Prospective Study of Exposure to Environmental Tobacco Smoke and Dysmenorrhea

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Dysmenorrhea is a common gynecologic disorder in women of reproductive age. Previous studies have found an association between current cigarette smoking and prevalence of dysmenorrhea. This study investigated the association between exposure to environmental tobacco smoke (ETS) and the occurrence of dysmenorrhea among women without a history of this disorder. The study population consisted of 165 newly wed, nonsmoking Chinese women (in Shenyang, China), who intended to get pregnant and who had no past history of dysmenorrhea at the time of enrollment. These women completed a baseline questionnaire interview upon enrollment and were prospectively followed by daily diary. Dysmenorrhea was defined as a diary recording of menstrual pain, thus introducing a potential confounder (10). Parity was also suggested to be associated with menstrual pain (8–10). Nulliparous women were reported to have a higher prevalence of dysmenorrhea than multiparous women. In our study, all the subjects were newly wed, nulliparous, nonsmokers who intended to conceive (thus, they used no contraceptives during the follow-up menstrual cycles). These characteristics minimize the confounding effects of contraceptive use, parity, and active smoking. This study also adjusted for a number of occupational exposures that may be associated with dysmenorrhea.

Dysmenorrhea, or painful menses, is a common gynecologic disorder in women of reproductive age. Reported prevalence ranges from 47 to 72% for various age groups (1–3). This condition accounts for significant school absenteeism, lost working time, and reduced quality of life (4–6). In the United States it is estimated that 600 million working hours are lost annually as a result of primary dysmenorrhea (5), and it is now recognized as an important women’s health issue (7).

A growing body of evidence demonstrates an association between environmental and occupational exposures and adverse reproductive outcomes. Although limited data are available for dysmenorrhea, epidemiological studies have shown a link between dysmenorrhea and several environmental risk factors, including current cigarette smoking (8–11). An even greater proportion of women are exposed passively to environmental tobacco smoke (ETS). The question of whether exposure to ETS also increases the risk of dysmenorrhea has been studied only to a limited extent. In a study by Hornsby et al. (8), women exposed to ETS reported more days with dysmenorrhea on average (2.6 days) compared to unexposed women (2.0 days), adjusting for duration of menses and other confounders. There are a number of methodologic challenges in studying the health effects of ETS exposure. First, quantification of ETS exposure has been problematic, in part because such exposure takes place in multiple locations. The contribution of each environment to total personal exposure varies with the amount of time spent and the concentration of ETS. Most studies are retrospective or cross-sectional in nature, so that the validity of these data depends on the accuracy of a subject’s recall. Furthermore, a temporal relation cannot be established, and thus causal inference cannot be made. As estimated by a previous study (12) using urine cotinine as a biomarker of cigarette smoke exposure, current smoking may result in urine cotinine levels 30- to 100-fold higher than ETS. It is likely that the magnitude of effect from ETS is small and more difficult to detect than that of current smoking. Among smoking women who are also exposed to ETS, it is difficult to sort out the independent contribution of current and passive smoking.

The purpose of this report is to examine the association of ETS exposure with dysmenorrhea among a cohort of newly wed, nonsmoking women who had no history of dysmenorrhea in Shenyang, China. Our study has several unique features. Dysmenorrhea and exposure to ETS were defined by the use of a daily diary. This prospective study design eliminates potential recall bias, a common drawback of retrospective or cross-sectional studies. In China, few women smoke cigarettes, but exposure to ETS is very high because of the high prevalence of smoking among men (15). This setting provides a good opportunity to study the effect of ETS exposure on dysmenorrhea. Oral contraceptives were sometimes used clinically to alleviate menstrual pain, thus introducing a potential confounder (10). Parity was also suggested to be associated with menstrual pain (8–10). Nulliparous women were reported to have a higher prevalence of dysmenorrhea than multiparous women. In our study, all the subjects were newly wed, nulliparous, nonsmokers who intended to conceive (thus, they used no contraceptives during the follow-up menstrual cycles). These characteristics minimize the confounding effects of contraceptive use, parity, and active smoking. This study also adjusted for a number of occupational exposures that may be associated with dysmenorrhea.

