Alcohol 54 (2016) 39–44

Contents lists available at ScienceDirect

Alcohol

journal homepage: http://www.alcoholjournal.org/

Did you drink alcohol during pregnancy? Inaccuracy and discontinuity of women's self-reports: On the way to establish meconium ethyl glucuronide (EtG) as a biomarker for alcohol consumption during pregnancy

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ARTICLE INFO

Article history:
Received 22 February 2016
Received in revised form
4 July 2016
Accepted 5 July 2016

Keywords:
Alcohol
Pregnancy
Self-report
Meconium
Ethyl glucuronide
EtG

ABSTRACT

Consuming alcohol during pregnancy is one of the most verified prenatal risk factors for impaired child development. Information about the amount of alcohol consumed prenatally is needed to anticipate negative effects and to offer timely support. Women's self-reports are not reliable, often influenced by social stigmas and retrospective recall bias, causing biomarkers of intrauterine ethanol exposure to become more and more relevant. The present study compares both women's gestational and retrospective self-reports of prenatal alcohol consumption with levels of ethyl glucuronide (EtG) in meconium. Women (n = 180) gave self-reports of prenatal alcohol consumption both during their 3rd trimester (gestational self-report) and when their children were 6–8 years old (retrospective self-report). Child meconium was collected after birth and analyzed for EtG. No individual feedback of children's EtG level was given to the women. All analyses were run separately for two cut-offs: 10 ng/g (limit of detection) and 120 ng/g (established by Goecke et al., 2014). Mothers of children with EtG values above 10 ng/g (n = 42) tended to report prenatal alcohol consumption more frequently. There was no trend or significance for the EtG cut-off of 120 ng/g (n = 26) or for retrospective self-report. When focusing on women who retrospectively reported alcohol consumption during pregnancy, a claim to five or more consumed glasses per month made an EtG over the 10 ng/g and the 120 ng/g cut-off more probable. Women whose children were over the 10 ng/g EtG cut-off were the most inconsistent in their self-report behavior, whereas the consistency in the above 120 ng/g EtG group was higher than in any other group. The next step to establish EtG as a biomarker for intrauterine alcohol exposure is to correlate EtG values in meconium with child developmental impairments.

Introduction

Consuming alcohol during pregnancy is one of the most verified prenatal risk factors (Polańska, Jurewicz, & Hanke, 2015). However, prevalence of gestational alcohol consumption is still approximately 20% (Lanting, van Dommelen, van der Pal-de Bruin, Bennebroek Gravenhorst, & van Wouwe, 2015; Melchior et al., 2015; O'Keeffe et al., 2015). Epidemiological data are based on women's self-reports, which are prone to understatement (Todorow, Moore, & Koren, 2010), and many cases are likely to go unreported. The most severe consequence of prenatal alcohol consumption is Fetal Alcohol Syndrome (FAS), which is characterized by smaller size, lighter weight, and distinct facial abnormalities at birth (Landgraf, Nothacker, & Heinen, 2013). However, in cases of low to moderate alcohol consumption, developmental

Conflict of interest: The authors declare that they have no conflict of interest.

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http://dx.doi.org/10.1016/j.alcohol.2016.07.002
0741-8329/

consequences are often not immediately obvious: Newborns seem to be unimpaired, there are no physical abnormalities, but effects on brain development are subtle and probable (Dörrie, Föcker, Freunscht, & Hebebrand, 2014). In particular, earlier findings suggest neurobehavioral and cognitive impairments comparable to symptoms of Attention Deficit Hyperactivity Disorder (ADHD) (Burger et al., 2011). Information about the consumed amount of alcohol during pregnancy is needed to anticipate negative effects on child development. There are three current options for the assessment of prenatal alcohol consumption:

A. Measure child developmental impairments.
B. Ask the woman.
C. Analyze biomarkers of the woman or child.

Options to measure child developmental impairment are restricted and this method often results in a very late diagnosis. In one study, 100% of children diagnosed in childhood with FAS had no detectable symptoms at birth (Little, Snell, Rosenfeld, Gilstrap, & Gant, 1990). Therefore, it seems essential to ask the woman about gestational alcohol consumption, which is the most direct and cheapest assessment method, but simultaneously the least reliable.

When asking women about alcohol consumption during pregnancy, the majority deny consumption (Derauf, Katz, & Easa, 2003: 95%; Goecke et al., 2014: 79%). In populations with heavy drinking (risk sample populations), where gestational alcohol consumption is not generally socially discouraged, percentages of denying self-reports are lower (Himes et al., 2015: 31%). However, even in these populations systematic underreporting is an issue. In their review concerning the influence of low to moderate alcohol consumption during pregnancy on child development, Todorow et al. (2010) drew the conclusion that the underreporting in women's self-reports is influenced by retrospective recall bias and social stigmas regarding alcohol use during pregnancy.

