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Review

The Effects of Alcohol and Drugs of Abuse on Maternal Nutritional Profile During Pregnancy

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Abstract: The consumption of alcohol and drugs of abuse among pregnant women has experienced a significant increase in the last decades. Optimal maternal nutritional status is of great importance for proper fetal development, yet is often altered with alcohol or drugs consumption. There is a lack of information on the effects of alcohol and drugs on maternal nutritional status, so the focus of this review was to provide an overview on nutrional status of mother and fetus in abusers pregnant women. Alcohol and drugs consumption can adversely affect the quality and quantity of proper nutrient supply and energy intake, resulting in malnutrition especially of micronutrients (vitamins, omega-3, folic acid, zinc, choline, iron, copper, selenium). When maternal nutritional status is compromised by alcohol and drugs essential nutrients are not available for the fetus, this can result in suboptimal outcomes like Intrauterine Growth Restriction (IUGR) or Fetal Alcohol Spectrum Disorder (FASD). It is critical to determine a means to resolve and reduce the physical and neurological malformations that develop in the fetus as a result of prenatal alcohol and drugs exposure combined with poor maternal nutrition. Prenatal nutrition interventions are required that may prevent or alleviate the development of such abnormalities.

Keywords: Alcohol; Drugs of abuse; Pregnancy; Maternal Nutrition; Fetal Nutrition; FASD; IUGR.

1. Introduction

The consumption of alcohol and drugs of abuse among pregnant women has experienced a significant increase in the last decades.

In Spain the prevalence of alcohol consumption during pregnancy through maternal hair analysis at the delivery is about 60%. In the general population of Europe about a quarter of women drink alcohol during pregnancy. Although negative consequences of alcohol consumption during pregnancy are well covered by the media, government promotion, and educational programs, pregnant women continue to consume alcohol frequently (defined as more than 7 drinks/week) or binge drink (when more than 5 drinks are consumed per occasion) [1].

Recent estimates of the prevalence of cannabis use among pregnant women in the US range between 3% and 16%. Population-based surveillance data from the National Survey on Drug Use and Health suggests that cannabis use among pregnant women in the US has increased as much as 62% between 2002 and 2014.The potency of cannabis has increased 6- to 7-fold since the 1970s [2]. Health from

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2002-2003 estimated that 4.3% of pregnant women aged 15 to 44 years reported illicit drug use. Approximately 250,000 women in the United States, of whom 90% are of childbearing age, meet criteria for intravenous drug abuse. This suggests, conservatively, that approximately 225,000 infants born each year could be exposed to illicit drugs in the prenatal or postpartum time period [3]. Opioid use during pregnancy has also increased nationally in recent years. The percentage of Medicaid-enrolled women who filled at least one opioid prescription during pregnancy increased 23% during 2000–2010, from 18.5% to 22.8% [4]. The prevalence of opioid abuse or dependence among pregnant women has increased from 1.7 per 1,000 delivery admissions in 1998 to 3.9 in 2011 [5].

Optimal nutritional status is required in producing healthy offspring. When maternal nutritional status is compromised with alcohol or drugs essential nutrients are displaced or not obtained, which results in suboptimal health outcomes in the developing fetus due to deprivation of essential nutrients required for growth [6]. The literature focusing on maternal nutritional status of alcohol and drug abusers during pregnancy is scarce. The aim of this review was to analyse the existing studies about the effects of drugs of abuse and alcohol on maternal nutritional status and fetal nutrition during pregnancy. We didn't analyse the effect of drugs and alcohol on pregnancy, the effect of drugs and alcohol on fetal development, neither the effect of nutritional status of the mother on drugs and alcohol.

2. Review

Effects of Alcohol exposure on maternal nutritional status

It is known that women who drink alcohol during pregnancy have poor nutritional status especially heavy drinkers. While food intake can, in the short term, exert a protective effect from the toxic effects of alcohol consumption, alcohol consumption over time can adversely affect the quality and quantity of proper nutrient supply and energy intake, particularly for women [7]. When consumed in excess alcohol can cause diseases by interferring with the nutritional status of the drinker, moreover many alcoholics do not consume a balanced diet. Excessive alcohol can alter the intake absorption into the body and utilization of various nutrients. In addition light to moderate drinkers who consume one to two glasses or less of an alcoholic beverages per day, consider those beverage a part of their normal diet and acquire a certain numbers of calories from them. Accordingly many alcoholics can suffer from various degrees of malnutrition. Primary malnutrition occurs when alcohol replaces other nutrients in the diet, resulting in overall reduced nutrients intake. Secondary malnutrition occurs when the drinker consumes adequate nutrients but alcohol interferes with the absorption of those nutrients from the intestine so they are not available to the body. Alcohol can interfere with uptake of essential aminoacids and vitamins particularly B1 (thiamine), B2 (riboflavin), B6 (pyridoxine), vitamin A and C and folic acid. The severity of these deficiencies correlates with the amount of alcohol and with the corresponding decrease in vitamin intake [8].

