**Figure.** Percentage of neonates with RDS by delivery gestational age, stratified by duration of ACS exposure.

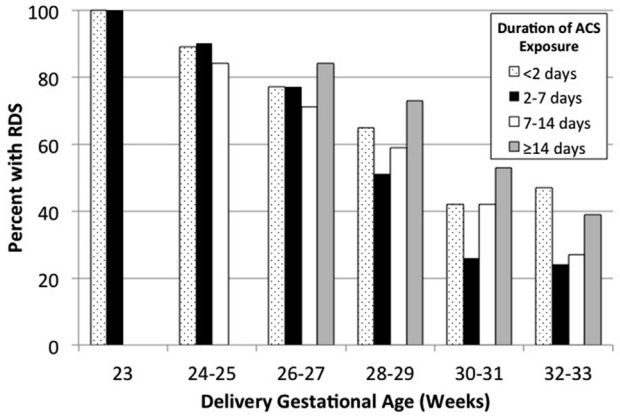


Table. Regression model examining factors associated with RDS.

| Characteristic | aOR | 95% CI | p-value |
|---|---|---|---|
| ACS Duration: <2 days | 1.41 | 1.06-1.86 | 0.017 |
| ACS Duration: 2-7 days | -Referent- | - | - |
| ACS Duration: 7-14 days | 1.38 | 1.04-1.82 | 0.024 |
| ACS Duration: ≥14 days | 2.64 | 1.99-3.50 | <0.001 |
| Delivery gestational age (per 1 week increase) | 0.66 | 0.63-0.69 | <0.001 |
| Male neonate | 1.24 | 1.02-1.52 | 0.035 |
| GPN study enrollment | 3.11 | 2.42-4.01 | <0.001 |
| Received antenatal magnesium sulfate | 0.85 | 0.69-1.03 | 0.104 |

## 529 The effects of antenatal corticosteroids in twin pregnancies complicated by preterm birth

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**OBJECTIVE:** Data regarding the effects of antenatal corticosteroids (ACS) in twins are limited due to the insufficient number of twin pregnancies enrolled in randomized controlled trials on ACS. Furthermore, the interpretation of available data is limited by the fact that the administration of ACS-to-delivery interval is greater than 7 days in a large proportion of twins, a factor that been shown to affect the efficacy of ACS and has not been controlled for in some of the previous studies. The objective of the current study was to assess the effect of ACS on neonatal outcomes in women with twin pregnancies who completed a course of ACS 1-7 days prior to delivery.

**STUDY DESIGN:** In this retrospective cohort study, data on twin infants born between 24+0 and 33+6 weeks and admitted to tertiary neonatal units in Canada during 2010-2013 were obtained from the Canadian Neonatal Network. Neonatal outcomes were compared between twins who received ACS between 24 hours and 7 days prior to delivery (twins-ACS group) and those who did not receive ACS (twins-control group).

**RESULTS:** 1) Out of 3,024 twin neonates who met the inclusion criteria, 1382 (69.5%) received a complete course of ACS 1-7 days prior to delivery and were compared to 607 (30.5%) who did not receive ACS. 2) Neonates in the twins-ACS group had a lower rate of mortality (2% vs. 7%, p<0.001) and grade 3-4 intraventricular hemorrhage (IVH) (7% vs. 12%, p=0.01). 3) Following adjustment for confounding factors including gestational age at delivery, hypertension, outborn status, parity, small for gestational age, and mode of delivery, administration of ACS in twins was associated with a lower odds of neonatal mortality, but was not associated with any of the neonatal morbidity outcomes (Table). 4) Findings were similar for the subgroup of twins delivered at less than 30+0 weeks of gestation.

**CONCLUSION:** Administration of ACS 1-7 days prior to delivery in twin pregnancies is important as it is associated with a lower odds of neonatal mortality, and the magnitude of effect is similar to that previously observed in singletons.

| Effect of ACS administrated 1-7 days prior to delivery compared to no ACS | |
|---|---|
| Outcome | Adjusted Odds Ratio (95% CI) |
| Mortality | 0.34 (0.17, 0.66) |
| Bronchopulmonary dysplasia | 0.62 (0.37, 1.04) |
| Intraventricular hemorrhage grade 3 or 4 | 0.60 (0.33, 1.09) |
| Retinopathy of prematurity >= stage 3 | 3.14 (0.78, 12.72) |
| Necrotizing enterocolitis | 1.07 (0.53, 2.18) |

## 530 Preterm umbilical cord blood is enriched for progenitor cells

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**OBJECTIVE:** Umbilical cord blood (CB), an established cell source for hematopoietic stem cell transplant, is also a potential source for emerging cell therapies to treat perinatal brain injuries. CB collection is often restricted to full-term deliveries, as preterm units are ineligible for public banking. We sought to determine feasibility of collecting preterm CB and to compare the cell content to full-term CB.

