Maternal Exposure to Neighborhood Carbon Monoxide and Risk of Low Infant Birth Weight

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Synopsis . . . .

This case-control study investigated the potential association between ambient levels of carbon monoxide in a pregnant woman's neighborhood of residence and her chance of delivering a low birth weight infant. Low birth weight infants and normal birth weight infants were contrasted with respect to ambient levels of CO during the 3 months prior to delivery in the neighborhoods where their mothers lived at birth.

After adjustment for the confounding effects of maternal race and education, there was no association between higher CO exposure and higher odds of low birth weight. These data do not support a strong association between maternal exposure to neighborhood CO during pregnancy and odds of delivering a low birth weight infant. Further investigation of the effects of CO exposure on birth weight, with direct measurement of total CO exposure, is needed.

THE DELETERIOUS EFFECTS of maternal smoking on infant birth weight have given rise to the theory that maternal exposure to carbon monoxide (CO) during pregnancy may increase the risk of delivering a low birth weight infant (*1–3*). The possibility that CO air pollution, in particular, adversely affects infant birth weight has caused significant concern among residents of Denver, CO (*4*), who are exposed to the highest levels of residential carbon monoxide in the United States. The annual "Better Air Campaign" has urged Denverites not to drive by publicizing the risk of fetal damage attributable to maternal CO exposure.

There is, however, little epidemiologic evidence regarding the effects of CO air pollution on birth weight. A report of a previous study concluded that mothers residing in Los Angeles residential areas with high levels of air pollution delivered infants of substantially lower birth weight than mothers residing in areas with low levels of total air pollution (*5*). A complete analysis of the effects of CO air pollution alone was not presented, however.

Further investigation of the effects of CO air pollution on infant birth weight is required to direct policy decisions regarding acceptable ambient levels of CO. This retrospective case-control study examined the relation between low birth weight and individual maternal exposure to neighborhood CO during the last 3 months of gestation.

Methods

Air pollution monitoring data of the Colorado Department of Health were used to calculate individual CO exposure for each mother. CO exposure was defined in this study as the time-weighted geometric mean ambient CO level in the mother's neighborhood of residence during the last 3 months of gestation. The selection of the last 3 months of gestation was based on the assumption that the adverse effects of smoking, and thus the potential adverse effects of CO air pollution, are mediated by chronic hypoxia during the last trimester of gestation (*6,7*).

Low birth weight and normal birth weight infants were identified through birth certificates obtained from the Colorado Department of Health. In order to obtain the most accurate data on maternal CO exposure, the study was restricted

to infants born to mothers residing near stationary CO air pollution monitors. A previous study conducted in Denver revealed that stationary monitors provide a good measure of neighborhood exposure within a 2-mile radius (*8*).

Infants born to mothers residing in the 54 census tracts which have at least 60 percent of their areas within 2 miles of a CO monitoring site were eligible for inclusion in the study. The entire area of 39 tracts lay within a 2-mile radius of a monitor; more than 80 percent of 10 tracts lay within a 2-mile radius of a monitor, and more than 60 percent of 5 tracts was within a 2-mile radius.

An expert from the Colorado Department of Health, Air Pollution Control Division, was asked in advance of the study to estimate the radius, in miles, within which each stationary monitor accurately reflected ambient levels of CO. On the basis of this information, subjects were divided in advance into two groups on the basis of the presumed accuracy of exposure data. Subjects residing in the census tracts which have 60 percent or more of their areas lying within the radius specified by the expert were considered to have more accurate assessment of exposure, and subjects residing in other census tracts were considered to have less accurate assessment of exposure to carbon monoxide.

All infants weighing 2,500 grams (g) or less born between 1975 and 1983 to mothers residing in those census tracts were included in the study (low birth weight infants), along with a 17 percent random sample of those infants who weighed more than 2,500 g at birth (normal birth weight infants). Birth certificates provided information about several known risk factors for low birth weight that might modify or confound the relationship with neighborhood CO exposure (table 1). Those items consisted of maternal age, race, education, marital status, parity, history of prior pregnancy loss before or after 20 weeks, history of loss of the most recent pregnancy, delivery interval, month of initiation of prenatal care, and infant's sex (*7*). Information on mother's smoking habits was not available.