A population-based research in the Western Cape province of South Africa showed that pregnant women who drink alcohol have poor maternal nutritional status, lower intake of vitamins A, C, D, E, B2, calcium, omega-3 fatty acids and choline if compared to nondrinking mothers [9].

Alcohol consumption during pregnancy depletes maternal vitamin A stores, which can interrupt normal cell growth of the fetus. The proposed mechanism for this is that when both retinol and

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alcohol are present, the enzyme alcohol dehydrogenase (ADH) preferentially metabolizes alcohol instead of retinol. This results in a deficiency in retinoic acid synthesis which is required to signal and control the cells involved in fetal development, organogenesis, organ homeostasis, cell and neuronal growth and differentiation, development of the Central Nervous System (CNS), and limb morphogenesis [10].

Halsted et al. reported that jejunal folate absorption is reduced to <20% in acute and chronic alcoholics, therefore resulting in deficiency. Under deficiency states, DNA and RNA synthesis is altered because of incorrect nucleotide incorporation, causing instability and cellular apoptosis. Deficiency is also attributed to reduced hepatic folic acid storage and increased catabolism and urinary excretion [11]. If alcohol is consumed, the ethanol competes with water for the phospholipase D– catalyzed reaction of phosphatidylcholine, and this affects protein expression and cell signaling. Choline-related mechanisms have been suggested to be a major part of the molecular etiology of Fetal Alcohol Spectrum Disorder (FASD) comprehend developmental abnormalities due to excessive maternal alcohol intake during pregnancy [12].

A recent study realized in pregnant women in Ukraine and Russia showed that mothers that consumed alcohol during pregnancy had low levels of plasma zinc and copper than non-drinking mothers [13]. Alcohol consumption on a chronic basis itself reduces the availability of zinc because there is decreased intake and absorption and increased urinary excretion. When acute zinc deficiency occurs as a result of ethanol exposure, metallothionein, a low-molecular-weight protein body, sequesters plasma zinc to the liver, resulting in a reduction in plasma zinc [14].

May et al. showed that BMI in drinking mothers was significantly lower than controls [9]. They found that lighter (lower BMI) women population who binge drink was less able to eliminate alcohol allowing more alcohol to cross the placenta. Conversely, in heavier mothers the additional adipose tissue helps distribute the alcohol, and therefore, protects the fetus. In addition micronutrients intake was insufficient for drinking women. May et al. confirmed that mothers of children with FASD had less vitamin D, C, thiamin, pantothenic acid, B12, phosphorus, magnesium, selenium, sodium, potassium, Eicosapentanoic acid (EPA), decosapentanoic acid (DPA) and docosahexaenoic acid (DHA) [15].

In animal models, selenium deposits and plasma concentrations are low in chronic alcoholics because of decreased dietary intake and increased production of free radicals resulting from alcohol metabolism [16]. Maternal alcohol consumption during pregnancy has not only decreases maternal intake of n– 3 Fatty Acids– rich foods, it also decreases maternal DHA status and reduces placental transfer of DHA to the fetus [17].

Nutrition is a protective factor against alcohol teratogenity. When maternal nutritional status is compromised by the presence of alcohol, essential nutrients are unavailable for the fetus which can result in suboptimal outcomes such as physical abnormalities, cognitive delays or FASD [18]. For these reasons some experimental studies tried to treat women with choline, minerals and antioxidants in order to reverse nutritional deficits seen in FASD [19,20].

May et al. described that mother of children with FASD consumed more total protein, vitamin E, C, B6, magnesium, phosphorus, EPA, DHA, DPA than mothers of controls but these differences did not have biologically significant since all mother were found to be deficient because excessive alcohol consumption likely nullified the beneficial effects of additional nutrient intake in the mothers of

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children with FASD. Despite an increase in total food consumption in mothers of children with FASD, there was no corresponding increase in diet quality [15].