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Methods

Study population. Beginning in July 1996, we established a cohort of newly wed couples in two districts (Tiexi and Dadong) in Shenyang, China. These couples were recruited to participate in a comprehensive prospective study designed to investigate the effects of various environmental and occupational exposures on reproductive outcomes. Newly wed couples were enrolled when they had obtained permission to become pregnant. Using daily diaries, these couples were followed until occurrence of clinical pregnancy or for up to 1 year. Women who had a prior marriage or a medically diagnosed gynecologic or endocrine disease were ineligible. Eligible subjects were recruited upon their consent and participated at a rate of > 90%. In total, 472 women have enrolled, and among these, 274 reported having a history of dysmenorrhea (58.1%). For the current analysis, we defined the ETS exposure for each complete menstrual cycle according to the diary, which was used to link with the occurrence of menstrual pain in the next follow-up menstrual period. Therefore we only included 388 (82.2%) women who had been followed for at least one complete menstrual cycle. Of the 388 women, 223 reported having history of dysmenorrhea (57.5%) and were excluded from the analysis for the purpose of examining the effect of ETS exposure on the incidence of dysmenorrhea. The final analysis was based on 165 women who did not report a history of dysmenorrhea at baseline interview and who had at least one complete menstrual cycle. This study was approved by Institutional Review Boards at Harvard School of Public Health and Beijing Medical University.

Baseline survey. We used the Chinese marriage registration system to identify newly wed couples and those planning a first pregnancy. Upon enrollment, physical examination was performed, and height and weight were measured according to a standard protocol. A structured baseline questionnaire was administered by a trained interviewer to all the women and their husbands at enrollment to collect information concerning occupational exposures, personal habits such as cigarette smoking and alcohol consumption, living environment, exposure to passive smoking, dietary intake, menstrual and reproductive history, and contraceptive use.

Daily diary. The current analysis is a part of longitudinal study to examine reproductive outcomes including fecundity. Each woman was followed monthly by the field staff. When a woman decided to stop contraception in order to become pregnant, she began recording a daily diary on menstrual bleeding and associated symptoms and exposure to tobacco smoke and other occupational exposures. Daily diary collection was terminated if a woman became clinically pregnant, dropped out of the study, or did not become pregnant within 1 year of cessation of contraception.

Assessment of dysmenorrhea. A menstrual cycle was defined from the first day of menstrual bleeding to the day immediately before the next menstrual bleeding. Menstrual pain was defined as abdominal pain or low back pain during menstrual bleeding. In this report, dysmenorrhea was defined as 2 or more days of menstrual pain during menstrual bleeding. From the baseline questionnaire, a positive history of dysmenorrhea was defined as any menstrual pain during the previous 12 months.

Assessment of environmental tobacco smoke. Each woman recorded in her daily diary the number of cigarettes smoked by the regular household members. The specific question in the diary form was, “What is the number of cigarettes someone smoked indoors at home yesterday while you were exposed?” For each menstrual cycle, we calculated an average number of cigarettes smoked per day at home over the entire cycle. This summary variable of ETS exposure at home was used to predict the occurrence of dysmenorrhea during the following menstrual period. It was evaluated as both a continuous and a categorical variable in the subsequent analysis. Exposure to ETS at the workplace was recorded as a binary variable (yes or no).

Data analysis. The major question of interest is whether ETS exposure at home independently affects the incidence of dysmenorrhea among women who did not have a history of dysmenorrhea, and whether the relation is modified by the population characteristics and various occupational factors. All data were double entered with Epi-Info (version 6.0; Centers for Disease Control and Prevention, Atlanta, GA, USA). The standard computer program SAS (version 6.12; Cary, NC, USA) was used for data analysis.

We first compared the population characteristics by ETS exposure status. We then computed the incidence of dysmenorrhea among prospectively followed menstrual cycles by four ETS exposure subgroups: no exposure and low, medium, and high tertiles of exposure. We also used local regression smoothing scatter plots (S-PLUS, version 3.4, MathSoft Inc., Cambridge, MA, USA) to examine the dose–response relationship between ETS exposure and dysmenorrhea and logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of dysmenorrhea associated with “low,” “middle,” and “high” ETS exposure, adjusting for

### Table 1. Characteristics of 165 women by passive smoking status at the first follow-up menstrual cycle, Shenyang, China.

| Characteristics | Passive smoking at home | p-Value<sup>a</sup> |
|-----------------|------------------------|---------------------|
| Physical        |                         |                     |
| Age (years)     | 25.9 ± 2.3             | 26.1 ± 2.6          | 0.688 |
| Height (m)      | 1.62 ± 0.04            | 1.60 ± 0.05         | 0.046 |
| Weight (kg)     | 54.1 ± 6.8             | 54.0 ± 7.4          | 0.943 |
| Body mass index (kg/m²) | 20.6 ± 2.8          | 21.0 ± 2.5          | 0.465 |
| Age at menarche (years) | 14.1 ± 1.3       | 14.0 ± 1.4          | 0.627 |
| Education       |                         |                     |
| Middle school or lower | 21.2                  | 23.5                | 0.911 |
| High school     | 42.4                   | 43.9                |       |
| College or above | 36.4                  | 32.6                |       |
| Occupation      |                         |                     |
| Technician      | 51.5                   | 47.0                | 0.892 |
| Administrative staff | 24.2                  | 27.3                |       |
| Factory worker  | 24.3                   | 25.7                |       |
| Occupational exposure |                 |                     |
| Toxin           | 3.7                    | 8.5                 | 0.400 |
| Noise           | 14.8                   | 10.4                | 0.120 |
| Dust            | 0.0                    | 6.5                 | 0.449 |
| Shift work      | 27.3                   | 28.0                | 0.882 |
| Perceived stress | 9.1                   | 13.7                | 0.725 |
| Passive smoking at work | 33.3                  | 45.4                | 0.258 |
| Season follow-up started |               |                     |
| Spring          | 39.4                   | 28.8                | 0.630 |
| Summer          | 12.1                   | 18.9                |       |
| Fall            | 30.3                   | 32.6                |       |
| Winter          | 18.2                   | 19.7                |       |
| No. of cycles followed |           |                     |
| 1              | 24.3                   | 23.5                | 0.961 |
| 2–4            | 51.5                   | 47.7                |       |
| 5–7            | 12.1                   | 13.6                |       |
| > 8            | 12.1                   | 15.2                |       |

