行政院國家科學委員會專題研究計畫　期中進度報告

懷孕婦女暴露二手菸之生殖危害評估(1/2)

計畫類別：個別型計畫
計畫編號：NSC91-2320-B-039-020-
執行期間：91 年 08 月 01 日至 92 年 07 月 31 日
執行單位：中國醫藥學院環境醫學研究所

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報告類型：精簡報告

處理方式：本計畫可公開查詢

中　華　民　國 92 年 5 月 19 日

孕婦在懷孕期間暴露到二手煙

NSC 91-2320-B-039-020

Exposure to environmental tobacco smoke (ETS) during pregnancy among pregnant women

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摘要

孕婦在懷孕期間暴露到二手煙或鉛物質，對其胎兒之發育有不同程度之影響，此研究在國外相關文獻均有詳細討論過。然而，限於部份研究對二手煙暴露之評估均無法準確地測量及未有效控制影響變項，使得部分研究報告無法證明其因果關係。台灣地區男性吸煙之比例一直維持在五成左右，且女性吸煙比例亦有上升之趨勢。且大部分民眾對二手煙之暴露一直多未加注意、防範，尤其是配偶與孕婦。因此本研究之目的在建立一個懷孕婦女之世代，從其懷孕期間監測其暴露二手煙及鉛之濃度直至其生產間，並評估胎兒健康狀況及再繼續觀察生長發育情況，以進一步分析二手煙或鉛對生殖危害之影響，作為政府機關管制菸害之佐證。研究對象以中部地區三所區域級醫院以上之婦產科，預計第一年收案 300 位孕婦，其中依孕婦特性可分為吸煙組、暴露二手煙組及非吸煙組。當孕婦在第一次產檢時即詢問其參加本研究之意願，經其同意每位孕婦均在懷孕 8 至 12 週內填寫完整問卷（調查二手煙之暴露在家中或工作場所、個人基本資料、對菸害之基本認知等）並收集其尿液、血液及唾液，以分析此檢體中可丁寧（cotinine）及鉛濃度，並由醫師評估胎兒發育情況等。追蹤懷孕孕婦至 20 週時，再依前述方式收集此相關資料，並評估營養攝食狀況。直至孕婦生產(約 28 週)時，評估出生胎兒之健康狀況，並設法收集孕婦與胎兒之頭髮及尿液，分析含可丁寧及鉛之濃度。第二年及第三年研究主題除繼續收集懷孕婦女之世代，再對其孕婦及胎兒世代繼續追蹤觀察，除對評估孕婦暴露二手煙及鉛外，著重胎兒生長發育情況，並瞭解其體內可丁寧及鉛濃度之變化，以評估二手煙暴露對其健康狀態之危害性。在本研究初期之研究結果顯示，在 190 位孕婦之血中可丁寧濃度平均為 1.8ng/ml。而尿

中可丁寧濃度平均為 1.4ng/ml；在排除濃度低於偵測極限（0.268ng/ml）之樣本後，尿中可丁寧濃度平均為 3.6ng/ml，若以肌酸酐校正則平均濃度為 0.23ng/g Creatinine。本研究中有 95%的婦女為非吸菸者，與先前之研究相似。本研究結果除對國內進一步分析孕婦暴露二手煙之危害性外，並可建立本土性之資料與國外研究報告相比較，以確實瞭解國人暴露二手煙或鉛對其生殖危害之影響。

