The Association of Marijuana Use with Outcome of Pregnancy

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Abstract: We analyzed interview and medical record data of 12,424 women to evaluate the relationship between marijuana usage and adverse outcomes of pregnancy. Low birthweight, short gestation, and major malformations occurred more often among offspring of marijuana users. When we used logistic regression to control for demographic characteristics, habits, and medical history data, these relationships were not statistically significant. The odds ratio for the occurrence of major malformations among marijuana users was 1.36, higher than odds ratios for other exogenous variables, and the 95 per cent confidence interval was 0.97–1.91. More data are needed to establish firmly or rule out an association between marijuana usage and major malformations. Until more information is available, women should be advised not to use marijuana during pregnancy. (*Am J Public Health* 1983; 73:1161–1164.)

Introduction

Recent data have shown a peak of marijuana usage among 18 to 25 year olds, raising questions about marijuana usage and effects in pregnancy.[1] Yet, little is known about the effect of marijuana on the development and well-being of the human fetus. There have been three case reports of abnormalities in infants who were born to mothers who used marijuana among other drugs, such as lysergide (LSD).[2–4] In a prospective study in which 57 of 291 mothers reported the use of marijuana during their pregnancy, the newborn of users and non-users did not differ in terms of medical indices, such as data about delivery, obstetrical complications, birthweight, and Apgar scores; however, a number of behavioral differences were observed among neonates born to users.[5] Regular marijuana smoking before and during pregnancy was associated with a dose-related decrease in the neonatal response to light and an increase in tremors and startles among offspring of marijuana users. Another study performed of 1,690 mother/child pairs at Boston City Hospital has found a statistically significant association between marijuana use during pregnancy and the occurrence of low birthweight.[6] Users of marijuana were five times more likely than non-users to deliver infants with features considered compatible with fetal alcohol syndrome.

Most of the research about the effects of marijuana on pregnancy has been done with animals.[7] Data from rats, mice, hamsters, rabbits, and primates have indicated that marijuana and its main active constituent, delta-9-tetrahydrocannabinol (9-THC), might have teratogenic potential.[8–10] Other effects of the drug have been fetal resorption and intrauterine growth retardation. Abel has indicated the methodologic difficulties in the interpretation of many of the animal studies.[10] The administration of the drugs produced a marked reduction in the consumption of food and water, and malformations occurred in association with relatively high doses administered by routes that would not be comparable to human usage.

We have been conducting a series of studies designed to obtain information on the relationship of late pregnancy outcomes to a variety of exposures including single and multiple induced abortions, use of alcohol, and use of tobacco. We here report the demographic characteristics and pregnancy outcomes of 12,424 women, 1,246 of whom reported some usage of marijuana during pregnancy.

Methods

The Study Population and Data Collection

The Delivery Interview Program (DIP) at the Boston Hospital for Women Division of the Brigham and Women's Hospital was designed to obtain information on the relationship of late pregnancy outcome to a variety of exposures. Between August 1977 and March 1980, we approached 14,458 women, 84.4 per cent of those who had delivered in this period (Table 1). Reasons for not being approached were lack of sufficient personnel to cover all deliveries (14.1 per cent) and treatment by the only physician who did not agree to let his patients participate in this study (1.5 per cent). On days when there were not sufficient personnel to interview all delivery patients, a random selection was made.

Of those who were approached and who had singleton deliveries, 90.0 per cent were interviewed. Failure to interview was due to early discharge (5.4 per cent), refusal (2.9 per cent), language barrier (1.6 per cent), and medical conditions that precluded an interview (0.1 per cent).

Women were interviewed following delivery but during the delivery admission. They were asked whether they used marijuana during pregnancy. If so, they were asked whether on the average they used the drug occasionally, weekly, or daily. We did not obtain more detailed information about patterns of marijuana usage during pregnancy. Other data collected included demographic characteristics, other habits and exposures, previous medical and obstetric history, and information on the current pregnancy and its outcome.[11]

From analysis of the 12,825 women interviewed, we excluded those for whom the medical record could not be found and those who were diabetic. Also, we excluded the 16 women whose records indicated a problem of "drug abuse," since these patients if they used marijuana at all invariably used other drugs.

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This paper, submitted to the Journal November 12, 1981, was revised and accepted for publication March 15, 1983.
Editor's Note: See also related article p 1164.

TABLE 1—Number of Potential Subjects, Exclusions, and Number of Subjects Included in the Final Analysis*

Boston Hospital for Women	Number
Deliveries in study period‡	17,136
Subjects approached	14,458
Singleton deliveries	14,255
Subjects interviewed	12,825
Medical records found	12,718
Non-diabetics	12,440
No "drug abuse" recorded by physician	12,424

*Each category is a subset of the higher category.
‡Note: Study period was August 1977–March 1980.

