ADVERSE EFFECTS ON OFFSPRING OF MATERNAL ALCOHOL ABUSE DURING PREGNANCY

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Abstract To evaluate the risk to offspring of heavy drinking during pregnancy, we administered a questionnaire to 633 women at the first prenatal visit. Nutritional status, smoking, drug and alcohol use were determined. Women were classified into three groups: abstinent and rare drinkers; moderate drinkers; and heavy drinkers. After delivery, detailed pediatric, neurologic and developmental examinations were administered by a physician without prior knowledge of any history. Infants born to heavy drinkers had twice the risk of abnormality of those born to abstinent or moderate drinkers (P<0.001). Thirty-two per cent of infants born to heavy drinkers demonstrated congenital anomalies, as compared to 9 per cent in the abstinent and 14 per cent in the moderate group (P<0.001). Microcephaly and multiple congenital anomalies were much more frequent in this group (P<0.001). Heavy drinking during pregnancy increases the risk to offspring. (N Engl J Med 297:528-530, 1977)

RECENT retrospective studies have reported possible teratogenic effects of chronic maternal alcohol abuse during pregnancy on offspring, termed the fetal alcohol syndrome. The features of this syndrome are reported as a recognizable pattern of multiple congenital anomalies with microcephaly, micrognathia, microphthalmia, cardiac defects, prenatal growth retardation and developmental delay. Increased perinatal mortality has also been reported.

Little is known about the frequency and spectrum of a fetal alcohol syndrome, and its very existence has been questioned. Obviously, not all offspring of women who drink heavily are abnormal. This paper reports the risk of abnormalities in these children.

METHOD

In May, 1974, a prospective study was begun at the Boston City Hospital. After informed consent had been obtained women registering for prenatal care were interviewed with a structured interview questionnaire. We evaluated nutritional status on the basis of replies to the question, "What did you eat yesterday, and were yesterday's meals typical?" We analyzed responses according to the recommended dietary allowances of the National Research Council. Adequacy of nine nutrients was assessed on the basis of the recommended diet for women 20 to 30 years old.

We inquired specifically about the present and past use of alcohol, tobacco, narcotics, sedatives, amphetamines, hallucinogens and marihuana. No data were available on fathers, nor could blood samples on mothers be obtained for vitamin levels and other chemical determinations. Beginning in July, 1975, women were interviewed again after delivery to observe changes in drinking and nutritional patterns during the pregnancy.

We determined the volume and frequency of maternal alcohol intake. Separate inquiry was made about the use of wine, beer and distilled spirits. We classified drinking patterns using the Volume-Variability Index of Cahalan, Cisin and Crossley. We calculated the total monthly volume of alcohol by multiplying frequency of use of each beverage by the various quantities usually consumed. Division by 30 yielded the daily volume. Variability of alcohol intake was established as either high maximum, five or more drinks on an occasion, or low maximum, never consuming five drinks. Women who drank less than once a month were classified as abstinent or rare drinkers and placed in Group 1. Heavy drinkers constituted Group 3. They consumed five or more drinks on occasion and also had a consistent daily average of more than 45 ml of absolute alcohol. All women who drank more than once a month but did not meet the criteria for heavy drinkers were classified as moderate drinkers and placed in Group 2. We also calculated grams of alcohol consumed daily per kilogram of body weight.

On the second or third day after delivery, the same pediatric neurologist, without prior knowledge of the prenatal or delivery history, or of the mother's drinking status, administered detailed pediatric, neurologic and developmental examinations to all study offspring. The neurologist assessed gestational age by Dubowitz criteria. Length, weight and head circumference were plotted by percentiles, with use of standardized anthropometric charts for Boston newborns, and also the Lubcheno Tables. Congenital anomalies were recorded and classed as major or minor. The infant's functional state was evaluated, with special attention to jitters, sucking response and tone. After recording the data, additional information concerning pregnancy and delivery was obtained.

RESULTS

Of 685 women eligible, 633 agreed to be in the study, a participation rate of 92 per cent. Group 1 consisted of 326 women (52 per cent), Group 2 of 249 (39 per cent), and Group 3 of 58 (9 per cent). An average of 174 ml of absolute alcohol per day was consumed by women in Group 3 — a mean dose of absolute alcohol of 2.2 g per kilogram per day. Heavy drinkers had a mean age (±S. D.) of 25.7±5.9 years as compared to 22.8±5.5 years in the abstinent and moderate drinking groups (P<0.001 by t-test). Their parity was greater; 19 per cent had four or more children, as contrasted to 6 per cent in the abstinent and 9 per cent in the moderate groups. There were no racial differences across the three drinking groups.

Nutritional status did not differ significantly across the three drinking groups. When the daily allowances of all three groups were compared to the recommended daily allowances of the National Research Council, 22 per cent met the criteria for vitamin A, 58 per cent those for vitamin C, 24 per cent those for vitamin D, 57 per cent those for thiamine, 46 per cent those for riboflavin, 56 per cent those for niacin, 35 per cent those for calcium, 7 per cent those for iron, and 82 per cent those for protein. Heavy drinking was associated with heavy smoking. Of the women in Group 1, 14 per cent smoked a package of cigarettes or more per day as compared to 19 per cent in Group 2 and 60 per cent.
in Group 3 (P<0.001 by chi-square, with 2 degrees of freedom) although 20 per cent of the heavy drinkers did not smoke at all. Less than 4 per cent of all women reported using psychoactive drugs during pregnancy. Thirty-six per cent of heavy drinkers had previously used drugs, as compared to 9 per cent in the other two groups.