Abstract

Previous studies have shown that fetuses of pregnant women exposed to environmental tobacco smoke (ETS) and lead may develop congenital problems. However, the conclusions are contradictory and unclear, partly because of inaccurate measurements of ETS exposure and the large number of confounders, which were not well controlled. Over fifty percent of males in Taiwan smoke, and the incidence of smoking among females has risen sharply in recent years. The purpose of this study is to establish the cohort of pregnant women and to periodically monitor exposure to ETS and lead. The health status of the fetus and the newborn will also be evaluated. The study will be conducted over a three-year period, and will include 300 pregnant women (smokers, non-smokers and passive smokers) from three teaching hospitals. Written consent will be obtained from all subjects. The subjects will undergo regular health examinations during the first trimester and will be interviewed by a questionnaire to include items such as demographics, exposure to ETS at home and the workplace, health status, and knowledge of smoking. Urine, blood and saliva samples will be taken to measure cotinine, a metabolite of nicotine, and lead levels. Fetal development will be assessed by obstetrician/ gynecologists. At the 28^{th} week, subjects will undergo a second examination and the nutrition status of the women will be assessed. The health status of the newborn infants will be evaluated and data will be correlated to the ETS and lead data. Cotinine levels in newborn hair samples will also be measured. The sister chromatid exchange and chromosome aberration frequencies of the newborn infants and their mothers will be measured and correlated with cotinine levels in the biological samples. The development of the infants (such as language, gross motor, fine motor, adaptive behavior, eating problems and length of play) will be assessed periodically up to the age of one year. Our preliminary results showed that mean blood cotinine level was 1.8ng/mL among 190 pregnant women.

Excluding values below the detection limit (0.268ng/mL), the mean cotinine level was 3.6ng/mL. Mean urinary cotinine levels were 0.23ng/g creatinie and 1.4ng/mL. Most (95%) of the women in our study were non-smokers and our data are similar to those in previous studies. Further study is needed to elucidate the factors that affect urinary and blood cotinine levels in pregnant women and to correlate data obtained from questionnaires with biological parameters. The results will be used to understand how the fetuses of pregnant women exposed to ETS and lead are affected, and will be made available to the DOH for use in health promotion campaigns aimed at pregnant smokers.

Introduction

Harger et al. (1990) studied a diverse group of pregnant women and weighed the relative risk of 41 potential factors influencing preterm premature rupture of membranes. Of all 41 factors, smoking, vaginal bleeding in more than one trimester, and previous preterm delivery had the strongest correlations. Naeye (1980) demonstrated a 23% lower frequency of abruption and a 33% lower frequency of placenta previa in women who quit smoking compared to those who continued to smoke throughout their pregnancy. Infant mortality from abruption was decreased by 50% and death by placenta previa was decreased by 33% in the mothers who stopped smoking. The incidence of low birth weight infants is directly proportional to the number of cigarettes smoked. MacArthur and Knox (1988) looked at women who started their pregnancy as smokers and found that those who quit smoking before 16 weeks' gestation had significantly larger infants than those who remained smokers throughout.

Maternal use of alcohol, tobacco, and/or marijuana during pregnancy has been implicated in the compromised development of children born to mothers who used these substances while pregnant (Coles et al., 1992; Day et al., 1991; Fried, 1988,

1990; Jacobson et al., 1994, Streissguth et al., 1985; Zuckerman et al., 1989). Prenatal maternal cigarette smoking was shown to be associated with less optimal Brazelton orientation performance (Oyemade et al., 1994), lower mental scores at 12 months, and altered responses on auditory items at 12 and 24 months (Fried, 1988), decreased BSID scores at 19 months (Richardson et al., 1995), almost doubled risk of the infant being a nonbabbler at 8 months (Obel et al., 1998), and persistent neurobehavioral effects in the language and motor areas at 1, 2, and 3 years of age (Fried, 1989). By contrast, Richardson et al. (1995) found no relationship between prenatal tobacco exposure and BSID scores at 9 and 19 months.

Another important consideration is the relationship of the physical and neuropsychological development of children with maternal substance use. Studies have shown general growth retardation, smaller head size, and lower birth-weight (Coles et al., 1992; Day et al., 1991; Mills, et al., 1984; Streissguth et al., 1985) among women who used substances during pregnancy. There is a significant relationship between prenatal substance use and neurological or neuropsychological development (Fried, 1991; Fried, 1990; Mattson & Riley, 1998; Richardson et al., 1995; Streissguth, et al., 1990). Kallen (2000) evaluated the registry of birth cohort of 1.3 million Swedish newborns and found that there were significant head developmental problems among infants whose mothers smoked during pregnancy with a dose-response effect. Faden (2000) showed that there were significant specific behavioral and developmental problems among three-year-olds whose mothers used substances during pregnancy. It has been well established that smoking during pregnancy results in increased infant mortality and morbidity, and adversely affects the child's physical and mental development. In Taiwan, there are few data available on this important topic. The purpose of this study was to establish the cohort of pregnant women and to periodically monitor exposure to ETS and lead. The health

status of the fetus and the newborn was also evaluated.

