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Intra-amniotic infection and the fetal corpus callosum in women with preterm labor

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Objective

To evaluate if fetal corpus callosum changes exist in fetuses of mothers admitted for preterm labor (PTL) or preterm prelabor rupture of membranes (PPROM) and the influence of intra-amniotic infection and/or inflammation (IAI).

Methods

In this prospective cohort study, fetal neurosonography and amniocentesis were performed at admission in singleton pregnant women with PTL and/or PPROM between 24.0-34.0 weeks. This group was further subdivided into two groups that were: 1) PTL/PPROM with intra-amniotic infection and/or inflammation (IAI group), and 2) PTL/PPROM without IAI (non-IAI group). The control group included outpatient pregnant women without PTL or PPROM matched for gestational age at study ultrasound. Fetal corpus callosum was evaluated by neurosonography. Corpus callosum total length, body maximum thickness, total area and Witelson subdivisions areas (rostrum, genu, rostral body, anterior midbody, posterior midbody, isthmus and splenium) were evaluated. Corpus callosum areas were assessed offline using a semi-authomatic in-house Matlab tool. Data was adjusted for fetal weight percentile, fetal sex, head circumference, non-cephalic presentation and for PPROM at admission. Protein S100B concentrations were measured in amniotic fluid from women with PTL/PPROM and compared to 20 amniotic fluid Biobank samples for reasons other than PTL/PPROM or fetal brain pathology, matched for gestational age at amniocentesis. Data was adjusted for fetal weight percentile, fetal sex, gestational age at amniocentesis and PPROM at admission.

Results

From 2018-2021, 143 fetuses were included: 95 fetuses were from mothers admitted with symptoms of PTL or PPROM: 41 (28.7%) were in the IAI group and 54 (37.8%) in the non-IAI group. 48 (33.6%) fetuses were included in the control group. There were no significant differences in maternal age, BMI, race, smoking habit, nulliparity, assisted reproductive techniques, gestational age at ultrasound or fetal sex. There were higher prevalence of fetuses below 10th percentile (26.8% in the IAI group, 13.0% in the non-IAI group and 8.3% in the control group) without fetal-placental Doppler significant differences. Only 65% of patients with PTL/PPROM had the optimal CC image to be processed to assess the CC areas. Corpus callosum total area (mm2) was smaller in the PTL/PPROM groups (IAI and non-IAI) when compared to control group, but similar between them (IAI: 0.72mm2 (0.59;0.81); non-IAI: 0.71mm2 (0.63-0.82) vs control: 0.78mm2 (0.71;0.91), p=0.038 (IAI vs. control) and p=0.004 (non-IAI vs control)). These differences seem to be at the expense of the rostral body (IAI: 0.158 (0.126-0.169); non-IAI: 0.156 (0.136-0.175) vs. 0.179 (0.147-0.203), p= 0.015 and p=0002), posterior midbody (IAI: 0.074 (0.054-0.084); non-IAI: 0.076 (0.067-0.090) vs. control: 0.088 (0.073-0.107), p= 0.017 and 0.021) and isthmus areas (IAI: 0.052 (0.046-0.066); non-IAI: 0.058 (0.047-0.076) vs. control: 0.069 (0.058-0.088), p= 0.003 and p=0.007). . Amniotic fluid concentrations of protein S100B were higher in the IAI group compared to control group (2030.6pg/ml (993;4883.5) vs. 74.8 (44.7;93.7), p=0.048) after adjustment for possible confounding factors. The non-IAI group seems to be an intermediate group different from the IAI group and the control group (1070.3 pg/ml (365.1-1463.2), p=0.038 and p<0.001, respectively).

Conclusion

Fetuses with PTL / PPROM present smaller corpus callosum total area, mostly at the expense of the posterior regions, and higher amniotic fluid concentration of protein S100B, a white matter damage biomarker. These findings support that the neurological damage observed in children born preterm have, at least in part, a prenatal origin.