**STUDY DESIGN:** CB was collected by trained staff or OB providers via in utero or ex utero collection immediately following infant deliveries of <34 weeks gestation. After the umbilical cord was prepped with chlorhexidine/isopropyl alcohol, CB was collected via venipuncture into either an attached bag or vials containing citrate phosphate dextrose anticoagulant. CB volume, cell concentrations, viability, microbiologic cultures, and potency (ALDH bright cells and colony forming units (CFU)) were compared to an existing dataset of full-term (=34 weeks) CB units from a public cord blood bank.

**RESULTS:** CB from 101 umbilical cords was collected at 93 preterm deliveries. Data from multiple pregnancies (n=7) were excluded from analysis if more than one CB unit was collected. Median gestational age was 31 weeks (range 23-33), and median birth weight was 1,595 gms (range 510-3,710). While no babies had positive blood cultures, 10 units had positive sterility cultures. Median total nucleated cell count (TNCC)/kg was 13.2x10e7 (range 0.9-154.7x10e7/kg). As expected, preterm CB units had lower CB volumes and TNCCs than full-term units. While the median concentration of CFUs was lower in preterm CB, the concentration CD34+ and ALDH bright cells were significantly higher than full-term CB.

**CONCLUSION:** Preterm CB collection is feasible, and doses well above those utilized in recent brain injury trials can be obtained. Compared to full-term CB, preterm CB has a higher concentration of CD34+ and ALDH bright cells, suggesting that progenitor cells may be highly mobilized early in fetal gestation.

Comparison of premature and full-term cord blood units; median (range)

| | Preterm (N=86) | Full Term (N=5,282) | p value* |
|---|---|---|---|
| Volume (mL) | 21 (1-85) | 93 (24-286) | <0.0001 |
| TNCC (x10e8) | 2.0 (0.1-25.2) | 11.8 (2.9-55.5) | <0.0001 |
| CD34+ (per uL) | 45.0 (2.5-393.2) | 35.7 (0.0-1045.0) | 0.0167 |
| % of CD45+ that are ALDH bright (N=76/5,271) | 0.46 (0.07-3.29) | 0.38 (0.00-3.63) | 0.0039 |
| CFU (x10e3 per ml) (N=82/5,279) | 25 (3-176) | 37 (0-173) | <0.0001 |
| *Wilcoxon | | | |

| Analysis | Bayley-III cognitive composite score | | Mean difference (95% CI) adjusted | Bayley-III language composite score | | Mean difference (95% CI) adjusted | Bayley-III motor composite score | | Mean difference (95% CI) adjusted |
|---|---|---|---|---|---|---|---|---|---|
| | Pessary | Control | | Pessary | Control | | Pessary | Control | |
| Survivors only | N=111 | N=60 | | N=107 | N=56 | | N=109 | N=58 | |
| mean score (+/-SD) | 101.3 (14.1) | 103.9 (8.2) | -2.3 (-5.1 to 0.5) | 104.4 (14.6) | 104.7 (8.3) | -0.1 (-3.1 to 2.8) | 106.2 (15.4) | 105.9 (8.9) | 0.7 (-2.4 to 3.8) |
| Survivors + deceased children | N=118 | N=80 | Relative Risk (95% CI) | N=114 | N=76 | Relative Risk (95% CI) | N=116 | N=78 | Relative Risk (95% CI) |
| Survival without disability n(%) | 109 (92.4) | 59 (73.8) | 1.25 (1.24 to 3.78) | 98 (86.0) | 53 (69.7) | 1.23 (1.04 to 1.45) | 110 (94.8) | 57 (73.1) | 1.30 (1.13 to 1.49) |

## 531 Long-term effects of cervical pessary for preterm birth prevention in twin pregnancy with short cervix: a 3 years follow-up of the ProTwin trial

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**OBJECTIVE:** Recently it has been shown that cervical pessary might be effective in the prevention of preterm birth in women with a multiple pregnancy and a cervical length (CL) <38mm. Here, we report the long-term outcome of the children included in that study.

