Current Cigarette Smoking and Risk of Acute Pelvic Inflammatory Disease

ABSTRACT

Objectives. Further information is needed on modifiable factors associated with the occurrence of acute pelvic inflammatory disease (PID). Cigarette smoking has been implicated as a risk factor for PID sequelae, but the association between smoking and PID has yet to be fully examined.

Methods. We conducted a population-based case-control study to evaluate smoking as a risk factor for acute PID. The case patients (n = 131) were women health maintenance organization (HMO) enrollees between the ages of 18 and 40 years who were treated for a first episode of PID. The control patients (n = 294) were randomly selected from the HMO enrollment files.

Results. Relative to never smokers, current smokers were at increased risk of PID. Women who smoked 10 or more cigarettes per day had a higher risk than did those who smoked less. Available data indicate that smoking status is not serving as a marker for uncontrolled confounding by lifestyle factors.

Conclusions. Our study results suggest that smoking represents a modifiable risk factor for acute PID. (*Am J Public Health.* 1992;82:1352–1355)

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Introduction

Cigarette smoking has been implicated as a risk factor for ectopic pregnancy[1–5] and tubal infertility.[6] One way in which smoking may affect both of these outcomes is by increasing a woman's risk for pelvic inflammatory disease (PID), a severe upper genital tract infection that may result in scarring and obstruction of the fallopian tubes. Although one study[7] found an increased risk for smokers, the relationship between smoking and PID has yet to be fully examined. We evaluated this association in a population-based series of cases and controls from the Group Health Cooperative of Puget Sound.

Methods

The case patients consisted of women aged 18 to 40 years who experienced their first episode of acute PID between September 1984 and November 1985. The Group Health Cooperative automated hospital information system was used to select inpatients who had received a primary discharge diagnosis of acute PID or salpingitis. The automated pharmacy database was used to select potential ambulatory care PID cases. Medical records of women who were prescribed either doxycycline or a high-dose regimen of tetracycline[8] were reviewed for a diagnosis of PID. All medical records were reviewed for the presence of three clinical inclusion criteria: abdominal pain of 1 month's duration or less, cervical motion or uterine tenderness, and adnexal tenderness. Patients were included only if all three symptoms and signs were noted.

The control patients were part of a control group for a concurrent population-based study of ectopic pregnancy conducted at Group Health Cooperative. These women were selected randomly from the enrollment files. Control patients with reference dates (dates assigned to approximate the date of conception of the assigned case) between January 1984 and August 1986 were selected randomly from the enrollment files and matched to the women with ectopic pregnancies on age and county of residence.

The following inclusion criteria were applied to all potential research subjects: resident of King County; no prior history of PID; sexually active within the preceding year; no prior hysterectomy or bilateral salpingo-oophorectomy; not pregnant; no pelvic surgery or uterine instrumentation within the preceding 6 weeks; no vasectomized partner at reference date.

An in-person interview was used to collect information on cigarette smoking status at diagnosis/reference date, duration and amount smoked, and, for former smokers, length of time since quitting. Similar information was obtained on respondents' partners where applicable.

Unconditional logistic regression[9] was used to assess the role of smoking as

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This paper was submitted to the Journal May 10, 1991, and accepted with revisions May 13, 1992.

a risk factor while controlling for the confounding effects of age, race, gravidity, and number of sexual partners in the year prior to reference date. Risk estimates of smoking in relation to PID were not substantially altered when income, education, marital status, presence and type of contraception at reference date, and recent douching were added to the model.

Results

We interviewed 131 (72.4%) of the 181 case patients identified as eligible. Twelve percent of the 131 were hospitalized. Of the 428 women identified as potential controls, 314 (73.4%) were interviewed. We excluded 20 control patients with a history of PID.

Case patients were more likely to be younger, to have lower incomes and less education, to be non-White, to have been previously pregnant, and to have had more than one sex partner in the previous year (Table 1). They were less likely to be married at reference date.

More case patients (43.5%) than control patients (25.6%) were current smokers (Table 2). Current smokers experienced a twofold increase in risk (adjusted odds ratio [OR] = 2.1, 95% confidence interval (CI) = 1.3, 3.6) compared with never smokers. Women who smoked an average of 10 or more cigarettes per day were at higher risk than those who smoked less (OR = 2.4, 95% CI = 1.4, 4.2 vs OR = 1.2, 95% CI = 0.5, 3.0). The risks associated with current smoking were consistently higher among women with two or more recent sexual partners (Table 3). The percentage of current smokers did not differ between partners of case and partners of control patients (35% and 30%, respectively).