Analytic Techniques

We first examined the distribution of infant/maternal characteristics and other pregnancy data within categories of reported marijuana usage. Information about malformations was derived from the physician's notes in the medical records during the delivery hospitalization. Classification of malformations as major or minor was done without knowing the exposure status of the subjects. For this purpose we used coding schemes which have been developed for the Congenital Malformations Surveillance Program at the United States Centers for Disease Control (CDC) and for the Collaborative Perinatal Project (CPP).[12]

Hemangiomata and lymphangiomata (180 infants of non-users and 17 infants of users) and nevi (23 infants of non-users and three infants of users), which were categorized as "tumors" in the CPP, were regarded as minor malformations. Undescended testis (62 infants of non-users and seven infants of users) were recorded as minor malformations, according to the CDC classification, although these were regarded as major malformations in the CPP. Similarly, inguinal hernias (five infants of non-users and three infants of users) were recorded as minor malformations.

To control for confounding we performed analyses by logistic regression.[13] All variables including the dependent variable were recoded as binary variables. We chose cut-off points on the basis of the distribution of characteristics within categories of marijuana consumption or according to a natural cut-off point of interest (e.g., one or more prior pregnancies versus no previous pregnancy).

The crude odds ratio was computed by including in the model just one independent variable, the categories of marijuana usage. Several models with additional independent variables were then examined, including a model with 11 demographic characteristics, habits and medical history variables of *a priori* interest. These included age, race, education, welfare status, cigarette smoking at delivery, alcohol consumption during the first trimester of pregnancy, parity, previous stillbirths, induced abortions, miscarriages, and ponderal index. Then, to determine the contribution of marijuana consumption after controlling for all the other variables, we examined the ratio of likelihood for two models: a model that included all variables except marijuana consumption versus a model that included this information. The difference between the log likelihood under the two models multiplied by −2, i.e., the Wilks criterion, is known to follow the Chi-square distribution with one degree of freedom under the null hypothesis that, after controlling for the above variables, marijuana consumption offers no additional information in predicting the outcome.

Results

In Table 2, we present some of the characteristics of the study population. About 10 per cent of the interviewed population reported the usage of marijuana during pregnancy, the majority of them being occasional users. Thus, there were 880 women who reported the occasional use of marijuana (7.1 per cent), 229 women who reported the usage of marijuana once a week (1.8 per cent), and 137 women who reported daily usage of marijuana (1.1 per cent).

Reported marijuana usage in pregnancy was positively associated with a variety of demographic characteristics including young maternal age, being single, Black, having less than a college education, and being on welfare. Smoking tobacco was associated directly with marijuana usage. There was a weak positive association with alcohol use and a weak negative association with coffee use.

Whereas the percentage of multigravidas was essentially similar for all categories of marijuana users and for non-users, fewer of the users had prior live births. This discrepancy between gravidity and parity occurred mainly because users had a higher percentage of previous induced abortions.

Marijuana users were more likely to have had an unplanned pregnancy (Table 3). Bleeding in the first two trimesters was not related to marijuana consumption, but bleeding in the third trimester was slightly more prevalent among weekly and daily users.

The occurrence of premature labor and abruptio placenta increased with higher frequency of marijuana usage. For premature labor, the crude association with marijuana usage was statistically significant ($p < 0.001$). There was no consistent relationship between marijuana usage and premature rupture of membranes, breech presentation, placenta previa, or fetal distress.

Table 3 also shows infant outcomes in relation to marijuana usage. Children of marijuana users were more

TABLE 2—Percentage of Selected Demographic and Medical Characteristics within Categories of Marijuana Usage during Pregnancy

Characteristics	Marijuana Usage			
	None	Occasional	Weekly	Daily
Number of Subjects (total = 12,424)	11,178	880	229	137
Demographics				
Age 26+ years	71.5	46.3	38.0	38.0
Single	10.5	29.3	31.4	33.6
Black	13.8	25.8	29.7	37.2
College Education	66.8	51.0	41.9	35.8
On welfare	14.1	28.6	26.7	38.0
Habits				
Smoking 3+ cigarettes per day at delivery	19.4	39.4	45.9	53.3
Alcohol use, 1st trimester	21.9	28.1	37.6	29.9
Coffee use, 1st trimester	43.9	40.0	35.4	33.6
Previous History				
Gravidity >1	63.9	58.1	63.3	65.7
Parity >1	50.6	35.3	39.7	39.4
Previous induced abortion(s)	13.0	28.5	29.7	38.0
Previous stillbirth(s)	3.0	1.4	3.5	3.6
*Previous miscarriage(s)	17.7	11.5	13.1	10.2
Ponderal index >30 (obesity)*	11.9	10.9	15.3	9.5