Measurements of CO exposure were grouped into quintiles. Relative risks of low birth weight due to quintile of CO exposure were estimated by calculation of odds ratios standardized to the lowest quintile. The odds ratios were examined for effect modification or confounding by each of the previously reported risk factors, using stratified analysis (*9*). Odds ratios were adjusted for confounding by calculating the Mantel-Haenszel pooled point estimate with 95 percent test-based confidence intervals (*10,11*). The Mantel extension of the chi-square test for linear trend and one-tailed significance test were used to examine dose-response relationships. An additional analysis considered several of the potentially confounding factors simultaneously through logistic regression modeling.

In order to study subgroups of low birth weight infants with potentially different etiologies, the analysis was repeated for infants weighing 1,500–2,500 g at birth (moderately low birth weight), and for infants weighing 1,500 g or less at birth (very low birth weight). In a further effort to examine specifically the risk of growth retardation rather than prematurity, the analyses of moderately low and very low birth weight infants were repeated while controlling for gestational age. Another analysis was restricted to residents of census tracts for which CO monitors were considered to reflect ambient levels more accurately.

Results

There were 998 low birth weight infants and 1,872 normal birth weight infants from 47 census tracts available for study. Of the low birth weight infants, 849 had moderately low birth weights, while 149 had very low birth weights.

The risk of low birth weight increased irregularly with increasing exposure to ambient carbon monoxide (table 2). The stratified analysis of the risk of low birth weight did not reveal any effect modifier of the risk of low birth weight due to CO exposure.The risk estimates were, however, strongly confounded by maternal race. Black women were much more likely to bear low birth weight infants and to live in areas with high levels of CO. After adjusting for race, there was no increase in risk of low birth weight with increasing exposure to ambient CO (table 3).

The risk estimates were also confounded by the effects of maternal education. Adjustment for maternal education alone enhanced the increase in risk of low birth weight seen with increasing CO exposure. After adjusting for the effects of both maternal race and education, however, there was no increase in risk of low birth weight with increasing exposure to CO (table 3).

These results were not altered when the risk of low birth weight was analyzed by adjusting for gestational age. There was no evidence of a relationship between CO exposure and risk of

Table 1. Characteristics of 54 Denver census tracts grouped by stationary monitoring site

Data item	Monitoring site[1]							
	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7	Site 8
1980 Census data[2]								
Total population	38,045	38,234	32,439	1,491	27,247	21,812	14,117	10,665
Median age (years)	32.4	29.3	31.3	43.1	30.0	28.0	30.9	31.4
Per capita income	$5,802	$6,114	$9,304	$7,581	$8,859	$8,374	$7,823	$11,635
Percent with income 200 percent under poverty level	63.3	47.9	27.4	29.0	17.0	21.7	28.3	5.3
Percent persons over 16 who are in labor force	61.7	56.5	69.9	64.0	75.0	71.5	65.7	70.8
Percent labor force in managerial and professional jobs	48.8	48.7	69.8	45.4	65.0	56.8	57.6	83.5
Percent families with children under 18 and no husband at home	26.0	15.7	11.7	5.6	10.3	11.2	7.8	5.2
Percent females in the labor force with own child under 6	42.8	43.9	63.9	44.2	55.1	49.8	42.8	41.6
Percent persons over 5 years living in same house as 5 years ago	33.5	44.6	46.3	47.7	40.5	45.5	50.7	28.8
Percent children 5 to 17 who speak English not well or not at all	21.0	17.7	0.5	...	14.6	4.4	6.5	12.0
Study data								
Carbon monoxide exposure in ppm:								
Median	2.4	1.2	3.6	...	0.8	1.2	1.1	0.5
5th and 95th percentiles	1.8, 3.6	0.7, 2.0	1.6, 4.8	...	0.7, 1.3	0.8, 2.1	0.8, 1.6	0.4, 0.8
Number of cases	344	303	200	0	20	98	18	15
Number of controls	501	567	399	0	74	252	28	51
Percent black mothers	25.4	1.0	28.4	...	12.8	1.1	0	1.5
Percent mothers with education beyond high school	20.9	18.8	36.8	...	46.2	29.8	28.3	89.4