TABLE 1—Demographic Characteristics of Pelvic Inflammatory Disease Case and Control Patients

	Total Sample				Currently Smoking			
	Case Patients (n = 131)		Control Patients (n = 294)		Case Patients (n = 57)		Control Patients (n = 76)	
	No.	%	No.	%	No.	%	No.	%
Age, y								
18–24	60	45.8	76	25.9	28	46.7	18	23.7
25–29	31	23.7	75	25.5	12	38.7	12	16.0
30–34	22	16.8	86	29.3	10	45.5	24	27.9
35+	18	13.7	57	19.4	7	38.9	22	38.6
Race								
White	101	77.1	253	86.1	49	48.5	66	26.1
Black	23	17.6	23	7.1	8	34.8	7	30.4
Other	7	5.4	18	6.1	0	...	3	16.7
Income[a]								
<$15 000	55	42.3	57	30.6	26	47.3	16	28.1
$15 000–30 000	47	36.2	122	37.9	22	46.8	30	24.6
>$30 000	28	21.5	114	31.5	8	28.6	29	25.4
Education								
≤High school	58	44.3	69	28.0	33	56.9	28	40.6
>High school	73	55.7	225	72.0	24	32.9	48	21.3
Current marital status								
Never married	10	7.6	32	15.6	4	40.0	10	31.3
Married	34	26.0	164	44.5	15	44.1	39	23.8
Separated/divorced	4	3.1	15	3.8	3	75.0	5	33.3
Living as married	39	22.1	27	10.0	12	41.4	9	33.3
Regular partner	54	41.2	56	26.0	23	42.6	13	23.2
Gravidity								
Never	37	28.2	111	50.2	13	35.1	25	22.5
Ever	94	71.8	183	49.8	44	46.8	51	27.9
Recent douching[b]								
No	74	57.7	218	77.1	31	41.3	52	23.9
Yes	55	42.3	74	22.9	26	47.3	24	32.4
Current contraceptive method[c]								
None	24	18.5	58	18.6	11	45.8	16	27.6
Oral contraceptive	45	34.6	87	37.4	18	40.0	23	26.4
IUD	8	6.2	13	3.5	5	62.5	4	30.8
Barrier	29	22.3	86	28.3	11	37.9	16	18.6
Tubal ligation	15	11.5	38	8.9	8	53.3	15	39.5
Other	9	6.9	12	3.3	3	33.3	2	16.7
Number of sex partners in preceding 12 months[d]								
One	87	66.4	237	80.6	31	35.6	55	23.2
Two	22	16.8	32	13.7	10	45.5	14	43.8
Three or more	22	16.8	22	9.7	16	72.7	7	31.8

Note. Control percentages were adjusted to the age distribution of cases.
[a]One case and one control patient refused to provide this information.
[b]Data missing for two case and two control patients.
[c]Data missing for one case patient.
[d]Data missing for three control patients.

Discussion

Although we were able to represent a broader spectrum of disease by including outpatients and were able to use a population-based series of control patients, our data have certain limitations. Diagnostic misclassification was unavoidable because laparoscopic confirmation was not done in the majority of cases. Also, we could not obtain complete microbiological data, which prevented us from examining how types of infection might modify the association with smoking.

Since many of the variables associated with increased risk of PID are also associated with smoking,[10,11] the possibility remains that smoking is a marker for lifestyle attributes inadequately adjusted for in the analysis. Several factors argue against this possibility. First, although lifestyle may be crudely assessed in the available variables, the proportion of women who were current smokers was higher for cases than for controls in virtually all categories of each variable (Table 1). Second, the risk of PID was elevated only among current smokers, which is consistent with expectations for an acute infectious process; among current smokers, moreover, risk increased with increasing amount smoked and with increasing potential for exposure to a variety of infecting organisms (more than one recent sex partner).

