218. Viral respiratory infections in children: causes and consequences

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Effect of inhaled hypertonic saline solution to treat infants hospitalized with viral bronchiolitis

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Background and aims: At present only symptomatic treatment is available for acute viral bronchiolitis, none of these are evidence-based. Recent trials show a reduction in hospital stay after inhalation of 3% hypertonic saline solution. This randomised double-blind, placebo-controlled interventional multicenter trial, performed at 12 Dutch hospitals, compares nebulization with hypertonic saline, either a 3% or 6%, with 0.9% isotonic saline. The primary end point is the time to discharge, aiming to achieve a 25% reduction in hospital stay.
Methods: Children younger than two years with clinical diagnosis of viral bronchiolitis, not responding to a single inhalation with Salbutamol may be included after informed parental consent. Trial medication will be nebulized three times daily until discharge criteria are met. Calculated power of 80% requires totally 156 patients.
Results: The analysis was performed on the data of 160 patients, all included in the seasons 2009-january 2011. Patient characteristics and the number of exclusions didn't differ significantly. The duration of hospital stay, need for tube feeding and supplemental oxygen shows no significant difference, but there's a trend that 3% seems tob e more effective than the other 2 concentrations.
Conclusions: Preliminary analysis showed no significant reduction in hospital stay but a trend that 3% hypertonic saline is the most effective regarding duration of hospital stay, need for supplemental oxygen and tube feeding. The use of 6%

hypertonic saline seems safe but has no additional benefit even compared with 0,9%. More research will be necessary to clear up this trend.

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7% hypertonic saline and hyaluronic acid and in the treatment of infants mild-moderate bronchiolitis

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The treatment of bronchiolitis is only supportive. The aim of our study was to evaluate the efficacy of hypertonic saline and hyaluronic acid (HS-HA) given by inhalation, in infants hospitalized for mild-moderate bronchiolitis. In a double-blind placebo-controlled study, 42 infants (26 males) less than 6 months of age (median age 2 months) were enrolled and randomly assigned to receive either HS-HA (7% NaCl + 0.1% HA) (n:21) or normal saline (n:20) at a dose of 2.5 ml twice a day for three days. To all infants a clinical severity score was assigned at the admission and four times daily during the hospitalization. Main outcome measures of our study were: number of days of hospitalization and reduction of the severity score. No differences were observed between the two groups for sex, age and clinical severity score at the admission. One child interrupted the protocol in the study group and two in the placebo group. 21% of children in the study group and 11% in the placebo group had mild cough after the aerosol. No difference was observed between the two groups with regard to the number of days of hospitalization (placebo group: 3.5 days vs study group: 3.1 days, p=0.4) and to the clinical score reduction during the first three days of hospitalization (placebo group: 3.3 vs study group: 3.7, p=0.6). HS-HA is a safe but not effective therapy in treating infants hospitalized for mild-moderate bronchiolitis.

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Evaluating the risk of lower respiratory tract infection (LRTI) hospitalizations due to respiratory distress syndrome (RDS) in late preterm

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Background: Premature birth results in underdeveloped lung function that increases their risk for respiratory infection and morbidity. The prevalence of RDS requiring intervention in premature births is significant, including those considered late preterm. RSV is the most prevalent cause for LRTI hospitalizations in infants. This study sought to determine what the independent risk of RDS diagnosis at birth has on LRTI hospitalisations in late preterm infants during the first year of life.
Methods: Late premature infants (33-36 weeks gestational age) hospitalized within the first year of life for a LRTI were extracted from the Medical Claims I3 database (2000-2008). Univariate analyses were conducted to compare the differences between infants with and without an RDS event at birth. A multivariate model was developed to determine the independent association of RDS and LRTI hospitalization. Statistical significance was set at 0.05.
Results: 31178 late preterm infants (52% male) were identified during the study timeline. 2297 (7.4%) late preterm infants were hospitalized due to a LRTI; a hyaline membrane disease or RDS diagnosis (ICD-9 code: 769) was observed in 962 late preterms (3%). Multiple logistic regression analysis showed a strong and significant relationship between RDS and LRTI hospitalization (OR 5.2, 95% CI 4.4–6.2).
Conclusion: Late preterm infants with RDS event at birth are 5 times more likely to be hospitalized due to LRTI during the first year of life compared to late preterm without RDS event at birth. This risk factor should be considered when evaluating a premature infants risk for respiratory hospitalization.

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Rhinovirus lower respiratory tract infections and healthcare utilisation of prematurely born infants during infancy

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Aim: RSV lower respiratory tract infections (LRTIs) are associated with increased healthcare utilisation and cost of care in both term and prematurely born infants. Rhinovirus (RV) LRTI has been associated with increased respiratory morbidity at follow-up in term born infants. Our aim was to determine whether RV LRTIs were associated with increased health related cost of care in prematurely born infants and to compare any effect with that of RSV LRTIs.
Methods: 130 infants born <36 weeks GA were prospectively followed from birth until one year. A nasopharyngeal aspirate (NPA) was taken every time the infants had a LRTI either in hospital or in the community. NPAs were tested for RV, RSV A and B, human metapneumovirus, parainfluenza 1-3, influenza A and B and adenovirus. Healthcare utilisation was determined by examining hospital and GP records and the cost of care calculated from the NHS reference costing scheme and British National Formulary for Children.
Results: 16 infants developed RV LRTIs (RV group), 14 infants developed RSV LRTIs (RSV group), eight infants developed both RSV and RV LRTI ("RSV and RV" group); 68 infants had no LRTI (no LRTI group). Compared to the no LRTI group, the RV group had higher costs for GP attendances ($p<0.01$) and medications ($p<0.01$) and the RSV group had higher hospital admission costs ($p<0.05$). The "RSV and RV" group had more PICU days than the other three groups ($p<0.05$) and greater hospital admission costs than the no LRTI ($p<0.01$) and the RV group ($p<0.05$).
Conclusion: RV LRTIs were associated with increased health related costs of care, but these were greater for RSV LRTIs and, in particular, dual infections with RSV and RV.

