Meconium Testing to Detect Prenatal Alcohol Exposure: More Harm Than Good?

Nicky Cairncross

ncairncr@sfu.ca

Simon Fraser University

Abstract:

Meconium testing has been suggested as a novel approach to early identification and therefore intervention for Fetal Alcohol Spectrum Disorder (FASD), a set of characteristics associated with prenatal alcohol exposure leading to life-long developmental health impacts. Meconium (newborns’ first stool) can been tested for specific biomarkers to establish whether a newborn has been exposed to alcohol in utero. One common biomarker is Fatty Acid Ethyl Esters (FAEEs), which are directly formed from metabolism of alcohol. This policy proposal presents a summary of findings to present the current advantages and limitations of meconium screening. Currently, there is a lack of research following up with children who test positive for FAEE to establish predictability of this screening tool. Given the stigma of admitting to prenatal alcohol use and the lack of evidence correlating positive FAEE screens with subsequent FASD diagnoses, meconium screening should be approached with caution. Policy recommendations to consider include 1) prohibiting the use of targeted meconium screening and 2) implementing mandated annual reporting on FASD prevalence to establish population level data.

Introduction

Fetal Alcohol Spectrum Disorder (FASD) is the term used to describe a set of characteristics associated with prenatal alcohol exposure of the fetus, leading to life-long
developmental, health and behavioural challenges (Streissguth et al., 2014). Present discourse discusses the inherent preventability of FASD; however, 50% of pregnancies are unplanned (“Prevention of FASD”, n.d) and alcohol exposure prior to pregnancy recognition may occur — leading to the need for early identification in infants.

Meconium testing has been suggested as a novel approach to early identification and therefore intervention for FASD (Burd & Hoffer, 2008; Joya, et al., 2012). The presence of fatty acid ethyl esters (FAEEs) in meconium, a newborn’s first stool, may correlate with prenatal alcohol exposure (PAE) (Hutson et al., 2011). This paper will focus on whether meconium testing is an appropriate tool for early identification in children exposed to prenatal alcohol.

Methods

A scoping review utilizing systematic strategies (Appendix A) indicated that, while useful and economical (Hutson, et al., 2011), meconium screening has important limitations. Searching PubMed and PsycInfo, using key words (meconium, prenatal alcohol exposure, and fatty acid ethyl esters or FAEEs) to identify studies published from 2010-2018, resulted in one critical literature review, nine prospective cohort studies, and one case study. The studies varied in approaches and findings.

Findings

Before meconium testing continues to be utilized in postnatal services some important findings should be taken into consideration. First, meconium testing excludes PAE in the first trimester (Goecke et al., 2014; Hime et al., 2014 & Vaiano et al. 2016), which is a critically sensitive period for fetal development (Andrew, 2014). A screening program for PAE without first trimester exposure fails to identify all children with PAE accurately.
Research suggests further investigation into reliable cut-off limits of FAEEs citing no difference in FAEE levels between abstainers and light-to-moderate drinkers (Himes et al, 2015 & Kwak et al, 2014). Many studies concluded measuring both FAEE and Ethyl Glucuronide (EtG), another biomarker, in combination would be best practice (Hasted et al., 2013 & Bakadash et al., 2010), or using EtG alone (Himes et al., 2015). Others (Goecke et al.) found only EtG showed an association with alcohol history ($P < 0.01$). Studies raised the risk of false positive tests secondary to delayed sample collection (Zellner et al., 2012a), FAEE instability at various temperatures (Himes et al., 2014 & Zellner et al., 2011), and traces of FAEEs found in mothers who credibly reported abstinence during pregnancy (Hasted et al., 2013).

Screening would not reduce costs related to assessment and diagnosis. Testing positive for FAEEs is not enough for a diagnosis of FASD in isolation (Zellner, 2012b; Andrew, 2014). Once infants have tested positive for FAEE above the established cutoff limits, they would be flagged for a full FASD assessment at a later age. Following a voluntary screening program, Zellner et al. (2012 b & 2012c) followed an infant identified as being prenatally exposed and the infant was later diagnosed with neurocognitive challenges; however, one can not make a causal link before a full diagnostic assessment is complete.