TABLE 2—Current Cigarette Smoking and Risk of Pelvic Inflammatory Disease

	Case Patients (n = 131)		Control Patients (n = 294)			
	No.	%	No.	%	Odds Ratio[a]	95% CI
Never smoked	54	41.2	171	58.2	1.0	referent
Ever smoked	77	58.8	123	41.8	1.8	1.1, 2.8
Current smokers	57	43.5	76	25.9	2.1	1.3, 3.6
<10 per day	11	8.4	21	7.1	1.2	0.5, 3.0
≥10 per day	46	35.1	55	18.7	2.4	1.4, 4.2
Former smokers	20	15.3	47	16.0	1.3	0.7, 2.4
Until 3 years ago	12	9.2	16	5.4	1.8	0.8, 4.3
>3 years ago	8	6.1	31	10.5	0.9	0.4, 2.2

[a]Adjusted for age, race, gravidity, and number of sex partners in the preceding 12 months.

TABLE 3—Current Cigarette Smoking and Risk of Pelvic Inflammatory Disease According to Number of Sex Partners in the Preceding Year

	One Partner					Two or More Partners				
	Case Patients (n = 72)		Control Patients (n = 200)		Odds Ratio[a]	Case Patients (n = 39)		Control Patients (n = 45)		Odds Ratio[a]
	No.	%	No.	%	(95% CI)	No.	%	No.	%	(95% CI)
Never smoked	41	56.9	145	72.5	1.0 (referent)	13	33.3	24	53.3	1.0 (referent)
Current smokers	31	43.1	55	27.5	1.9 (1.0, 3.4)	26	66.7	21	46.7	2.9 (1.1, 7.5)
<10 per day	3	4.2	12	6.0	1.1 (0.3, 4.4)	8	20.5	9	20.0	1.6 (0.4, 5.5)
≥10 per day	28	38.9	43	21.5	2.1 (1.1, 3.9)	18	46.2	12	26.7	3.9 (1.3, 11.2)

[a]Adjusted for age, race, gravidity.

Finally, we noted that the current smoking patterns of respondents' partners were unrelated to respondents' risk.

There are a number of plausible ways in which smoking may increase the risk of PID. The effect of nicotine on tubal ciliary function and ovum transport has been documented,[12] and the same impaired ciliary wave action that can fail to move the ovum toward implantation in the uterus may result in an inability to effectively repel ascending infectious organisms.

Studies have also provided evidence that smoking impairs the immune response.[13–19] A recent examination of the effect of cigarette smoking specifically on local cervical immunity found that current smokers had a decrease in the concentration of Langerhans' cells in the cervical epithelium.[20] Because these cells help detect and present antigens to circulating T-lymphocytes, a decrease could affect susceptibility to PID pathogens.

The only other study to assess this relationship used hospital-based data from the Women's Health Study[7]; the OR for current smokers compared to never smokers was 1.7. Our findings agree with findings from studies of PID sequelae, as well.[1–6] An association between smoking and urethritis in men, which is caused by many of the same organisms that cause PID,[21] has also been reported.[22]

More information is needed about modifiable noninfectious factors that may be associated with the acquisition or spread of cervical infection. This population-based study describes an association between one such factor—current smoking—and acute PID. We provide evidence that uncontrolled confounding is not the source of these findings and show that there is reason to believe that smoking itself may be acting to increase the risk of acute PID. □

Acknowledgments

This research was supported in part by grants 1-R01-HD17657 and 3-R01-HD17657-S1 from the National Institute of Child Health and Human Development, National Institutes of Health.

These findings were reported in part at the Society for Epidemiological Research 23rd Annual Meeting in Snowbird, Utah, June 1990.

The authors would like to acknowledge Noel Weiss, Kathleen Saunders, Barbara Young, Sandra Howard, Carol Ure, Jude Ballard, and the interviewing team that collected these data for their assistance with this project.

