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Review

Toxic effects of prenatal exposure to alcohol, tobacco and other drugs

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ABSTRACT

Tobacco, alcohol, cannabis and cocaine are the most consumed psychoactive drugs throughout the population. Prenatal exposure to these drugs could alter normal foetal development and could threaten future welfare. The main changes observed in prenatal exposure to tobacco are caused by nicotine and carbon monoxide, which can impede nutrient and oxygen exchange between mother and foetus, restricting foetal growth. Memory, learning processes, hearing and behaviour can also be affected. Alcohol may cause physical and cognitive alterations in prenatally exposed infants, fundamentally caused by altered NMDAR and GABAR activity. Tetrahydrocannabinol, the psychoactive compound of cannabis, is capable of activating CB1R, inducing connectivity deficits during the foetal brain development. This fact could be linked to behavioural and cognitive deficits. Many of the effects from prenatal cocaine exposure are caused by altered cell proliferation, migration, differentiation and dendritic growth processes. Cocaine causes long term behavioural and cognitive alterations and also affects the uteroplacental unit.

Contents

Abbreviations: SHS, second hand smoke; PTE, prenatal tobacco exposure; SID, Ssudden infant death syndrome; CNS, central nervous system; nAChRs, nicotinic acetylcholine receptors; DNA, deoxyribonucleic acid; microRNA, micro ribonucleic acid; BDNF, brain-derived neurotrophic factor; mRNA, messenger RNA; PAE, prenatal alcohol exposure; FAS, foetal alcohol syndrome; NMDARs, N-methyl-D-aspartic acid receptors; GABARs, gamma-aminobutyric acid receptors; LTP, long term potentiation; LTD, long term depression; DNMT, DNA methyltransferase; HDAC, histone deacetylase; MeCP2, methyl CpG binding protein 2; THC, tetrahydrocannabinol; CB, cannabinoids receptor; PCE, prenatal cannabis exposure; MHPCD, maternal health practices and child developmental study; OPPS, ottawa prenatal prospective study; PCoE, prenatal cocaine exposure; Ppp1cb, β-catalytic subunit of the protein phosphatase type-1; PP1, protein phosphatase type-1; HAT, histone acetyltransferase; FASD, foetal alcohol spectrum disorder.

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1. Introduction

Drug use as well as alcohol and tobacco consumption during pregnancy are major risk factors that can impede normal child development and postnatal survival rates. The effects that accompany prenatal psychoactive drug exposure are complex and variable. Such effects are mainly determined by the compounds chemical nature, intake quantity, frequency of consumption and other many variables.

According to the latest publication regarding the Spanish domiciliary survey on alcohol and drugs the most consumed psychoactive substances are alcohol (76.6%) and tobacco (40.2%). Amongst illicit drugs, cannabis (27.4%) and cocaine (8.8%) have the highest consumption rate [1].

Considering the high consumption prevalence of these substances, as well as their known toxic effects during pregnancy, this paper will focus on the deleterious effects that may appear in the offspring, during early and later stages of life, after prenatal exposure to tobacco, alcohol, cannabis and cocaine.

2. Tobacco

Between 5–26% of smoking women will continue to smoke during pregnancy [2]. The dangers of prenatal exposure to smoke, whether it is in form of first hand smoke or second hand smoke (SHS) have been proven. SHS contains more than 4000 dangerous chemical substances which may cause many toxic effects when inhaled. Half of these substances are commonly found in tobacco and the other half of these compounds appear when combustion takes place. Approximately 250 of the chemical species are known to be toxic for humans and around 50 of these substances may cause cancer. Of these compounds, some of the most dangerous are nicotine, carbon monoxide, acetone, arsenic, benzene, cadmium, cyanide, formaldehyde, lead, mercury, nickel, phenol and styrene. Nicotine and carbon monoxide are especially interesting due to their capability to cause offspring alterations [3]. These components can accumulate in the foetal compartments as early as the seventh week of gestation in both active and passive smokers. These substances are normally found in higher concentrations and for longer periods of time in the foetus compared to the mother [4].

Many of the compounds found in tobacco can easily cross through the placental barrier and can influence the developing foetus. It is also known that the newborn can continue to be exposed to tobacco through breast milk or even through SHS, which can result in additional difficulties when assessing the effects of prenatal tobacco exposure (PTE) [5].

2.1. Prenatal tobacco exposure and its consequences for the newborn

The harmful effects that result from PTE may become apparent in different ways. One of the most outstanding dangers is an increase in the number of cases of sudden infant death syndrome (SIDS) [6]. From the moment of birth several newborn stress signs can be detected, especially those that affect the central nervous system (CNS), gastrointestinal system and vision functionality [7]. The stress/abstinence component is a checklist of "yes" or "no" items organized by organ system based primarily on the work of Finnegan [8] which is enclosed in a neurobehavioural examination specifically designed to measure drug effects (NICU Network Neurobehavioral Scale). This examination also provides an assessment of neurologic and behavioural functions [7,9]. It follows a fixed sequence of administration that starts with a preexamination observation, followed by the neurologic and behavioural components and the Stress/Abstinence scale that is further divided into the following subscores: physiologic, autonomic, CNS, skin, visual, gastrointestinal, and state [7,9].

2.1.1. Prenatal effects of tobacco exposure on the central nervous system, cognitive and executive functions

Recent studies describe tobacco's neurotoxic and neuromodulatory effects on the brain. These alterations cause impairments in learning, memory, hearing and behaviour. Other studies focus on genetic dysregulation and altered biochemical pathways that take place when PTE occurs [5].

Two of the most prominent characteristics that are present in the newborn with PTE are those associated with stunted prenatal head growth and brain volume [10].

Growth reduction in the foetus is most prominent in the later stages of pregnancy. In normal conditions, when tobacco is absent, certain foetal structures are protected by a blood flow redistribution system when the delivery of oxygen and nutrients is insufficient. Under a tobacco exposure situation, this phenomenon ceases to take place [11].

Tobacco's neuromodulatory effects include cell loss, cell hypertrophy and neurite formation, a marker of potential damage to neuronal projections. All these changes that appear in the CNS can alter certain aspects of cognition and behaviour [12].

A recent study examined the effects of prenatal smoking exposure on brain volumes and later childhood behaviour. Smaller brain volumes and cortical grey matter volumes have been reported as well as thinner superior frontal, superior parietal and precentral cortices. Exposed children also showed more effective problems at 6 years of age, assessed by the Child Behaviour Checklist.