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TITLE

MATERNAL UTERINE ARTERY AD.VEGF-A165 GENE THERAPY IMPROVES FETAL BRAIN WEIGHT AND DOES NOT ADVERSELY AFFECT NEUROLOGICAL ANATOMY IN FGR GUINEA PIGS

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ABSTRACT
Context:Fetal growth restriction(FGR) is the failure of a fetus to achieve normal intrauterine growth. FGR has no treatment, can impair motor function, cause behavioural disorders & has high mortality-rates. FGR fetuses have reduced brain size & increased neural cell inflammation. Evidence shows that uterine artery application of a VEGF-A165 adenoviral vector(Ad.VEGF-A165) to pregnant guinea pigs(GP) with FGR increases term fetal weight.
Objective:Is maternal Ad.VEGF-A165 gene therapy neuroprotective in FGR GP fetuses?
Methods:Patients- Dunkin Hartley GPs were fed normally (control=n=7) or 70% their diet to induce FGR one month before conception & during pregnancy. Interventions-FGR dams received Ad.VEGF-A165(n=9 FGR+VEGF group) or pluronic gel(n=7 FGR group) to their uterine arteries via laparotomy on day ~30 of pregnancy. Control dams underwent sham laparotomy. Main Outcome Measures-Evidence of fetal brain sparing from body & brain weights calculated at term post-mortem(~65days). Brain volumes, microglial ramification & apoptosis analysis was conducted in cresyl violet, IBA1 & TUNEL stained sections. Groups were compared using one-way ANOVA.
Results:Brain weight was reduced in FGR fetuses(2.268g±0.064g) but control(2.531g±0.093g) & FGR+VEGF groups were similar(2.517g±0.063g). Fetal weight was similar between the three groups(P>0.05). Brain sparing was lower in FGR fetuses(2.693g±0.082g) but FGR+VEGF group(3.040g±0.081g) was similar to controls(2.976g±0.120g). Microglial activation was increased in cortex, hippocampus, thalamus & striatum in FGR fetuses compared with control & FGR+VEGF groups. TUNEL staining showed no difference in apoptosis across the groups.
Conclusion:Mid-gestation uterine artery Ad.VEGF-A165 gene-therapy in FGR GP pregnancies improves fetal brain growth, normalises microglial activation & does not cause apoptosis or adversely affect neuroanatomy.

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