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Heavy in utero ethanol exposure is associated with the use of other drugs of abuse in a high-risk population

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Abstract

Many ethanol dependent women also use other drugs of abuse that may affect pregnancy outcome and long-term child neurodevelopment. This study investigated the association between drugs of abuse and concurrent use of ethanol in pregnancy. A study cohort of neonates with FAEE levels above 2 nmol per gram meconium, indicative of heavy in utero ethanol exposure, was identified ($n = 114$). Meconium and hair analyses for the presence of other drugs of abuse were obtained for some of these neonates and the rates of drug exposure were compared with the rates in a cohort of neonates who were tested negative (FAEE below 2 nmol per gram meconium) for ethanol exposure ($n = 622$). Odds ratios (ORs) for various drugs were calculated with ethanol exposure. A 15.5% positive rate for intrauterine ethanol exposure was detected. A high rate of in utero drug exposure was detected in neonates with and without in utero ethanol exposure, 60.5% versus 62.7% respectively. Neonates with heavy in utero ethanol exposure were almost twice as likely to be exposed to narcotic opiates (OR = 1.90; 95% confidence interval [CI]: 1.13–3.20) and 3.3 times as likely to be exposed to amphetamine (OR = 3.30; 95% CI 1.06–10.27) when compared to neonates with no ethanol exposure. Exposure to cannabinoids predicted less likely exposure to ethanol (OR = 0.61; 95% CI: 0.38–0.98) and no significant difference was noted in the exposure to cocaine (OR = 1.24, 95% CI: 0.81–1.91). Neonates suspected of heavy in utero ethanol exposure should be tested for other drugs of abuse and vice versa. Early detection of drug exposures can facilitate early intervention to both the neonate and the mother, thus decreasing the risk of long-term neurodevelopmental outcomes for the child, including secondary disabilities associated with fetal alcohol spectrum disorder.

Keywords: Alcoholism; Drugs of abuse; Ethanol; FAEE; Meconium; Neonatal hair

Introduction

Ethanol is legal and widely available substance. Canadian data from 2000 to 2001 estimate that 13.6% of pregnant women consume ethanol at some point in pregnancy, whereas 4.9% women drink throughout the entire pregnancy (Dell and Roberts, 2006). In utero exposure to ethanol may result in fetal alcohol spectrum disorder (FASD), which encompasses a range of physical, behavioral, and cognitive disabilities. In North America, FASD affects 0.9% of live births (Sampson et al., 1997). Illicit drug use in pregnancy is also a concern, as it has been associated with maternal, fetal, and neonatal complications, including prematurity, intrauterine growth retardation, low birth weight, fetal distress, and developmental delays (Bateman et al., 1993; Chouteau et al., 1988; Petitti and Coleman, 1990; Schneider and Chasnoff, 1992; Umans and Szeto, 1983).

Knowledge of alcohol or illicit drug exposure can serve to direct needed prevention methods and appropriate management. However, nonanonymous self-reporting is subjective and often unreliable while maternal blood markers of alcohol abuse have been deemed ineffective due to the lack of sensitivity and specificity (Bearer, 2001; Cook, 2003; Russell et al., 1996; Stoler et al., 1998). Neonatal hair and meconium testing, however, are optimal methods for identifying late pregnancy in utero exposures due to ease of collection, high sensitivity and specificity, and wide windows of detection.

Meconium is comprised of materials ingested during gestation, including amniotic fluid, mucus, bile, epithelial cells, and water, with its formation beginning in the second trimester (Gareri et al., 2006; Kwong and Ryan, 1997).

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Meconium methods have been extensively validated for detection of in utero drug exposures in the second and third trimesters of pregnancy, including heavy ethanol exposures where the test relies on the detected quantity of fatty acid ethyl esters (FAEEs), which are formed by enzyme-mediated esterification of ethanol and free fatty acids (Bearer et al., 1992, 1999, 2003; Best and Laposata, 2003; Chan et al., 2003, 2004; Ostrea et al., 1988; Pichini et al., 2003, 2004; Rosengren et al., 1993). It is important to note that with a positive cut-off value of 2 nmol total FAEE per gram of meconium, is 100% specific and 98.4% sensitive for identifying heavy or binge drinking in the second and/or third trimesters; occasional or moderate drinking does not produce a positive test result (Chan et al., 2003). For women, the Centers for Disease Control and Prevention define heavy drinking as consumption of more than one drink per day and binge drinking as "pattern on alcohol consumption that brings the blood alcohol concentration level to 0.08% or above," which corresponds to four or more drinks on a single occasion (CDC, online resource).