References

1. Campbell OM, Gray RH. Smoking and ectopic pregnancy: a multinational case-control study. In: Rosenberg M, ed. *Smoking and Reproductive Health.* Littleton, Mass: PSG Publishing Co; 1987.
2. Chow W-H, Daling JR, Weiss NS, Voigt L. Maternal cigarette smoking and tubal pregnancy. *Obstet Gynecol.* 1988;71:167–170.
3. Handler A, Davis F, Ferre C, Yeko T. The relationship of smoking and ectopic pregnancy. *Am J Public Health.* 1989;79:1239–1242.
4. Coste J, Job-Spira N, Fernandez H. Increased risk of ectopic pregnancy with maternal cigarette smoking. *Am J Public Health.* 1991;81:199–201.
5. Stergachis AS, Scholes D, Daling JR, Weiss NS, Chu J. Maternal cigarette smoking and the risk of ectopic pregnancy. *Am J Epidemiol.* 1991;133:332–337.
6. Daling JR, Weiss NS, Spadone L, Moore DE, Voigt L. Cigarette smoking and primary tubal infertility. In: Rosenberg M, ed. *Smoking and Reproductive Health.* Littleton, Mass: PSG Publishing Co; 1987.
7. Marchbanks PA, Lee NC, Peterson HB. Cigarette smoking as a risk factor for pelvic inflammatory disease. *Am J Obstet Gynecol.* 1990;162:639–644.
8. US Department of Health and Human Services. Sexually transmitted diseases: treatment guidelines, 1982. *MMWR.* 1982; 31(Suppl):43S.
9. Breslow NE, Day NE. *Statistical Methods in Cancer Research.* Vol 1. Lyon, France: IARC; 1980.
10. Novotny TE, Warner KE, Kendrick JS, Remington PL. Smoking by blacks and whites: socioeconomic and demographic differences. *Am J Public Health.* 1988;78: 1187–1189.
11. O'Malley PM, Bachman JG, Johnston LD. Period, age, and cohort effects on substance use among young Americans: a decade of change, 1976–86. *Am J Public Health.* 1988;78:1315–1189.
12. Weathersbee PS. Nicotine and its influence on the female reproductive system. *J Reprod Med.* 1980;25:243–250.
13. Thomas W, Holt PG, Keast D. Effect of cigarette smoking on primary and secondary humoral responses of mice. *Nature.* 1973;243:240–241.
14. Rozman TL, Rogers AS. The immunosuppressive potential of products derived from cigarette smoke. *Am Rev Resp Dis.* 1973; 108:1158–1163.
15. Schwartz SL. Interaction of nicotine and other amines with the endocytic and exo-

cytic functions of macrophages. *Fed Proc (Biochemical Aspects of Toxic Agents).* 1976;35:85–88.
16. Burton RC. Smoking, immunity, and cancer. *Med J Aust.* 1983;2:411–412.
17. Winkel P, Statland BE. The acute effect of cigarette smoking on the concentrations of blood leukocyte types in healthy young women. *Am J Clin Pathol.* 1981;75:781–785.
18. Chalmer J, Holt PG, Keast D. Cell-mediated immune responses to transplanted tumors in mice chronically exposed to cigarette smoke. *J Natl Cancer Inst.* 1975;55:1129–1134.
19. Andersen P, Pedersen OF, Bach B, Bonde GJ. Serum antibodies and immunoglobulin in smokers and nonsmokers. *Clin Exp Immunol.* 1982;47:467–473.
20. Barton SE, Jenkins D, Cuzick J, Maddox PH, Edwards R, Singer A. Effect of cigarette smoking on cervical epithelial immunity: a mechanism for neoplastic change? *Lancet.* 1988;ii(8612):652–654.
21. Thompson SE, Washington AE. Epidemiology of sexually transmitted chlamydia trachomatis infections. *Epidemiol Rev.* 1983;5:96–122.
22. Pessione F, Dolivo M, Casin I, et al. Sexual behavior and smoking: risk factor for urethritis in men. *Sex Trans Dis.* 1988;15:119–122.

Dr. Derrick B. Jelliffe to Receive Posthumous Award at APHA Annual Meeting

Dr. Derrick B. Jelliffe will posthumously receive the "Lifetime Achievement Award" from APHA's International Health Section at this year's APHA meeting in Washington, DC, November 8 to 12. (Dr. Jelliffe, a renowned pediatrician and advocate for international maternal and child health and nutrition, as well as professor emeritus at the University of California–Los Angeles School of Public Health, died March 18 at the age of 71.) The tribute will take place Tuesday, November 10, from 7:00 to 8:30 PM. Dr. Susi Kessler, chair of the International Health Section, will present the award. Dr. Michael C. Latham, professor and director of the Program in International Nutrition, Cornell University, will deliver the tribute's keynote address, "Derrick Jelliffe: Pioneer in Child Health and Infant Feeding." A reception will follow.