Contribution of intrauterine exposure to infection and inflammation in the neurodevelopmental outcome of premature infants up to 5 years of age

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Background

Infection and inflammation are leading responsible of spontaneous preterm delivery (sPTB) at earlier gestational ages. There are several references reporting an association between clinical chorioamnionitis, histological chorioamnionitis or funisitis and the occurrence of long-term disabilities. However, in women with **preterm labor (PTL)** or preterm prelabor rupture of membranes (PPROM) without any clinical suspicion of infection, there are no data assessing the influence of infection an inflammation on neurodevelopmental outcome when these women are managed with amniocentesis to rule out **microbial invasion of the amniotic cavity (MIAC) or intra-amniotic inflammation (IAI).**

Objective

To evaluate the contribution of infection and inflammation in the neurodevelopmental outcome of premature infants whose mothers with PTL or PPROM were managed with amniocentesis to identify MIAC or IAI.

Methods

- Prospective cohort study performed in infants up to **5 years old with sPTB <34.0 weeks. If undelivered** at time of amniotic fluid culture results, a **targeted antibiotic treatment** was initiated according to the microorganisms isolated in the amniotic fluid.
- MIAC was defined based on amniotic fluid **aerobic/anaerobic/*Mycoplasma* cultures** and IAI based on amniotic fluid **interleukin-6 levels**. Histological chorioamnionitis and funisitis were defined as **neutrophil infiltration of the chorion/amnion/umbilical vessel walls**
- **Neurodevelopment was evaluated by Ages & Stages Questionnaires®** mailed-out at 23.5 corrected months. We defined poor neurodevelopmental outcome when at least one of the areas evaluated (communication, fine and gross motor, problem solving and personal social) scored below expected for age
- Logistic regression analysis evaluated the independence of antenatal, intra-partum and neonatal outcomes to predict a poor neurodevelopmental outcome.

Results

- Among 97 infants evaluated, 43% were born from women with PPROM and 57% with PTL. MIAC and IAI occurred in 54% and 70% of cases, respectively, and funisitis in 34%. Only 21 infants (22%) scored below expected for age.
- Steroids administration was significantly lower in those premature infant who scored worse. **Among all variables evaluated, EOS and funisitis showed to be an independent factor of abnormal ASQ test being communication and gross motor those areas that significantly scored worse. No association was found with MIAC or IAI.**

	Abnormal neurodevelopmental outcome n 21	
	OR	95% CI
Smoking during pregnancy	1.25	0.36-4.38
Low social-economic status	4.13	0.51-33.5
Breastfeeding	0.73	0.27-1.96
Antenatal steroids	0.16	0.02-1.04
PPROM > 18 hours	1.12	0.41-3.02
Emergency cesarean section	0.94	0.35-2.54
Gestational age at delivery	0.88	0.73-1.06
Male gender	1.88	0.69-4.87
Birthweight	0.99	0.99-1.00
Umbilical artery pH <7.1	1.11	0.11-10.8
Apgar score < 7 at 5 minutes	3.00	0.68-14.6
NICU admission (days)	1.02	0.99-1.03
Early-onset sepsis	**4.00**	**1.38-11.56**
Intraventricular hemorrhage	2.06	0.62-6.88
Periventricular leukomalacia	3.89	0.51-29.5
Retinopathy of prematurity	1.06	0.15-7.34
Clinical chorioamnionitis at delivery	1.36	0.43-4.34
IAI	1.08	0.37-3.15
MIAC	0.99	0.37-2.60
'Sterile'"IAI	1.14	0.33-3.95
Histological chorioamnionitis	0.57	0.19-1.70
Funisitis	**3.01**	**1.06-8.51**

Conclusions

The occurrence of EOS and funisitis were considered independent factors of abnormal neurodevelopmental screening test meanwhile MIAC or IAI were not.