Ethanol exposure has also been shown to alter Iron (Fe) regulation and homeostasis. Chronic ethanol consumption increases body stores of Fe and is associated with a significant risk of Fe overload [21]

In animals models supplementations with antioxidants to pregnant female reduce oxidative stress. Nutrients such as choline, vitamin E, bataine, folic acid, methionine, zinc can attenuate alcohol-induced changes to the epigenome and oxidative damage [22]

Effects of Drugs exposure on maternal nutritional status

In general use of illicit drugs produces multiple nutrient deficiencies or malnutrition which is the most common cause of immunodeficiency [23]. Use of these drugs undermines appetite, affects food habits leading drug addicts to crave 'empty-energy', potentially nutrient-deficient foods and causes micronutrient deficiency [24].

The majority of drug addicts present below-normal BMI and biochemical values, and clinical signs of nutrient deficiency. The reduced nutritional indices may be possibly because of the consumption of poor quality nutrient-deficient foods [25]. The clinical signs of nutrient deficiency, particularly, are reported to be associated with micronutrient deficiencies [24]. The decreased BMI, haemoglobin and protein values in the drug addicts respectively indicate the presence of chronic energy deficiency, anemia and protein–energy malnutrition. In addition deficiency of antioxidant vitamins (A,C,E) in this population has recently been reported. It was recorded that the majority of drug addicts (about 60 %) had sexually transmitted diseases and were suffering from multiple nutrient deficiencies. This outcome is consistent with the fact of synergy between malnutrition and infection like HIV [26].

Metamphetamine

Amphetamines are powerful CNS stimulants with a profoundability to increase wakefulness and focus. The principle mechanism of action is increased release of norepinephrine, serotonin, and dopamine from neurons within the brain. At the same time, amphetamines inhibit re-uptake of these neurotransmitters.

However, amphetamine use, particularly among young pregnant patients, appears to be increasing. The effects of amphetamine use in the preconception period and pregnancy are difficult to establish because users of amphetamines will commonly use other illicit drugs while pregnant, making it difficult to separate the effects of amphetamines from those of other illicit drugs. As with virtually all other drugs of abuse, there is an important confounding effect. More important, perhaps, is the association of amphetamine use with risky sexual behaviors, teenage pregnancy, and potential increased risk of sexually transmitted infections [27].

Abuse have all been associated with poor maternal weight gain and nutritional status. In many cases, these substances are mixed, and most have fairly powerful appetite suppressant properties. Management of poor maternal nutrition is relatively concrete in theory but can be frustrating for the practitioner because sometimes little can be done to change established maternal behaviors in regard to nutrition. There is a significant number of substance-abusing pregnant patients who may be severely underweight; both of these conditions suggest poor overall nutritional status, if overeating

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is present it is often a consequence of abstaining from methamphetamine [28]. Methamphetamine has been shown to have vasoconstrictive effects resulting in decreased uteroplacental blood flow and fetal hypoxia, and anorexic effects on the mother which may result in intrauterine growth retardation (IUGR) [29].

Cocaine

Little is known about the nutrition-related effects of cocaine use. In one study, pregnant women with urine assays positive for cocaine weighted significantly less before the pregnancy, had lower hematocrit levels at the time of prenatal registration, and gained slightly less weight during the gestation than did those with negative assays [30]. Pregnant women who used cocaine or cannabis had low levels of ferritine and folate, and the fetus showed low birthweight and low craneal circumference. Although the deficit in birth weight did not achieve significance when prepregnancy weight and maternal weight gain were controlled for in the analysis, significant decreases in birth length and head circumference remained [31]. Thus, these data suggest that the association between cocaine use and growth retardation may be partially but not completely mediated by nutritional factors. Other factors, such as cigarette smoking, alcohol consumption, and other drug abuse, which were not controlled for in all the studies, may also have confounded some of the reported adverse effects. Isolating the influence of cocaine from other factors would nevertheless be difficult, since cocaine use is often accompanied by abuse of other substances as well as other life-style patterns that may be detrimental to the fetus.

Prenatal cocaine exposure has been associated with a variety of adverse effects in humans, including poor maternal weight gain, spontaneous abortion, placental abruption, premature and precipitous labor, fetal distress, IUGR, various birth defects, and neonatal neurobehavioral deficits. These effects in humans have largely been supported by animal studies [32]

The human data, however, are confounded by maternal risk factors and multiple drug abuse. Animal studies, on the other hand, can control for many confounding variables, providing a clearer view of drug-induced effects.

