

Fetal Alcohol Syndrome: Do Vitamins Have A Role?

Michael N. A. Eskin*

Department of Human Nutritional Sciences, University of Manitoba, Canada

Fetal Alcohol Syndrome (FASD) is a condition associated with alcohol consumption during pregnancy that results in dysmorphic facial features, impaired growth and central nervous system abnormalities [1]. The degree of damage depends on the extent and regularity of alcohol consumption during pregnancy, and is particularly prevalent in individuals of low socioeconomic status. In addition to vitamin A deficiency, those living at the poverty level may also be deficient in folate and choline, both of which are important for normal neural tube development. This editorial will focus on the potential of these vitamins in mitigating some of the effects of alcohol in the development of FASD.

Depletion of vitamin A stores, as a result of alcohol consumption, can lead to growth retardation, limb dysmorphogenesis, as well as dysfunction of the central nervous system [2]. This is due to the direct competition between vitamin A or retinol and alcohol for the enzyme alcohol dehydrogenase, which has a higher affinity for binding to alcohol. As a result, vitamin A metabolism is blocked, causing a deficiency in retinoic acid synthesis [2,3]. Retinoic acid is essential for fetal development, organogenesis, organ homeostasis, cell and neuronal growth and differentiation, development of the central nervous system, as well as limb morphogenesis [2,4]. By exposing *Xenopus laevis* frog embryos to ethanol, Yelin et al. [5] found a high incidence of malformations that resembled the phenotypic anomalies induced in individuals affected by FASD. Further work by Yelin et al. [6] on early molecular changes induced by ethanol exposure established the suitability of this model for studying FASD. Later work by using Zebrafish embryos as their model, confirmed the defects in retinoic acid signalling, resulting from embryonic exposure to alcohol. Supplementation of ethanol exposed Zebra fish embryos with low levels of retinoic acid (10^{-9} M), during gastrulation and somitogenesis, significantly restored some of the defects caused by alcohol exposure. However, fetal anomalies reported by excess consumption of retinoic acid, suggests there is only a very narrow safe range for this nutrient [7].

Folic acid, an essential nutrient that plays a key role in one-carbon transfers, is intimately involved in the biosynthesis of DNA and DNA methylation [8]. During pregnancy, there is an increased demand for folic acid to support the rapid growth of the fetus. However, ethanol exposure can severely impair folate by altering absorption, distribution and excretion [9-11]. Hewitt et al. [12] examined the effects of chronic ethanol exposure and folic acid supplementation on the folic acid status of a maternal and fetal guinea pig model. While folate supplementation did not alleviate the decrease of folic acid in the brain and hippocampus, it did prevent a decrease in hepatic levels, in both the mother and fetus. Previous work by Cano et al. [13] also found that folate supplementation had a protective effect by reducing oxidative stress in the offspring of pregnant rats exposed to ethanol [14]. Later reported that a high folate diet prevented ethanol-induced cardiac defects in pregnant mice exposed to an intraperitoneal injection, equivalent to a binge-drinking dose of ethanol.

Choline is another essential nutrient required for fetal development [15]. Addition of choline during early postnatal development was reported by Thomas et al. [16], to reduce the severity of memory deficits induced in adult rats subjected to prenatal alcohol exposure. Supplementation of adult rats with choline from postnatal days, 4-30 days was also found to reduce the severity of a number of behaviour

symptoms associated with ethanol exposure, such as spatial learning deficits and over activity [17], trace eye blinking conditioning [18], and trace fear conditioning deficits [19]. Such changes were associated with alcohol exposure during the third trimester equivalent brain growth spurt [20]. Choline supplementation, coincident with prenatal alcohol exposure in rats, was also shown by Thomas et al. [20] to protect against ethanol's teratogenic effects.

All these studies point to vitamin A, folate and choline mitigating some of the adverse effects of ethanol exposure, consistent with that presented recently by Ballard et al. [21]. Future studies, including epigenetics, will shed more light on the potential protective and preventive roles of these and other vitamins in reducing the abnormalities associated with the development of fetal alcohol syndrome.

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*Corresponding author: Michael N.A. Eskin, Professor, Department of Human Nutritional Sciences, University of Manitoba, Canada, E-mail: Michael.Eskin@ad.umanitoba.ca

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