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Spontaneous Abortions Among Women Employed in the Plastics Industry

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A matched case-control study was done to analyze whether certain occupational exposures in the plastics industry were related to the risk of spontaneous abortions. Information on spontaneous abortions (cases) and births (controls) was obtained from the hospital discharge register; data on occupational exposures were obtained from the occupational health services of the workplaces. No increased risk of spontaneous abortions was observed among workers processing polymerized plastics or heated plastics made of vinyl chloride or of styrene. Owing to the low statistical power of the study, only strong effects can be ruled out. The odds ratio for workers actually processing polyurethane was increased (1.9, not statistically significant), and that for all workers in polyurethane-processing factories was significantly increased (3.0, $p = 0.02$). The finding needs to be investigated further in future studies.

Key words: spontaneous abortion, occupational exposure, plastics industry, polyvinyl chloride, polyurethane, styrene plastics

INTRODUCTION

Observations of the carcinogenicity and mutagenicity of vinyl chloride and some other chemicals in plastics [IARC, 1979] have raised concern about their other biological effects. Increased fetal death rates have been reported among the wives of men exposed to vinyl chloride monomer [Infante et al, 1976]. A more recent study did not support this finding but did detect an increased rate of stillbirths among the exposed [Sanotsky et al, 1980]. Three other studies reported excesses of birth defects in communities with vinyl chloride polymerization plants, but the role of vinyl chloride has not been established [Infante, 1976; Edmonds et al, 1978; Thériault et al, 1983].

A Finnish study suggested that women employed in the plastics industry, especially in styrene processing, had more hospitalized spontaneous abortions than all Finnish women [Hemminki et al, 1980], but the excess was not confirmed in a follow-up study [Hemminki et al, 1984]. An interview study revealed no large difference in the number of spontaneous abortions between female lamination workers exposed to styrene and their controls [Härkönen and Holmberg, 1982]. A case-control study

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concerning mothers of children with central nervous system defects initially suggested an association with the reinforced plastics industry [Holmberg, 1977], but further data have been negative.

The present study is a continuation of our earlier efforts to examine the possibility that chemical exposures in the plastics industry affect spontaneous abortions among plastic workers. It is a part of a joint Nordic study coordinated by the Nordic Working Group on Occupational Reproductive Hazards. Here we focus on the possible effects of different types of plastics and their thermal degradation products, which include many potentially mutagenic and/or carcinogenic chemicals [Vainio et al, 1980]. The study concerns all Finnish women in the plastics industry who belong to the Union of Chemical Workers and has been done with a case-control design.

MATERIALS AND METHODS

The study population comprised all female workers in the plastics industry who belonged to the Union of Chemical Workers in 1979 or who had resigned from the Union during 1978 and 1979. According to the union, 9 of 10 workers in the plastics industry are union members. The workers' reproductive data for 1973–1980 were collected from the hospital discharge register maintained by the Finnish National Board of Health. The register includes information on all Finnish women treated for spontaneous abortion (ICD-8 codes 643 and 645) and for induced abortion (codes 640–642), and who have given birth (codes 650–662). The register records have been supplemented with data on spontaneous abortions treated on an outpatient basis. About 14% of the spontaneous abortion patients were treated as outpatients in 1973–1980. The majority of them were treated in Helsinki hospitals [Niemi et al, 1985]. In the population of this study 7% of the cases were outpatients.

Cases and controls were selected from the women who had been union members during the first trimester of pregnancy. All the women treated for spontaneous abortion were defined as cases. Three matched controls were selected from women who had given birth and who had not had a registered spontaneous abortion. The controls were matched to the cases for age at the beginning of pregnancy within 2 years (the nearest available matching). Only two controls were available for one case, and only one control could be found for four cases.

A questionnaire was sent to the occupational health physicians (occupational health services are now mandatory in Finland) to determine the occupational exposures of cases and controls during the first 2 months of pregnancy; 45% of the physicians were employed in municipal health centers, and 19% in private health stations; 36% of them were plant physicians. The physicians themselves or working-site nurses were asked to fill out the questionnaire forms. They were not informed whether they were dealing with a case or a control. The first part of the questionnaire dealt with the type of production, the type of plastics handled, and the manufacturing procedures in the factory. The second part requested information on the individual worker's occupation and main tasks, the type of plastics she handled, whether plastics were heated during the process, and other exposures. Information concerning industrial hygienic measurements and biological exposure tests was also requested.

Physicians who did not respond to the first mailing were sent a second questionnaire. Physicians who still failed to respond were contacted by telephone.

The information on occupation and main tasks was used to classify the study population into four occupational exposure categories: 1) processing of "cold" polymerized plastics, 2) processing of heated plastics, 3) processing of plastic monomers (epoxy resins were also included to this group), and 4) not processing plastics (ie, other employment). Exposure to solvents was also considered in the analysis. The types of plastics analyzed were vinyl chloride, styrene plastics (polystyrene, styrene-butadiene, styrene-acrylonitrile, acrylonitrile-butadiene-sytrene), and polyurethane.