Given the limited options preceding a positive test, other then flagging for further follow up, a FAEE test increases the potential harm and stigma associated with screening (McLennan & MacMillan, 2016). Clinical epidemiological studies have posed caution on the efficacy of imposed screening for various health issues when there is limited evidence on positive health outcomes (Finkelhor, 2018; McLennan & MacMillan, 2016). Children who test positive may funnel resources and clog waitlists with children who may not have been referred for an FASD
assessment otherwise. Provision of unnecessary services can outweigh benefits if it is hindering the provision of services to children in need (McLennan & MacMillan, 2016).

To be more cost-effective many researchers have postulated the use of targeted instead of universal screening programs. However, researchers caution that a targeted program may increase bias and stigma. This shame and stigma created by a targeted screening program can hinder health care provider relationships and reduce patients accessing services postnatally for fear of punishment.

Discussion

Although early interventions are critical, ethical considerations should be noted. Targeted screening can increase stigma and minimize trust in healthcare professionals (Zellner 2012a). Furthermore, in Canada, attention to initiatives that target ‘at risk’ populations, specifically Indigenous women, for FASD prevention is pervasive and troubling (Salmon, 2011). However, the feasibility of using a universal screening program remains to be seen. Substance use during pregnancy is a complex issue and should be analyzed with nuance. There is a prevailing idea that meconium screening will be an effective initiative creating positive health impacts on childhood development (Burd & Hoffer, 2008). There is a lack of research establishing cost effectiveness, earlier interventions, and improved health outcomes. Therefore, meconium screening should not be implemented in a universal or targeted way to establish infants who have been exposed prenatally to alcohol. Instead of using meconium screening to establish population level data on PAE, an alternative could, for example, be mandated annual reporting of FASD diagnoses from health care professionals. If more sound longitudinal research confirms a positive FAEE screen to an FASD diagnosis, and positive health outcomes can be established, then policies should be
revisited. However, at this time, given the plethora of ethical challenges and extensive social repercussion of meconium screening, it should not be used to test for prenatal alcohol exposure.

Policy recommendations:

1. Prohibit the use of targeted meconium screening
2. Mandate annual reporting on prevalence of FASD from all diagnosing health care professionals in British Columbia (to enable population-level estimates)
References

Andrew, G. (2014). To test or not to test and that is the question. Canadian Journal of Neurological Sciences, 41(1), 1-2.


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Appendix A: Literature Search

Records Identified via PubMed 2010-2018 (n=29)

Records Identified via Psychinfo 2010-2018 (n=10)

Records after Duplicates Removed (n=33)

Records after Exclusion Criteria (n=14)

Full Text articles Assessed for Eligibility (n=14)

Studies Included (n=11)

Records Excluded (n=3)
- FAEEs not focus of research
- Focus on ethics of meconium testing

Number of Duplicate Studies (n=6)

Records Excluded (n=20)
- Dissertations
- Prevalence studies
- Methadone usage
- Impact studies
### Appendix B: Articles Identified Using Systematic Approaches