*Kilogram/meter-squared

TABLE 3—Percentage of Selected Pregnancy Events, Delivery Characteristics, and Infant Outcomes within Categories of Marijuana Usage during Pregnancy

Characteristics	Marijuana Usage			
	None	Occasional	Weekly	Daily
Pregnancy Events				
Unplanned pregnancies				
on contraception	14.8	21.4	20.5	17.5
no contraception	23.3	35.5	38.4	48.2
Bleeding in:				
1st trimester	9.5	9.9	8.7	7.3
2nd trimester	3.9	4.0	3.5	2.2
3rd trimester	4.8	4.3	6.1	7.3
Toxemia or eclampsia	3.5	4.4	4.8	3.6
Pre-admissions for false labor	8.5	9.9	8.3	12.4
Premature labor	3.7	5.0	7.0	8.8
Delivery Characteristics				
Placenta abruptio	1.1	1.6	2.2	2.9
Premature rupture of membranes	4.3	5.8	7.9	2.9
Breech presentation	4.3	4.7	4.4	2.9
Placenta previa	0.6	0.2	0.4	0.0
Fetal distress	3.1	4.2	3.1	5.1
Infant Outcomes				
Major malformations	2.6	3.2	3.9	3.6
Minor malformations	6.2	7.8	5.2	5.1
Birthweight <2500 grams	7.6	9.8	13.5	11.7
Gestation <37 weeks	7.2	8.2	11.4	11.7
Neonatal jaundice	19.5	19.4	17.0	17.5
Stillbirth	0.6	0.6	1.3	1.5
Neonatal infection	1.0	1.0	2.2	2.9
Special care nursery	17.0	19.2	20.5	13.9
1 minute Apgar score less than 6	7.5	9.4	8.3	13.1
Respiratory problems	5.2	5.3	6.6	5.1

likely to have one or more major malformations than children of non-users, but there was no crude association with minor malformations. There were excesses of stillbirths and of neonatal infections among weekly and daily users, but the excesses are based on small numbers and are unstable.

One minute Apgar scores were statistically significantly lower for infants of marijuana users ($p < 0.05$), but this was related to the occurrence of low birthweight and short gestations among these infants.

Table 4 gives the general categories of the recorded major malformations that occurred in 42 infants of marijuana users compared to their occurrence among non-users. Only the most severe malformation for each infant is included. While each of these categories occurred more commonly among users than among non-users, this may simply be a reflection of random excess. Among non-users, the most prevalent of the "other" malformations were 25 cases of congenital hip dislocation and 18 cases of cleft lip/cleft palate; among the users there was one congenital hip dislocation and no cleft lip/cleft palates.

In Table 5 we present the results of the logistic regression model for major malformations. The odds ratio for major malformations among marijuana users versus non-users was 1.36 with a 95 per cent confidence interval of 0.97, 1.91. The Wilks criterion for introducing the information about marijuana usage after all other variables in the model were controlled was not statistically significant ($p = 0.09$). A similar analysis specifically for daily users resulted in similar results. The only variable statistically significant at the 0.05 level was parity of more than 1, and that was associated with a lowered odds ratio for major malformations.

Newborn infants of users of marijuana had a statistically significantly lower birthweight (Table 3), but when other variables were controlled, marijuana usage was not statistically significantly associated with low birthweight (Table 6 odds ratio = 1.07, 95 per cent confidence interval 0.87–1.31). Several other variables were more strongly associated with and statistically significantly related to the occurrence of low birthweight including smoking cigarettes, history of previous stillbirth or miscarriage, primiparity, low ponderal index, having less than a college education, and being Black.

Similar findings were obtained for the occurrence of short gestations. That is, there was a crude, statistically significant association between marijuana use and short gestation that disappeared with control of other variables by logistic regression. The logistic regression analysis, controlling for demographic characteristics, habits, and previous obstetric history yielded an odds ratio of 1.02 with a 95 per cent confidence interval of 0.82–1.27.

Discussion

This is an early report about marijuana usage in pregnancy. Like the recent report by Hingson, *et al,* the exposure variable—marijuana usage in pregnancy—is poorly quantified.[6] Future studies will undoubtedly need to ask more detailed questions about frequency of usage at each stage of pregnancy. Nevertheless, it is of interest and

TABLE 4—Major Malformations among Newborns of Marijuana Users and Non-users

Malformation (type of system)	Marijuana Usage			
	11,178 Non-Users		1,246 Users	
	Number of Malformations	Rate per 1000	Number of Malformations	Rate per 1000
Congenital heart disease	26	2.3	7	5.6
Hypospadias	47	4.2	7	5.6
Clubfoot	41	3.7	6	4.8
Upper alimentary tract	13	1.2	3	2.4
Respiratory tract	6	0.5	3	2.4
Genital	3	0.3	2	1.6
Face, neck and ear	15	1.3	2	1.6
Spina bifida	5	0.5	2	1.6
Hydrocephalus	6	0.5	2	1.6
All other malformations	132	11.7	8	6.7
Total major malformations	294	26.3	42	33.7

