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Neonatal screening for prenatal alcohol exposure: Assessment of voluntary maternal participation in an open meconium screening program

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ABSTRACT

Meconium fatty acid ethyl esters (FAEEs) are validated biomarkers of fetal alcohol exposure. Meconium FAEE testing can potentially be used as a screen by health-care professionals to identify neonates at-risk for Fetal Alcohol Spectrum Disorder, thereby permitting diagnostic follow-up of these children and early intervention in those who develop disabilities. The purpose of this study was to assess whether women would willingly partake in a screening program of this nature. This was determined by launching a pilot screening program for prenatal alcohol exposure in a high-risk obstetric unit previously shown to have a high prevalence of FAEE-positive meconium via anonymous meconium testing. The program involved voluntary testing of meconium for FAEEs and long-term developmental follow-up of positive cases through an existing public health program. The participation rate in the screening program was significantly lower than when testing was conducted anonymously (78% vs. 95%, respectively; $p < 0.05$), and the positivity rate was 3% in contrast to 30% observed under anonymous conditions ($p < 0.001$). These low rates suggest that the majority of mothers who consumed alcohol in pregnancy refused to participate. We conclude that despite the potential benefits of such screening programs, maternal unwillingness to consent, likely due to fear, embarrassment, and guilt, may limit the effectiveness of meconium testing for population-based open screening, highlighting the need for public education and social marketing efforts for such programs to be of benefit.

Introduction

Fetal Alcohol Spectrum Disorder (FASD) is a term that describes the broad range of physical, cognitive, and behavioral disabilities that can arise due to prenatal alcohol exposure (Chudley et al., 2005; Streissguth & O'Malley, 2000). Estimated to affect 9.1/1000 live births, FASD is a leading preventable cause of mental retardation in the western world and a substantial economic burden (Sampson et al., 1997). The annual costs in Canada alone exceed $5 billion in productivity losses, medical costs, special education, social services, and externalizing behaviors (Stade et al., 2009).

Although the primary alcohol-induced damage is permanent, early diagnosis is beneficial and associated with a decreased risk of secondary disabilities such as disrupted school experience, unemployment, institutionalization, and trouble with the law; likely because it permits early intervention and specialized support (Streissguth et al., 2004). Unfortunately, recognizing FASD is extremely challenging, and diagnosis is often contingent upon establishing a history of significant *in-utero* alcohol exposure (Chudley et al., 2005). Since maternal reports are unreliable in supplying this information due to recall bias and common underreporting (McNamara, Orav, Wilkins-Haug, & Chang, 2005; Russell et al., 1994), objective methods and biomarkers for ascertaining prenatal alcohol exposure have been investigated.

Fatty acid ethyl esters (FAEEs) are non-oxidative metabolites of ethanol formed by the esterification of ethanol to endogenous fatty acids or fatty acyl-CoA, which deposit and accumulate in fetal meconium (Best & Laposata, 2003; Koren, Hutson, & Gareri, 2008). Numerous studies have established that elevated meconium FAEE concentration can serve as a biomarker of heavy prenatal alcohol exposure occurring in the last two trimesters of pregnancy (Bearer,

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Gould, Emerson, Kinnunen, & Cook, 1992; Bearer et al., 1999, 2003, 2005; Brien et al., 2006; Chan et al., 2003; Klein, Karaskov, & Korent, 1999; Littner, Cudd, O'Riordan, Cwik, & Bearer, 2008; Moore, Jones, Lewis, & Buchi, 2003). Furthermore, agreement between meconium FAEEs and various alcohol-related outcomes has been demonstrated (Brien et al., 2006; Hutson, Magri, Gareri, & Koren, 2010; Jacobson, 2006; Noland et al., 2003; Peterson et al., 2008), and this test has been used anonymously to obtain epidemiological data on prenatal alcohol exposure in select populations (Garcia-Algar et al., 2008; Gareri, Lynn, Handley, Rao, & Koren, 2008; Goh et al., 2010; Hutson et al., 2010).

It has been recognized that meconium analysis for FAEEs may serve as a neonatal screening tool for the identification of alcohol-exposed newborns, which could potentially be implemented as a universal screen or targeted to high-risk populations (Goh et al., 2008). Such screening would not only provide accurate exposure history required for diagnosis, but if implemented along with a comprehensive follow-up program and interventions, could facilitate early recognition and treatment of FASD (Gifford et al., 2010; Goh et al., 2008; Hopkins et al., 2008). As an added value, it may identify and allow for intervention in problem-drinking mothers, which, in turn, may prevent future alcohol-exposed pregnancies (Koren et al., 2008). However, since informed consent from a competent patient or appointed guardian prior to treatment or testing is an ethical and legal component of medical practice (Etchells, Sharpe, Walsh, Williams, & Singer, 1996; Flagler, Baylis, & Rodgers, 1997), a screening program of this nature may require consent of the child's legal guardian (typically the parent). This could diminish the value of meconium screening in a clinical setting since embarrassment, guilt, and fears of stigma and child apprehension, may deter women who consumed alcohol from consenting to testing despite the potential value to child health.