<table>
<thead>
<tr>
<th>Authors/ Year</th>
<th>Study Type</th>
<th>Sample Size &amp; Methods</th>
<th>Purpose / Findings</th>
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</thead>
<tbody>
<tr>
<td>Bakdash, A., Burger, P., Goecke, T. W., Fasching, P. A., Reufbach, U., Bloch, S., &amp; Kornhuber, J. (2010)</td>
<td>Prospective Cohort Follow up study</td>
<td>602 meconium samples No Maternal self-report of alcohol use</td>
<td>- The cut-off of 500 ng/g for the cumulative FAEE concentration of four esters was derived in this study from the generally accepted value of 2 nmol/g=600 ng/g for seven esters and corresponds best with a cut-off of 274 ng/g EtG.</td>
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<td>Goecke, T. W., Burger, P., Fasching, P. A., Bakdash, A., Engel, A., Härberle, L., ... Kornhuber, J. (2014)</td>
<td>Prospective Cohort No follow up</td>
<td>557 Pregnant Women/ meconium samples Maternal self-report</td>
<td>- 21.2% of the 557 participants admitted low-to-moderate (Unspecified amount) alcohol consumption during (no time, dose response specified). - pregnancy - Of the parameters analyzed from meconium, only EtG showed an association with alcohol history</td>
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<td>Roukema, H., Lum, L., Eisinga, Zelner, I., Shor, S., Lynn, H., &amp; Koren, G. (2012a).</td>
<td>Prospective Cohort Follow up study</td>
<td>122 meconium samples</td>
<td>- Quantification of fatty acid ethyl esters from only 50 mg meconium was fully validated and applied to 122 samples from newborns whose mothers were suspected of drug and alcohol use. - It was found that even if mothers credibly reported abstinence during pregnancy, sometimes small amounts of FAEEs can be found in meconium.</td>
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<tr>
<td>Huneas, S. K., Conchero, M., Scheidweiler, K. B., &amp; Huestis, M. A. (2014)</td>
<td>Prospective cohort</td>
<td>107 Women Meconium samples used</td>
<td>- Testing stability of EtG and FAEEs under various freeze/thaw cycles and time spent in room temperature conditions. - Alternatives to FAEE or combined use of FAEE with EtG and EtS are increasingly recommended for meconium</td>
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<td>Huneas, S. K., Tripp, T., Petersen, J. M., Raffo, C., Burd, L., ... Prenatal Alcohol in SIDS and Stillbirth</td>
<td>Prospective Cohort</td>
<td>6 meconium samples</td>
<td>- A method was developed and validated to detect and quantify four FAEEs (ethyl palmitate, ethyl lactate, ethyl oleate, and ethyl stearate) from 0.5 g of meconium - The detection limits of the four FAEEs ranged from 0.020 to 0.042 nmol/g and are 6- to 25-fold lower than the individual FAEE threshold concentrations (0.5 nmol/g).</td>
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<td>Joos, A., Frigui, B., Ortiguera, S., Papasetr, E., Martinez, E. F., Manich, A., ... &amp; Pichinis, S. (2012).</td>
<td>Literature Review</td>
<td>Meconium samples purchased from newborns who exhibited Abstinence Phenomena Symptoms or known or supposed drug abuse in mothers</td>
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<td>Kwak, H.-S., Han, J.-Y., Choi, J.-S., Ahn, H.-K., Kwak, D.-W., Lee, Y.-K., ... - Nava-Ocampo, A. A. (2014).</td>
<td>Prospective Cohort</td>
<td>294 pregnant women</td>
<td>- No significant differences were identified between the levels of each FAEE in meconium from babies born to abstainers and those born to mothers with history of light-to-moderate prenatal alcohol exposure during their pregnancy. - Light-to-moderate prenatal alcohol exposure cannot be predicted by the FAEE concentrations</td>
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<tr>
<td>Zelner, I., Hutson, J. R., Kapur, B. M., Feig, D. S., &amp; Koren, G. (2012a).</td>
<td>Prospective Cohort</td>
<td>136 meconium samples</td>
<td>- First collected meconium sample tested negative in all 30 newborns - Later samples tested about the 2 nmol/g cut-off in 19 of 30 babies</td>
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<td>Zelner, I., Shor, S., Lynn, H., Roukema, H., Lum, L., Eisinga, K., &amp; Koren, G. (2012b).</td>
<td>Prospective Cohort</td>
<td>47 pregnant women</td>
<td>- Children with positive meconium results were followed through Ontario's Healthy Babies Healthy Children program - The participation and positivity rates were significantly lower than those when testing anonymously in the same unit which highlights the hesitancy of women to participate in such screening programs even when researchers are promising there will be no punitive measures taken</td>
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<td>Zelner, I., Shor, S., Lynn, H., Roukema, H., Lum, L., Eisinga, K., &amp; Koren, G. (2012c).</td>
<td>Case Study</td>
<td>1 mother/child pair</td>
<td>- First case of a child identified as part of a research study (the research study above Zelner, I., et al. (2012b) on a neonatal screening program for FAEE. - The meconium tested high for FAEEs (52 nmol/g; positive cut-off ≥ 2 nmol/g), which prompted active follow-up of the infant's development, identifying early neurocognitive problems</td>
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