167 MSC-CONCENTRATED SUPERNATANT: A NOVEL THERAPEUTICAL APPROACH IN INFLAMMATION-INDUCED PRETERM BRAIN INJURY?

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Background and aims Preterm brain injury of premature born infants is a main cause of disability and represents an enormous individual, familial and social burden. Up to 50% of these children suffer from disabilities such as cerebral palsy and cognitive disorders. The aetiology of brain injury has been considered to be multifactorial. Factors such as hyperoxia or inflammation are important pathomechanism in the development of brain injury.

As infections and subsequent inflammation are almost unavoidable on NICUs, new anti-inflammatory approaches are needed. In differend experimental settings, mesenchymal stem cells (MSCs) show these anti-inflammatory abilities. Although intravenously administered MSCs get trapped in the lung, therapeutic effects in target tissue are detectable, thereby indicating paracrine mechanisms. Since MSC-supernatants contain molecules with immunosuppressive functions, such as the identified TSG-6, we wondered whether MSC supernatants contain additional, maybe synergistically acting factors. The objective of this study is to evaluate the effect of concentrated MSC-supernatant on brain damage caused by inflammation.

Methods Wistar rats were randomized in 4 groups (vehicle/vehicle, vehicle/concentrated MSC-supernatant, LPS/vehicle, LPS/concentrated supernatant). LPS (0.25mg/kg) was administered at p3, concentrated MSC-supernatant at p3 and p4. At p5, animals were transcardially perfused, brains were removed and snap-frozen for molecularbiological analysis.

Results At p5, LPS-treated animals show a marked increase in apoptosis, whereas additional treatment with concentrated MSC-supernatant results in a decrease in neural apoptosis.

Conclusions Concentrated MSC-supernatant showed promising effects on inflammation-induced brain damage in an experimental model of encephalopathy of prematurity.

168 SERUM VEG F LEVELS IN PRETERM INFANTS: EFFECTS OF GESTATION AND LASER OR BEVACIZUMAB THERAPY FOR RETINOPATHY OF PREMATURITY

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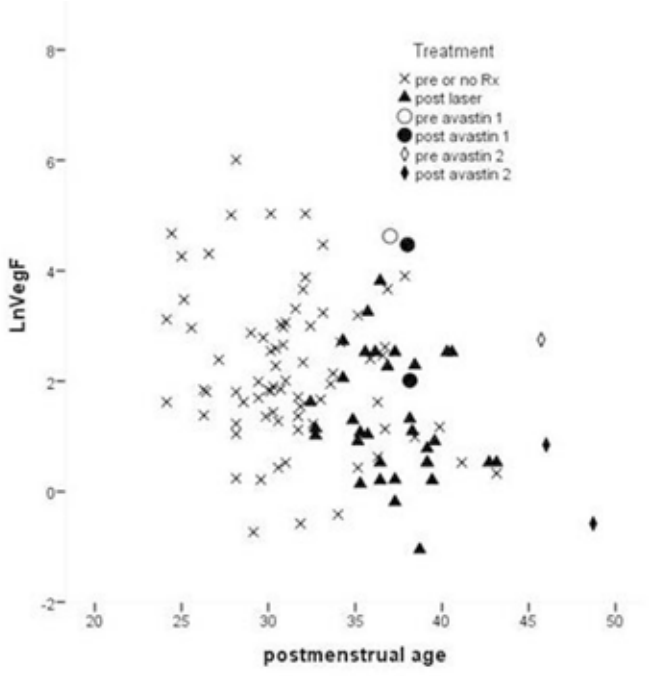
Background Bevacizumab, a monoclonal antibody to the vascular endothelial growth factor Veg F appears to offer successful treatment of severe retinopathy of prematurity (ROP), but there are no human data addressing potential systemic absorption and effects on systemic Veg F levels in preterm infants. We measured Veg F in preterm infants during their stay in intensive care including some infants treated with laser or bevacizumab for ROP.

Methods Serum and plasma were salvaged as part of a consented research study in preterm infants from delivery to discharge. Veg F levels were measured using flow cytometry and analysed in relation to gestation, postmenstrual age and any ROP treatment.

Results 26 infants, median 26 wks gestational age (range 23–29 wks) contributed 114 samples. 5 received laser treatment for ROP, 2 bevacizumab. Serum VegF levels decreased with increasing postmenstrual age. Levels for those treated for ROP did not differ from those untreated. The two infants that received bevacizumab had lower VegF levels after treatment than before.



Abstract 168 Figure 1

Conclusions This first data in human preterm infants with and without ROP treatment show trends with increasing postmenstrual age, and that VegF levels in infants treated with bevacizumab do not appear to differ from those untreated or those treated with laser. Individual infants receiving bevacizumab had lower VegF levels in the first week after injection than before. As bevacizumab treatment increases efforts should be made to further assess effects on circulating VegF.