Neonatal hair has also been used in determination of in utero drug exposures. Growth of neonatal hair begins in the last 3–4 months of pregnancy and thus can provide information of exposure in the last trimester. This method has also been extensively validated and is routinely used (Graham et al., 1989; Kintz and Mangin, 1993; Klein et al., 1994). Previous studies have shown that women who abuse ethanol abuse other drugs, such as nicotine, cocaine, and opiates (Gladstone et al., 1997; Kokotailo et al., 1992; Lester et al., 2001; Ostrea et al., 1992). However, to the best of our knowledge, no previous study has looked into the association of heavy in utero ethanol use and that of other drugs of abuse in a high-risk Canadian population where ethanol or illicit drug use was suspected in pregnancy and confirmed with laboratory testing.

This study assessed the trends in neonatal exposure to drugs of abuse that are associated with heavy ethanol use in pregnancy. It was hypothesized that heavy ethanol use in late pregnancy will be associated with an increased exposure of other drugs of abuse. Such a determination is clinically important, as neonatal drug analysis is commonly done for cocaine, amphetamine, and other drugs of abuse, but rarely for ethanol.

Patients and methods

All the neonatal meconium and hair analyses performed by the Motherisk Laboratory at The Hospital for Sick Children between June 1997 and July 2008 were reviewed. All the samples were collected by either Children's Aid Societies or physicians who suspected intrauterine drug exposures and were sent to Motherisk Laboratory for clinical testing. The criteria for suspicion included personal or third-party reports, evidence of alcohol, and/or drug abuse.

Neonates who were tested for intrauterine ethanol exposure, using meconium FAEE measurements were identified. All the available meconium and hair analyses for those neonates were reviewed.

Other drugs of abuse that were tested in some of these neonates, in addition to meconium FAEE, were amphetamines (amphetamines and methamphetamines), barbiturates, benzodiazepines, cannabinoids, cocaine (cocaine and benzoylecgonine), opiates (heroin, morphine, codeine, hydrocodone, hydromorphone), oxycodone, phencyclidine, tricyclic antidepressants, meperidine, and methadone.

All the neonatal meconium samples were stored at −80°C, and all the hair samples were stored at room temperature. Analyses were conducted within 2 weeks of receipt of a sample. Prior to June 2007, all the meconium FAEE analyses were conducted via liquid–liquid extraction followed by gas chromatography with flame ionization detection as proposed by Chan et al. (2003), with positive drug samples being sent out for confirmation via gas chromatography with mass spectrometry. As of June 2007, all the meconium FAEE analyses were conducted via headspace solid-phase microextraction followed by gas chromatography with mass spectrometry, obtained from Shimadzu, Columbia, MD (Hutson et al., 2009). All the other drugs of abuse exposures were tested via methanol extraction followed by enzyme-linked immunosorbent assay obtained from Immunalysis Corporation, Pomona, CA.

Positive results for heavy in utero ethanol exposure were cases that had over 2 nmol FAEE per gram meconium (Chan et al., 2003). Positive drug of abuse test were defined as a corresponding meconium and/or hair analysis positive for the specific drug of abuse as asked by the child protection worker.

Statistical analysis

Descriptive statistics were used to identify the rate of drug exposures, where the rate was determined via division of positive cases over the sum of the negative and positive cases (unknown cases were not included in the calculations). Odds ratios (ORs) were used to obtain the relative likelihood of drug exposure in combination with heavy in utero ethanol exposure.

Results

Nine hundred and forty three neonates were tested for intrauterine ethanol exposure using meconium FAEE measurements. There were 207 cases of insufficient meconium quantity for FAEE analysis; these cases were excluded from the statistical calculation. Out of the 736 cases with meconium FAEE results, 114 were positive results and 622 were negative, resulting in a 15.5% positivity rate for heavy in utero ethanol exposure.

In addition to FAEE testing documenting ethanol exposure, neonates were most frequently tested for cocaine, followed by cannabinoids, opiates, and amphetamines.