

Short Communication

Parental smoking and allergic sensitization in offspring defined by skin prick testing

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Investigations of parental smoking during childhood and allergic sensitization have produced contradictory results, but this may be because of variations in the definition of allergy and other influences. We investigated associations of parental smoking with an objective measure of allergy, skin prick testing (SPT), and considered associations with maternal and paternal smoking, independently of each other. A stratified random sample, aged 22–74 yr, of 720 Swedish FinEsS-study members were skin prick tested for 15 allergens. Subjects with at least one positive SPT were defined as atopic. Data on childhood exposures, including parental smoking, were collected by structured interview. Logistic regression used atopy as the dependent variable. After adjustment, paternal smoking was statistically significantly associated with an increased risk and maternal smoking a non-statistically significant decreased risk in offspring, with odds ratios (and 95% confidence intervals) of 1.48 (1.04–2.10) and 0.73 (0.48–1.12), respectively. Analysis of families with a non-smoking mother produced an odds ratio for paternal smoking of 1.61 (1.09–2.37). The negative association between maternal smoking and atopy may not operate through passive smoke exposure and could conceal a significant increased risk associated with passive exposure to tobacco smoke in childhood.

Reported associations of parental smoking with offspring's allergy are contradictory, (1, 2) possibly because of at least two potential confounding or modifying factors. The first is failure to separate maternal and paternal smoking. Some studies looking specifically at maternal smoking reported a protective association (3, 4). Therefore, potentially different associations with allergy for maternal and paternal smoking should be considered. Another potential source of error and variation in association is the use of symptoms and diagnoses such as wheeze and asthma to define allergy. Such symptoms have been associated with passive exposure to tobacco smoke in childhood (5) but do not represent allergy and may result from smoke-induced exacerbation of symptoms such as wheezing. Such a definition of allergy may obtain false positive associations with parental smoking. Here, we investigated associations of maternal and paternal smoking during offspring's childhood separately and used skin prick testing (SPT) as an objective measure of allergic sensitization.

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Methods

A stratified random sample of 1200 Swedish FinEsS (5, 6). respondents, aged 22–74 yr, was selected for SPT. The FinEsS study was designed as a general population-based study investigating putative risks for asthma, chronic bronchitis, type-1 allergy and respiratory symptoms; and details of the sample have been described in full elsewhere (5). Some 720 (60%) participated in this sub-study, providing SPT data for 704 subjects after exclusions for illness, pregnancy or breastfeeding. The variations in proportion in the attained sample compared with the original population were within two percent for sex, smoking and allergic rhinitis, but there was a slight age shift such that there was 5% increase in second oldest age category.

Standardized SPT (7, 8). was performed on the forearm for 15 allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Lepidoglyphus destructor*, *Acarus siro*, cat, dog, cow,

horse, birch pollen, timothy, mugwort, *Alternaria alternata*, *Cladosporium herbarum*, latex and German cockroach. The definition of atopy used here is a positive test to at least one allergen. Subjects reacting to the negative reference ($n = 12$) were excluded, leaving 692 for analysis.

A structured interview conducted by a research nurse, recorded information on exposures and characteristics during childhood, including parental smoking behaviour (whether mother or

father regularly smoked at home), urban or rural place of residence, bedroom sharing with a sibling, house type and the presence of pets during the first 5 yr of life. Other information recorded by the interview included: number of older and younger siblings and own smoking behaviour.

Multiple logistic regression in SPSS used atopy as the dependent variable with mutual adjustment for all of the measures shown by the Table 1, modelled as binary dummy variables.

