**ID:** 91  
**TITLE:** TWO-YEAR OUTCOMES OF PREMATURE INFANTS ENROLLED IN THE FIRST-IN-HUMAN STUDY OF AMNION CELLS FOR BRONCHOPULMONARY DYSPLASIA  
**AUTHORS:** Atul Malhotra 1,2,3, Rebecca Lim 3,4, Joanne C Mockler 3,4, Euan M Wallace 3,4  
**AFFILIATIONS:** 1 Monash Newborn, Monash Children's Hospital, Melbourne, Australia  
2 Department of Paediatrics, Monash University, Melbourne, Australia  
3 The Ritchie Centre, Hudson Institute of Medical Research, Melbourne, Australia  
4 Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia  

**CONTENT:**

We have previously reported on the immediate safety and neonatal outcomes of six premature infants with severe bronchopulmonary dysplasia (BPD) who were administered human amnion epithelial cells (hAECs). (Reference 1) One infant died in the neonatal period due to unrelated causes. In this study, we aimed to assess the follow-up outcomes of the five surviving infants till 2-year corrected age (CA). The focus of the study was to assess long-term safety of low dose hAEC administration in neonates.

References:

Study follow-up consisted of assessment of any serious adverse events, growth, respiratory, cardiac and neurodevelopmental outcomes at four time points (6, 12, 18 and 24 months corrected age). Study follow-up investigations included chest x-rays, cranial, abdominal ultrasounds, and echocardiograms at regular intervals and an MRI brain at 2-years CA.

All five infants were alive at 2 years CA. Median time to wean off home oxygen was 24 (10-36) months. Two infants had associated pulmonary hypertension, which resolved by 2 years of age. Three infants were re-hospitalised briefly for viral infections during the follow-up period. There were no cranial or abdominal ultrasound abnormalities noted. MRI brain findings included normal (n=2), and mild-moderate white matter loss (n=2). Neurodisabilites diagnosed included hemiplegic cerebral palsy (n=1), global developmental delay (n=2), and severe hearing loss (n=3). All infants were ambulant. No evidence of tumour formation was noted on serial physical examinations or on any imaging.

There were no long-term adverse events observed in the study infants that could be attributed to hAEC administration. We observed long-term effects of extreme prematurity, and severe BPD in the cohort. A dose escalation study to establish the optimum dose of hAECs in infants at risk of BPD is currently underway. (Reference 2)

**COI:** None declared
ID: 434

TITLE: SEMI-QUANTITATIVE LUNG ULTRASOUND EVALUATION OF DEVELOPING BPD IN EXTREMELY PRETERM NEONATES: PRELIMINARY RESULTS OF A MULTICENTER PROSPECTIVE COHORT STUDY

AUTHORS: Valentina Dell’Orto 1
Giulia Vigo 2
Roberto Raschetti 3
Roberta Centorrino 4
Nadya Yousef 5
Valentina Condo 6
Silvia Lama 7
Virgilio P. Carnielli 8
Fabio Mosca 9
Daniele De Luca 10

AFFILIATIONS: 1 Department of Neonatology, G. Salesi University Hospital, Ancona, Italy
2 APHP-South Paris University Hospitals, Medical center “A.Beclere”, Paris, France
3 APHP-South Paris University Hospitals, Medical center “A.Beclere”, Paris, France
4 APHP-South Paris University Hospitals, Medical center “A.Beclere”, Paris, France
5 APHP-South Paris University Hospitals, Medical center “A.Beclere”, Paris, France
6 Neonatal Intensive Care Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy
7 Neonatal Intensive Care Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy
8 Department of Neonatology, G. Salesi University Hospital, Ancona, Italy, and Marche Polytechnic University, Ancona, Italy
9 Neonatal Intensive Care Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy, and Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy
10 APHP-South Paris University Hospitals, Medical center “A.Beclere”, Paris, France

CONTENT:

Lung ultrasound (LUS) is a non-invasive, radiation-free, point-of-care technique used to diagnose acute neonatal respiratory disorders, and to guide respiratory care using semi-quantitative LUS aeration scores. LUS findings of bronchopulmonary dysplasia (BPD) have not yet been formally characterized, and the role of LUS in developing BPD remains to be defined.

