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MATERNAL CAFFEINE INTAKE AND LOW BIRTH WEIGHT: IS THERE A RELATIONSHIP?

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In 1974, the first studies looking at the effect of caffeine use on pregnancy were published. These studies have continued, partly due to the conflicting nature of the results. Some have concluded that caffeine use in pregnancy is safe, while others believe caffeine use can increase risks for intrauterine growth retardation and low birth weight infants. The hypothesis that caffeine may affect a fetus is plausible, as caffeine crosses the placental barrier, increases maternal epinephrine and is metabolized more slowly by the mother during pregnancy. There has also been the suggestion that a relationship between caffeine use and fetal growth is confounded by tobacco use. Since 1980, the FDA has recommended that women refrain from caffeine during pregnancy. Regardless, 75 percent of women continue to use some form of caffeine during pregnancy. The purpose of this study is to review literature on the epidemiologic relationship between caffeine use during pregnancy and low birth weight infants.

Review

Fenster et al (1) used surveys to determine maternal caffeine consumption, and determined that high levels of caffeine intake increase the risk for fetal growth retardation. Participants in this study were women who had served as controls in a case-control study for spontaneous abortions. Evaluation was made of 1,230 singleton births. Women were interviewed by phone nine months after giving birth, and were asked about their caffeine intake during pregnancy, the amount consumed the month before pregnancy, and how caffeine intake changed during pregnancy. Caffeine consumption was calculated by assuming an average amount in tea, coffee and cola, and summing these amounts based on subject reports.

In the analysis, caffeine use was divided into no caffeine, light use of 1-150mg/day, moderate use of 151-300mg/day and heavy use of more than 300mg/day. Caffeine use was analyzed using these divisions, as well as on a continuous scale. Confounding variables were included if they were strongly correlated with low birth weight, or caffeine use and low birth weight. Additionally, women who reduced their caffeine intake early in pregnancy were analyzed separately.

The results of this study show four variables are associated with increased caffeine use; multiparty, one or more therapeutic abortions, being employed and the use of cigarettes or alcohol. A dose-response effect was found as caffeine intake increased ($p=0.05$). After adjusting for confounders, the risk in women with high caffeine consumption was nearly twice that of women with no caffeine consumption. This association remained after adjusting for smoking status and alcohol use. Women who reduced their caffeine intake early in pregnancy had a decreased risk of delivering a low birth weight infant (OR 0.65, CL 0.2, 2.11) than women who continued to drink heavy amounts (OR 3.05, CL 1.09, 8.51).

This study found an association between caffeine use during pregnancy and low birth weight infants, when the caffeine use continued past week 6. A major problem if this study is that women were not interviewed until nine months after they had given birth. Asking a woman to recall caffeine consumption from 18 months ago raises the potential for recall bias. Although studies have shown that reports of coffee consumption have good reliability for up to 6.5 years, this risk still exists. This study did not consider caffeine intake from food sources. Additionally, researchers did not question women's method of beverage preparation.

Vlajanic et al (2) did a retrospective cohort analysis of the effect of caffeine during pregnancy on birth weight. Of 1,268 women in Belgrade, Yugoslavia, 1,032 were interviewed within three days of giving birth. Interviewers obtained information on coffee, tea and cola consumption, and caffeine intake was calculated based on average caffeine per serving of the beverages listed above. Data on other possible confounders such as weight, smoking status, alcohol use and socioeconomic status were also collected. Infant data such as weight and gestational age were also collected. While information was collected on caffeine consumption during all three trimesters of pregnancy, this paper only presented information on the third trimester.

13.55 percent of the women reported no caffeine use during pregnancy, while mean intake for the rest of the subjects was 133.44 mg per day. The main source of caffeine was coffee, and coffee intake was positively correlated to smokers. Caffeine intake was positively correlated to occupational and housekeeping activities as well as parity. Birth weight decreased as caffeine consumption increased. This correlation remained after adjustments were make for gestational age, infant sex, parity, smoking and maternal height and weight ($p=0.027$). In women who consumed more than 141 mg per day, birth weight was reduced by 114 grams, ($p=0.06$). When comparing caffeine intake among non-smokers, those who consumed 71-140mg/day had infants weighing 116 grams less than women consuming less than 10mg/day. Additionally, women consuming more than 140mg/day had infants weighing 153 grams less than women consuming 0-10mg/day. This study found a dose response effect of caffeine on birth weight, which remained even with modest amounts of caffeine intake.

