Teratogenic Risks from Exposure to Illicit Drugs

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KEYWORDS

• Addiction • Fetal effects • Illicit drug use • Teratogenic risk
• Pregnancy complications

KEY POINTS

- This article presents issues pertaining to limitations with reports about fetal risks and describes current information in humans about fetal effects for specific illicit drugs.
- Associating illicit drug use with eventual pregnancy outcome is difficult. Concurrent use with multiple substances is frequent, and many users are economically disadvantaged, which contributes to unfavorable perinatal outcomes.
- Teratogenic effects may be manifested not only as an intrauterine demise or dysmorphism, but also as growth restriction or behavioral changes.
- Except for maternal alcohol exposure, no birth defect syndrome has been described for specific illicit substances or prescription drugs of abuse.

INTRODUCTION

Substance use is prevalent in the United States, especially in the reproductive-age population. The 2012 National Survey on Drug Use and Health indicated that 14.7% of the US population aged 12 or older used an illicit drug and 4.9% used prescription-type pain relievers for nonmedical reasons in the past year.[1] Furthermore, 9% of this population had some form of substance use disorder. Cigarette and binge alcohol use (five or more drinks on at least one occasion in past 30 days) involved 24.1% and 23.2% of the population, respectively.

Chronic substance use may affect menstrual cycles and semen analysis, but these effects are generally reversible with discontinuation of the drug.[2–5] For this reason, reproductive-age women with addiction disorders may still conceive at any time. Delivery of a drug or chemical by the sperm to the oocyte may be associated with

The authors have nothing to disclose.
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Obstet Gynecol Clin N Am 41 (2014) 229–239
http://dx.doi.org/10.1016/j.ogc.2014.02.008 **obgyn.theclinics.com**
0889-8545/14/$ – see front matter

developmental toxicity, although less is understood and toxicity has not been well-demonstrated in humans.

Illicit drugs include cannabis, stimulants, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. According to the 2012 National Survey on Drug Use and Health, an estimated 4.4% of pregnant women reported illicit drug use in the past 30 days.[1] A second study showed that whereas 0.1% of pregnant women were estimated to have used heroin in the past 30 days, 1% of pregnant women reported nonmedical use of an opioid-containing pain medication.[6] Even though a reduction in substance use may occur during pregnancy, some women may not alter their drug use patterns until at least pregnancy is confirmed. For these reasons, a large number of fetuses are exposed to illicit substances, including during critical stages of organogenesis.

Associating illicit drug use with eventual pregnancy outcome is difficult, because concurrent use of multiple substances is frequent and many users are members of economically disadvantaged segments of society in which unfavorable perinatal outcomes are more common. It is also difficult to follow infant outcomes in such pregnancies and to analyze research data. This article presents issues pertaining to limitations with published investigations about fetal risks and describes the most current information in humans about fetal effects from specific illicit substances (**Table 1**).

LIMITATIONS WITH INVESTIGATIONS ABOUT FETAL RISKS

Difficulties in accurately monitoring dose and exposure of a substance continue to undermine the strength of many observations regarding adverse perinatal effects. Illicit drugs and prescription medications for recreational reasons may be intentionally or inadvertently taken at potentially toxic doses. An accurate evaluation of dosage and the exact period of exposure are often not possible. Addiction or the recreational use of illicit substances may lead to the intake of these drugs in large and uncontrolled doses. For example, when amphetamine use has been studied among addicted mothers, it has been difficult to identify which adverse effects may have resulted from these drugs or the simultaneous use of other substances (eg, ethanol), and poor maternal nutrition, hygiene, and attendance at prenatal visits.

Any illicit drug unbound to proteins can freely pass from the maternal compartment, across the placenta, and into the fetal compartment. Concentrations in the fetal serum can be the same or even higher than in the mother. Little doubt exists that passage of the drug or metabolite into the fetal central nervous system is unimpeded. Effects on the developing embryo and fetus depend on gestational timing, extent of drug distribution, uteroplacental perfusion, and drug or metabolite amount.

Teratogenic effects may be manifested not only as an intrauterine demise or dysmorphism, but also as growth restriction or behavioral changes. Although an association between a substance and an anomaly (eg, midline facial defects) may be suggested with a particular genetic susceptibility, subsequent epidemiologic studies often do not ascribe any substance exposure with an increase in human malformations. It is also not possible to conclude in human beings that heritable birth defects are increased after exposure to a certain drug or chemical.

Small population sizes and unblinded evaluations of drug-exposed newborns raise questions about the significance of any teratogenic observations. Other causes for adverse pregnancy outcome may also exist within drug-abusing populations. Impurity of most illicit drugs and the common practice of using multiple substances either combined or at separate times make it difficult to ascribe specific fetal effects to a certain compound.