Objective. To describe semi-quantitative LUS findings in extremely preterm infants with developing BPD and investigate the reliability of a LUS score to predict BPD.

Preterm neonates (30 weeks’ gestation or less) were eligible and underwent serial LUS examination (d0, d7, d14, d28 and at 36w of postconceptional age): LUS score was calculated as previously described. Blood gases were measured by arterialized capillary samples, or adequately calibrated transcutaneous devices, within 1h from LUS. Basic clinical data were also registered. BPD was diagnosed according to NICHD criteria at 36 weeks post-gestational age.

We enrolled 38 neonates (GA 26.9 (1.9);BW 904 (291);5’Apgar 7 (2.8);CRIB2 11.4 (3.9) Males 17(44.7%), of whom 27(71%) were diagnosed with BPD. LUS score correlates with oxygenation index at any time point (min p=0.35) and remains stable over time (p=0.196 RM-ANOVA within patient analysis). LUS values are significantly different betweenpatients who develop BPD and those who don’t (RM-ANOVA between patients’ analysis p=0.002; post-hoc p<0.0001 at 36 weeks’ post-conception; Fig.1). LUS calculated in the first day of life is not predictive of BPD (AUC:0.58;p=0.467), but LUS calculated at 1 week of life can reliably predict BPD (AUC: 0.813 (0.63-0.93);p=0.01; best cut-off: 5, sensitivity 90%; specificity 63%; Fig.2).

Conclusions. LUS findings described by a semi-quantitative score do not change over time but the LUS score is significantly higher in babies with BPD as compared to those who do not develop BPD. LUS at 7d of life may reliably predict the diagnosis of BPD at 36 weeks post-conceptional age.
Images: https://www.eisewhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=63e6566d098aae10e5f2c6edac8616cf-MjAxOS0wNSM1Y2UyNjY2YzViYzkx

Fig 1 LUS score in patients with bronchopulmonary dysplasia (BPD) and without bronchopulmonary dysplasia (No BPD), at different end points: 1-7-14-28 day of postnatal age and at 36 weeks of GA.

Fig 2 ROC curves for BPD prediction. ROC curve plots sensibility and 1-specificity for LUS score at 1 (LUS0)-7 (LUS 7)-14 (LUS 14)-28 (LUS 28) days of life and 36 weeks of gestational age (LUS 36).

COI: None declared
ID: 809

TITLE: GESTATIONAL HYPERTENSIVE DISORDERS AND INTRAUTERINE GROWTH RESTRICTION AS RISK FACTORS FOR BRONCHOPULMONARY DYSPLASIA: A META-ANALYSIS AND META-REGRESSION.

AUTHORS: Maria Pierro 1; Eduardo Villamor-Martinez 2; María Álvarez-Fuente 3; Steven H. Abman 4; Eduardo Villamor 2

AFFILIATIONS: 1 Mother’s and Baby’s Health Department, Division of Neonatology, Fondazione Poliambulanza, Brescia, Italy
2 Department of Pediatrics, Maastricht University Medical Center (MUMC+), School for Oncology and Developmental Biology (GROW), Maastricht, the Netherlands.
3 Hospital Ramón y Cajal, Madrid, Spain
4 Department of Pediatrics, University of Colorado School of Medicine, Denver, Colorado, USA.

CONTENT:

Gestational hypertensive disorders (GHD), including gestational hypertension and preeclampsia, are major risk factors for preterm birth and intrauterine growth restriction (IUGR). The adverse intrauterine environment associated with GHD and/or IUGR is considered to play a pathogenic role in some complications of very preterm birth, including bronchopulmonary dysplasia (BPD). We aimed to conduct a systematic review of studies reporting on GHD and IUGR/small for gestational age (SGA) as risk factors for BPD.

