Poster

Impact of Myo-inositol supplementation in the prevention of neural tube defects

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ABSTRACT

Motivation: Neural tube defects (NTDs) occur during early development by failure of neural tube closure and cause severe birth problems like spina bifida. It has been demonstrated that the mechanisms required during neural tube closure are regulated by genetic and environmental factors, such as maternal diet. Folic acid supplementation during pregnancy prevents the appearance of NTDs in 70% of the cases and the remaining 30% are considered folate resistant. For that reason, there is a need to find new supplements that could help preventing NTDs. One compound that is being tested is inositol, a simple carbon six sugar alcohol that participates in a diverse range of cellular functions. In clinical trials, inositol was used to prevent NTDs and the offspring from mothers that included inositol and folic acid in their diet during pregnancy did not develop NTDs. In our laboratory we are using Loop-tail, mutant of the member of the Wnt-PCP Vangl2, that in heterozygosity presents an incidence of 6% spina bifida. Previous studies using Loop-tail, revealed that a cellular aggregate originates in neural tube dorsal zone of heterozygous embryos. This aggregate, Sox10 positive, is formed by cells from the neural crest which did not migrate correctly. Besides, this cellular aggregate shares similarities with lipomyelomeningocele, the most common type of spina bifida occulta. In order to prevent the appearance of this cellular aggregate our laboratory previously used D-Chiro-inositol in Loop-tail mice as a supplement. Although the aggregate size and prevalence was reduced, crown-rump length of heterozygous embryos was significantly shorter than control embryos. Therefore, we are currently testing Myo-inositol, the isomeric form of inositol used in the human trials designed to prevent NTDs.

Methods: Myo-inositol was administered in the drinking water to pregnant females from day E1.5 of gestation until E11,5 and embryos were collected at stage E12,5. From each litter, data referring to number of implants, resorptions and genotype of the embryos was registered for possible effects on embryotoxicity. In situ hybridization using a Sox10 probe, neural crest marker, was later performed in order to study the presence and intensity of cellular aggregates.

REFERENCES

Greene, N. D., Leung, K. Y., & Copp, A. J. (2017). Inositol, neural tube closure and the prevention of neural tube defects. Birth defects research, 109(2), 68–80. https://doi.org/10.1002/bdra.23533

Nikolopoulou, E., Galea, G. L., Rolo, A., Greene, N. D., & Copp, A. J. (2017). Neural tube closure: cellular, molecular and biomechanical mechanisms. Development (Cambridge, England), 144(4), 552–566. https://doi.org/10.1242/dev.145904