Does Maternal Tobacco Smoking Modify the Effect of Alcohol on Fetal Growth?

ABSTRACT

Smoking and drinking habits were registered by a self-administered questionnaire in 36th week of gestation in 11,698 pregnant women, more than 80 percent of all such women in two Danish cities 1984–87. Alcohol consumption of 120 g/week or more was associated with a greater reduction in the average birthweight in the babies of smokers than of non-smokers (about 40 grams for the non-smokers and about 200 grams for the smokers). This is particularly striking considering that the average birthweight for smokers is lower than for non-smokers. A birthweight difference of more than 500 grams was found between babies of mothers who neither smoked nor drank and mothers who smoked and drank heavily. Our data suggest that women's smoking habits should be taken into consideration when giving pregnant women advice about drinking. (*Am J Public Health* 1991; 81:69–73)

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Introduction

It has been known for many years that smoking during pregnancy reduces fetal growth[1] and it is also well established that growth retardation is part of the fetal alcohol syndrome.[2] Tobacco smoking relates to fetal growth and birthweight in a dose-response manner[1] but the association with alcohol consumption remains less clear. In a recent publication,[3] only alcohol intake of 120 grams or more per week was associated with low birthweight, and it was suggested that health education should be directed mainly toward mothers who drink 100 grams of alcohol or more per week. Another recent study[4] found that alcohol had an effect on birthweight only in smokers.

The purpose of our study was to investigate whether it is reasonable to assume a threshold for the effect of alcohol on birthweight and other growth parameters according to smoking habits.

Methods

Detailed information was collected on drinking and smoking habits of pregnant women attending the midwife centers in Odense and Aalborg, Denmark during their 36th week of gestation, from April 1984 to April 1987. The mothers sent a completed questionnaire directly to the Department of Social Medicine, Odense University. The medical records and questionnaires were given a study number which was not related to the personal identification number. After delivery, obstetrical information was extracted from the medical records and linked to the questionnaire data by means of the study number.

More than 95 percent of all pregnant women in two defined geographical areas at the 36th week of gestation were covered, for a total of 13,815 women. After excluding multiple births, data were available from the questionnaires and medical files for 11,850 women. Most of the non-responders failed to answer reminders, and some left the study area before delivery so that no data were available regarding the child. Also excluded were 152 women who gave birth before the 36th week of gestation; the data file thus consisted of 11,698 women.

Detailed questions were asked concerning beer, wine, spirit, coffee, and tea consumption before and during pregnancy. The number of alcoholic drinks per week was calculated; each drink was considered to contain 12 grams of absolute alcohol according to normal quantities of alcoholic beverages per glass (or bottle of beer) in Denmark. The data on smoking and drinking were self-reported and referred to average consumption during the first 36 weeks of gestation.

Data on gestational age, weight increase during pregnancy, placental weight and measurements of the child (weight, length and head circumference) were recorded from the mothers' and infants' hospital records. All were measured blind to knowledge of questionnaire data. All deliveries took place at one central hospital in each region. The midwives who car-

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ried out the recording had a comparable training and conducted the assessments in a standardized way. The study was part of a large community trial among pregnant women in Denmark.[5]

In the data analysis, multiplicative as well as additive models have been used (logistic regression and analysis of variance). The variables which were most closely associated with alcohol consumption and which were known to be predictors of fetal growth were included as confounders.

Results

Table 1 displays the characteristics of the participating women. Smoking and drinking habits during the first 36 weeks of gestation are shown in Table 2. Thirty-five percent were non-smokers who drank 1–29 grams of alcohol per week. Almost 200 women reported that they consumed 120 grams (10 drinks) or more per week and 832 indicated a smoking history of 15 cigarettes or more per day. The proportion of newborns with a birthweight of less than 2500 grams varied widely with a tendency to correlate with the frequency of alcohol and tobacco use.

Most newborn measures decrease with increasing cigarette and alcohol intake. Among smokers the decrease associated with alcohol is greater than among non-smokers (see Table 3).

In Table 4, the results of the analysis of variance of the data shown in Table 3 are presented. Among non-smokers, alcohol consumption was found to be statistically significantly associated with placental weight and birthweight (test for trend). Among smokers of 1–9 cigarettes, alcohol was associated with birth length, and in the subgroup of heavy smokers alcohol was significantly associated with all measures (except birth length).

All of the variables in Table 4 depended upon the duration of pregnancy and in two additional analyses of variance, confounding by gestational age was addressed (data not shown). In one model, gestational age was included as a covariate and, in another model, the analyses were restricted to women who gave birth between the 39th and 41st weeks of gestation. In these analyses, the adjusted differences from the mean were in the same direction but usually a little smaller. A statistically significant association between alcohol consumption and placental weight was still found for non-smokers. In the group of moderate smokers, significant associations were found for placental weight, birthweight and birth length (but not in the restricted analyses). In the group of heavy smokers, all associations remained statistically significant at the 0.05 level (except in the restricted model with birth length).