[1] Census tracts by site are as follows:
site 1: 16, 17.01, 17.02, 20, 23, 24.01, 24.02, 25, 26.01, 26.02, 27.01, 27.03, 31.01, 31.02
site 2: 3.02, 3.03, 4.02, 5.01, 5.02, 6, 7.01, 7.02, 8
site 3: 33, 37.01, 37.02, 37.03, 41.03, 42.01, 43.01, 43.02
site 4: 90.03
site 5: 70.15, 70.17, 70.18, 74, 75, 76, 77.02, 77.03, 77.04
site 6: 103.04, 103.05, 103.07, 103.08, 104.02
site 7: 14.03, 30.01, 30.02, 54.01, 54.03, 58
site 8: 56.09, 56.15
[2] See reference *16*.

Table 2. Estimated risk of low birth weight related to neighborhood carbon monoxide levels during the last 3 months of pregnancy, among births to Denver residents of selected census tracts, 1978–83

Carbon monoxide level	Number of infants weighing 2,500 g or less	Number of infants weighing 2,500 g or more	Odds ratios	95 percent confidence interval
< 1 ppm	198	410	1.0	...
≥ 1 and < 2 ppm	304	652	1.0	0.8, 1.2
≥ 2 and < 3 ppm	248	393	1.3	1.0, 1.7
≥ 3 and < 4 ppm	171	277	1.3	1.0, 1.7
≥ 4 ppm	77	140	1.1	0.8, 1.6

moderately low or very low birth weight, with or without control for gestational age. Logistic regression analysis yielded similar results. Analysis restricted to census tracts where the monitor was expected to reflect more accurately neighborhood exposure did, however, reveal a slightly stronger relation of CO exposure and low birth weight (table 4).

Discussion

The results of this study do not support a strong relation between risk of low birth weight and maternal exposure to CO in the neighborhood of residence during the last 3 months of pregnancy. The authors considered several potential sources of bias which may have influenced the results of this study.

The most important potential source of bias in these results lies in the measurement of CO exposure. The measurement of exposure to ambient outdoor CO in the neighborhood of residence may have been misclassified due to local variations not reflected by data from stationary monitors. This possibility is supported by the finding of a somewhat stronger relation between CO exposure

Table 3. Risk of low birth weight related to neighborhood carbon monoxide exposure, adjusted for mother's race and education, among births to Denver residents of selected census tracts, 1978–83

	Race[1]		Education[2]		Race and education[3]	
Carbon monoxide level	Odds ratios	95 percent confidence interval	Odds ratios	95 percent confidence interval	Odds ratios	95 percent confidence interval
< 1 ppm	1.0	...	1.0	...	1.0	...
≥ 1 and < 2 ppm	0.9	0.8, 1.2	0.9	0.7, 1.2	0.9	0.7, 1.1
≥ 2 and < 3 ppm	1.1	0.9, 1.4	1.3	1.0, 1.6	1.1	0.8, 1.4
≥ 3 and < 4 ppm	1.1	0.8, 1.5	1.3	1.0, 1.7	1.1	0.9, 1.5
≥ 4 ppm	0.9	0.6, 1.3	1.3	0.9, 1.8	1.0	0.7, 1.5

[1] Number of subjects = 2,866, χ^2 test for linear trend = 0.10, P = 0.75.
[2] Number of subjects = 2,802, χ^2 test for linear trend = 9.43, P = 0.002.
[3] Number of subjects = 2,800, χ^2 test for linear trend = 0.85, P = 0.36;

Table 4. Risk of low birth weight related to neighborhood carbon monoxide exposure, adjusted for mother's race and education, for 2 groups according to monitor accuracy[1]

	Monitor accurately reflected CO level[2] (N = 456)		Monitor less accurately reflected CO level[3] (N = 2,344)	
Carbon monoxide level	Odds ratios	95 percent confidence interval	Odds ratios	95 percent confidence interval
< 1 ppm	1.0	...	1.0	...
≥ 1 and < 2 ppm	0.6	0.3, 1.2	1.0	0.8, 1.2
≥ 2 and < 3 ppm	1.3	0.7, 2.7	1.0	0.8, 1.4
≥ 3 ppm	1.5	0.7, 3.5	1.1	0.8, 1.5