PubMed/MEDLINE and EMBASE databases were searched. A random-effect model was used to calculate odds ratios (OR) and 95% confidence intervals (CI). Sources of heterogeneity were determined by subgroup and meta-regression analyses. BPD was defined as supplemental oxygen requirement on postnatal day 28 (BPD28), or at the postmenstrual age of 36 weeks (BPD36). K=number of studies.

We found 148 studies meeting the inclusion criteria. Meta-analysis could not detect an association between GHD and BPD28 (k=24, OR 1.04, CI 0.79-1.37) or BPD36 (k=48, OR 1.04, CI 0.90-1.20). Gestational age (GA) was significantly higher in the GHD group and meta-regression revealed that the higher GA in this group was significantly associated with a lower odds of BPD. Analysis restricted to the studies without significant differences in GA, revealed a positive association between GHD and BPD36 (OR 1.51, CI 1.24-1.83). Regarding IUGR/SGA, meta-analysis showed a significant association with BPD36 (k=73, OR 1.44, CI 1.24-1.68) but not BPD28 (k=16, OR 1.06, CI 0.70-1.70). GA was significantly higher in the IUGR/SGA group, and meta-regression showed that the higher GA in this group was significantly associated with a lower risk of BPD.

Our data suggest that IUGR/SGA and GHD are risk factors for developing BPD but the association is significantly confounded by the lower GA of the “control” group.

COI: None declared
ID: 854

**TITLE:** PREVENTIVE EFFECTS OF MATERNAL CDP-CHOLINE, ADMINISTERED EITHER ALONE OR IN COMBINATION WITH A STEROID, ON LUNG INJURY IN A NEONATAL RAT MODEL OF HYPEROXIA

**AUTHORS:** Cansu Koc1, Mehmet Cansev1, Tulin Alkan2, Ilker Mustafa Kafa3, Meri η Cetinkaya4

**AFFILIATIONS:** 1 Department of Pharmacology, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey
2 Department of Physiology, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey
3 Department of Anatomy, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey
4 Department of Neonatology, Health Sciences University, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey

**CONTENT:**

Bronchopulmonary dysplasia (BPD) is the major cause of chronic lung disease in preterm infants. As current management approaches have little efficacy due to multifactorial pathogenesis, novel preventive and therapeutic options are required. CDP-choline, an endogenous intermediate in phosphatidylcholine (PC) synthesis was shown to reduce hyperoxia-induced severe lung damage when injected to newborn rats. However, the effect of maternal CDP-choline on neonatal lung structure was not evaluated yet. The aim of this study was to evaluate the effect of maternal administration of CDP-choline, alone or in combination with betamethasone, for prevention of hyperoxic lung injury in newborn rats.

Pregnant Spraque-Dawley rats were grouped to receive either single or combined therapies of CDP-choline and/or betamethasone. Pups born to these dams were subjected to hyperoxia for 10 days after the first day of life. After decapitation at 11 days of life; lung phospholipid levels, apoptotic cell death and alveolarization were evaluated. Radial alveolar count was used for determination of alveolarization. Both total phospholipid and PC levels were established in lung tissues. Western blot analysis was performed for evaluation of apoptotic cell death.

Maternal CDP-choline administration significantly enhanced total phospholipids and PC levels, improved alveolarization, and reduced apoptosis in rat pups subjected to hyperoxic lung injury. Antenatal betamethasone significantly increased lung phospholipid levels, but had no significant effect on apoptosis and alveolarization. The lung phospholipid levels were significantly higher and apoptosis was potently reduced in pups whose dams received the combination of betamethasone and CDP-choline, compared to single administration of both agents.

This is the first study that shows the preventive effect of maternal CDP-choline treatment on hyperoxic lung injury in newborn rats. Our findings show that the combination of betamethasone and CDP-choline provides greater benefit in reducing neonatal hyperoxic lung injury by both increasing phospholipid levels and improving alveolarization and decreasing apoptosis. These data suggest the clinical utility of this combination for prevention of BPD.

**COI:** None declared