*<sup>a</sup>-values for physical characteristics are derived by t-test; all others are derived by chi-square test.

Except as noted, all values are percent of total subjects; other values are mean ± SD.
Table 3 presents the crude and adjusted ORs of dysmenorrhea in relation to ETS exposure. Compared with cycles without ETS exposure, the adjusted ORs of dysmenorrhea associated with low, middle, and high tertiles of ETS exposure were 1.1 (CI; 0.5–2.6), 2.5 (CI, 0.9–6.7), and 3.1 (CI, 1.2–8.3), respectively. The findings were again consistent when the analysis was limited to the first menstrual cycle from each woman. Three variables as a group—namely, age, body mass index, and occupational category—explained most of the difference between the crude and adjusted results. When these three variables were excluded from the full model, the ORs for the exposure categories were 1.08, 2.20, and 2.46, respectively, leading to results similar to the unadjusted effect estimates. However, exclusion of any single variable from the model did not lead to such a change from the full model. When ETS exposure was treated as a continuous variable, the estimated OR of dysmenorrhea was 1.3 (CI, 1.0–1.8) for exposure to two cigarettes per day; that is, the risk of dysmenorrhea increased by 30% for each two cigarettes smoked at home.

Finally, we performed several subset analyses to exclude the possibility of potential confounding. We first excluded the women who had used either oral contraceptives or an intrauterine device before the study. The ORs of dysmenorrhea for women with low, middle, and high exposure to ETS were 1.1 (CI, 0.5–2.6), 2.6 (CI, 0.9–7.1), and 3.1 (CI, 1.2–8.2), respectively, which were consistent with those from the total sample.

The number of available cycles varied by each individual woman. Moreover, both dysmenorrhea and ETS have a high intra-class correlation coefficient within cycles (0.44 and 0.67, respectively), and therefore women with fewer cycles will have smaller weight in the evaluation of passive smoking effect. We addressed this potential bias by only including each woman’s first menstrual cycle in the analysis. As shown in Table 3, the results were similar to those of the analysis that included all available cycles.

Table 3. Crude and adjusted odds ratios of dysmenorrhea associated with passive smoking from 625 follow-up cycles.

| Passive smoking (cigarettes/day) | Total cycles | Dysmenorrhea No. | Percent |
|----------------------------------|--------------|------------------|---------|
| All cycles                       |              |                  |         |
| None                             | 145          | 14               | 9.7     |
| Low (< 0.8)                      | 160          | 15               | 9.4     |
| Middle (0.8–2.5)                 | 160          | 22               | 13.8    |
| High (> 2.6)                     | 160          | 27               | 16.9    |
| First cycle only                 |              |                  |         |
| None                             | 33           | 2                | 6.1     |
| Low (< 0.8)                      | 44           | 5                | 11.4    |
| Middle (0.8–2.7)                 | 44           | 7                | 15.9    |
| High (> 2.9)                     | 44           | 13               | 29.5    |

Exposure to ETS at work was another potential confounder. Because we did not have detailed information on workplace exposure, we could only include it as a binary variable (yes, no) in the regression analysis. ETS at work may also be considered as a component of exposure. To address this concern, we first restricted our analysis to women who did not report exposure to ETS at work before enrollment. The results remained consistent; the ORs of dysmenorrhea for low, middle, and high passive smoking were 1.1 (CI, 0.4–3.5), 1.9 (CI, 0.6–6.3), and 2.0 (CI, 0.6–6.7), respectively. Second, we combined ETS at home (no, low, middle, high) with ETS at work (no, yes), creating eight categories of exposure. Compared to the group with neither exposure, the ORs for the groups were 1.3 (low, no), 0.9 (low, yes), 2.5 (middle, no), 2.4 (middle, yes), 3.0 (high, no), and 3.1 (high, yes).

