Fetal Alcohol Spectrum Disorders: Biomarkers and Treatments

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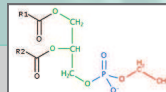
Introduction

Exposure to ethanol during pregnancy can have devastating effects on the developing fetus. Depending on time of exposure, pattern of alcohol consumption and genetic and environmental factors, the symptoms can go from mild to severe, referred to as Fetal Alcohol Spectrum Disorders (FASD). The main symptoms are growth retardation, facial abnormalities and central nervous system dysfunction. Due to its low molecular weight and solubility, alcohol freely crosses the placenta, causing teratogenic effects such as oxidative stress, apoptosis, cell migration impairing, signalling interferences and epigenetic effects.
FASD is 100% preventable and has no cure.

Biomarkers

As maternal self report is not always reliable, there is a need of molecular biomarkers of fetal alcohol exposure.
So far, meconium has been proposed to be the best matrix to detect biomarkers of fetal exposure, although it is mainly formed during the last 8 weeks of pregnancy (and provides information about this period only).
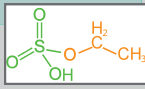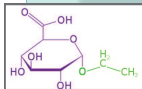
Fatty Acid Ethyl Esters

FAEEs are the result of alcohol conjugation with a fatty acid. Only a few are useful for fetal exposure to alcohol.

Phosphatidylethanol
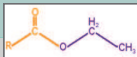
PEth is suggested as a biomarker for early pregnancy detection.

Ethyl Glucuronide and Ethyl Sulphate

EtG and EtS are both direct minor alcohol metabolites.

Baby with Fetal Alcohol Syndrome

Facial Characteristics:
small eye openings...........
smooth philtrum................
thin upper lip.............

Facial Abnormalities

When present, facial characteristics are a good indicator of FASD.

	Advantages	Disadvantages
FAEEs	They cannot cross the placenta (indicate fetal exposure)	Possible false results. Information about the last 8 weeks (when meconium is mainly formed)
EtG and EtS	High specificity and sensitivity	They cross the placenta (indicate maternal exposure). Information about the last 8 weeks (as it is detected in meconium)
PEth	High sensitivity and long life in maternal matrices	Bad results in neonatal matrices detection
Facial abnormalities	Easy to evaluate	Not always present

*R, R_1 and R_2 are fatty acid chains

Treatments

Based on alcohol teratogenic mechanisms, several molecules have been proposed to prevent or avoid FASD symptoms during fetal exposure to ethanol.

- Choline Supplement
- Serotonin agonists
- Neurotrophic and growth factors
- Neurotransmitter interference
- NDMA antagonists
- Signal pathway interference
- Overstimulation of NDMA Receptors
- Only during ABSTINENCE
- Vitamin A Supplement
- CELL DEATH
- Cell-cell adhesion disrupted (CAM L1)
- Oxidative Stress
- NAP and SAL Peptides
- 1-octanol
- Antioxidants
- Nfr-2 transcription factor induction
- Treatment
- Damage mechanism

Conclusions

* Although further studies are needed to correlate chronic or acute consumption with biomarkers concentration, FAEEs and/or EtG and EtS are good indicators of prenatal exposure to ethanol.

* PEth could be used to detect ethanol consumption in early pregnancy.

* If a cheap, easy and quick method of screening is developed, it would be possible to establish a neonatal diagnosis for ethanol exposure using this biomarkers.

* Several therapeutic agents have been suggested, although none of them act in all mechanisms of damage.

* Therapeutic strategies based on vitamin or nutrient supplement have better perspectives to reach clinics because of security concerns.

* The best prevention is to avoid total consumption of ethanol during pregnancy.