ORIGINAL ARTICLES

Caffeine and alcohol as risk factors for sudden infant death syndrome

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Abstract

***Objective*—To assess whether alcohol and caffeine are independent risk factors for sudden infant death syndrome (SIDS).**

***Materials and methods*—Analyses based on data from the Nordic epidemiological SIDS study, a case control study in which all parents of SIDS victims in the Nordic countries from 1 September 1992 to 31 August 1995 were invited to participate with parents of four controls, matched for sex and age at death. Odds ratios (ORs) were calculated by conditional logistic regression analysis.**

***Results*—The crude ORs for caffeine consumption > 800 mg/24 hours both during and after pregnancy were significantly raised: 3.9 (95% confidence interval (CI), 1.9 to 8.1) and 3.1 (95% CI, 1.5 to 6.3), respectively. However, after adjustment for maternal smoking in 1st trimester, maternal age, education and parity, no significant effect of caffeine during or after pregnancy remained. For maternal or paternal alcohol use, no significant risk increase was found after adjusting for social variables, except for heavy postnatal intake of alcohol by the mother, where the risk was significantly increased.**

***Conclusions*—Caffeine during or after pregnancy was not found to be an independent risk factor for SIDS after adjustment for maternal age, education, parity, and smoking during pregnancy. Heavy postnatal but not prenatal intake of alcohol by the mother increased the risk.**

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Keywords: sudden infant death syndrome; caffeine; alcohol; risk factors

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Caffeine is believed to act by inhibiting phosphodiesterase, thereby increasing cAMP. It stimulates the cerebral cortex, increases wakefulness, and in larger doses stimulates respiration.[1] One report[2] has suggested that there might be an association with sudden infant death syndrome (SIDS) because of an increased tendency of apnoea seen in the offspring of rats treated with large doses of caffeine during pregnancy. In a recent study in New Zealand, high doses (> 400 mg/24 hours) of caffeine were found to increase the risk of SIDS (odds ratio (OR), 1.46; 95% confidence interval (CI), 1.05 to 2.05).[3]

Ethyl alcohol has been shown to have deleterious effects on fetal development, causing the fetal alcohol syndrome, which consists of short stature, mental retardation, and cerebral and ocular malformations.[4] The association between alcohol and SIDS has been less well investigated,[5–9] but most studies have found no association between prenatal alcohol use and an increased risk of SIDS.[6–9]

The effects on SIDS of maternal use of caffeine[2 3] and alcohol[5–9] have not been clarified. Therefore, we used data from the Nordic epidemiological SIDS study to assess the effects on SIDS of prenatal and postnatal intake of caffeine and alcohol.

Material

Between 1 September 1992 and 31 August 1995, parents of 294 cases of SIDS in the Scandinavian countries were invited by the local paediatrician (Norway and Sweden) or forensic institute (Denmark) to participate in the study. Of these, 244 families (83%) accepted. For each case, six controls matched for sex, date of birth plus two weeks, and maternity hospital were selected. The delay period of two weeks was allowed to obtain a similar age of the controls and the SIDS victims when the questionnaire was completed. The first four were invited to participate in the study. If a family was reluctant to enter the study, one of the two remaining controls was invited. Of a total of 1207 invited control families, 869 (72%) were willing to participate. The cases and controls received a questionnaire consisting of 272 questions without any written guidance included. The material is described in detail elsewhere.[10]

Methods

Odds ratios (ORs) were calculated by conditional logistic regression,[11] using the SPSS statistical software package.[12] To evaluate confounding, the Mantel-Haenszel procedure[13] in the EpiInfo program[14] was used. In the alcohol analysis, adjustment was made for maternal age, education, smoking during pregnancy, and paternal unemployment. In the caffeine analysis, adjustment was made for maternal age,

Table 1 Prevalence of caffeine consumption in four strata during and after pregnancy in SIDS cases and controls with crude and adjusted odds ratios (ORs) in Scandinavia 1992–95, the Nordic epidemiological SIDS study