Discussion

Previous studies demonstrated the adverse effects of current smoking on menstrual cycle (4.8–10.14). Few studies are available on ETS exposure in relation to the risk of dysmenorrhea. In this report, we found a significant dose–response relation between ETS exposure and the risk of dysmenorrhea, even after adjustment for important covariates. It is noted that our study reported the incidence rate of dysmenorrhea among those who did not have a history of dysmenorrhea at enrollment. Most previous studies reported prevalence. According to the baseline questionnaire, the prevalence of dysmenorrhea in our population was 58.1%, which is comparable to the prevalence reported in the previous studies (47–72%). The effect of passive smoking on dysmenorrhea observed in this study appears stronger than that in a longitudinal study by Hornsby et al. (8), in which the authors observed a 30% increase in the mean number of days with dysmenorrhea. Some features of our study may contribute to a stronger effect compared to the previous studies. Our study population was

Table 2. Crude incidence rate of dysmenorrhea in the 625 follow-up menstrual cycles by passive smoking status.

| Passive smoking (cigarettes/day) | Total cycles | Dysmenorrhea No. | Percent |
|----------------------------------|--------------|------------------|---------|
| All cycles                       |              |                  |         |
| None                             | 145          | 14               | 9.7     |
| Low (< 0.8)                      | 160          | 15               | 9.4     |
| Middle (0.8–2.5)                 | 160          | 22               | 13.8    |
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Discussion

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Table 3. Crude and adjusted odds ratios of dysmenorrhea associated with passive smoking from 625 follow-up cycles.

| Passive smoking (cigarettes/day) | Unadjusted OR 95% CI | p-Value | Adjusted OR 95% CI | p-Value |
|----------------------------------|----------------------|---------|-------------------|---------|
| Model I                          |                      |         |                   |         |
| None                             | 1.0                  | 0.000   | 1.0               | 0.000   |
| Low (< 0.8)                      | 1.1                  | 0.5–2.5 | 0.841             | 0.001   |
| Middle (0.8–2.5)                 | 2.1                  | 0.8–5.6 | 0.150             | 0.079   |
| High (> 2.6)                     | 2.4                  | 0.9–6.1 | 0.072             | 0.024   |
| Model II                         |                      |         |                   |         |
| Two cigarettes/day               | 1.3                  | 1.0–1.6 | 0.038             | 1.3     |

*The logistic regression model adjusted for district (Tiexi vs. Dadong), age tertiles (21.5–24.6, 24.7–26.5, 26.6–31.6), education (middle school or lower, high school, college or above), area of residence, occupation (technician, administrative staff, factory worker), shift work, perceived stress, occupational exposure to chemical hazards, noise and dust, passive smoking at work, and the season (winter and spring vs. summer and fall) of the starting cycle. Generalized estimating equations were used to account for multiple cycles per woman.
younger than those included by Hornsby et al., who included women 37–39 years of age. We measured the amount of ETS by estimating the number of cigarettes smoked in the women’s presence, whereas Hornsby et al. defined ETS as living or sharing a workplace with a smoker. In addition, our study focused on new occurrence of dysmenorrhea, excluding women who reported a history of dysmenorrhea. All the women in our study were nonsmokers and thus current smoking was not a confounder here.

The biological mechanisms by which cigarette smoke may affect dysmenorrhea are not well understood. Some researchers have suggested that because nicotine is a vasoconstrictor, it can result in reduced endometrial blood flow, which is common in women with dysmenorrhea (9). It is suggested that cigarette smoke may have an antiestrogenic effect (16,17).

When the results of this study are interpreted, several methodological limitations should be taken into account. We did not have biochemical measurements of ETS exposure. Our sample size was relatively small and did not allow further analysis of subgroups with recurrent/severe dysmenorrhea or of the timing of ETS exposure within a specific menstrual cycle in relation to the risk of dysmenorrhea. We did not have detailed information on exposure to ETS at work and could not fully assess the joint effect of ETS exposure at home and at the workplace. Our measurement of potential confounders was based on self-report rather than objective measurements, which may have limited our ability to control some confounders. Finally, although we excluded women with a history of dysmenorrhea, we did not have clinical information of unrecognized gynecological disorders that may produce new dysmenorrhea symptoms. Although our findings from observational study are biologically plausible and highly consistent, they are only suggestive, not conclusive. Further studies are needed to corroborate our findings.

From a public health perspective, dysmenorrhea is a highly prevalent gynecological morbidity accounting for significant medical cost, absenteeism, lost working time, and reduced quality of life. Identification of modifiable risk factors of dysmenorrhea has important implications for women’s reproductive health. Our study findings reiterate that preventing both active and passive smoking among women of reproductive age is likely to have a significant beneficial impact on their reproductive health.

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