169 HOSPITAL MORTALITY IN 2,437 INFANTS IN THE AUSTRALIAN, NEW ZEALAND AND UK BOOST II TRIALS OF NEONATAL OXYGEN SATURATION TARGETING

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Background The optimal oxygen saturation (SpO_2) for preterm infants is unknown. Three BOOST II trials in Australia, New Zealand and UK are comparing outcomes in infants < 28 weeks after randomisation to SpO_2 targeting of 85–89% vs 91–95%, using masked oximeters.[1] In interim analysis the high target increased 36 week survival in infants whose oximeter had been upgraded with new, more accurate software.[2,3]

Methods Pooled analysis of hospital mortality by target, overall and by old or new software.

Results

Abstract 169 Table 1

Hospital mortality of infants by SpO2 target overall

	SpO2 85–89%	SpO2 91–95%	Risk Ratio (95% CI)	p value
Hospital mortality	235/1220 (19.3%)	202/1217 (16.6%)	1.16 (0.98–1.38)	0.09

Abstract 169 Table 2

Hospital mortality of infants by SpO2 target, by old vs new software

	Old software				New software			
	SpO2 85–89%	SpO2 91–95%	Risk Ratio (95% CI)	p value	SpO2 85–89%	SpO2 91–95%	Risk Ratio (95% CI)	p value
Hospital mortality*	98/629 (15.6%)	109/630 (17.3%)	0.90 (0.70–1.16)	0.41	137/591 (23.2%)	93/587 (15.8%)	1.46 (1.15–1.85)	0.0015**

There was no significant mortality difference between SpO_2 targets overall. There was significant heterogeneity between old and new software on mortality (test for interaction p=0.006).* Using new software, targeting 91–95% increased hospital survival by 7.4% (from 76.8% to 84.2%) versus targeting 85–89% (p=0.0015).**

Conclusions Pending the primary outcome of disability free survival at 2 years it appears wise not to target 85–89%.

References

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170 MATERNAL ALLOPURINOL ADMINISTRATION DURING TERM LABOR IS NEUROPROTECTIVE IN CASE OF FETAL HYPOXIA; A MULTICENTER RANDOMIZED PLACEBO CONTROLLED TRIAL

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Background Hypoxic-ischemic encephalopathy due to perinatal hypoxia-induced free radical formation is an important cause of long-term neurodevelopmental disabilities. Allopurinol reduces the formation of free radicals, which potentially limits hypoxia-induced reperfusion damage. With this trial we aimed to assess whether maternal allopurinol treatment during fetal hypoxia would reduce the release of brain-tissue-specific biomarkers associated with neonatal brain damage.

Methods We performed a randomized double blind placebo controlled multicenter trial (NCT00189007) studying laboring women at term with imminent fetal hypoxia. Fetal distress was suspected in case of an abnormal fetal heart rate trace, ST-wave abnormalities on fetal ECG or fetal scalp pH<7.20. Women were allocated to receive allopurinol 500 mg IV or placebo immediately prior to delivery. Endpoints were S100B and neuroketal in cord blood, which are brain-tissue-specific biomarkers for brain damage. Because S100B followed a non-normal distribution, we used a poisson regression model with associated RR (95%CI). For neuroketal we report geometric mean differences.

Results We randomized 222 women to allopurinol (n=111) or placebo (n=111). S100B was significantly lower in the allopurinol-group (median 43.4; IQR 20.2–71.5) compared to the placebo-group (median 54.9; IQR 26.8–94.7), RR 0.91 (95%CI 0.88–0.94). Neuroketal did not significantly differ between groups, geometric mean difference –7.57 (95%CI –15.6; 3.57).

Post-hoc analysis showed a marked gender difference in treatment effect in favor of girls for S100B (RR 0.63 (95%CI 0.59–0.68)) and neuroketal (geometric mean difference –16.5 (95%CI –24.6; -1.83)).

Conclusion Maternal treatment with allopurinol during fetal hypoxia reduces damage to neuronal cells as indicated by brain-tissue-specific chemical biomarkers.

171 NIPPV DOES NOT REDUCE BRONCHOPULMONARY DYSPLASIA (BPD) OR DEATH IN EXTREMELY LOW BIRTH WEIGHT INFANTS - A RANDOMISED TRIAL

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Background Standard care of preterm infants includes nCPAP & NIPPV. We compared rates of BPD or death in a randomised trial of NIPPV or nCPAP.

Methods Eligible infants were preterm, birth weight < 1000g; requiring either (i) non-invasive respiratory support within first seven days, "no intubation/early extubation group", or (ii) were < 28 days at first extubation - "prior intubation". Central block randomisation to NIPPV or nCPAP was conducted via the web. Primary outcome was a composite of death (prior to 36 weeks' gestational age [GA]) or BPD at 36 weeks' GA: defined as requiring ventilation; $FiO_2 > 30\%$; or positive oxygen reduction test (ORT). Sample size 1000 (β 80%; 2-tailed α 5%) to demonstrate 20% reduction in primary outcome.

Results 36 international sites enrolled 1007 infants. Observed rates of BPD or death were similar in the two groups. BPD outcome,