Clear "dose-response" relationships were not seen in any models in Table 4, except for birthweight among heavy smokers. However, random variation due to small numbers in the sub strata should be taken into consideration. Among heavy smokers, women who drank more than 30 grams of alcohol per week had a substantially lower birthweight. This is particularly striking considering the generally low mean for that group of women.

Table 5 presents odds ratios for low birthweight according to alcohol consumption compared with frequency of low birthweight for non-drinkers. Each smoking stratum represents a separate analysis. A two- to three-fold increase was seen for all consumers of 120 grams of alcohol or more per week. The marginal values in the table show an excess risk of low birthweight in the group of "heavy drinkers" only. The prevalence of low birthweight increased steadily with increasing cigarette consumption, as can be seen in the right hand column.

All analyses in Table 5 were repeated with the subset of women who gave birth in the 39th–41st weeks of gestation and weight increase during pregnancy was also included in the models. By restricting analyses to deliveries at term, a four-fold increase of low birthweight was found for consumers of more than 120 grams of alcohol per week (data not shown).

After controlling for average alcohol consumption, no association between binge drinking and any of the pregnancy outcome measures was seen (data not shown).

According to the present data set, neither the additive nor the multiplicative model of interaction between alcohol consumption and tobacco smoking on any of these measured outcomes fitted the data very well, despite the fact that both models were acceptable according to formal statistical testing of interaction terms.

Discussion

Birthweight was closely correlated with the combined exposure to alcohol as

TABLE 1—Age, Parity, Gestational Age at Birth and Weight Increase during Pregnancy for 11,698 Participating Women

Characteristics	N. Cases	%
Age (years)		
under 24	3,473	29.7
25 to 34	7,356	62.9
35 or more	869	7.4
Parity		
0	5,628	48.1
1	4,412	37.7
2 or more	1,658	14.2
Gestational age in weeks		
under 39	1,890	16.2
39 to 40	6,122	52.3
41 or more	3,686	31.5
Weight increase in kg*		
under 11	2,923	34.4
12 to 15	2,970	35.0
16 or more	2,599	30.6

*3,206 missing from start of pregnancy to the time of delivery

TABLE 2—Number of Pregnancies According to Maternal Drinking and Smoking Habits: Bottom line, Newborns < 2500 g in percent

Number of Cigarettes per Day	Grams of Alcohol per Week: 0	1–	30–	60–	90–	120+	All
0	1,267	4,088	1,082	404	103	101	7,045
	2.0	1.6	1.8	1.5	1.0	4.0	
1–4	102	368	110	55	10	15	660
	2.9	3.5	2.7	3.6	0.0	13.3	
5–9	294	839	213	74	26	28	1,474
	5.1	4.2	2.8	1.4	0.0	10.7	
10–14	315	894	218	70	31	24	1,552
	4.1	4.8	7.2	5.7	9.7	0.0	
15+	172	433	132	40	26	29	832
	3.5	6.2	5.3	7.5	11.5	25.0	
All	2,150	6,622	1,755	643	196	197	11,563*

*135 missing cases

TABLE 3—Means of Placental Weight, Birthweight, Birth Length and Head Circumference According to the Mother's Alcohol Consumption during Pregnancy, Stratified by Smoking Status

Smoking Status (Daily)	Alcohol in g/Week	Placental Weight in g	Birthweight in g	Birth Length in cm	Head Circumference in cm
Non-smokers	0	569	3,572	52.6	35.4
	1–	561	3,579	52.6	35.4
	30–	557	3,602	52.8	35.5
	60–	537	3,582	52.6	35.5
	90–	532	3,554	52.8	35.4
	120+	534	3,536	52.4	35.5
Subtotal	Mean	560	3,580	52.6	35.4
	(Stddev)	(132)	(483)	(2.3)	(1.5)
1–4 cigarettes	0	567	3,487	52.2	35.1
	1–	557	3,493	52.3	35.3
	30–	572	3,479	52.0	35.4
	60–	564	3,573	52.6	35.3
	90–	626	3,727	53.4	35.6
	120+	450	3,141	51.3	34.7
Subtotal	Mean	560	3,492	52.2	35.3
	(Stddev)	(135)	(510)	(2.5)	(1.6)
5–9 cigarettes	0	555	3,330	51.6	35.0
	1–	548	3,321	51.5	35.0
	30–	528	3,261	51.5	34.9
	60–	522	3,379	51.9	34.8
	90–	524	3,444	52.1	35.5
	120+	489	3,144	50.6	34.6
Subtotal	Mean	544	3,316	51.5	35.0
	(Stddev)	(121)	(458)	(2.2)	(1.6)
10–14 cigarettes	0	572	3,357	51.5	35.0
	1–	548	3,282	51.4	34.9
	30–	535	3,259	51.4	34.8
	60–	528	3,291	51.4	34.7
	90–	540	3,123	50.5	34.4
	120+	493	3,116	50.9	34.4
Subtotal	Mean	549	3,289	51.4	34.9
	(Stddev)	(132)	(467)	(2.2)	(1.5)
15+ cigarettes	0	546	3,270	51.4	34.9
	1–	561	3,266	51.3	34.8
	30–	531	3,207	51.3	34.6
	60–	524	3,123	50.8	34.6
	90–	539	3,169	50.8	34.8
	120+	472	3,023	50.8	34.0
Subtotal	Mean	548	3,239	51.2	34.7
	(Stddev)	(128)	(459)	(2.3)	(1.5)
Total	Mean	556	3,478	52.2	35.2
	(Stddev)	(132)	(497)	(2.4)	(1.6)

