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Second-hand exposure to tobacco smoke and its effect on disease activity in Swedish rheumatoid arthritis patients. Data from BARFOT, a multicentre study of RA

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ABSTRACT

Objective. *We studied the prevalence and effect on disease activity of ever having had second-hand exposure to tobacco smoke in Swedish rheumatoid arthritis (RA) patients who had never smoked.*

Methods. *Between 1992 and 2005, 2,800 patients were included in the BARFOT early-RA study in Sweden. Disease Activity Score 28 joints (DAS28), C-reactive protein (CRP), Health Assessment Questionnaire (HAQ), rheumatoid factor (RF), general health and pain visual analogue scales (VAS), and drug treatment were registered at inclusion and at follow-up at 3, 6, and 12 months and 2 and 5 years. EULAR response criteria were applied at the same follow-up points. In 2010, a self-completion postal questionnaire was sent to 2,102 patients in the BARFOT study enquiring about lifestyle habits such as whether they had ever been exposed to tobacco smoke as a result of someone else smoking.*

Results. *A total of 963/1,421 patients (68%) had had second-hand exposure to tobacco smoke. At 3, 6, and 12 months, at 2 years, and at 5 years of follow-up, there were no differences in EULAR response between patients who had never smoked and who had been exposed or had not been exposed second-hand to tobacco smoke (p=0.91, p=0.88, p=0.84, p=0.61 and p=0.85, respectively).*

Conclusions. *We did not find any association between second-hand exposure to tobacco smoke and disease activity in RA.*

Introduction

Worldwide, second-hand exposure to tobacco smoke is a major public health problem, as 40% of children, 35% of women, and 33% of men are regularly exposed to tobacco smoke indoors as a result of someone else smoking and a total of 603,000 deaths were attributed to second-hand smoking in 2004 (1). In Sweden, 15% of women and 19% of men were regularly exposed to second-hand smoking in 2010, representing 17% of the adult population (Swedish National Institute of Public Health). Smoking has been shown to cause rheumatoid arthritis (RA) (2) and to have a detrimental effect on therapy response in RA in some (3-5), but not all studies (6). We studied second-hand exposure to smoke and its effect on disease activity in a large multicenter longitudinal observational study of RA patients in southern Sweden.

Material

During the period 1992–2005, 2,800 adult patients were enrolled in the BARFOT (Better Anti-Rheumatic FarmacOTherapy) study, a multicentre longitudinal observational study of patients with early RA in southern Sweden (7-9). All patients fulfilled the American College of Rheumatology RA classification criteria from 1987 (10). Disease activity was evaluated at inclusion, at 3, 6, and 12 months, and also at 2 and 5 years in this study. The number of swollen joints (28-joint count) (SJC), number of tender joints (28-joint count) (TJC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), the Swedish version of the Stanford Health Assessment Questionnaire (HAQ) (11, 12), and visual analog scale (VAS) for pain and general health were measured on every follow-up occasion. The Disease Activity Score using 28-joint count (DAS28) was calculated at inclusion and at every follow-up occasion (www.das-score.nl). Disease duration was calculated from the start of the symptoms.

EULAR (European League Against Rheumatism) response was calculated from the DAS28 scores (13). The DAS28 is a composite score consisting of the number of swollen joints (of 28), tender joints (of 28), ESR, and the patient's global assessment (www.das-score.nl). The patients were classified into three EULAR response groups: no response, moderate response, or good response. A EULAR good responder had to demonstrate an improvement of at least 1.2 units and achieve an absolute score of <3.2. A non-responder should show an improvement of <0.6, or >0.6 and ≤1.2, and have a final DAS28 of >5.1. Moderate responses fall in-between. Treatment with DMARDs (disease-modifying anti-rheumatic drugs) and glucocorticoids was registered at inclusion and at each follow-up point.

Table I. Baseline demographics and disease characteristics stratified according to second-hand exposure to tobacco smoke in patients who had never smoked. The values are mean (SD) unless otherwise stated.

Variable	Never-smokers Second-hand smoking status n=501		*p*-value
	Not exposed n=211	Exposed n=290	
Women, %	83	79	0.33
Age	52 (16)	56 (15)	0.003
Disease duration, months	6.8 (4.0)	6.9 (4.0)	0.55
HAQ	0.96 (0.59)	0.97 (0.59)	0.76
DAS28	5.3 (1.2)	5.2 (1.3)	0.31
VAS pain, mm	46 (23)	45 (24)	0.73
VAS general health	44 (24)	45 (26)	0.47
Number of swollen joints (28)	11 (6.0)	10 (5.5)	0.62
Number of tender joints (28)	9 (7.0)	8 (6.4)	0.45
ESR, mm, median, interquartile range	27 (16–44)	26 (14–45)	0.72
CRP, mg/L, median, interquartile range	16 (9–34)	14 (8–37)	0.75
RF, % positive	56	58	0.60
DMARD, %	76	79	0.31
Glucocorticoids, %	37	37	0.96

HAQ: Health Assessment Questionnaire; DAS28: Disease Activity Scale (28 joints); VAS: visual analogue scale; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor.

Rheumatoid factor (RF) was analysed using the current laboratory methods in each participating hospital. Serum antibodies to cyclic citrullinated peptide were analysed using the Immunoscan-RA ELISA CCP2 test (Euro-Diagnostica, Malmö, Sweden). A titer above 25 units/ml was regarded as positive. The choice of DMARD treatment in the BARFOT study was left to the discretion of the rheumatologist.