TABLE 5—Odds Ratios and Confidence Interval Estimation by Logistic Regression for Major Malformations*

Characteristics	OR	95% Confidence interval
Marijuana usage (any frequency)	1.36	0.97–1.91
Previous miscarriage(s)	1.27	0.96–1.67
White	1.21	0.89–1.67
Alcohol use in pregnancy	1.19	0.93–1.64
Age 35+	1.19	0.83–1.72
Previous stillbirth(s)	1.05	0.55–1.99
On welfare	1.03	0./2–1.47
Smoking 3+ cigarettes per day at delivery	0.84	0.63–1.11
Previous induced abortion(s)	0.82	0.59–1.14
Parity >1	0.74	0.59–0.92

*Listed are the odds ratios (OR) of having a baby with a major malformation controlling simultaneously for the other characteristics in the list. The analysis was performed for 11,178 women who reported no use of marijuana during pregnancy and 1,246 women who reported some marijuana use.

TABLE 6—Odds Ratios and Confidence Interval Estimation by Logistic Regression for Low Birthweight*

Characteristics	OR	95% Confidence interval
Marijuana usage (any frequency)	1.07	0.87–1.31
Previous stillbirth(s)	2.63	1.98–3.49
Ponderal index <18	2.14	1.30–3.52
No college education	1.71	1.47–2.00
Smoking 3+ cigarettes per day at delivery	1.56	1.34–1.81
Black	1.39	1.16–1.67
Previous miscarriage(s)	1.37	1.15–1.62
Previous induced abortion(s)	1.12	0.94–1.34
Age <18 years	1.08	0.80–1.46
On welfare	1.06	0.87–1.28
Alcohol in 1st trimester	0.97	0.82–1.14
Parity >1	0.73	0.64–0.84

*Listed are the odds ratios (OR) of having a baby with low birthweight, controlling simultaneously for the other characteristics in the list. The analysis was performed with data from 11,178 women who reported no usage of marijuana during pregnancy and 1,246 women who reported some marijuana use.

concern that 10 per cent of the women who gave birth at the Boston Hospital for Women during the study period admitted some use of marijuana during pregnancy. This is likely to be a minimum estimate of the actual per cent of users.

More marijuana users had infants who had lower birthweight, short gestations, and major malformations. After controlling for demographic characteristics, smoking, alcohol consumption, and medical history, these excesses in poor outcomes were not statistically significant. The association of marijuana usage and major malformations remains suggestive (odds ratio = 1.36), but we could not detect any specific malformation that was strongly related to marijuana usage. Nevertheless, the question of whether marijuana usage is related to the occurrence of major malformations merits further investigation.

If marijuana use indeed caused congenital malformations, our failure to find a statistically significant association could be explained in part by difficulties in detecting malformations during the delivery hospitalization. It is known that certain malformations are detected later. Misclassification of exposure status is another possibility. Perhaps only marijuana usage in the first trimester is important; some women may use marijuana in the first trimester only; an interview at delivery may fail to detect first trimester exposure.

Still another explanation for our inability to find a statistically significant association would be a biased selection of subjects, i.e., those who smoked marijuana were excessively excluded from the study. We have no indication that this happened, however. Subject selection was made without reference to exposure status. Moreover, information about outcome was collected by trained record reviewers, who used a standard questionnaire and were unlikely to be award of specific exposure while recording outcomes.

An alternative explanation for the observed (weak) relationship between marijuana usage and adverse outcomes of pregnancy could be that women who have an undesirable outcome of pregnancy are more likely to report prior usage of marijuana. This recall bias cannot be excluded without a prospective study in which exposure is ascertained before the outcome is apparent.

The results of this report should be considered cautiously until they are confirmed by more detailed investigation, but they are not reassuring. The data were collected before there was much publicity about the possible effects of marijuana use on pregnancy, and it is disturbing that a sizable percentage of women delivering in our hospital admitted use of marijuana in pregnancy. When compared to non-users, our marijuana users were younger, more often Black, less likely to be married, less educated, more often on welfare, and had more unplanned pregnancies. Educational programs aimed at the reduction of marijuana usage during pregnancy might be focused toward women with these characteristics. Until more information is available, like every other unnecessary drug, women should be advised not to use marijuana during pregnancy.

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ACKNOWLEDGMENTS

This research was supported by a grant from the National Birth Defects Foundation.