CONCLUSION: This trial failed to demonstrate a benefit of antioxidant supplementation in reducing the rate of gestational hypertension, preeclampsia and adverse conditions among patients with or without risk factors.

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3 Magnesium sulfate to prevent adverse neurological injury: providing biological evidence

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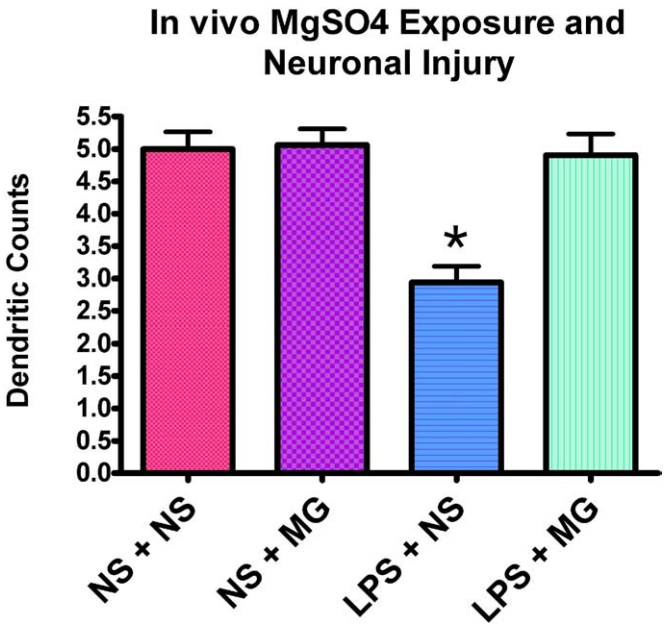
OBJECTIVE: Recent clinical trials suggest that antenatal exposure to magnesium sulfate (MG) reduces the risk of adverse neurological outcomes in ex-preterm children. About 70% of preterm infants result from spontaneous preterm birth (PTB) which is highly associated with intrauterine inflammation. Using a mouse model of intrauterine inflammation, these studies sought to assess if MG prevents brain injury.

STUDY DESIGN: CD-1 mice on E15-16 were randomized to intrauterine infusion (IU) of LPS or saline (NS). After IU, dams were randomized to intraperitoneal (IP) treatment with MG (270mg/kg X1, then 27mg/kg q20 min for 4 hrs and 2nd dose of 270mg/kg) or equal volumes of NS. From the 4 treatment groups, (IU NS+IP NS; IU LPS+IP NS; IU LPS+IP MG; and IU NS+IP MG), fetal brains (FB) were collected and neuronal cultures were created. Immunocytochemistry and confocal microscopy were performed to assess morphology and number of dendritic processes. FB from the 4 groups were used to investigate mRNA expression of cytokines, cell death, and neuronal and glial differentiation.

RESULTS: IL1 mRNA was differentially expressed between the treatment groups (P=0.009); LPS+NS and LPS+MG had increased IL1 levels compared to controls. Markers of pro-oligodendrocytes were altered by LPS+NS but not by LPS+MG (P=0.06). Caspase-1 mRNA was increased 1.3-fold in LPS and 1.6-fold in LPS+MG compared to controls (P=0.03). Neuronal cultures from LPS+NS demonstrated fragility, decreased aggregation, and a reduced number of dendritic processes; this neuronal injury was prevented by MG (*P<0.001, FIG).



CONCLUSION: Prevention of neuronal injury in inflammation-associated PTB may be a key mechanism by which MG prevents cerebral palsy. These studies provide biological plausibility for the clinical use of MG in preterm deliveries.

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4 Induction of labour versus expectant monitoring for intrauterine growth restriction at term (The Digitat Trial): a multicentre randomised controlled trial

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OBJECTIVE: Induction of labour is common treatment for pregnant women with a fetus suspected of intrauterine growth restriction (IUGR) at and near term, but its effectiveness has never been assessed in a randomised controlled trial.

STUDY DESIGN: We conducted a multicentre randomised controlled trial in 52 hospitals in the Netherlands, between November 2004 and November 2008. Pregnant women with a singleton pregnancy suspected of IUGR beyond 36+0 weeks of gestation were randomly allocated to either induction of labour or expectant monitoring using a web-based allocation system. The primary outcome was a composite measure of adverse neonatal outcome, defined as death before hospital discharge, a 5-minute Apgar score <7, an umbilical artery pH <7.05 or admission to the neonatal intensive care. Secondary outcome was operative delivery. Analysis was by intention-to-treat. This trial has been assigned the ISRCTN 10363217.

RESULTS: We randomly allocated 321 women to induction of labour and 329 women to expectant monitoring. Time until delivery was 0.9 days (IQR 0.7-1.7) in the induction group vs 10.1 days (IQR 5.5 −16.0) in the expectant monitoring group (difference of the mean -9.6 days [95% CI −10.9; −8.4], p<0.001). Median birth weight was significantly lower in the induction group; 2410 grams ([QR 2212 - 2655] vs 2580 grams ([IQR 2267 - 2870]; mean difference −147 grams [95% CI −208; −87], p<0.001). Composite adverse neonatal outcome occurred in 16 cases in the induction group versus 16 cases in the expectant monitoring group (6.2% vs 6.1%; difference 0.1% [95% CI −4.0%; 4.1%], p=1.0). The number of caesarean sections was also comparable in both groups (n=41 versus n=41; 13.6% vs 13.3%; difference 0.3% [95% CI −5.2%; 5.7%], p=0.9).

CONCLUSION: In women with a singleton fetus suspected of growth retardation at term, a strategy of induction of labour is equally effective as a strategy of expectant monitoring.

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