[1] Separated into 2 groups according to expert opinion of monitor's accuracy in reflecting neighborhood carbon monoxide levels.
[2] Census tracts 17.02, 24.01, 24.02, 25, 26.01, 5.02, 90.03, 14.03, 30.01, 30.02, 54.01, 54.03, 58, 56.09, and 56.15; χ^2 test for trend = 3.26, P = 0.07.
[3] All other tracts; χ^2 test for trend = 0.34, P = 0.56.

and low birth weight among individuals for whom neighborhood CO measure was predicted to be most accurate. The accuracy of stationary monitor readings in measurements of neighborhood CO exposure was enhanced, however, by restricting the study to infants born to mothers residing near a monitor. Of equal importance is the possibility that the observed effect of neighborhood CO may have been confounded by exposure to unmeasured sources of CO. Determinants of individual exposure levels are numerous, and accurate prediction of short-term individual exposure would require accounting for exposure to a myriad of microenvironments (*8*). It should be noted, however, that any effect of CO on birth weight is likely to result from chronic exposure to elevated levels of CO rather than exposure to local short-term elevations.

Evidence that stationary monitoring values of CO correlate rather highly with indoor levels (*12*) suggests that the exposure measure employed in this study reflects long-term neighborhood and indoor exposure in spite of numerous local perturbations such as operation of a gas stove. The unmeasured source of CO exposure of greatest concern is cigarette smoking, in view of its strength as a predictor of low birth weight. The fact that adjustment for education increased the magnitude of the relationship between CO exposure and low birth weight suggests that control of smoking, for which education is a proxy, might have elevated the risk estimate.

An additional limitation is the range of CO exposures available for study. Denver has historically had relatively high CO levels (up to an average of approximately 8 ppm in the early 1970s), (*4*) but there has been a marked reduction in urban CO concentrations over time. Supportive laboratory evidence regarding CO and birth weight resulted from exposures of 90 ppm or greater (*13,14*). Therefore, this study was only capable of identifying effects over a range of exposure which is modest relative to past urban levels and those shown to affect laboratory animals adversely.

Another potential source of bias is overadjustment for the effects of extraneous variables. In this study, overadjustment could have occurred if the relationship between black maternal race and low birth weight was mediated in part by CO

exposure. In that case, controlling for race would obscure a real relationship between CO and low birth weight. The observation that there was no increase in risk of low birth weight with increasing CO exposure among black women or white women suggests that this is unlikely.

The definition of low birth weight also warrants comment. Evidence from research on smoking suggests that carbon monoxide may result in intrauterine growth retardation. Controlling for gestational age or conducting analyses restricted to moderately low or very low birth weight infants may not classify infants as well as direct physical assessment of growth retardation. In addition, this study would have had more power if the potential effect of CO on mean birth weight had been studied. The case-control design, on the other hand, facilitates estimation of the risk of low birth weight, which is of interest because of its relation to morbidity and mortality (*15*).

The results of the previous study conducted in Los Angeles suggested that a retrospective study such as this one might detect an effect of long-term, low-level environmental CO exposure on the risk of low birth weight. This study did not, however, detect an effect. The method used to measure CO exposure in this study may have contributed to this negative finding because it did not include measurement of individual exposure to all sources of CO.

Further investigation of the relation between CO air pollution and birth weight should include an assessment of total individual exposure to CO from all sources, including smoking and indoor sources. Because previous experience indicates that follow-back studies based on birth certificate data provide incomplete data on smoking (*5*), and that questionnaire data on CO exposure do not closely approximate directly measured CO exposure (*8*), further study of the effects of environmental CO exposure on birth weight may necessitate direct measurement of CO exposure. This observation is particularly true given that small effects, which would be difficult to detect if CO exposure were misclassified or its effects confounded, may still have notable public health consequences and be important to consider in formulating air quality standards.

Conclusion

In conclusion, the results of this study do not support a strong relation between risk of low birth weight and maternal exposure to neighborhood CO (as reflected by data from stationary monitors) during the last 3 months of gestation. More definitive study of the issue will likely require direct measurement of total CO exposure.

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