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Review

Novel approaches to the diagnosis of fetal alcohol spectrum disorder

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Abstract

The diagnosis of fetal alcohol spectrum disorder is a difficult task, especially in cases where clear, physical markers of in utero alcohol exposure are not apparent. Reviewed in the following paper are some older tools for screening alcohol use in pregnancy and present novel approaches to the diagnosis of FASD, including ethanol biomarker development to behavioural phenotyping. Improving current FASD diagnostic methodology through more novel approaches may provide the possibility of earlier and wider diagnosis, allowing intervention and treatment at stages where the advanced effects of alcohol can still be mitigated.

Keywords: Fetal alcohol spectrum disorder; Diagnosis; TWEAK; T-ACE; Fatty acid ethyl esters; Hair and meconium screening; Behavioral phenotyping

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1. Introduction

Most consequences of in utero alcohol exposure are irreversible. However, with proper support, stimulation and educational efforts, children with fetal alcohol spectrum disorder (FASD) can learn to integrate themselves effectively into society to lead normal lives. Studies have shown the younger the age at which an affected child is identified, the lower the frequency of secondary disabilities (Streissguth et al., 2004). Thus the early diagnosis of FASD in newborns is fundamental for the successful intervention in the course of this devastating disorder. Moreover, the diagnosis of the child may lead to the identification of an often unknown alcohol dependent mother in urgent need for help.

Pre-natal alcohol exposure is associated with a spectrum of effects categorized by FASD. Fetal alcohol syndrome (FAS) is the most severe form of FASD and is the most preventable cause of birth defects in the western world (Bratton, 1995). The clinical characteristics of FAS include pathognomonic facial malformations (short palpebral

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fissures, flat philtrum, thin upper lip), complex brain dysfunction, cognitive impairments, behavioural disturbances and neurological damage (Battaglia et al., 1996). When these distinct facial malformations are present, the diagnosis of FAS can be established without the confirmation of maternal alcohol consumption. However, this ideal scenario occurs only in the minority of cases. One of the most difficult issues regarding FASD lies in the diagnosis of less apparent forms of the disorder where no physical markers have manifested. As such, the majority of these cases go undetected until secondary disabilities develop and the child has begun their schooling (Abel, 1996).

Hence it is apparent that the diagnosis of FASD is difficult since this often requires positive confirmation of heavy maternal drinking. This confirmation may be based on clinical observation, self-reports, medical records, positive biological markers for alcohol in blood, hair or meconium and from behavioural and facial feature measurements of the infant after birth. In this paper we review some older tools for screening alcohol use in pregnancy and present novel approaches to the diagnosis of FASD, including ethanol biomarker development to behavioural phenotyping. Improving current FASD diagnostic methodology through more novel approaches may provide the possibility of earlier and wider diagnosis, allowing intervention and treatment at stages where the advanced effects of alcohol can still be mitigated.

2. Screening for maternal alcohol consumption: maternal testimony and questionnaires

Without the distinctive pathognomonic features seen in FAS at birth, confirmation of in utero alcohol exposure often requires maternal admission to gestational drinking. Unfortunately, maternal self-reporting is often unreliable because of the countless stigmas associated with a pregnant mother's admission to risky behaviours, including alcohol and drug consumption (Russell et al., 1996). As such, obtaining an accurate maternal history of alcohol use in pregnancy may be a difficult task.

Alcohol screening tools have been used for years in adults to help identify problem drinkers in a primary care setting. Questionnaires, such as the Alcohol Use Disorders Identification Test (AUDIT), the CAGE and its modified versions (i.e. TWEAK, T-ACE), the Michigan Alcoholism Screening Test (MAST), and the Timeline Followback calendar (TLFB), have all been effective in distinguishing risk drinkers from non-risk drinkers (Bradley et al., 1998; Russell et al., 1994; Sokol et al., 2003). However, not all of these screening tools have been developed and validated for use within a pregnant population.

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines recommend that any woman who drinks more than seven drinks per week or more than three drinks on any given day in the past month should be further assessed for risk of alcohol-related problems (US Department of Health and Human Services, 2000). To date, moderate evidence indicates that the T-ACE and the TWEAK are effective at identifying women who would benefit from an intervention for their alcohol use during pregnancy (Chudley et al., 2005). Physician documentation alone in comparison to screening tests has been shown to yield lower prevalence estimates (Gupman et al., 2002). Sensitivities and specificities for these two screening tools have been well documented. The four-item T-ACE has demonstrated a 76% and 89% sensitivity and specificity, respectively, in identifying gestational risk drinkers (Savage et al., 2003). The 5-item TWEAK performs with similar accuracy in identifying heavy gestational drinkers, with a sensitivity and specificity ranging from 70% to 79% and 63% to 83%, respectively. Furthermore, Dawson et al. (2001) have shown that by using a threshold of one point rather than two points to assess moderate-risk drinking, the TWEAK performed with a 65.6% sensitivity and a 63.7% specificity. Thus, it may be possible to implement alcohol questionnaires in pregnancy to not only screen for high-risk heavy gestational alcohol consumption but also for equally worrisome cases of moderate-risk drinking in pregnancy. In fact, 2005 Canadian guidelines for the diagnosis of FASD recommend that all pregnant and post-partum women should be screened for alcohol use by their heath care provider with a validated screening tool (i.e. T-ACE, TWEAK) (Chudley et al., 2005).

Although the effectiveness of the T-ACE and TWEAK are well recognized, some cited disadvantages to this screening process have been raised. It has been suggested that a screening protocol to identify in utero alcohol exposure should assess both the mother and the fetus (Savage et al., 2003). The T-ACE and TWEAK may be considered inadequate since they only assess the alcohol dependence of the mother and may fail to identify fetuses exposed to alcohol whose mothers are not alcohol dependant (Savage et al., 2003). Thus a screening protocol should include two different types of screening tools to help identify fetuses at risk for the effects of in utero alcohol exposure; a screen for mothers who report alcohol use for alcohol dependence and a screen for fetal exposures to alcohol (Savage et al., 2003). Maternal screening may still be done using tools such as the TWEAK and T-ACE. To screen infants for *in utero* alcohol exposure, TLFB calendars which include the date of conception and date of pregnancy recognition may be useful in accurately assessing the timing, frequency, and amount of alcohol consumed during pregnancy (Savage et al., 2003). TLFB calendars have been proven to be highly reliable and valid in general populations and include a method for determining the timing of alcohol use (Sobell et al., 1988; Sobell and Sobell, 1992). Combing these two screening methods to identify mothers and infants at risk for gestational alcohol use and exposure may increase the accuracy and effectiveness of screening for maternal alcohol consumption in pregnancy.

Although screening may be a reliable method to help identify at-risk women and fetuses, it should not be