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Alcohol and Fetal Damage

Peter Allebeck and Jørn Olsen

Since the identification of fetal alcohol syndrome in the end of the 1960s, substantial evidence has accumulated on a number of adverse effects that alcohol consumption during pregnancy may have on the fetus. Long-term effects on child development has also been observed. Although the various types of effects are well documented, less is known about threshold levels of consumption, under which there is no risk of damage. Few studies have assessed the risk associated with high episodic drinking. From a theoretical point of view, binge drinking in critical stages in organ formation may constitute a particularly high risk for adverse outcomes.

Key Words: Alcohol, Pregnancy, Fetal Effects.

IT IS well documented that fetal damage in pregnancy due to alcohol exposure is dose-dependent. A high level of alcohol exposure increases the risk of fetal growth retardation, craniofacial malformations, and impaired brain development. A number of other reproductive failures have also been associated with intrauterine exposure to alcohol, but the evidence is less convincing for these outcomes. We consider alcohol to be teratogenic in susceptible individuals, because epidemiological evidence is backed up by results from experimental animal studies and reasonable biological theories. Alcohol is not a sufficient cause in the "strong-Hume" sense, but requires additional component causes to trigger the effect. These other component causes are not known, but could be of a genetic nature or related to diet or other living conditions. Most epidemiological studies suffer from the fact that heavy drinking often is associated with poor social conditions, change in dietary habits, and smoking and drug use. Two recently published books summarize the existence knowledge in the field.[1,2] In the following review, we summarize the existing evidence with regard to various outcomes and particularly what is known about risk levels for adverse outcomes.

MISCARRIAGE AND INTRAUTERINE DEATH

Some studies have shown an increased occurrence of miscarriage[3] and intrauterine death.[4] Other studies have not found such an association.[5] An important methodological problem is that not all miscarriages are recorded, and there is a possibility that use of alcohol affects the likelihood of a miscarriage being treated in hospital, and thus recorded. Heavy users of alcohol might be less likely to seek care for the problem. Larroque[6] concluded that there probably is an association between alcohol and miscarriage, as well as intrauterine death, but that it is unclear at which levels of alcohol abuse.

An alcohol intake of more than 7 drinks per week in females is apparently associated with reduced fecundity,[7] which could be due to an increased occurrence of very early spontaneous abortions.

PREMATURE LABOR

There is weak evidence of increased occurrence of premature labour in high consumers of alcohol,[8,9] but confounding due to socioeconomic factors cannot be ruled out.

GROWTH DISORDERS

Body Length

Several studies have found that children born to women with high alcohol consumption are shorter than other children.[10–12] Other studies have failed to find such an association.[3,4] It should be pointed out that, in follow-up of children to alcoholic mothers, it is difficult (or impossible) to separate prenatal from postnatal risk factors.

Cranial Circumference

Reduced cranial circumference, often associated to lower birthweight, has been observed in a number of studies.[10,12]

Birthweight

A number of studies have analyzed the association between alcohol consumption and birthweight. Larroque[6] reviewed 24 studies, and half of these found such an association. Confounding (e.g., by smoking and social conditions) might be considerable. Some studies have taken account of confounding factors and still found significant risks of low birthweight at consumption levels of at least 2 to 3 drinks per day.[4,13] It has also been shown that children of mothers who continue to drink throughout the pregnancy have a lower birthweight than those whose mothers decrease their consumption.[14,15]

CONGENITAL MALFORMATIONS

Craniofacial Malformations

These have in general been found in children to mothers with high alcohol consumption. A dose–response relation

From the Department of Social Medicine (P.A.), Göteborg University, Göteborg, Sweden; and the Department of Epidemiology and Social Medicine (J.O.), University of Aarhus, Aarhus, Denmark.

Reprint requests: Peter Allebeck, M.D., Ph.D., Department of Social Medicine, Vasa Hospital, S-411 33 Göteborg, Sweden.

has been found between level of alcohol intake and the risk for craniofacial malformations.[16] It has also been suggested that they are more common in children to mothers with high consumption in the first trimester or around conception. It is to be expected that binge drinking at critical stages is more important than a daily, moderate consumption, and there is some empirical support for this.[17,18]

Other Malformations

Some studies have shown an increased occurrence of malformations also after a moderate alcohol consumption in mother.[19,20] Mills et al.[21] did not find any increased risk of malformation after consumption of up to 2 drinks per day. It should be pointed out that congenital malformations are relatively common (around 9/1000 births in Sweden) and that very large materials are needed to show an increased occurrence in relation to alcohol abuse.

LEFT-HANDEDNESS

Left-handedness has been considered a sensitive marker of neurotoxic exposure in fetal life, and the prevalence of left-handedness in early childhood was assessed in children exposed to moderate to high levels of alcohol in pregnancy.[22] No statistically significant increased prevalence was found.

FETAL ALCOHOL SYNDROME (FAS)

FAS was first described in 1968 by LeMoine et al.[23] It consists of three types of congenital defects: growth disturbances, deviant appearance, and symptoms from the CNS. A less pronounced form of the syndrome is called fetal alcohol effects.

Growth disorders can occur before and after birth, and may effect length, weight, and cranial form, as described.

The deviant appearance is characterized by a flat middleface, a thin upper-lip, epicantus fold, and other malformations in the face or on the extremities. The appearance is difficult to diagnose at birth, but becomes more characteristic in early childhood.

The CNS effect may consist of cramps, mental retardation, hyperactivity, memory disturbances, and structural changes, such as mild reduced brain size. To make the diagnosis of FAS, some symptoms from each of these groups should be present, as well as a record of heavy alcohol consumption in the mother. Thus, alcohol exposure is made a necessary cause of FAS by a circular argument that includes the "cause" in the definition of the disease.