**STUDY DESIGN:** In the ProTWIN trial, women with a multiple pregnancy had been randomised to pessary or no pessary. As positive effects of pessary on prolongation and improvement of neonatal outcome had only been seen in women with a CL <38mm, we limited follow-up to that group (133 mothers, 157 vs 111 children in pessary and control group respectively). At 3 years corrected age, the children were invited to undergo a Bayley Scales of Infant and Toddler Development-third edition (Bayley-III) assessment. We compared mean cognitive, language and motor function scores between the pessary and control group, adjusted for dependence of twins and triplets and potential confounders in survivors (Table). Analysis including deceased children was performed to calculate the survival rate without disability (disability defined as any Bayley III <1SD below the mean). In sensitivity analysis we used multiple imputation to deal with missing cases resulting from loss-to-follow-up.

**RESULTS:** Of 268 children born to 133 women in our study group, 241 surviving children were eligible for follow-up of whom 171 children (71%, 111 pessary vs 60 control group) underwent a Bayley-III assessment. In total 27 children died (7 in pessary vs 20 control group) of whom only 2 in the follow-up period. Analysis including deceased and disabled children showed a higher survival without disability in the pessary group when compared to controls (92.4 vs 73.8%, p=0.006). When analysis was limited to survivors, we found neither statistical nor clinically relevant differences in Bayley-III scores between both groups (Table). Analysis using multiple imputation showed comparable results.

**CONCLUSION:** In women with a twin pregnancy and a CL < 38 mm, cervical pessary increases survival without neurodevelopmental disability in children at 3 years corrected age. As among survivors Bayley-III scores were similar between pessary and non-pessary users, use of a pessary seems to be without adverse long term neurodevelopmental effects for children.

## 532 The effects of nifedipine and atosiban on the neonatal brain: a secondary analysis of the APOSTEL III trial

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**OBJECTIVE:** To compare the effects of nifedipine and atosiban on the neonatal brain in neonates born at less than 32 weeks of gestation.

**STUDY DESIGN:** We performed a secondary analysis of the APOSTEL III-trial (NTR 2967), a randomized clinical trial which allocated women with threatened preterm labor between 25-34 weeks of gestation to nifedipine or atosiban. Women delivering at = 32 weeks of gestational age in the two main participating centers were included for this study. To evaluate difference in type and severity of preterm brain injury, all neonatal ultrasounds made during neonatal admission and at term age were systematically scored (table 1). To identify variables associated with preterm brain injury, logistic regression was performed for predictors and protectors for brain injury obtained from the international literature.

**RESULTS:** We included 117 neonates, born from 104 women, of which 66 neonates were exposed to atosiban and 51 to nifedipine. Baseline characteristics were comparable between the groups. Brain injury was observed in 22 (43.1%) in the nifedipine group and in 37 (56.1%) neonates in the atosiban group (p = 0.26). Logistic regression showed no association between type of tocolysis and brain injury (OR 0.6; 95% CI: 0.29-1.24). Factors independently associated with decreased or increased brain injury were respectively caesarean section (OR 0.31; 95% CI: 0.12-0.83) and mechanical ventilation (OR 2.73; 95% CI: 1.04-7.12).

**CONCLUSION:** Brain injury in children born before 32 weeks of gestation was comparable between tocolysis using nifedipine or atosiban. The possible protective effect of a cesarean section in extreme preterm birth should be further explored in this selected population.

**Table 1. Scoring table for the degree of brain injury**

| Grade | Severity of Injury | Type of Injury |
|---|---|---|
| **Grade 0** | No brain injury | None |
| **Grade 1** | Mild brain injury | • Grades I and II intraventricular hemorrhage<br>• Persistent pathologic non-decreasing inhomogeneous flaring between day 7-14<br>• Thinning of the corpus callosum<br>• Pronounced or dilated ventricles (increased anterior horn width, ventricular index or thalamo-occipital distance) with the ventricular index < p97. |
| **Grade 2** | Severe brain injury | • Intraventricular hemorrhage grade III / IV or parenchymal/ periventricular hemorrhagic infarction<br>• Post hemorrhagic ventricular dilatation (ventricular index >p97)<br>• Intracerebral local cystic lesions<br>• Cystic periventricular leukomalacia<br>• Cerebellar hemorrhage<br>• Parenchymal infarction<br>• Intraparenchymal hemorrhage. |