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Material and Methods

Three hundred and ninety-three pregnant women completed and returned the questionnaire in two antenatal clinics. Informed written consent was obtained form all participants. A structured questionnaire was developed to interview the pregnant women's stage of change relating to smoking and health status. Demographic information, details of previous pregnancies, details of other children and prenatal health status, details of the current pregnancy (including whether or not pregnancy was planned, intention to attend antenatal classes, intention to breastfeed etc.), current smoking habit (allocating the respondents to the appropriate stage of change) were obtained. A smoker was defined as a person who smoked at least one cigarette per day. Ex-smokers were asked how long they had given up smoking and were ascribed to the action stage if they had quit less than six months ago or the maintenance stage if they had quit more than six months ago. Six months is the widely accepted cut-off point between action and maintenance used in other studies. Subjects were interviewed using a questionnaire and subjects with renal dysfunction were excluded from the study. Subjects were classified into three groups (smokers, ETS exposed and non-smokers) according to the answers given in the questionnaire.

Determination of urinary and serum cotinine using HPLC

Pretreatment for HPLC

HNO3 was added to 2ml of urine, heated at 60

3000rpm for five minutes. Methanol, chloroform and NaOH were added to 1 ml of supernatant and centrifuged at 3000rpm for ten minutes. Nitrogen was used to purge the chloroform layer and 0.5ml methanol was added to dissolve the precipitate before measurement using HPLC.

Strict quality control measures were observed in all measurements of urinary and salivary cotinine concentrations. Table 1 shows the detection limits and calibration curves for each of the three measurements of urinary and salivary cotinine concentrations. The relative prediction deviation (RPD) percentage of the calibration curves were less than 7%. The recovery rate for urine using HPLC was 84.0%. Reproducibility for HPLC was low (4%). Fig.1 shows the stability of the urinary cotinine at 4 and –20 using HPLC. Urinary cotinine in Fig.1 (b) was unstable over 14 days at both concentrations (14.3 μg/ml and 45.7 μg /ml).

All data were analyzed using SAS/PC+6.12. Frequency and mean were used to describe the univariate analysis for urinary and serum cotinine among pregnant women.

Results and Discussion

Figure 1 shows the distribution of cotinine levels in the blood of 190 pregnant women. Mean concentration of cotinine was 1.8ng/mL and the maximum concentration was 15ng/mL. The blood cotinine level of 97 women was below the detection limit. Excluding these subjects, the mean concentration of cotinine was 3.6ng/mL (Fig.2). Over 90% of subjects had blood cotinine levels equal to or over 7.36ng/mL. Figures 1 and 2 show a right-skewed distribution. These data are similar to those obtained from non-smokers in previous studies.

Figures 3 and 4 show the distribution of urinary continine concentrations. Mean urinary continine concentrations were 0.23ng/g creat. (SD = 0.61) and 1.4ng/mL (SD = 3.4). In over 90% of the subjects, urinary cotinine level was at least 1.55ng/g creat. Under 10% of subjects had a urinary cotinine level equal to or below 0.015ng/g creat.There was a right-skewed distribution in Fig.3 and 4. Excluding values below the detection limit, the mean concentrations of urinary cotinine were 0.50ng/g creat. (SD = 0.88) and 3.0ng/mL (SD = 4.87) (Fig.5 and 6).

In summary, about 95% of pregnant women in our study were non-smokers and were not exposed to ETS. Therefore, the distributions of blood and urinary cotinine levels were right-skewed. These data are consistent with those reported in previous studies of non-smokers. Further studies will be conducted to

investigate the relationships between questionnaire items and biological parameters.