			Crude			Adjusted for smoking in 1st trimester			Adjusted for maternal age, education, parity, and smoking in 1st trimester		
Caffeine consumption	Cases	Controls	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
During pregnancy											
Nil	34	160	1.0	Ref	Ref	1.0	Ref	Ref	1.0	Ref	Ref
1–400 mg/24 h	102	465	0.9	0.6 to 1.5	0.74	0.9	0.6 to 1.5	0.70	1.1	0.6 to 1.9	0.79
401–800 mg/24 h	57	119	2.0	1.2 to 3.4	0.009	1.2	0.7 to 2.2	0.46	1.5	0.8 to 3.0	0.20
> 800 mg/24 h	24	24	3.9	1.9 to 8.1	< 0.001	1.7	0.8 to 3.8	0.19	2.5	1.0 to 6.7	0.06
After pregnancy											
Nil	28	109	1.0	Ref	Ref	1.0	Ref	Ref	1.0	Ref	Ref
1–400 mg/24 h	98	478	0.7	0.4 to 1.2	0.16	0.7	0.4 to 1.2	0.12	0.9	0.5 to 1.5	0.60
401–800 mg/24 h	59	158	1.2	0.7 to 2.1	0.45	0.9	0.5 to 1.6	0.20	1.0	0.5 to 2.0	0.91
> 800 mg/24 h	30	30	3.1	1.5 to 6.3	0.002	1.4	0.6 to 3.1	0.62	2.0	0.8 to 5.2	0.14

CI, confidence interval.

Table 2 Prevalence of caffeine consumption in two strata during and after pregnancy in SIDS cases and controls with crude and adjusted odds ratios (ORs) in Scandinavia 1992–95, the Nordic epidemiological SIDS study

			Crude			Adjusted for smoking in 1st trimester			Adjusted for maternal age, education, parity, and smoking in 1st trimester		
Caffeine consumption	Cases	Controls	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
During pregnancy											
0–400 mg/24 h	136	625	1.0	Ref	Ref	1.0	Ref	Ref	1.0	Ref	Ref
> 400 mg/24 h	81	143	2.5	1.8 to 3.6	< 0.001	1.5	1.0 to 2.2	0.07	1.6	1.0 to 2.5	0.053
After pregnancy											
0–400 mg/24 h	126	587	1.0	Ref	Ref	1.0	Ref	Ref	1.0	Ref	Ref
> 400 mg/24 h	89	188	2.0	1.5 to 2.9	< 0.001	1.3	0.9 to 1.9	0.18	1.4	0.9 to 2.1	0.15

CI, confidence interval.

education, parity, and smoking during pregnancy, as well as only for smoking during pregnancy. Information about when in pregnancy caffeine was consumed was not requested in the questionnaire. Daily intake of caffeine was calculated as 107 mg × the number of cups of coffee each day + 34 mg × the number of cups of tea each day.[15]

We chose to categorise caffeine ingestion in four strata (0, 1–400, 401–800, and > 800 mg/24 hours) because there were effects above 600–800 mg/24 hours in the preliminary analyses. Because there were very few cases in the highest stratum, we also analysed caffeine categorised in two strata (0–400 mg/24 hours and > 400 mg/24 hours).

To evaluate a possible dose response relation in the caffeine data, we used caffeine categorised in four strata as above. A conditional logistic regression was performed with caffeine as a categoric variable in the four strata, and caffeine as a linear variable through these strata. We tested the significance of the difference in goodness of fit χ^2 with the difference in degrees of freedom (df).

Alcohol doses were measured in alcohol units (AU), 1 AU representing one glass of beer or wine or the equivalent amount of alcohol in fortified wine or spirits.

Table 3 Caffeine consumption during pregnancy by maternal smoking in 1st trimester in controls in Scandinavia 1992–95, the Nordic epidemiological SIDS study

	Caffeine consumption							
	Nil		1–800 mg/24 h		> 800 mg/24 h		Total	
Maternal smoking	n	%	n	%	n	%	n	%
Nil	123	22.7	413	76.2	6	1.1	542	100
1–4 cigarettes/day	24	19.7	92	75.4	6	4.9	122	100
5–9 cigarettes/day	8	9.5	64	76.2	12	14.3	84	100
10–14 cigarettes/day	1	10	9	90	0	0	10	100
>15 cigarettes/day	0	0	0	0	0	0	0	100

$\chi^2 = 48.6$; degrees of freedom (df) = 6; $p < 0.001$.