well as smoking, but a number of limitations of the study should be kept in mind. The sample was truncated at 36 weeks, and therefore precluded study of babies born at earlier gestation. Since data on smoking and drinking habits are self-reported, intake of alcohol especially was likely to be underreported, particularly high consumption levels. For this reason, no estimates were made for alcohol consumption of more than 120 grams per week. Few women indicated no drinking at all during pregnancy, which agrees with our impression that Danish women usually report moderate and socially acceptable levels of drinking without hesitation.

It is likely that the heavy drinkers were more prevalent among non-responders than responders, but since exposure data were collected prior to the deliveries, bias is not a serious problem. Nevertheless, the effects shown may be underestimates.

Sulaiman, *et al*,[3] suggested that health education during pregnancy should be directed toward mothers who drink more than 100 grams of alcohol per week since no statistically significant effect was seen below this level. However, that study was rather small with only a few women consuming more than 100 g absolute alcohol per week. Lumley, *et al*,[6] did not detect any harmful effect on fetal outcome of alcohol consumption during pregnancy at levels below two glasses a day. Our data indicate that health education should take smoking habits into consideration when giving advice about alcohol use during pregnancy. If pregnant women do not give up smoking while pregnant, a much lower level of alcohol intake should be aimed at. Furthermore, it must be taken into consideration that only a limited set of potential adverse effects of alcohol or smoking combined have been studied. Martin, *et al*,[7] found that maternal alcohol intake, coupled with smoking, exerted an interactive and deleterious effect upon newborn learning.

Our data to some extent supported the findings that consumption of beer is more closely related to adverse outcomes of pregnancy,[3,9,10] but it is likely that the association was confounded by social factors not recorded in the study (data not shown). We cannot recommend that health education should address the types of beverages differently at present.

We found that the average consumption of alcohol was much more important than binge drinking (data not shown). However, this may not be true for other adverse outcomes of pregnancy. Keeping alcohol's teratogenic effect in mind,[2] it is still wise to warn against binge drinking while pregnant.

Kariniemi, *et al*,[11] found that maternal alcohol consumption only decreased the birthweight among female fetuses. However, no such effect was seen in our study (data not shown).

Low birthweight remains the most important determinant of perinatal mortality and impaired development. When alcohol consumption increases among women, one should be aware of the fact that combined exposure of both alcohol and tobacco may reduce birthweight to a substantial degree, as illustrated by the increased ORs of low birthweight. The difference in birthweight between the lowest level of alcohol and tobacco use and the highest levels was found to be more than 500 grams.

In a large scale study, Mills, *et al*,[12] found somewhat different effects than we did. In our data, heavy alcohol consumption seemed to have a stronger effect on birthweight among smokers than non-smokers, whereas this phenomenon was apparently absent in Mills' data. Like

TABLE 4—Adjusted Differences from Mean Values of Placental Weight, Birthweight, Birth Length and Head Circumferences According to the Mother's Alcohol Consumption during Pregnancy, Stratified by Smoking Status: Analysis of Variance*

Smoking Status (Daily)	Alcohol in g/Week	Placental Weight in g	Birth-weight in g	Birth Length in cm	Head circumference in cm
Non-smokers	0	9	1	−.0	−.0
	1−	2	−2	−.0	−.1
	30−	−1	21	.1	.1
	60−	−29	−14	−.1	.0
	90−	−34	−48	.0	−.1
	120+	−35	−44	−.2	.0
	Mean	565	3,582	52.6	35.4
1–9 cigarettes	0	12	24	.1	.0
	1−	2	1	−.0	.0
	30−	−9	−45	−.1	−.0
	60−	−9	72	.4	−.1
	90−	−3	121	.5	.4
	120+	−65	−245	−1	−.5
	Mean	554	3,377	51.7	35.1
10+ cigarettes	0	13	63	.1	−.0
	1−	5	−9	−.0	.1
	30−	−19	−61	.1	−.2
	60−	−22	−31	−.1	−.1
	90−	−6	−145	.0	−.9
	120+	−73	−206	−.2	−.7
	Mean	554	3,283	51.3	35.4

*All values have been adjusted for parity (0, 1, 2, +), school education (−9y, 10y, 11 + y) and age. Multiple classification analysis, adjusted for main effects and covariates in 3 separate subgroups according to smoking habits.