To determine if women would willingly participate in a neonatal screening program for prenatal alcohol exposure, we offered meconium testing with subsequent follow-up, interventions, and social supports, to women from a regional Ontario population delivering in a high-risk obstetric unit previously shown to have a high prevalence of alcohol-exposed neonates as determined by anonymous meconium testing. We assessed the rates of voluntary participation and positivity for alcohol exposure in this pilot screening program, and compared these with the rates observed with anonymous testing.

Methods

Subject recruitment

The target population to whom screening was offered were women residing in the region of Grey-Bruce, Ontario, who were delivering at St. Joseph's Health Care (SJHC) in London, Ontario. Grey-Bruce is located in Mid Western Ontario, Canada, and occupies an area of 8586 km^2, comprising of a midsized city (Owen Sound, ~22,000 people), smaller towns, farming communities, first nation communities, and Mennonite settlements. There are ~1200–1400 births per year in the region, but high risk or complicated pregnancies are often transferred out of the region to tertiary and more specialized health-care centres, one of which is the high-risk obstetric unit of SJHC in London, Ontario (~50 births/year). We chose to launch the screening program at this high-risk obstetric unit since a previous study, using anonymous meconium testing, observed a 12-fold higher risk of FAEE-positive meconium in women referred to this site as compared to the general population of the region (30% vs. 2.5%) (Goh et al., 2010).

Written informed consent for meconium FAEE analysis and follow-up of those testing positive was sought from all Grey-Bruce women delivering at SJHC in London, Ontario from November 1st, 2008 to May 31st, 2010. Briefly, Grey-Bruce residents identified by nurses were informed of the study, offered screening, and given an *Informed Consent* document to review and sign if they chose to participate. Women were also informed of the study through pamphlets and posters in the maternity ward. It was stressed that a positive test or self-report of drinking in pregnancy would not necessitate involvement of child protection agencies, but would be used to initiate follow-up by the public health unit and to mobilize support services if needed.

Meconium collection, handling, and analysis

Meconium specimens from neonates born to consenting women were collected into 50-mL screw cap conical polypropylene tubes (Sarstedt AG & Co., Numbrecht, Germany) by nursing staff and labeled with the subject number to ensure confidentiality. Samples were stored onsite at −20 °C and shipped on dry ice to the Motherisk Laboratory at Hospital for Sick Children in Toronto, Ontario on a biweekly basis, where they were stored at −80 °C until analysis.

Meconium FAEEs were measured using headspace solid-phase microextraction and gas chromatography-mass spectrometry. The method involves the detection and quantification of four FAEEs (ethyl palmitate, linoleate, oleate, and stearate) using corresponding d_5-ethyl esters as internal standards. It has been developed and validated in our laboratory, and published in detail elsewhere (Hutson, Aleksa, Pragst, & Koren, 2009; Hutson, Rao, Fulga, Aleksa, & Koren, 2011). Heptane, ethyl esters (palmitate, linoleate, oleate, stearate), fatty acids (palmitic, linoleic, oleic, stearic), anhydrous ethanol-d_6, and thionyl chloride were obtained from Sigma–Aldrich Co. (St. Louis, MO). Acetone was obtained from EMD Chemicals Inc. (Gibbstown, NJ). Chromatograms were analyzed using LabSolutions GCMSsolution software version 2.50SU1 (Shimadzu, Kyoto, Japan). A cumulative sum of ≥2.00 nmol FAEE/gram meconium was considered positive for heavy alcohol exposure, as established in a population baseline study that measured meconium FAEEs in neonates born to abstainers, social drinkers, and confirmed heavy drinkers (Chan et al., 2003). The same cut-off was used in the previous anonymous prevalence study conducted at this site (Goh et al., 2010).

Maternal and neonatal characteristics

Subject characteristics along with pregnancy and delivery information were obtained from charts of consenting women. Additionally, information on alcohol use was obtained by the nursing staff using the Parkyn Screening Tool; a routine postpartum questionnaire administered to all women as part of Ontario's Ministry of Health and Long Term Care "Healthy Babies Healthy Children" program. This questionnaire is meant to assess families with a new baby for risks of future health concerns and includes a question regarding alcohol use in pregnancy.

Follow-up and neurodevelopmental assessment

Children with positive meconium results were followed-up through Ontario's Healthy Babies Healthy Children program, which involves postpartum home visits by public health nurses, who provide personalized support and education to families with newborns (Ontario Ministry of Health and Long-Term Care, 2003). In this study, the nurse assigned to a positive case was notified of the meconium test results, conducted an in-depth family assessment (including a screen for alcohol use disorders), and enrolled the family in an ongoing home-visiting program with an individualized family service plan that included regular assessments of