All cocaine treatments in animal models resulted in significant decreases in maternal weight gain and food consumption. Undernutrition is a sufficient cause of fetal weight reduction [32].

In animals models during pregnancy cocaine increased water consumption suggests that cocaine, like a number of drugs, caused excess thirst. This excess thirst could be caused by increased locomotor activity or a dryness in the mouth similar to that caused by adrenaline and other sympathometic drugs or by a possible diuretic effect. Cocaine provoked diarrhoea in some of cocaine treated dams. This suggests that cocaine can act as a gastrointestinal irritant, causing malabsorption and fluid loss in at least some animals receiving very high doses. Cocaine-induced diarrhoea or diuresis could cause natriuresis (sodium loss) and the loss of other electrolytes and nutrients causing malnutrition [32].

Studies in humans showed that malnutrition in the population of cocaine addicted may be multifactorial and could involve lower caloric intake, abnormal metabolic and gastrointestinal functions, and even deleterious drug effects. Cocaine and amphetamines are appetite suppressants that tend to reduce body weight with their anorexic effects [33]. A population of Brazil cocaine addicted was found to have hemoglobin and hematocrit levels below normal, indicate

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protein-energy malnutrition and anemia associated with a diet poor in micronutrients, especially iron, as well as insufficient protein intake and clinical problems. They were found to have low levels of HDL cholesterol and high levels of triglycerides. LDL cholesterol, total cholesterol, and glucose also presented alteration, but at lower percentages [34]. Islam et al. found lower concentrations of antioxidant vitamins E, C, and A in this population, suggesting a lack of access to certain foods [35]. In pregnant women high maternal serum concentrations of illicit drugs were accompanied by less concentrations of folate and ferritin and significant increase in leukocyte count than those of subjects with lower serum illicit drugs suggesting malabsorption problems [36]

Cannabis

There are few data on the nutritional status of pregnant marijuana users, nor is it known what effect marijuana exposure may have on specific nutrients. Although marijuana reportedly stimulates the appetite [37], studies of women who have consumed marijuana during pregnancy have provided conflicting results regarding their nutritional status. One study found that marijuana users consumed significantly more calories and protein and gained slightly more weight during the pregnancy than did their controls [38]. Another study reported that women who had a positive assay for marijuana use weighed slightly less before the pregnancy and gained significantly less weight during the pregnancy as a compared with those who had a negative assay [31].

Van Gelder et al. described that Women who reported use of any illicit drug were less likely to have used folic acid in the periconceptional period and during pregnancy were also more often underweight (BMI<18.5kg/m2) than women who did not report use of illicit drugs [39]. Roberson et al. used the pregnancy risk assessment monitoring system data and found that women who used marijuana in pregnancy were more likely to report severe nausea that would explain the undernutrition in that population [40]

Knight et al. showed that subjects whose serum values were above the ADAMHA/NIDA (National Institute on Drug Abuse) ranges for marijuana, phencyclidine and cocaine had concentrations of folate and ferritin that were significantly less than those of subjects with lower serum drug levels [36].

In a study realized In animals models, female wistar rats were exposed to cannabis smoke, placebo smoke, or no smoke while concurrently consuming 1 of 3 diets differing in protein concentration (8%, 24%, 64%). 12 variables were affected by the low-protein diet, 8 were significantly potentiated when undernutrition was combined with cannabis treatment, these included a lengthened gestation period, an increase in occurrence of stillbirths and litter destruction, and decreased activity in the rat pups so low-protein diet potentiated worse effect of cannabis [41].

Heroine

Heroin is the most commonly abused illicit opiate and women who use heroin are likely to use other harmful substances, such as tobacco, alcohol, and cocaine, all of which have their own potential adverse effects on pregnancy. Therefore, it is difficult to separate the effects of heroin from these other substances. In addition, intravenous drug use is a risk factor for many infectious diseases, including human immunodeficiency virus (HIV) infection [28]. Opiates are CNS depressant and analgesics and create physical and psychological dependence.