Results

CAFFEINE

Mean caffeine intake during pregnancy was higher among mothers of cases than among mothers of controls (345 *v* 218 mg/24 hours; 95% CI of the difference, −167 to −87; $p < 0.001$), as was caffeine intake after pregnancy (375 *v* 263 mg/24 hours; 95% CI of the difference −153 to −71; $p < 0.001$).

When analysing caffeine in four strata (table 1), the crude OR for caffeine consumption during pregnancy was increased for doses > 400 mg/24 hours. For doses between 401 and 800 mg/24 hours, the OR was 2.0 (95% CI, 1.2 to 3.4) and for doses > 800 mg/24 hours, the OR was 3.9 (95% CI, 1.9 to 8.1). After pregnancy, the crude OR was significantly increased only in the highest stratum; that is, above 800 mg/24 hours, where it was 3.1 (95% CI, 1.5 to 6.3) (table 1). After adjustment for smoking in 1st trimester, no significant effects remained during or after pregnancy, and after adjustment for maternal age, education, parity, and smoking in 1st trimester we found an effect of caffeine > 400 mg/24 hours during pregnancy, but it was not significant even in the highest stratum. After pregnancy we found an OR of 1.4 (95% CI, 0.6 to 3.1) in the highest stratum after adjusting for smoking, and 2.0 (95% CI, 0.8 to 5.2) after adjusting for smoking, maternal age, education, and parity.

During pregnancy, the difference in χ^2 between a linear and a categorised model was 9.2 (2 df; $p < 0.02$) for caffeine; after pregnancy the difference was 14.0 (2 df; $p < 0.001$).

Table 4 Maternal alcohol dose, usually ingested and ingested the days before death/interview in SIDS cases and controls with crude and adjusted odds ratios (ORs) in Scandinavia 1992–95, the Nordic epidemiological SIDS study

			Crude			Adjusted		
	Cases	Controls	OR	95% CI	p Value	OR	95% CI	p Value
Maternal alcohol dose (AU)								
Nil	85	263	1.0	Ref	–	1.0	Ref	–
1–4 AU	120	504	0.8	0.5 to 1.1	0.11	0.8	0.5 to 1.2	0.24
⩾ 5 AU	19	40	1.5	0.8 to 2.7	0.23	0.7	0.4 to 1.5	0.41
Recent maternal alcohol ingestion								
No	207	774	1.0	Ref	–	1.0	Ref	–
Yes	34	85	1.5	1.0 to 2.4	0.07	1.4	0.8 to 2.5	0.20
Alcohol dose today or yesterday								
Nil	216	788	1.0	Ref	–	1.0	Ref	–
1–4 AU	21	79	1.0	0.6 to 1.6	0.86	1.0	0.5 to 1.9	0.91
⩾ 5 AU	7	2	12.2	2.5 to 59.3	0.002	5.9	1.0 to 33.9	0.047

Adjustment was made for maternal age and education, maternal smoking during pregnancy, and paternal unemployment.
AU, alcohol units; CI, confidence interval.

Table 5 Maternal and paternal alcohol consumption during and after pregnancy in SIDS cases and controls with crude and adjusted odds ratios (ORs) in Scandinavia 1992–95, the Nordic epidemiological SIDS study

			Crude			Adjusted		
Alcohol use	Cases	Controls	OR	95% CI	p Value	OR	95% CI	p Value
Maternal use during pregnancy								
Never	155	571	1.0	Ref	–	1.0	Ref	–
Less than weekly	79	264	1.1	0.8 to 1.5	0.67	1.5	1.0 to 2.2	0.06
More than weekly	7	18	1.1	0.4 to 2.7	0.83	1.3	0.4 to 4.3	0.70
Maternal use after pregnancy								
Never	124	407	1.0	Ref	–	1.0	Ref	–
Less than weekly	111	407	0.8	0.6 to 1.1	0.28	0.9	0.6 to 1.3	0.64
More than weekly	7	45	0.4	0.2 to 1.0	0.06	0.6	0.2 to 1.7	0.31
Paternal use during pregnancy								
Never	39	91	1.0	Ref	–	1.0	Ref	–
Less than weekly	145	578	0.6	0.4 to 0.9	0.015	0.8	0.5 to 1.3	0.38
More than weekly	40	174	0.5	0.3 to 0.9	0.016	0.7	0.4 to 1.4	0.35
Paternal use after pregnancy								
Never	44	92	1.0	Ref	–	1.0	Ref	–
Less than weekly	141	568	0.5	0.3 to 0.7	<0.001	0.7	0.4 to 1.1	0.12
More than weekly	41	178	0.4	0.3 to 0.7	0.001	0.6	0.3 to 1.1	0.11

Adjustment was made for maternal age and education, maternal smoking during pregnancy, and paternal unemployment.
CI, confidence interval.