TABLE 5—ORs (and 95% CI) of Low Birthweight (< 2,500 g) According to the Mother's Smoking and Drinking Habits during Pregnancy (logistic regression)

Smoking* Status (Daily)	Alcohol in g/Week 0	1−	30−	60−	90−	120+	Adjusted for Alcohol All
0	1.0	0.8 (0.5–1.3)	0.9 (0.5–1.6)	0.8 (0.3–1.9)	0.5 (0.1–3.8)	2.2 (0.7–6.5)	1.0
1–9 cigarettes	1.0	0.9 (0.5–1.6)	0.6 (0.3–1.4)	0.5 (0.1–1.7)	—	2.7 (0.9–8.0)	2.2 (1.7–3.0)
10+ cigarettes	1.0	0.8 (0.5–1.3)	0.6 (0.3–1.1)	0.9 (0.4–2.2)	1.6 (0.6–4.1)	2.1 (0.8–5.2)	3.4 (2.6–4.3)
Adjusted for smoking All	1.0	1.0 (0.7–1.3)	1.0 (0.7–1.5)	0.9 (0.5–1.5)	1.1 (0.5–2.5)	2.7 (1.5–4.8)	

*Logistic regression made on those subgroups of women according to smoking habits and on all in the study (marginal row and column) all analyses adjusted for age, school education, and parity. Alcohol and smoking entered the model as "dummy variables."

Mills, *et al*, we found little effect of low to moderate drinking among non-smokers but among heavy smokers reductions in average birthweight tended to appear already at an alcohol consumption of 30–59 g/week, and this pattern was not evident from the Mills data. One problem of comparing the two studies is that they did not use the same standards for alcohol and smoking exposure. More important, however, is the fact that our exposure data were collected at the 36th week of gestation while Mills' data were collected at the first visit in the first trimester. The generally stronger effects of alcohol on birthweight seen in our study may thus reflect the impact of a more relevant time period.

Although the significance of placental weight is disputed, it has been found to be a predictor of growth later in the childhood.[13] It is therefore interesting that alcohol consumption was found to be associated with relatively large reductions in average placental weight, although it should be kept in mind that the effects might have been exerted via fetal growth since birthweight and placental weight are closely associated.

Unfortunately, only some of the potential confounders could be controlled in this study. Nutrition, in particular, may be an important confounder in a study of alcohol consumption and fetal growth. Furthermore, it is likely that heavy drinkers may be less willing to follow prenatal care. Use of other drugs may be a confounder in some countries but it is unlikely in this sample.

The combined effect of alcohol and tobacco smoking should be taken into consideration when advising on health behavior during pregnancy. □

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Pew Commission Advances Agenda Action for Nation's Health Professional Schools

The Pew Health Professions Commission met for the second time on November 7 and 8 in Washington, DC to advance 18 reform recommendations as part of a national Agenda for Action that addresses health care and educational issues challenging the nation's health professional schools. This agenda is built on an analysis of the current health care environment and the major forces and trends which will shape health care in the United States over the next 15 years.

The Commission's recommendations for discussion include a redefinition of the core science curriculum; a reorientation of the teacher-learning process; a shift in patient care training setting; a dissolution of the boundaries between the health professions; a redirection of faculty incentives; the creation of new governance and organizational arrangements; and a change in the orientation of the health professions from illness to health.

The Pew Commission will continue to refine the Agenda for Action over the next three months, and is expected to announces its final Agenda for Action in April 1991. The five objectives of the Pew Commission are to: establish a national Agenda for Action; develop appropriate policy recommendations for federal, state, professional and institutional agencies which will support implementation of the Agenda for Action; communicate the Agenda for Action; provide institutional change resources; and explore and fund demonstration projects at health professional schools across the nation.

The Pew Health Professions Commission is an outgrowth of the Future of the Health Professions project, a program of Duke University and The Pew Charitable Trusts. Over the past six years, The Pew Charitable Trusts has invested over $60 million of programming support in its Strengthening the Health Professions initiative and has secured an additional $40 million of leveraged support from other foundations for this initiative. For further information, contact Pew Health Professions Commission, Duke University Medical Center, 3101 Petty Road Suite 1106, Durham, NC 27707. Tel: (919) 490-6695; Fax (919) 489-5907.