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Studies about opiate addiction disorders have proven extreme nutritional deficiencies of key proteins, fats, vitamins, minerals like zinc, iron, calcium, chromium, magnesium, potassium and other essential nutrients. Drug abusers show weight loss and dietary patterns changes, which disrupt their ability to digest carbohydrates efficiently. Changes in specific nutrient status can lead to develop barriers in withdrawal from opiates addiction [42]. Metabolic problems are often associated with heroin, cocaine, and ecstasy drug although there is a wide range of medical problems produced. The use of heroin has been implicated in blood sugar disorders in a number of mechanisms. Fasting insulin levels were found to be four times higher in heroin addicts than in control subjects and insulin resistance stemming from opioid use may be coupled with beta cell dysfunction [43].

In opiate addicts unhealthy eating behaviours have been shown due to lack of nutritional knowledge, food preparation skills, and environments [44,45].

During withdrawal from heroin, nicotine, marijuana, and cocaine, weight gain or loss occurs, which is caused by major changes in food intake selection. Nutrition is related with conditions and diseases, such as diabetes which decreases sensitivity to dependence on morphine and vitamin D deficiency that slows down morphine dependency as well as protein deprivation which generates preferential fat intake with low cocaine use [24].

Heroin addicts consume less than the minimum amount of vegetable, fruit and grains recommended by the food pyramid and are more eager to have sweets [44].

Increasing the dietary intake of protein and reducing simple carbohydrates in the form of vegetables and whole grains can manage the carbohydrate-metabolism health problems [46]. Management of pregnant substance abusers must address the needs of poorly nourished, homeless, and /or in carcerated pregnant substance abusers. In addition to education about nutrition and weight gain, some of these women may need referral to food assistance programs and shelters, and provision of transportation vouchers and prenatal multivitamins [47].

Outreach and educational resources targeting younger pregnant women and women living below the federal poverty level about the dangers of misusing prescription pain relievers may be especially beneficial [48].

No specific studies about nutritional impairment in pregnant women addicted to heroin have been reported.

Effects of alcohol and drugs of abuse exposure on fetal nutritional status

Nutrients available to the fetus are dependent on the mother's intake, her metabolism, her partitioning of nutrients among maternal stores and circulation, and the placental transport mechanism.

Ethanol crosses the placental barrier so maternal consumption generates prolonged periods of exposure in the fetus causing a severe damage to developing structures [49].

After alcohol consumption placenta generates oxidative stress (ROS) which modify several placental function such as signalling, production, release of hormone and enzymes, transport of nutrients, implantation, cellular growth and maturation [50]. Ethanol decreases nitric oxide (NO) availability causing a deregulation of fetal blood flow and ethanol exposure can alter the expression of several

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placental genes playing critical roles in fetus development. All theses abnormalities described difficult the delivery of nutrients to the fetus and generates IUGR and FASD [49,50].

Alcohol can disrupt the fetal supply of nutrients through multiple mechanisms including: 1) quality and quantity of intake can decrease; 2) gastrointestinal changes may lead to abnormal digestion and malabsorption of nutrients [8]; 3) decreased renal function/reabsorption and increased urine excretion of key micronutrients; 4) alterations in the composition and function of gut microbiome [51]; and 5) altered placental transport and placental metabolism of nutrients [52]. Independent of the shortage of micronutrients, which may have aided or protected fetal development, it is plausible that the alcohol further reduced the available nutrients for the fetus [15].

Alcohol and drugs of abuse induced fetal growth retardation that is potentiated by maternal inadequate nutrient intake and smaller body size [9]. Cocaine's and heroin's vasoconstrictive ability may lead to fetal hypoxia [53] and reduced nutritional supply to the fetus. Since cocaine, like amphetamines, acts as a suppressant of appetite [54,55], an inadequate maternal diet may play a role in the growth retardation seen in fetuses of cocaine abusers. Cocaine readily crosses the placenta however, the vasoconstrictive effect of cocaine may reduce placental transport of nutrients [56].

Methamphetamine can causes fetal growth restriction by several proposed mechanisms including maternal vasoconstriction leading to restricted nutrient delivery to the fetus and fetal vasoconstriction and hypertension leading to decreased fetal oxyhemoglobin saturation [57].

Marijuana smoking, like tobacco smoking, is also associated with increased carboxyhemoglobin levels which in turn may impair fetal oxygenation and, consequently, fetal growth [58]. Furthermore, marijuana use tends to increase the heart rate and blood pressure which may lead to reduced uteroplacental blood flow to the fetus [59]. Abnormalities in growth are biologically plausible, given the passage of cannabinoids across the placenta. There are some data suggesting that cannabis affects glucose and insulin regulation and therefore may affect the fetal growth trajectory [60].