The estimates of odds ratios for exposure were calculated with the logistic regression model for individually matched data based on the conditional maximum likelihood. The likelihood ratio test was used to evaluate the significance of the parameter estimates [Breslow and Day, 1980].

RESULTS

This study population comprised 167 female workers, of whom 44 had had a spontaneous abortion (cases) and 123 had given birth (controls). The mean ages of the cases and the controls were 26.4 and 25.3 years, respectively. Questionnaires on the exposures of the cases and the controls during the first 2 months of gestation were sent to 47 occupational health physicians. The response rate to the questionnaires was 83%, with no difference between the response rates for the cases and the controls (Table I). However, the proportion of workers whose employment was identified was higher for the cases (82%) than for the controls (72%). Information about the workplace was reported as unknown during the early pregnancy for 12% of the controls, whereas it was known for all the cases. The controls with unknown workplaces had been employed in the factory before or after pregnancy but not during early pregnancy.

The distribution of cases and controls by occupational exposure was nearly the same (Table II). Almost 80% were employed in the production of plastic goods; one third was engaged in the heating of plastics, and exposure to thermal degradation products of plastics was possible. Only two women had handled plastic monomer (one case and one control). Some 18% of the cases and 16% of the controls were exposed to solvents. Table III shows odds ratios for processing polymerized plastics, heated plastics, and solvent exposure. All the odds ratios are close to unity.

The numbers of workers who had processed various types of plastics were small. Many of the women (28%) had handled more than one type of plastics. Table IV shows the proportions of cases and controls separately for all workers processing

TABLE I. Cases of Spontaneous Abortion and Their Controls According to Employment (in percent)

	Cases (N = 44)	Controls (N = 123)	Total (N = 167)
Employment identified	82	72	75
Processing of plastics	64	55	58
Other employment	18	17	17
Employment not identified	18	28	25
Employment unknown	—	12	8
No response	18	16	17
Total	100	100	100

TABLE II. Cases of Spontaneous Abortions and Their Controls According to Occupational Exposure During Early Pregnancy

	Cases		Controls	
Occupational exposure	N	%	N	%
Processing of:				
Polymerized "cold" plastics	14	39	32	36
Heated plastics	12	33	32	36
Plastic monomers	1	3	1	1
Unknown	1	3	3	3
Other employment	8	22	21	24
Total	36	100	89	100

TABLE III. Odds Ratio of Spontaneous Abortion for the Processing of Polymerized Plastics and Heated Plastics, and for Solvent Exposure, Matched Logistic Regression Analysis

Occupational exposure	Exposed cases	Exposed controls	Odds ratio	95% Confidence interval
Polymerized plastics	14	32	1.1	0.4–3.3
Heated plastics	12	32	0.8	0.3–2.5
Solvents	6	13	1.1	0.3–3.9

TABLE IV. Odds Ratio of Spontaneous Abortion for the Processing of Polyvinyl Chloride and Styrene Plastics, Matched Univariate Analysis

	Exposed cases		Exposed controls			
Occupational exposure	N	%	N	%	Odds ratio[a]	95% Confidence interval
Workers processing:						
Polyvinyl chloride plastics	5	14	8	9	1.1	0.3–4.2
Styrene plastics	4	13	17	22	0.4	0.1–1.2
Workers processing heated:						
Polyvinyl chloride plastics	3	9	7	8	1.2	0.3–5.4
Styrene plastics	4	11	12	14	0.6	0.2–2.3

[a]Calculated for each variable separately by logistic regression analysis.

polyvinyl chloride and styrene plastics and for those processing heated polyvinyl chloride and styrene plastics. Work with polyvinyl chloride plastics was more common among the cases; work with styrene plastics was more common among the controls. Odds ratios and their confidence limits were calculated for each plastics variable individually by logistic regression analysis. None of the odds ratios were significantly different from unity (Table IV).

The odds ratios for workers in polyurethane-processing factories are given in Table V. The risk estimate for women handling polyurethane plastics was increased (odds ratio = 1.9) but not significantly. The relative risk of spontaneous abortions was also estimated for all the workers employed in the factories in which polyurethane plastics were processed, even though not all of the women studied were listed as exposed. The odds ratio for this group was 3.0 ($p = 0.02$), with 95% confidence limits of 1.2–7.8.

The variables for polyurethane, polyvinyl chloride, and styrene plastics and for solvents were included simultaneously in the same logistic regression model in order

TABLE V. Odds Ratio of Spontaneous Abortion for Workers in Polyurethane-Processing Factories, Matched Univariate Analysis

Group	Exposed cases		Exposed controls		Odds ratio[a]	95% Confidence interval
	N	%	N	%		
Workers processing polyurethane	4	13	6	7	1.9	0.4–8.5
All workers employed in factories processing polyurethane	12	31	14	14	3.0	1.2–7.8

[a]Calculated for each variable separately by logistic regression analysis.

TABLE VI. Odds Ratios of Spontaneous Abortion for Exposure to Various Types of Plastic Materials, Matched Multivariate Analysis*

Handling of:				Heating of:		
Polyurethane	Styrene plastics	Polyvinyl chloride	Solvents	Styrene plastics	Polyvinyl chloride	χ^2 of the model
2.2	0.4	1.0	1.0	—	—	3.16
2.1	—	—	1.0	0.5	1.1	1.95

*None of the odds ratios or models were statistically significant.

to control for their interdependences. Table VI shows the odds ratios for these exposures yielded by two models. None of the odds ratios changed essentially.