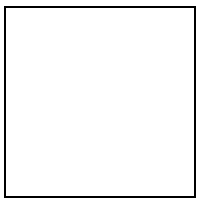

Fig.1 Distribution of blood cotinine levels in 190 pregnant women

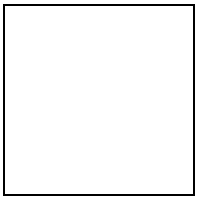

Fig.2 Distribution of blood cotinine levels above the detection limit in 93 pregnant women

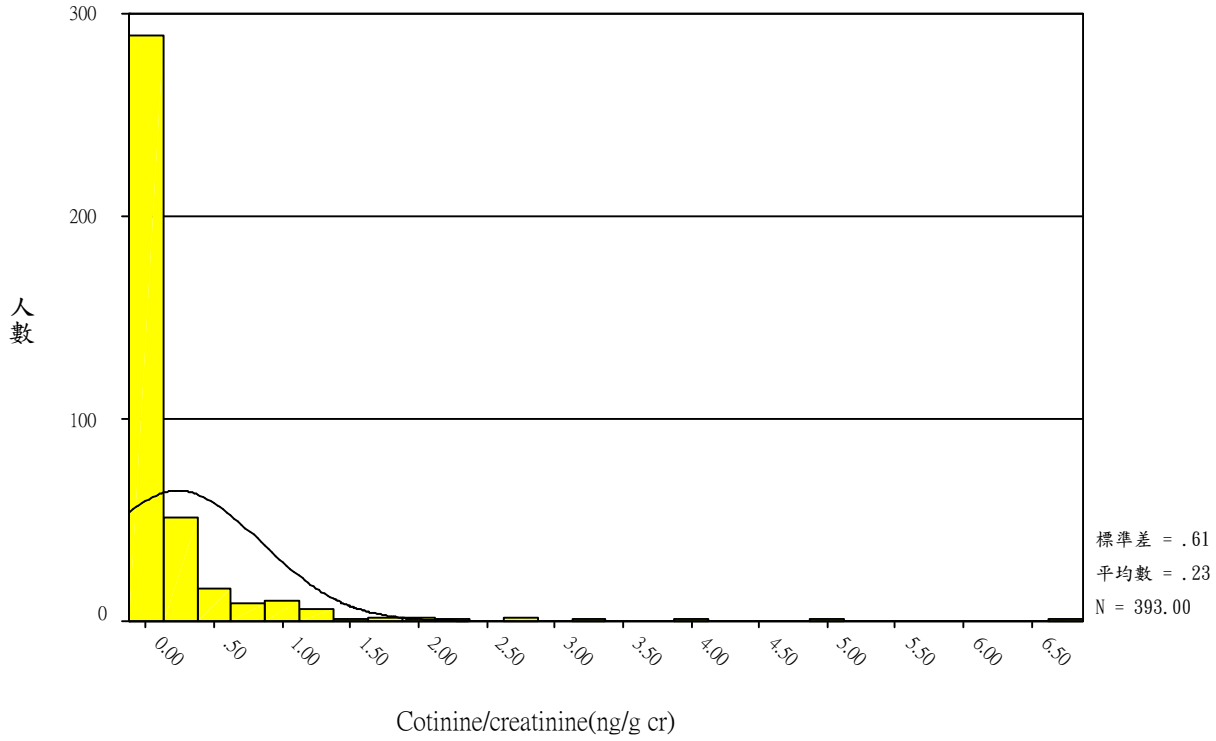

Fig.3 Distribution of urinary cotinine levels (ng/g creat.) in 393 pregnant women