Long-Term Effects

Reduced body weight, length, and cranial circumference has, in several studies, been shown to remain throughout childhood. Day et al.[24] showed an association between the age of 3 years and alcohol use in the mother, even after control for nutritional and environmental factors. Streissguth et al.[25] showed reduced IQ, learning problems, concentration disorders, and behavioral deficits in 7-year-old children of mothers with alcohol problems. Aronsson and Hagberg[26] reported behavioral disturbances and poor performance on psychological tests in 12- to 13-year-old children of mothers with high alcohol consumption. These mothers also had considerable social problems.

In the EUROMAC study, children were assessed at 18 months according to the Bayley scales and other instruments. In none of the tests did children of mothers with a moderate to high alcohol consumption have poorer results than other children.

OCCURRENCE

Because FAS is the only defined disorder for which alcohol has been attributed as the main cause, this is the only diagnosis for which prevalence rates has been reported. Abel and Sokol[27] identified in a review 19 studies in which occurrence of FAS had been calculated. It should be noted that the majority of these 19 studies had none or only one case of FAS. They nevertheless calculated an overall prevalence of 1.9 of 1000. This figure was based on a total number of FAS children (164) identified in a total sample size of 88,236 live births. Another way to present the results is to conclude that, in 9 of these 19 studies, there was no FAS child among the remaining 10, the prevalence figures vary between 0.4 to 0.6/1000[28,29] and 3.0 to 3.1/1000.[30,31]

Attempts have been made to calculate prevalence of FAS among children with mental retardation. Abel and Sokol[32] have reviewed five studies of prevalence of FAS among children with mental retardation. In the same way as described, they collapsed all cases identified in all studies and devided by the sum of the study populations, and found a prevalence of 23/1000. The figures reported varied from 8/1000[33] to 88/1000.[34]

It should be pointed out that FAS is difficult to diagnose; and the interobserver, and perhaps even intraobserver, agreement is expected to be low. All prevalence estimates are thus observer-specific and not necessarily comparable over time or between different populations.

RISK LEVELS

EUROMAC[35] is the only study that specifically has been designed to assess risk associated with moderate alcohol consumption and to identify a threshold for harmless alcohol consumption. 8448 pregnancies were followed from eight regions in Europe. Alcohol consumption was assessed by trained interviewers and transformed into grams of alcohol. The children were assessed with regard to their stational age, length, weight, and Apgar score, and follow-up at 18 months was performed according to the Bayley scales.

No case of FAS was identified; reduced birthweight was

noted at consumption levels above 120 g/week. Assessment at 18 months of age showed that children of high consumers did not have poorer results on the Bayley scales than nonconsumers of alcohol. A threshold effect for low birthweight was noted at 60 g/week, although the authors refrain from drawing strong conclusions from this single value. They concluded that alcohol consumption around 120 g/week (about 2 drinks/day) can be considered harmless for the child. This is consistent with other findings that fully developed, and even partial FAS seems to occur only at high consumption levels.[27,36] They also concluded that reduced fetal growth probably is the most sensitive measure of a prenatal alcohol effect. Reduced birthweight is found after an exposure of 80 g/week.

Besides EUROMAC, a number of studies have attempt to analyze effects of various outcomes of different levels of alcohol consumption.

Birthweight

In a review by Larroque,[6] a number of studies are presented in which birthweight has been related to level of alcohol consumption. Most studies have found effects on birthweight at high consumption levels; >400 g/week according to Kaminsky et al.[4] and >250 g/week according to Mills et al.[21] Rosett et al.[13] found reduced birthweight already at a consumption level of >126 g/week. Those studies who have found reduced birthweight at even lower consumption levels have been criticized for a low number of cases and methodological problems. Larroque concludes that there is no evidence of risk of reduced birthweight at a consumption level of <120 g/week.

Abortions

Some studies have found an increased occurrence of spontaneous abortion,[37,38] as well as premature birth[12] at consumption levels around 1 to 2 drinks/week. These studies have been criticized on methodological grounds.[6] The higher number of studies have not found such an association, even at higher consumption levels.[39,40] It should be noted that the occurrence of spontaneous abortion is difficult to assess, because many cases do not come to the hospital and are not recorded. Thus, there is no strong evidence for increased risk of spontaneous abortion or premature birth at lower consumption levels.

Long-Term Effects on the Child

The most important work in this area has been performed by Streissguth et al.[10,41,42] Lower scores on the Bayley scales was noted at 8 months in children whose mothers had consumed >165 g/week. At 4 years age, reduced attention, prolonged reaction time, and lower IQ were noted in children whose mother had consumed >250 g/week; at 7 years age, poor development and increased occurrence of behavioral disturbances were noted in children of mothers who consumed >165 g/week. They also found learning disturbances and lower IQ after binge drinking (i.e. five drinks or more on any occasion), which, if confirmed, is of major public health importance.

A few other studies have followed children over time. Harmful effects have usually been observed at consumption levels of >165 g/week. In a review by Forrest et al.,[43] it is concluded that the lowest level at which developmental disorders have been observed is around 150 g/week.

Summary of Evidence Regarding Risk Levels

The most serious fetal effects, FAS and fetal alcohol effects, apparently occur only at high consumption levels. Risk of low birthweight increases from consumption levels of around 60 to 80 g/week, but a clear threshold is difficult to establish. Risk of spontaneous abortion and premature birth increases possibly at high consumption levels, but it is uncertain if exposure at lower levels increases the risk. Risk of long-term effects, such as neurological and mental development disorders, is found at consumption levels not less than 150 g/week. From a theoretical point of view, binge drinking at critical stages in organ development may cause damage even in pregnancies with an otherwise low level of intake.

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