DISCUSSION

The present study investigated the main group of plastics workers in Finland. Although the overall rate of spontaneous abortions was not increased in this group of women [Hemminki et al, 1984], the heterogeneity of plastics work warranted a detailed study on individual exposures.

The results suggested that neither the processing of polyvinyl chloride or styrene plastics nor exposure to thermal degradation products was associated with spontaneous abortions. A significant difference between the cases and the controls was found however, in the frequency of employment in the polyurethane-processing industry.

Although this was a nationwide study, the statistical power of the investigation was low because of the small size of the study population. Calculated with the method provided by Miettinen [1969], the likelihood of detecting a twofold risk was 38% for exposure to thermal degradation products. This likelihood was smaller for specific types of plastics. Thus the absence of a significant association between spontaneous abortions and exposures rules out only a strong effect.

Below we discuss some sources of bias in reproductive studies in some detail and show how we tried to eliminate them. We feel that the present results can hardly be explained by systematic bias but, of course, we are unable to rule out chance findings.

Bias in recalling exposures related to pregnancy and response bias are the most serious problems of case-control studies based on interview data. In this study information on exposure was obtained from occupational health physicians who did not know whether they were dealing with a case or a control. They were requested to

fill out the questionnaires by themselves and without worker contacts. Even though we cannot rule out that medical records revealed the case or control status of the subjects to the physicians, the physicians can be considered relatively objective sources of exposure data.

Information on pregnancy outcome was collected from the hospital discharge register. This procedure may cause selection that is dependent on how patients seek hospital care. The length of gestation is probably the main selective factor in seeking hospital care; therefore it is obvious that our results do not apply to abortions that occurred in the very first weeks of gestation. As the study subjects had a homogeneous social background, we consider selection due to exposure unlikely and certainly not agent-specific. No information was available on such potential confounding factors as prior obstetric history, smoking, or the use of alcohol. The homogeneous social background makes it unlikely that these factors were major confounders. In addition, matching for age probably minimized the differences in parity between the cases and the controls.

Another potential source of bias in this study is that no information was available on union members who had resigned before 1978. Inclusion of the year of pregnancy in the logistic regression model did not, however, change the odds ratios for employment in the plastics industry or for exposure to thermal degradation products.

The third potential source of bias in this study is the difference between cases and controls in the number of workers whose employment could not be identified. The nonresponse rates were similar for cases and controls, but there were 14 controls (12%) who during pregnancy had not worked at the factory specified in the union register. Comparison of the distribution of detected and undetected controls by age, year of pregnancy, and workplace revealed no essential differences.

An attempt was made to examine further potential bias involved by creating a separate variable for missing data in logistic analysis. The inclusion of this variable in the equations did not change essentially the odds ratios for exposure variables.

The results of the present study suggested an association between employment in a polyurethane-processing factory and an increased risk of spontaneous abortion. The odds ratio for workers actually processing polyurethane was increased (1.9, not statistically significant), and the odds ratio for all workers in polyurethane-processing factories was significantly increased (3.0, $p = 0.02$). The latter group included not only polyurethane workers but also workers who handled other types of plastics or whose work did not involve plastics handling. Workers processing polyurethane may have been exposed to isocyanates and amines. Exposure of other workers is also possible if they have been working in areas where isocyanates are handled. Isocyanates irritate the respiratory tract and can act as sensitizers that produce asthma-like symptoms in sensitized workers exposed to very low concentrations [NIOSH, 1978]. Symptoms have been reported also in workers not employed themselves in polyurethane processing.

The literature contains no information on the reproductive effects of isocyanates other than a case report on the impotency of two men heavily exposed to toluene diisocyanate [Barlow and Sullivan, 1982]. Because of the high reactivity of isocyanates it is not easy to envisage that they would systemically reach the human embryo. Yet indirect immunological or other mechanisms cannot be excluded. It may also be that working conditions other than isocyanates are responsible for the findings.

The questionnaire asked for the results of industrial hygienic measurements that would represent the situation during the study subjects' pregnancy. Two factories

answered this question. The concentration of toluene diisocyanate was reported to be 0.002 cm^3/m^3 and that of 4,4'-methylenediphenyl diisocyanate, <0.002 cm^3/m^3. These replies indicate a low level of exposure (hygienic standard = 0.02 cm^3/m^3). However, as the results were obtained for only two measurements, neither of which had been performed during the pregnancy of the study subjects, they cannot be used to assess the exposure level of all polyurethane workers.

This study detected no increased risk of spontaneous abortions among workers processing polymerized plastics or heated plastics made of polyvinyl chloride, or styrene. Because of the low statistical power of the study, only strong effects could be ruled out. Studies in other countries are needed before final conclusions can be made. The same conclusion applies to the observation of a positive association between polyurethane plastics and the risk of spontaneous abortion. This finding, therefore, should be considered a hypothesis that needs to be tested in future studies.

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