This study considered infant sex and age as potential confounders, a consideration not seen in many of the other studies reviewed. The study did choose not to consider alcohol consumption as a confounder, as only 1.1 percent of participants consumed more than six drinks per week. This decreases the strength of the study, as we have no indication that any amount of fetal alcohol exposure is safe, and any exposure should be considered a potential risk for low birth weight. Additionally, researchers failed to consider sources of caffeine other than tea, cola and coffee. Finally, as in many other studies of this nature, interviewing after the mother has given birth presents problems for recall bias.

In contrast to Vlajanic's findings, a case control study determined that caffeine use during pregnancy had no significant effect on an infant's birth weight (3). Santos et al looked at a population of pregnant women in Pelotas, Brazil. Caffeine is consumed primarily in the form of coffee, and a local beverage called mate. Population based controls were selected, regardless of whether or not they had the outcome of interest. Two controls were selected for each of the 400 cases. Cases included all singleton babies born at Pelota hospitals in 1992, while controls consisted of the next two babies born after a case, regardless of their birth weight. Using this method, a baby could serve as both a case and a control. Structured interviews were conducted with mothers during their stay in the hospital and examined caffeine intake as well as other potential confounders. A low birth weight was defined as less than 2,500 grams, and intrauterine growth retardation was defined as less than 2,500 grams at 37 weeks or more.

Mothers were considered caffeine users if they consumed caffeine at least once a week. Analyses were done of in-home samples of caffeinated beverages to determine actual caffeine content. Only 1.6 percent of mothers were lost to follow-up, and 22 percent of cases also served as controls for other cases. Additionally 1.6 percent of subjects served as controls twice.

Mean daily caffeine intake was similar between cases and controls. Results of this study show that, even after allowing for confounders, higher caffeine consumption was associated with lower risks of low birth weight babies, but not significantly. Interestingly, there was an association, although not significant, between increased risk of low birth weight and moderate caffeine intake. However, low caffeine intake showed a protective effect against low birth weight, although again, not significant. Overall this case control study shows no association between caffeine intake and low birth weight.

The results of this study must be reviewed with consideration of some of the experimental methods. Caffeine intake was reported after mothers gave birth. This introduces the potential for recall bias, as mothers with low birth weight babies may have a better recollection of caffeine intake than women with normal weight babies. However, this is most likely not the case in Brazil, as women are not advised to avoid caffeine during pregnancy. Additionally, using some babies as cases as well as controls may have a negative impact on the validity of the results. One important factor that these researchers failed to consider was weight for gestational age. Infants gain a significant amount of weight during the last few weeks of gestation. This study did not factor in gestational age when assessing whether a baby had a low birth weight. Thus, a case weighing 2,400 grams born at 37 weeks could have been matched with a control, weighing 3,600 grams, born at 41 weeks. It is important to note that this is one of the few studies of this kind done in South America, and cultural or genetic factors may play a role. The researchers did actually measure the caffeine content of food and beverages consumed by the women, and paid special attention to variations in content, cup sizes and preparation method.

Eskenazi et al (4) examined the effect of decaffeinated as well as caffeinated coffee on fetal growth and gestational duration in a cohort study. This is one of only a few studies to look at decaffeinated as well as caffeinated coffee. Such consideration will help establish if caffeine, or another compound in coffee, may have an effect on birth weight. Study participants came from all women delivering in and residing in four counties in San

Joaquin, CA in 1992. Of 7,855 women who were eligible to participate in the survey, 202 drank both caffeinated and decaffeinated coffee, 1,480 consumed caffeinated coffee only, 504 consumed only decaffeinated coffee, and 5,669 consumed no coffee during pregnancy. Mothers received a survey attached to their child's birth certificate, which asked for information on caffeine intake only during the fourth and fifth months of pregnancy. Researchers also assessed smoking status, BMI, gestational age and quality of prenatal care.