If self-reports at one assessment time are of low reliability, perhaps repeating the surveys at different assessment points could help. Currently, it remains unclear if there are specific patterns of self-reporting, for example, denying alcohol consumption when asked during pregnancy and reporting in retrospect. Gollenberg and colleagues (Gollenberg, Mumford, Cooney, Sundaram, & Louis, 2011) have already demonstrated that self-report of alcohol consumption shows the most lack of reliability in comparison with other behavioral self-reports (caffeine, nicotine), both asked during pregnancy and 10 years later.

The last option, establishing child biomarkers which represent alcohol consumption during pregnancy, focuses on metabolites of ethanol. Ethyl glucuronide (EtG) is a minor ethanol metabolite and can be detected in the first stool (meconium) of the newborn, passed within 72 h after birth. EtG has been established in several studies as a biomarker of fetal ethanol exposure during the third trimester of pregnancy (see for review Burd & Hofer, 2008; Joya et al., 2016). Meconium accumulates in the fetal gut from around the 20th week of gestation until birth. The majority of the meconium (75%) is created during the last 8 weeks of pregnancy. Positive cut-off (limit of detection) for intrauterine alcohol exposure varies slightly from study to study, but a minimum of 10 ng/g EtG argues for fetal alcohol exposure during the 3rd trimester (Bakdash et al., 2010; Himes et al., 2015).

In order to establish EtG as a biomarker for low to moderate gestational alcohol consumption, for use in clinical practice, earlier studies focused on correlation with women's self-reports. However, it has been demonstrated in several studies that women's self-reports during pregnancy, due to the above-named biases, do not satisfactorily correlate with meconium biomarkers. Specifically, in general population samples and at times when EtG was high, the correlation was small (Goecke et al., 2014). Correlations were higher in heavy alcohol-consuming populations, indicated by fewer social stigmas and a wider range of reported drinking levels (Himes et al., 2015). Nonetheless, in a review by Lange et al (Lange, Shield, Koren, Rehm, & Popova, 2014) comparing the amount of ethanol metabolites in meconium with women's self-reports during pregnancy, a four-fold understatement of alcohol consumption by self-report was found. Correlation of retrospective women's self-report (for example, when the child has reached school age) with meconium biomarkers has been missing until now.

The present study includes, for the first time, both gestational women's self-reports and retrospective women's self-reports simultaneously. Additionally, two EtG thresholds were compared for significance (10 ng/g and 120 ng/g). The hypotheses were:

1. *Inaccuracy: Between-subject effects.* Mothers of EtG-positive children and mothers of EtG-negative children do not differ in their gestational (3rd trimester) and retrospective (child 6–8 years old) self-report of alcohol consumption during pregnancy. The hypothesis applies to both groups separated by 10 ng/g and 120 ng/g EtG thresholds.
2. *Discontinuity: Within-subject effects.* There is no significant correlation between gestational and retrospective women's self-reports of alcohol consumption during pregnancy for mothers of EtG-positive children. Mothers of EtG-negative children are more consistent. This hypothesis applies to both the groups separated by 10 ng/g and 120 ng/g EtG thresholds.

Materials and methods

Study design

The present study included two assessment times: 2005–2007 (first assessment) and 2012–2015 (second assessment). In the first assessment, pregnant women, recruited as outpatients at the department of obstetrics and gynecology during their 3rd trimester without preselection, took part in FRAMES (**Fra**nconian **M**aternal Health **E**valuation **S**tudies, Goecke et al., 2014; Reulbach et al., 2009). Child meconium was collected after birth (Bakdash et al., 2010). The second assessment took place when the children were 6–8 years old. Both women and children were re-assessed in the follow-up study FRANCES (**Fran**conian **C**ognition and **E**motion **S**tudies). At both time points, women completed a self-rating question concerning their alcohol consumption during pregnancy (question seen in Fig. 1). Women never received individual feedback of their child's meconium EtG levels.

The study was approved by the Local Ethics Committee and was conducted in accordance with the Declaration of Helsinki. All patients gave informed consent.

Participants

The present paper reports the results of $n = 180$ women with complete data sets, who took part in both FRAMES and FRANCES data collection. At the time of childbirth, participants were an average of 32.8 ($SD = 4.67$) years of age, ranging from 19 to 44. Of the 180 participants, 42 (23%) children were EtG-positive with ≥10 ng/g and 26 (14%) with ≥120 ng/g in meconium. Women with EtG-negative vs. EtG-positive children, based on both the 10 ng/g and 120 ng/g thresholds, did not differ during their third trimester in age [10 ng/g: $t(178) = -.37$, $p = .711$; 120 ng/g: $t(178) = -.02$, $p = .982$], secondary education level [10 ng/g: $\chi^2(1, N = 179) = .00$, $p = .962$; 120 ng/g: $\chi^2(1, N = 179) = .00$, $p = .963$], marital status [10 ng/g: $\chi^2(1, N = 179) = .25$, $p = .620$; 120 ng/g: $\chi^2(1,$