Between March and September 2010, all patients who were still alive in the BARFOT study (n=2,102) received a self-completion postal questionnaire assessing lifestyle factors such as smoking and second-hand smoke exposure. The questions assessing whether the patient had ever been exposed to second-hand smoking were "Have you lived or spent time together with one or more persons who have smoked indoors on a daily basis?" and "At your workplace, have you been in rooms where people have smoked?" The socioeconomic status was assessed as blue-collar worker, lower white-collar worker, upper white-collar worker, self-employed, or other. All patients received written information about the questionnaire in 2010 and the ethical committee of Lund University approved the BARFOT study and the self-completion postal questionnaire in 2010.

Results

In total, 1,524 of 2,102 patients (73%) answered the self-completion postal questionnaire. Of these, 1,460 patients (96%) were >18 years of age and had disease duration of ≤24 months, and these patients were included in the study. Reliable smoking data as reported from the self-completion postal questionnaire in 2010 were available for 1,379 of the 1,460 patients (94%). Five hundred and fourteen (37%) of the patients were never-smokers, 634 (46%) were previous smokers, and 231 (17%) of the patients were current smokers in 2010.

A total of 963 out of 1,421 patients (68%) had reliable data on exposition to second-hand smoking. Second-hand exposure to tobacco smoke was gender-related: 66% of women had been exposed as compared to 72% of men (p=0.02). Second-hand exposure to smoke was also related to socioeconomic class: of the blue-collar workers, 71% were exposed; of the lower white-collar workers, 64% were exposed; of the upper white-collar workers, 74% were exposed; of those who were self-employed, 31% were exposed; and of the others, 70% were exposed (overall p=0.0003). Exposed patients were also older (mean 66 years exposed *vs*. mean 62 years not exposed; p=0.0001). There was no correlation between second-hand exposure to tobacco smoke and RF positivity (p=0.59) or immigrant status (p=0.10). We had anti-CCP antibody data on 388 patients. Anti-CCP antibody status was not associated with second-hand exposure to smoke (p=0.87).

Never-smokers

Of the never-smokers, data on ever being exposed to second-hand smoking were available for 501 of 514 patients (97%). Of these patients, 290 of the 501 (58%) had been exposed to second-hand smoking. Baseline data stratified according to second-hand exposure to smoke are shown in Table I. The patients who had never smoked but who had been exposed to second-hand smoking were older. There were no differences in DMARD and glucocorticoid treatment at inclusion, stratified according to exposure to second-hand smoking, but patients exposed to second-hand smoking had significantly fewer ongoing DMARDs, as reported from the self-completion questionnaire in 2010 (ongoing DMARDs exposed 0.76 *vs*. not exposed 0.94; p=0.003). After stratification according to second-hand smoke exposure, there were no differences in the number of previous DMARDs used or current or previous use of biologics (data not shown).

There were no differences in EULAR response between the patients who had never smoked and who had or had not been exposed to second-hand smoking at 3, 6, 12 months, 2 years, or 5 years of follow-up (p=0.91, p=0.88, p=0.84, p=0.61 and p=0.85, respectively). We could we see no differences in the absolute DAS28 values stratified according to smoke exposure second-hand, up to 5 years of follow-up (data not shown). Anti-CCP status was available for 138 never-smokers (62 were anti-CCP negative and 76 were anti-CCP positive). There were no differences in EULAR response in patients who had never smoked, stratified for anti-CCP status and second-hand exposure to smoke (data not shown).

Discussion

In this large Swedish longitudinal observational RA patient study in which patients were included between 1992

and 2004, we found an alarmingly high prevalence of ever being exposed to second-hand smoking (68%). In the study, blue-collar workers and upper white-collar workers had high second-hand exposure to tobacco smoke (71% and 74%, respectively). We could see no effect of second-hand exposure to smoke on disease activity in RA patients who had never smoked. Active smoking has been shown to cause RA in genetically and serologically predisposed patients (2) and to have a detrimental effect on RA as reported from this same cohort (3, 4) and in other studies (5), but not from all studies (6). The exact pathogenetic mechanism is at present unknown.

The Swedish Tobacco Act was introduced in 1993 and amended in 1994, and it banned direct tobacco advertising, concerned smoke-free public premises, and established regulations concerning health warnings and tar limits. Smoking in restaurants has since been banned in Sweden. The Swedish National Institute of Public Health has kept records of second-hand smoke exposure in the normal population in Sweden since 2004. Then, 27% of the population was exposed to second-hand smoking as compared to 15% in 2010. Exposure was related to lower socioeconomic class and lower education. A large study on 8,270 working individuals in Skåne, the southernmost part of Sweden, in 2000 showed that 30% of the individuals had second-hand exposure to smoke, 33% of men and 27% of women, and that the exposure was related to lower socioeconomic class and young age (14). A large study assessing second-hand exposure to smoke in 5,420 individuals from the normal population of Sweden in 1993 showed that the prevalence of second-hand exposure to smoke ranged from 0.9% to 26% in men and 0% to 30% in women, depending on occupation (15). We report a high lifetime exposition to second-hand smoke (68%) as compared to these cross-sectional studies.

In this study, we were not able to assess whether the second-hand exposure to smoke was before or after the diagnosis of RA, or both, and we were unable to quantify the time of second-hand exposure to tobacco smoke. Clearly, more studies on this are needed.

In conclusion, in this large study of Swedish RA patients included between 1992 and 2005, having ever been exposed to second-hand tobacco smoke was very prevalent (68%). We could not show any effect of second-hand exposure to smoke on disease activity in RA patients who had never smoked. It is not known whether second-hand exposure to tobacco smoke has a pathogenetic role in RA, and further studies on this subject are needed.

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