The subject population was primarily Hispanic, and non-Hispanic whites. Only 11 percent of subjects smoked, and 78 percent of subjects reported caffeine use during pregnancy, with 36 percent consuming tea, 68 percent cola and 21 percent caffeinated coffee. Compared with women who drank no coffee at all, those who drank either caffeinated or decaffeinated coffee were not more likely to have low birth weight babies, or small for gestational age infants. Women who consumed only caffeinated coffee had infants that weighed an average of 17 grams less than women who drank neither type of coffee. Women who drank caffeinated coffee delivered infants that weighed less than infants of women who drank no coffee, with an average weight reduction of 3.0 grams per week per cup [OR -5.9, -0.6]. When examining the amount of coffee women drank, a trend emerged where infants of women who consumed more than one cup of either type of coffee daily weighed 16-19 grams less than women who drank only caffeinated coffee (not significant). Additionally, women who consumed two cups of cola per day experienced an average infant weight reduction of 20 grams, but this was not statically significant. There was no association between birth weight and tea intake.

When confounders such as smoking status and race were factored in, the effect of caffeine on birth weight was reduced. Smoking reduced birth weight by an average of 200 grams, while black infants weighed 265 grams less than white infants.

This study has a large sample size, and considered weight for gestational age. However, the use of survey data after birth introduces the potential for recall bias, especially when women are questioned on caffeinated as well as decaffeinated beverages. Additionally, only asking about a two-month period of time may have affected results, as women may have altered their consumptions at other times during pregnancy. Additionally, many of the initial subjects were excluded from the study as they did not provide information on caffeine intake. These subjects could be different from subjects who provided information. Finally, there are other factors that simply could not be accounted for, such as maternal nutrition, substance abuse and exercise.

Cook et al (5) performed a prospective, population based study in London. This is one of the few prospective studies done on this subject. Women were interviewed three times during pregnancy, initially around 14 weeks, and then again at 28 and 36 weeks. Interviewers used a structured questionnaire to interview the women. A blood sample on at least one of the visits was provided by 1,500 women, and 640 women provided blood samples at all three visits. Blood samples were collected and assayed for cotinine and caffeine. Caffeine intake was determined by amounts of coffee, tea, cocoa and cola ingested in the previous week. Obstetric data was obtained from obstetric records, and birth weight ratio was calculated. Due to the short half-life of caffeine, most statistics were done on women who gave all three blood samples. Results were adjusted for smoking status, alcohol intake and social class.

Overall, birth weight ratio decreased with increasing caffeine intake, with a regression coefficient of -1.29 percent (CL -2.05, -0.53), which was reduced to -0.6 percent when cotinine levels were accounted for. However, this relationship seemed to only be present in smokers. When adjusting for smoking status, the regression was only significant in smokers (-1.55 percent/g per week (-2.86-0.24)). When blood caffeine levels were examined, there was no relationship to birth weight regardless of smoking status (p=0.35).

This study found no relationship between blood caffeine concentrations and birth weight, however there was a relationship between caffeine intake and birth weight. Caffeine is rapidly metabolized in the body. It is possible e that blood levels were just too low at the time of testing, as only three tests were performed on the subjects. It is important to note that as pregnancy progresses; the metabolism of caffeine slows, as evidenced by this study. Additionally, smoking increases the metabolism of caffeine. Cook et al suggest that previous studies that have found an association between caffeine intake and birth weight may not have accounted for differences in smoking status. While this study reduced the potential for recall bias by doing surveys during pregnancy, measuring blood caffeine levels may not be the most accurate way of assessing caffeine use in this study. With a maximum of only three blood levels, and considering the rapid rate of caffeine metabolism, a slight alternation in timing of testing could result in drastically different conclusions.

The final cohort analysis reviewed was conducted between 1996 and 2000 in Connecticut and Massachusetts. (6) Women were recruited from obstetric practices and clinics whose pregnancies were less than 24 weeks in gestation. 2,478 women enrolled in the study. Women were interviewed in their homes before the 25th week of pregnancy and asked detailed questions regarding consumption of caffeinated and decaffeinated beverages, brand of beverage and preparation method. Subjects were shown model cup sizes to better estimate intake amounts. Intake was computed by intensely monitoring a select subgroup of subjects and directly measuring the caffeine in their beverages. Respondents were then placed into three subgroups, telephone monitoring, intense monitoring and biochemical monitoring. Obstetric records were used to identify pregnancy outcomes, and low birth weight was defined as less than 2,500 grams.