When comparing caffeine ⩽ 400 mg/24 hours with caffeine > 400 mg/24 hours (table 2), the crude OR for caffeine > 400 mg/24 hours was 2.5 (95% CI, 1.8 to 3.6) during pregnancy, and 2.0 (95% CI, 1.5 to 2.9) after pregnancy. Adjustment for smoking lowered ORs considerably (OR, 1.5; 95% CI, 1.0 to 2.2 and OR, 1.3; 95% CI, 0.9 to 1.9 during and after pregnancy, respectively). When adjusting for smoking, maternal age, education, and parity the OR was 1.6 (95% CI, 1.0 to 2.5) during pregnancy and 1.4 (95% CI, 0.9 to 2.1) after pregnancy.

There was a strong relation between caffeine consumption and smoking (table 3). Among the controls, we found that only 1% of the non-smokers consumed > 800 mg caffeine each day, whereas the corresponding figure was 5% of those who smoked 1–4 cigarettes each day and 14% of those who smoked 5–9 cigarettes each day ($p < 0.001$).

INTERACTIONS

We found no significant interactions with country, maternal smoking, maternal age, education, or parity. However, there was a significant interaction between breast feeding and caffeine in pregnancy ($p = 0.027$), but not with caffeine after pregnancy ($p = 0.06$).

Table 6 Paternal alcohol dose, usually ingested and ingested the days before death/interview in SIDS cases and controls with crude and adjusted odds ratios (ORs) in Scandinavia 1992–95, the Nordic epidemiological SIDS study

			Crude			Adjusted		
	Cases	Controls	OR	95% CI	p Value	OR	95% CI	p Value
Paternal alcohol dose								
Nil	71	184	1.0	Ref	–	1.0	Ref	–
1–4 AU	115	512	0.5	0.3 to 0.7	<0.001	0.7	0.4 to 1.2	0.20
⩾ 5 AU	58	173	0.7	0.5 to 1.1	0.15	0.7	0.4 to 1.3	0.27
Recent paternal alcohol ingestion								
No	178	687	1.0	Ref	–	1.0	Ref	–
Yes	50	160	1.2	0.8 to 1.8	0.28	0.8	0.5 to 1.2	0.22
Alcohol dose today or yesterday								
Nil	200	719	1.0	Ref	–	1.0	Ref	–
1–4 AU	33	132	0.9	0.6 to 1.3	0.56	1.2	0.7 to 1.9	0.54
⩾ 5 AU	11	18	2.2	1.0 to 4.9	0.047	1.5	0.6 to 3.9	0.38

Adjustment was made for maternal age and education, maternal smoking during pregnancy, and paternal unemployment.
AU, alcohol unit; CI, confidence interval.

ALCOHOL

If the mother ingested alcohol on the reference day or the day before, the risk was increased with an alcohol dose of 5 AU or more (crude OR, 12.2; 95% CI, 2.5 to 59.3) (table 4). After adjusting for paternal unemployment, maternal smoking, age, and education, the effect was still significant (OR, 5.9; 95% CI, 1.0 to 33.9; p = 0.047). However, there was no influence of either prenatal or postnatal maternal ingestion of alcohol on the risk of SIDS.

Paternal use of alcohol in moderate doses was associated with low ORs (tables 5 and 6). Crude ORs were 0.6 (95% CI, 0.4 to 0.9) for use of alcohol less than once a week and 0.5 (95% CI, 0.3 to 0.9) for use of alcohol more than once a week during pregnancy. After pregnancy, the crude ORs were 0.5 (95% CI, 0.3 to 0.7) and 0.4 (95% CI, 0.3 to 0.7), respectively. When adjusting for paternal unemployment, smoking, maternal age, and education, the ORs were 0.8 (95% CI, 0.5 to 1.3) for less than weekly and 0.7 (95% CI, 0.4 to 1.4) for more than weekly use during pregnancy, and 0.7 (95% CI, 0.4 to 1.1) for less than weekly and 0.6 (95% CI, 0.3 to 1.1) for more than weekly use after pregnancy.