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Human respiratory syncytial virus infection *in vivo* and *in vitro* induces expression of the B cell differentiation factor BAFF

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Background: In RSV disease, innate immune mediators expressed by infected airway epithelial cells are known to strongly influence both early inflammatory responses and the subsequent development of an adaptive immune response. The B lymphocyte differentiation factor, B cell activating factor of the TNF family, BAFF or TNFSF13B, has been shown to be present in autopsy samples from RSV Infected infants (Reed, J.L. *et al.* JID; 199:1128-38)
Aims: To determine if BAFF expression is elevated in the airways of infants with severe RSV Bronchiolitis and if RSV infection of primary Airway epithelial cells *in vitro* induces BAFF expression.
Methods and results: BAFF protein, as measured by ELISA, was elevated in bronchiolar alveolar lavage fluid collected from the lungs of infants with severe RSV infection (n=10, mean 833pg). Non infected control group infants, admitted for elective surgery had lower levels (n=7, mean 12pg, $p<0.027$). To further confirm these results BAFF mRNA was measured by taqman real-time PCR in bronchial brushings from patients with RSV bronchiolitis (n=5) and healthy infants (n=6). Average BAFF mRNA expression was around 20 fold higher in samples obtained from infected infants ($p<0.01$). When *In vitro* cultures of primary airway epithelial cells isolated from healthy children were infected with RSV A2 strain, BAFF mRNA expression was induced 200 fold with maximum expression at 12 hours post infection (n=4, $p<0.01$). Protein analysis showed expression of up to 170pg BAFF protein at 48 hours post infection.
Conclusions: Airway Epithelial cell expression of the B cell differentiation factor BAFF is induced by RSV infection both *in vivo* and *in vitro*.

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Prenatal exposure to PCBs and dioxins is associated with increased risk of wheeze and infectious diseases in 2-year old children

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Food may contain toxicants (from environmental pollution or formed during food preparation). These toxicants may cross the placental barrier and affect the foetus' immune system. The aim of this study was investigated if prenatal exposure to acrylamide, dioxins and polychlorinated biphenyls (PCBs) affect the childrens immunological health status.
Pregnant women were recruited to the birth cohort BraMat (n=205). The occurrence of common childhood infections and periods of more than 10 days of dry cough, chest tightness or wheeze in the children was assessed by annual questionnaires (n = 195 and 184, respectively). Maternal intake of toxicants was estimated from a validated food frequency questionnaire filled in by the mothers at midterm. The sum of six non-dioxin-like PCBs (PCB 28, 52, 101, 138, 153, 180), and the sum of toxic equivalents of 29 dioxins and dioxin-like PCBs were used. Logistic and linear multivariate regression analyses were performed. Adjustments were made for gender, mode of delivery, Apgar score, breast-feeding, parity, birth season and maternal history of atopy, age, BMI, education and smoking.
No associations between prenatal exposure to acrylamide and the health outcomes were found. At age one year, prenatal exposure to PCBs and dioxins was associated with increased risk of wheeze and exanthema subitum, and increased number of upper respiratory tract infections. Similar results were obtained in preliminary anaylsis for wheeze and upper resiratory track infections at two year of age.
Our findings suggests that prenatal exposure to dioxins and PCBs increase the risk of wheeze and infectious diseases during the first two years of life.

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Airborne transmission of respiratory syncytial virus (RSV) infection

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Introduction: RSV is a highly contagious pathogen and spreads among groups of young children, within families and between patients in hospital. RSV is thought to spread predominantly by hands contaminated with infectious respiratory secretions [1]. However, it remains unclear if RSV can be spread by aerosol. Knowledge of this is important as it is assumed in many hospitals that aerosol transmission of RSV does not occur.

Aim: To determine if patients with RSV bronchiolitis produce aerosolised particles containing RSV capable of infecting human respiratory epithelial cells (A549).

Method: 18 infants with "RSV Bronchiolitis" were recruited. An Andersen microbial impactor was placed 100cm from the head of the patient and run for 30min fractionating collected particles into different aerosol size distributions. Room air was impacted into 20ml of RPMI growth media and its infectivity of A549 was determined using plaque assays. Immunofluorescence staining of the infected A549 cells was used to confirm RSV infection.

Results: 17 infants produced infectious airborne particles less than 4.7μ. We estimated the number of infectious RSV within aerosols of less than 4.7μ produced from 12/17 patients to be 188.5±68 (mean ± SEM, range 2.4 to 4044) in 10 litres of air. This volume would be inhaled by a 3.1kg baby in 10 minutes (respiratory rate 40/min; tidal volume 8ml/kg).

Conclusion: Infants with RSV bronchiolitis produce aerosols that contain infectious RSV in aerosols small enough to deposit in the lower airways. These findings may influence infection control strategies to prevent aerosol transmission of RSV in a hospital setting.

Reference:

[1] Goldmann DA. Pediatric Infectious Disease Journal 2000;19(10 Suppl).