Higher caffeine consumption was associated with younger age, increased parity and smoking. The overall rate of low birth weight in the study was 4.7 percent. First trimester caffeine consumption was associated with low birth weight (p=0.045) with women who took in at least 300mg of caffeine daily having an OR of 2.55 (CI 1.14, 5.70). Women with caffeine intake in the third trimester greater than 300 mg daily also had increased risk of a low birth weight baby (p=0.037). However, when the eight confounders, age, parity, number of prior pregnancies, marital status, race, education, height, smoking status and weight were accounted for, caffeine effect was reduced and there was no statistically significant effect on birth weight. When urinary caffeine levels were examined, there was a protective effect of caffeine on low birth weight (OR=0.74, CI 0.54, 1.00). There was an association between small decreases in birth weight (28 grams) per 100mg of caffeine consumed per day (p=0.002). A comparison was also done with women who consumed only decaffeinated coffee versus women who drank caffeinated, or a mixture of the two. No meaningful difference was found for any prenatal outcomes.

Although this study found a significant caffeine effect on birth weight, this is likely to be clinically important only for women who consume more than 600mg of caffeine a day. Birth weight was decreased by an average of 28 grams per cup of coffee, and this small decrement is not likely to have a negative impact on the fetus, except at extremely high levels of maternal caffeine intake. This study factored in confounders, as well as level of caffeine intake, both important for statistical soundness. Additionally, these researchers analyzed women in three different ways and still found only a slight association. These different analyses also help increase the strength of this study.

Summary and Conclusions

After reviewing the literature on a possible relationship between maternal caffeine intake and decreased fetal birth weight, a statistically significant decrease in birth weight appears to exist when mothers intake >300mg of caffeine per day. However, this effect does not become clinically significant until women exceed 600mg/day. While most of the studies reviewed made an exceptional attempt at quantifying caffeine intake, no study monitored all sources of intake for the entire nine months. Asking a woman who had just given birth, or gave birth nine months ago to recall her caffeine intake throughout her pregnancy introduces a large potential for error. Additionally, many of the studies that found a significant effect at low levels of caffeine had large potential for recall bias. Both of the prospective studies found much more modest effects of caffeine on birth weight than the case-control or retrospective cohort studies.

There may be a small effect of caffeine on birth weight, but it is not nearly as profound as the effects of smoking or alcohol use during pregnancy. Women who are planning to become pregnant or who are pregnant should be advised to limit their intake to less than 300mg/day. More importantly, they should be advised to exercise, eat healthy and avoid tobacco or alcohol use.

REFERENCES

1. Fenster L, Eskenazi B, Windham G, Swan S. Caffeine consumption during preg nancy and fetal growth. Am J Public Health 1991;81:458-461.

2. Vlajinac H, Petrovic R, Marinkovic J, Sipetic S, Adanja B. Effect of caffeine intake on birth weight. Am J Epidemiology 1997;145(4):335-338.

3. Santos I, Victoria C, Huttly S, Carvalhal J. Caffeine intake and low birth weight: a population-based case-control study. Am J Epidemiology 1998;147(7):620-626.

4. Eskenazi B, Stapleton A, Kharrazi M, Chee W. Associations between maternal decaffeinated and caffeinated coffee consumption and fetal growth and gestational duration. Epidemiology 1999;10(3):242-249.

5. Cook D, Peacock J, Feterabend C, Carey I, Jarvis M, Anderson H, Bland M. Relation of caffeine intake and blood caffeine concentrations during pregnancy to fetal growth: prospective population based study. BMJ 1996;313(7069)1358-1362.

6. Bracken M, Triche E, Belanger K, Hellenbrand K, Leaderer B. Association of maternal caffeine consumption with decrements in fetal growth. Am J Epidemiology 2003;157(5) 456-466.