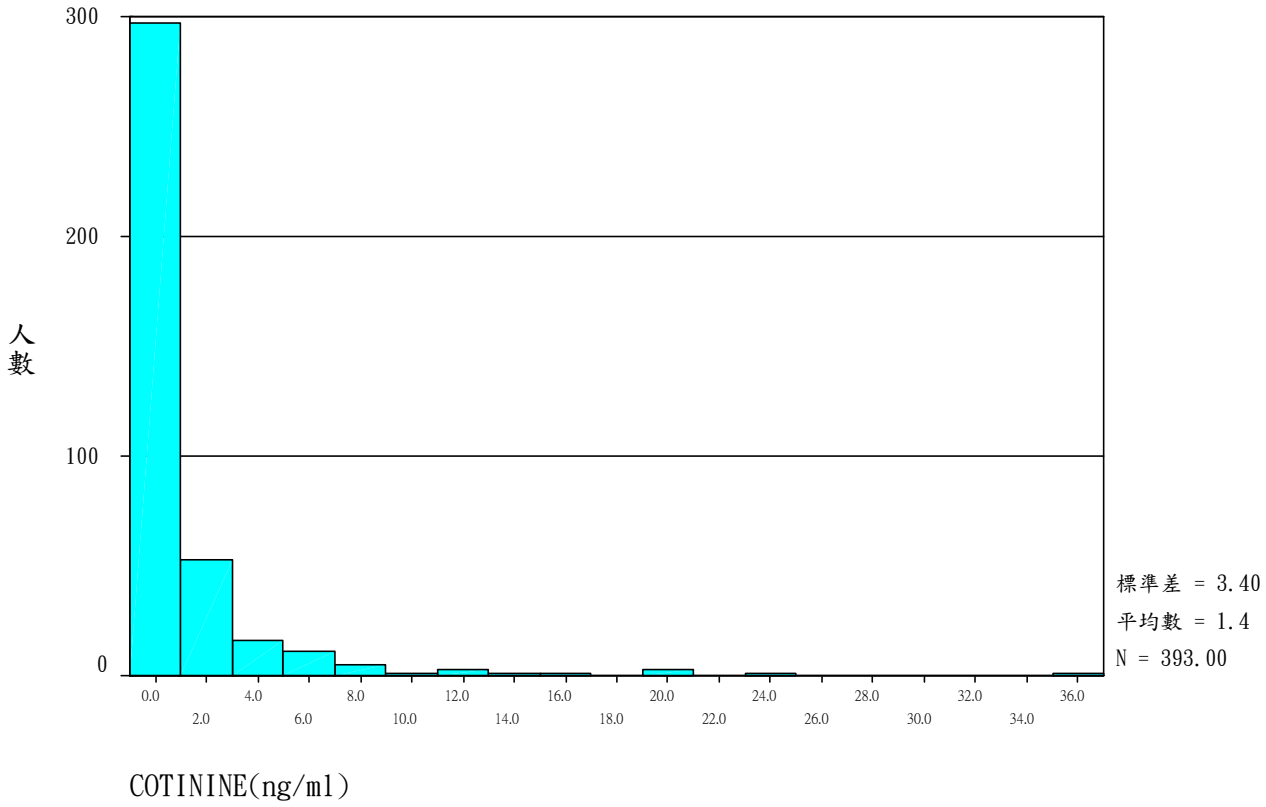

Fig.4 Distribution of urinary cotinine levels (ng/mL.) in 393 pregnant women

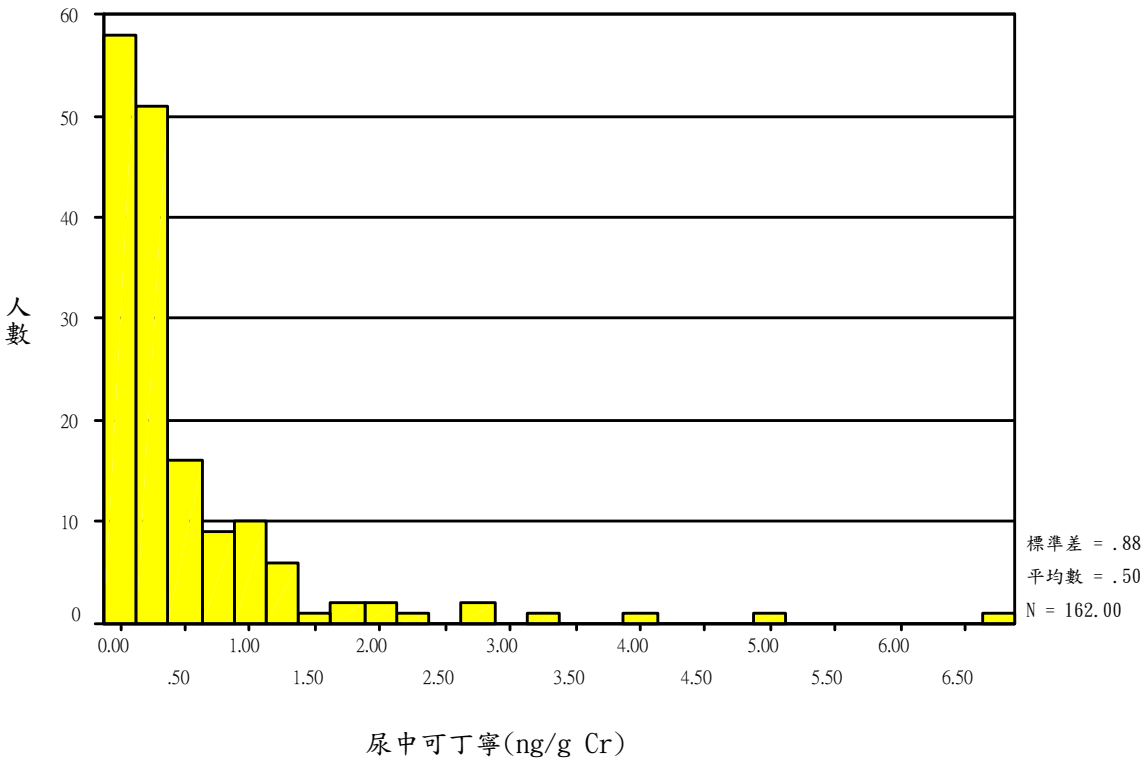

Fig. 5 Distribution of urinary cotinine levels (ng/g creat.) above the detection limit in 162 pregnant women

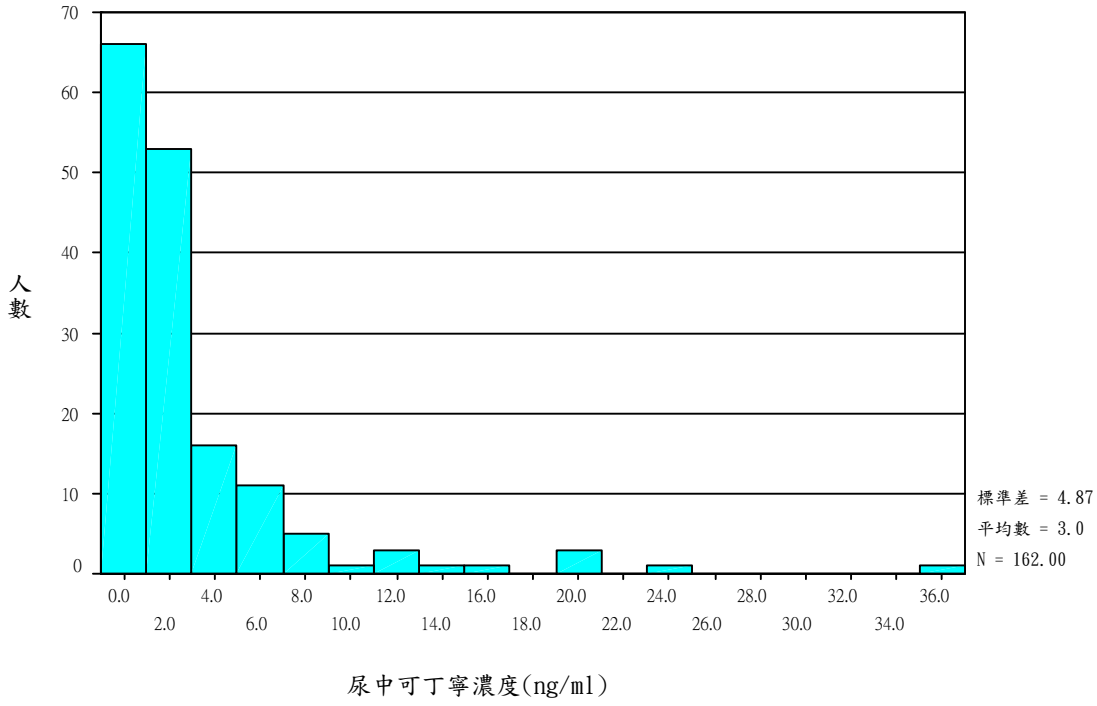

Fig. 6 Distribution of urinary cotinine levels (ng/mL) above the detection limit in 162 pregnant women

Table 1. The reproducibilities between and within for measurement if urinary cotinine levels

	Between day		Within day	
	Rt （mins）	area（mA）	Rt （mins）	area（mA）
means±SD	7.86±0.05	198.33±9.98	7.68±0.27	198.51±0.81
CV （%）	0.61	5.03	3.55	0.41