Of the 322 babies born to the cohort of 633 women, 152 (47 per cent) were in Group 1, 128 (40 per cent) in Group 2, and 42 (13 per cent) in Group 3. At the conclusion of the study, 180 women were undelivered, 21 had miscarried, seven had had therapeutic abortions, and 84 had been lost to follow-up observation. When the results of infant examinations were compared across drinking groups, no differences were found in Apgar scores, nor in the frequency of acquired medical illness.

Infants were classified as abnormal if they displayed congenital anomalies, growth abnormalities or abnormalities on neurologic examination. Of 42 infants born to heavy drinkers, 29 (71 per cent) were considered abnormal at the time of the newborn examination. This rate compared with 52 (35 per cent) infants in Group 1, and 45 (36 per cent) of those born to women in Group 2 (P<0.001 by chi-square, with 2 degrees of freedom). This population at Boston City Hospital is a high-risk group with 35 per cent of all newborns delivered there admitted to the intensive care unit. This finding correlates well with the overall proportion of abnormal infants as defined by the above criteria (40 per cent) of 322 infants.

Hypotonia was seen more frequently in Group 3 infants (17 per cent), as compared to 12 per cent in those in Group 1 and 9 per cent of those in Group 2 (P = 0.300 by chi-square). Jitteriness was three times as frequent in infants in Group 3, being present in 29 per cent as compared to 10 per cent in Group 1 and 11 per cent in Group 2 (P = 0.001 by chi-square, with 2 degrees of freedom). The ability to suck well was decreased in 12 per cent of infants in Group 3, as compared to 6 per cent in Group 1 and 2 per cent in Group 2 (P = 0.05 by chi-square, with 2 degrees of freedom). There was no clustering of any two of these signs.

Prematurity rose from 5 per cent of births in Group 1 and 3 per cent in Group 2 to 17 per cent in Group 3 (P = 0.05 by chi-square, with 2 degrees of freedom) (Fig. 1). The proportion of postmature infants rose slightly but not significantly from 8 per cent and 9 per cent in infants born to abstinent mothers and moderate drinkers to 20 per cent in offspring of women in Group 3 (Fig. 1). Only P values less than 0.01 were considered low enough to indicate the presence of a real difference because of multiple testing of the data. A marked increase in infants small for gestational age was noted with increased alcohol intake, ranging from 8 per cent and 7 per cent in infants born to mothers in Groups 1 and 2, to 27 per cent in Group 3 (P<0.001 by chi-square, with 2 degrees of freedom). The concurrence of more than one feature was not statistically significant.

Major differences were found in growth measurements among the three groups of babies (P<0.001 by chi-square, with 2 degrees of freedom). Birth length was less in offspring of heavy drinkers (P = 0.05 by chi-square, with 8 degrees of freedom), as was birth weight (P<0.001 by chi-square, with 8 degrees of freedom). Smaller head circumferences were found more frequently among the offspring of heavy drinkers than in the offspring of the abstinent women or moderate drinkers (P<0.001 by chi-square, with 8 degrees of freedom). Five of the 42 infants (12 per cent) born to heavy drinkers were microcephalic, as compared to one of 274 infants (0.4 per cent) in the other two groups combined (P<0.001 by chi-square, with 1 degree of freedom). (Microcephaly is defined as a birth head circumference greater than 2 standard deviations below the mean for gestational age.)

Congenital anomalies were found in offspring of women in all three drinking groups, but were present in 32 per cent of infants in Group 3, as compared to 9 per cent in Group 1 and 14 per cent in Group 2 (P<0.001 by chi-square, with 2 degrees of freedom) (Fig. 2). Minor anomalies rose from 5 per cent in
The frequency of all abnormalities was twice as great in offspring of heavy drinkers as the frequency of those in the other two groups. Nutritional intake, drug use and sociologic factors were not significantly different among women in all three drinking groups and do not account for these findings. Heavy drinking was associated with several variables that may affect fetal outcome. When chi-square analyses were used, however, few relations were found between outcome measures and maternal age, parity, marital status and smoking.

The presence of single and multiple, major and minor congenital anomalies was significantly increased in infants of heavy drinkers, but a specific pattern of abnormalities was not noted, in contrast to previous reports in the literature in which a "fetal alcohol syndrome" has been reported.

Animal studies of experimental alcoholism have also shown offspring with low birth weight, central-nervous-system abnormalities and congenital anomalies when pregnant animals have been fed ethanol and nutrition has been well controlled.14-22

It is not yet clear whether alcohol itself is acting as a direct toxin, via its metabolites, or whether other factors must be present to produce abnormalities. The quantity and variability of alcohol consumption around conception and during the various stages of pregnancy in human beings may have different effects. It is likely that heavy drinking during the first trimester has the greatest effect on fetal maldevelopment, whereas heavy alcohol consumption near term may have a greater effect on fetal nutrition and size. It does appear clear, however, that there is a definitively increased risk to offspring of women who drink heavily during pregnancy.

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