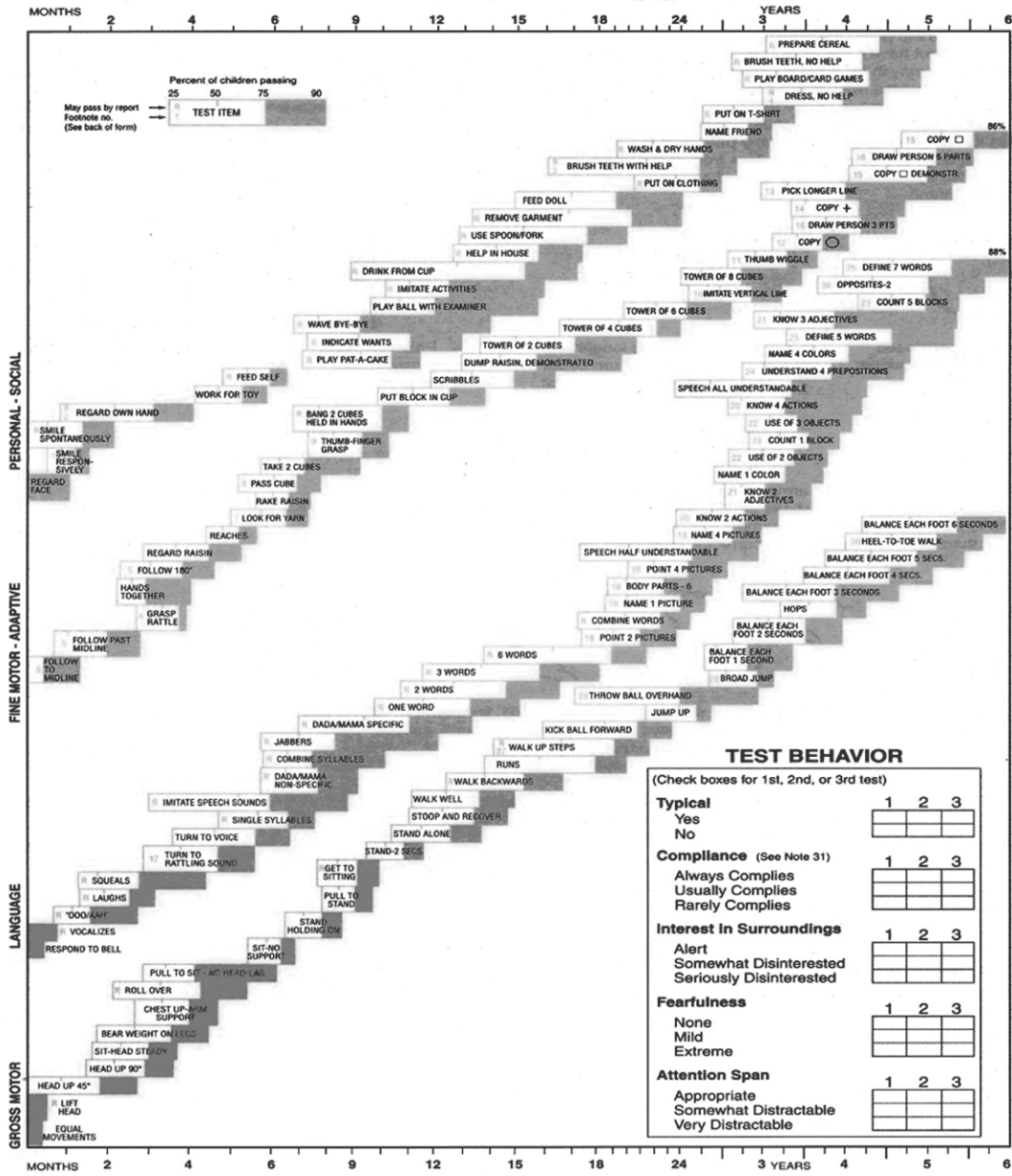
Helicobacter pylori is the principal cause of peptic ulcer disease and gastric cancer. Most children infected with *H. pylori* are asymptomatic. Antral gastritis is the most common manifestation in children. Duodenal and gastric ulcers may be associated with *H. pylori* gastritis in adults but is uncommon in children. The risk of gastric cancers, including non-Hodgkin lymphoma (eg, mucosa-associated lymphoid tissue [MALT]) and adenocarcinoma, is increased in adults. Eradication of *H. pylori* has been shown to prevent the recurrence of peptic ulcer disease, to reverse gastric atrophy – a precursor of gastric cancer – and to cure some localized low-grade gastric lymphomas. Sequential therapy seems to be better than triple therapy in terms of eradicating the *H. pylori* infection however further studies requires to make the change in the protocol.

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