397 Treatment with DHA after hypoxia ischemia improves functional outcome in a rat model of perinatal hypoxia-ischemia

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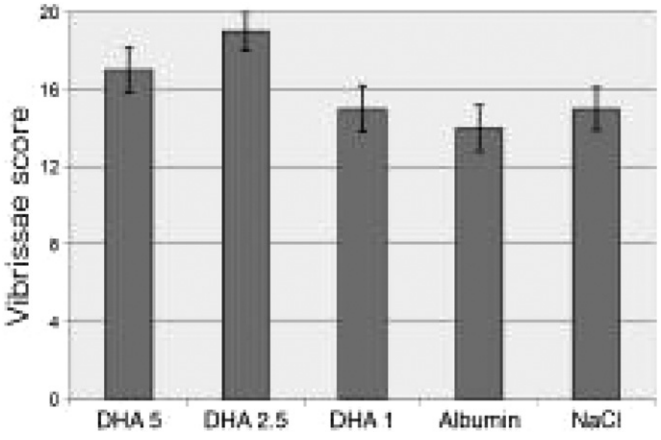
OBJECTIVE: Docosahexaenoic acid (DHA) is a dietary polyunsaturated fatty acid with neuroprotective properties. We hypothesized that DHA treatment after hypoxia-ischemia (HI) would improve functional outcome and reduce brain volume loss in a rat model of perinatal HI.

STUDY DESIGN: Seven-day-old Wistar rat pups from 8 litters (N=96) were divided into 3 treatment groups and 2 control groups. Treatment groups received intraperitoneal (IP) injections of DHA 1, 2.5 or 5 mg/kg as DHA-albumin complex. Control groups received 25% albumin or normal saline (NaCl). Pups underwent right carotid ligation followed by 1.5 hours recovery at 37°C, then 90 minutes in 8% O2 to simulate cerebral HI. Fifteen minutes after HI, pups received control or treatment IP injections. At 14 days, rats underwent bilateral sensorimotor testing using vibrissae-stimulated forepaw placing response. Bilateral hemisphere and regional volumes were calculated from cortex, striatum, and hippocampus, and right hemisphere volume loss was calculated [100*(L−R)/L)].

RESULTS: Post HI treatment with DHA significantly improved vibrissae forepaw placing response (16.9±0.8 treatment vs. 14.7±0.8 controls; normal function=20 $p<.035$, t-test). The predominant effect was limited to the two higher doses (Figure). Post injury DHA treatment did not attenuate brain volume loss in any region compared to controls.

CONCLUSION: Although brain volume loss is not affected by post-ischemia DHA treatment, treatment significantly improves functional outcome, particularly in higher doses.



0002-9378/$ – see front matter • doi:10.1016/j.ajog.2009.10.563

398 DHA pretreatment changes the relationship between subventricular zone volume and contralateral sensorimotor function

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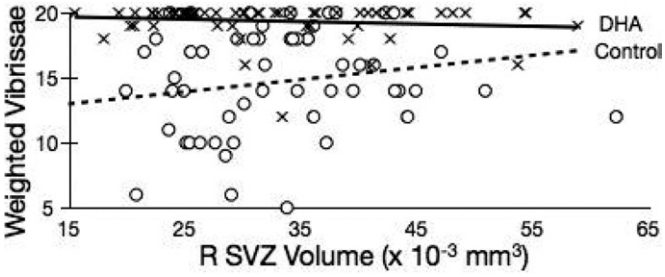
OBJECTIVE: Neurogenesis and proliferation occur in the rodent subventricular zone (SVZ) after cerebral hypoxia-ischemia (HI). We hypothesized that (1) SVZ volumes in rats pretreated with neuroprotective doses of docosahexaenoic acid (DHA) would increase in our model of perinatal HI and (2) this volume increase would have a positive correlation with sensorimotor function.

STUDY DESIGN: Seven-day-old Wistar rat pups from 10 litters (N=120) were divided into 3 treatment groups (intraperitoneal injections of DHA 1, 2.5 or 5 mg/kg as DHA-albumin complex) and 3 control groups (25% albumin, normal saline or no injection). Injections were given, right carotid ligation was performed, followed by 90 minutes in 8% O2, simulating cerebral HI. As we previously reported, at 14 days, DHA pretreated rats demonstrated reduction in sensorimotor deficits using vibrissae-stimulated forepaw placing response. SVZ volumes were calculated by summing bilateral SVZ areas obtained from regularly spaced coronal sections through the dorsolateral SVZ at 2.5X.

RESULTS: SVZ volumes significantly increased in right hemispheres relative to left and did not differ among treatment groups. There was a positive linear relationship between right SVZ volume and contralateral weighted vibrissae score in pooled control groups ($p<.05$). In contrast, in pooled DHA groups with higher vibrissae scores, there was no relationship between SVZ volume and function ($p=.64$). Overall there was no difference in right SVZ volume or in its relationship with right hemisphere damage severity among treatment groups.

CONCLUSION: In controls, bigger SVZ volumes correlated positively with improved function. Although SVZ volumes increased in DHA treated rats similarly to controls, function was sufficiently improved in DHA treated rats such that SVZ expansion did not correlate with improved function.



0002-9378/$ – see front matter • doi:10.1016/j.ajog.2009.10.564

399 Hemodynamic changes in the middle cerebral artery of fetuses undergoing laser surgery for twin-twin transfusion syndrome: evidence of cerebral autoregulation?

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OBJECTIVE: We hypothesized that laser surgery for twin-twin transfusion syndrome (TTTS) would result in fetal hemodynamic alterations, manifested by changes in cerebral vessel resistance with autoregulation of blood flow. The study objective was to compare the middle cerebral artery (MCA) pulsatility index (PI) and mean velocity (mean V) before and after laser surgery for TTTS.

STUDY DESIGN: A prospective observational study of TTTS patients was conducted. MCA Doppler examination was attempted within one day before and after laser surgery for TTTS. Patients were excluded from analysis if MCA Doppler measurements were unavailable (n=41) or if gestational age (GA) was less than 18 weeks (n=13). The pre- and postoperative mean (S.D.) of the MCA PI and mean V z-scores of the recipient and donor fetuses were calculated and compared. Demographic and outcome data were analyzed in relation to the MCA PI and mean V. Data were analyzed using paired t-tests and multivariable linear regression models.

RESULTS: Of 157 patients, 103 met study criteria. The MCA PI z-scores of the recipients increased from −1.29 (1.20) preoperatively to 0.14 (1.52) postoperatively ($p<0.0001$), while the donors' decreased from −0.31 (1.67) to −0.67 (1.29), $p=0.07$. MCA mean V z-scores did not change following surgery in donors and recipients. Some significant associations were identified between changes in the MCA PI and mean V and Quintero stage, GA at surgery, numbers of vessels lasered, donor growth restriction, and outcomes (GA of delivery, survival).