Discussion

We could not demonstrate an independent effect of prenatal caffeine on the risk of SIDS. Alcohol consumption by the mother during pregnancy did not increase the risk, but large amounts of alcohol on the reference day or the day before increased the risk. Paternal alcohol consumption did not result in an increased risk; in fact, the ORs were low because of an association with beneficial social circumstances, which is supported by the non-significant results after adjusting for social variables.

CAFFEINE

Caffeine has been found to cause malformations in rodents[16–19] and to induce long term effects on sleep, locomotion, learning abilities, emotivity, and anxiety in rodent offspring.[18] In humans, teratogenic effects are questionable.[20] Caffeine does not change breast milk composition, and stimulates milk production.[21] Several studies have suggested an increased risk of spontaneous abortion or intrauterine growth retardation.[22–24] However, after adjustment for smoking[15 25] this effect seems to be low. Recent studies seem to agree that there is no risk of preterm delivery,[26–29] but the effect on birth weight is still disputed.[26 29–31]

Thus, several studies have been published on the association between caffeine and pregnancy outcome, but to our knowledge, only one on SIDS.[3] In our study, however, we could not demonstrate such an effect. The OR estimate in the highest dose range (> 800 mg/24 hours) was 2.5 during and 2.0 after pregnancy, which was not significant (table 1), and the same applies to the dichotomised variable in table 2. Unfortunately, we do not have sufficient data to verify an effect, regardless of the model chosen. Also, with the results from the difference in χ^2 between a categoric and a linear model, we could not verify a dose response relation. The results might be caused by misclassification—mothers might be more honest when answering questions concerning coffee and tea consumption than questions regarding smoking, especially as it is well known that smoking is harmful to the baby. Alternatively, it could be that we did not have enough cases to verify an effect. Because smoking and coffee consumption are strongly correlated (table 3), unreported smoking would tend to increase the ORs for caffeine consumption.

The interaction between breast feeding and caffeine is presumably the result of confounding by smoking. It has been shown that mothers who smoke breast feed less than those who do not.[32] Among our controls, 30% of smokers were breast feeding at the interview, in contrast to 70% of the non-smokers. We found that in a model containing smoking in early pregnancy, the interaction term loses its significance.

Because it has been suggested that caffeine could stimulate milk production,[21] one might expect an association between caffeine intake and breast feeding, and thus a protective effect of caffeine, because breast feeding seems to lower the OR. Our data showed no such association.

ALCOHOL

In view of the harmful effects of alcohol on the fetus, we found it remarkable that there was no increase in SIDS with prenatal alcohol use. In a case control study, it is possible that mothers with alcohol problems would not admit them, and the consequence would be an underestimation of its effects. Thus, the increased risk attached to high intake of alcohol by the mother within the last days before the event was surprising and might suggest that the lack of effects of prenatal use is true. However, this result is based on only seven cases and two controls. The small numbers render analyses of interactions impossible.

The seemingly protective effect of paternal alcohol ingestion reflects an association with beneficial social circumstances, and thus is a confounder. This is supported by the disappearance of significance after adjusting for maternal age and education, maternal smoking during pregnancy, and paternal unemployment. It has been shown recently that the pattern of alcohol use differs between social classes, and that men in Sweden with a higher socioeconomic index consume more alcohol than men with a lower socioeconomic index (Rosengren A, Dotevall A, Wilhelmsen L, the MONICA study of Göteburg. Unpublished data, 1999). Thus, a moderately high alcohol consumption could be a marker of high social status.

Conclusions

We found no association between caffeine consumption, during or after pregnancy, and increased risk of SIDS. Prenatal alcohol consumption by the mother was not associated with an increased risk, but heavy postnatal intake by the mother might be a risk factor in a

very small subgroup. Paternal alcohol consumption prenatally or postnatally is associated with a lower OR, but this is a result of confounding.

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