Heroin is not considered to be grossly teratogenic, but it is highly lipophilic and readily crosses the placenta. Untreated heroin use is associated with IUGR, premature delivery, increased neonatal mortality and neonatal abstinence syndrome (NAS) [61].

In general as maternal and fetal nutritional status are inter-relationed when maternal nutritional status is compromised by alcohol and drugs essential nutrients are not available for the fetus, this can result in suboptimal outcomes like IUGR or FASD. Specific nutrients deficits (iron, copper and choline) were linked to slow growth trajectories and others criteria of FASD [13].

Undernourished mothers may be limited in their ability to appropriately support the fetus. In utero malnutrition, followed by poor postnatal nutrition, can perpetuate the effect of malnutrition, which can cause severely stunted growth and negatively influence reasoning, visuospatial functions, IQ, language development, attention, and learning [62].

From work with experimental animals, it is well documented that deficiencies of certain nutrients, including folate, vitamin B12, Zn, Fe and Copper (Cu), during pregnancy can result in abnormal CNS development, and other abnormalities [63]. The metabolism of Fe, Zn and Cu are interrelated, and it has been demonstrated in experimental animal models that a maternal deficit of anyone of the above elements can result in alterations in the metabolism of the other elements in the mother as well

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as the fetus [64]. This leads to decreased amounts available for placental transport, resulting in fetal zinc and Cu deficiency that lead to IUGR and fetal dysmorphogenesis [65].

When maternal dietary calcium intake is low, fetal bone development and mineralization may be compromised. The lack of omega-3's directly and adversely affects fetal brain development and cognitive function later in life. Folate is a major requirement for brain and spinal cord development and riboflavin also plays a role in brain development. Vitamin B12 is critical to the process of DNA methylation and deficiencies in vitamin B12 can cause abnormalities in DNA methylation and neurodevelopmental deficits. Choline deficiency during pregnancy and lactation may cause deficient of motor function and memory in the offspring [9]. Miller and Carter reported that ethanol consumption by rat dams perturbs the temporal patterns between Fe concentrations and Fe-regulatory proteins in brain regions of offspring. Fetal alcohol exposure can result in low Fe stores in the human infant [66, 67].

Alcohol consumption during pregnancy depletes maternal vitamin A stores, which can interrupt normal cell growth of the fetus. Retinol is essential because it allows the transcription of genes that are required in regulating cell and neuronal differentiation for the limbs, brain, and nervous system to be transcribed [68]. Nutrients such as folate, vitamin C (ascorbic acid), vitamin E (**a**tocopherol), selenium, and zinc are important contributors to antioxidant activity so tha lack of these nutrients cause by alcohol and drugs produces oxidative stress [6].

It has been described a reduction in perinatal body fat in fetal cocaine exposed fetus, implied restricted nutrient supply to the fetus. There are several possible mechanisms by which this can occur in addition to reduced maternal undernutrition: cocaine can reduce amino acid uptake by the placenta and it can cause nutrient restriction through vasoconstriction of the uterine arteries [69]. Several recent observations suggest that prenatal cocaine exposure may impair the delivery of nutrients to the fetus. For example, cocaine exposure during pregnancy reduced placental sodium transport in mice, caused hyponatremia in human neonates, decreased uterine blood flow in rodents and sheep, reduced amino acid uptake in rat and human placentae [70], decreased the percentage of body fat content and the whole-body weights of rat fetuses and human infants [71], altered bone composition in human and rat offspring [72].

3. Conclusions

Few studies report the effects of alcohol and drugs of abuse on maternal nutritional status. Despite public health efforts to reduce alcohol and drugs consumption during pregnancy an important number of pregnant women continue consuming them. Alcohol and drugs of abuse cause maternal and fetal malnutrition with consequent developmental fetal problems. Maintaining optimal nutrition during pregnancy is critical, which raises questions regarding how much and what should be provided during pregnancy to alleviate the severity of the outcome of FASD, IUGR or fetal dysmorphogenesis. Although maternal nutrition intervention appears to be a promising strategy, robust information on the role of nutrients and nutrition interventions is scarce. In this regard, this review tries to find evidence of potential target nutrients for prenatal nutritional support by focusing specifically on alcohol and drugs metabolism, effects on fetal development, and several nutrients and their interactions with alcohol or drugs consumption. The identification of such nutrients can led to successful public health prevention programs and policies.

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