Table 1. Skin prick tests for atopy by parental smoking and potential confounding factors

	Skin prick		Odds ratios with 95% CI			
	Positive	Negative	Unadjusted	p-value	Adjusted*	p-value
Mother smoked						
No	173 (76.2)	357 (76.8)	1		1	
Yes	54 (23.8)	108 (23.2)	1.03 (0.71–1.50)	0.870	0.73 (0.48–1.12)	0.148
Father smoked						
No	107 (47.1)	256 (55.1)	1		1	
Yes	120 (52.9)	209 (44.9)	1.37 (1.00–1.89)	0.051	1.48 (1.04–2.10)	0.029
Subject's smoking						
Never smoked	115 (50.7)	224 (48.2)	1		1	
Ex-smoker	69 (30.4)	140 (30.1)	0.96 (0.67–1.38)	0.827	1.09 (0.74–1.61)	0.664
Current smoker	43 (18.9)	101 (21.7)	0.83 (0.54–1.26)	0.384	0.90 (0.58–1.40)	0.640
Older siblings						
None	124 (54.6)	199 (42.8)	1		1	
1	61 (26.9)	120 (25.8)	0.82 (0.56–1.19)	0.295	0.77 (0.51–1.17)	0.223
2	22 (9.7)	59 (12.7)	0.60 (0.35–1.02)	0.062	0.64 (0.36–1.15)	0.135
3 or more	20 (8.8)	87 (18.7)	0.37 (0.22–0.63)	<0.001	0.42 (0.23–0.75)	0.003
Younger siblings						
None	94 (41.4)	197 (42.4)	1		1	
1	63 (27.8)	130 (28.0)	1.02 (0.69–1.50)	0.938	0.94 (0.61–1.46)	0.798
2	40 (17.6)	78 (16.8)	1.08 (0.68–1.69)	0.755	1.06 (0.64–1.76)	0.820
3 or more	30 (13.2)	60 (12.9)	1.05 (0.63–1.73)	0.855	1.12 (0.64–1.96)	0.686
Pets from birth to age 5 yr						
No	116 (51.1)	201 (43.2)	1			
Yes	111 (48.9)	264 (56.8)	0.73 (0.53–1.00)	0.051	0.79 (0.55–1.13)	0.201
Home from birth to age 5 yr						
House	102 (44.9)	248 (53.3)	1		1	
Flat	99 (43.6)	174 (37.4)	1.38 (0.99–1.94)	0.060	1.02 (0.66–1.56)	0.938
Both	26 (11.5)	43 (9.2)	1.47 (0.86–2.52)	0.161	1.18 (0.66–2.10)	0.568
Place of residence birth to age 5 yr						
Urban	142 (62.6)	256 (55.1)	1		1	
Rural	85 (37.4)	209 (44.9)	0.73 (0.53–1.02)	0.061	0.99 (0.65–1.51)	0.957
Age at SPT (yr)						
20–29	24 (10.6)	33 (7.1)	0.89 (0.46–1.72)	0.725	0.87 (0.44–1.70)	0.685
30–39	45 (19.8)	55 (11.8)	1		1	
40–49	42 (18.5)	102 (21.9)	0.50 (0.30–0.86)	0.012	0.48 (0.28–0.84)	0.010
50–59	53 (23.3)	116 (24.9)	0.56 (0.34–0.93)	0.025	0.50 (0.29–0.87)	0.013
60–69	54 (23.8)	139 (29.9)	0.48 (0.29–0.79)	0.004	0.44 (0.25–0.77)	0.004
70	9 (4.0)	20 (4.3)	0.55 (0.23–1.33)	0.183	0.52 (0.21–1.32)	0.168
Sex						
Male	113 (49.8)	232 (49.9)	1		1	
Female	114 (50.2)	233 (50.1)	1.00 (0.73–1.38)	0.978	1.02 (0.73–1.42)	0.922
Shared a bedroom with siblings from birth to age 5 yr						
Yes	96 (42.3)	167 (35.9)	1.32 (0.95–1.82)	0.101	1.03 (0.69–1.54)	0.876
No	125 (55.1)	286 (61.5)	1		1	
Uncertain	6 (2.1)	12 (2.6)	1.14 (0.42–3.12)	0.792	0.80 (0.28–2.34)	0.689
Total	227	465				

The measures of parental smoking are for smoking during the subject's childhood.

*Adjustment is for all variables shown.

Results

In univariate analysis, maternal smoking was not associated with offspring's atopy risk, while paternal smoking was associated with a marginally statistically significant increased risk of atopy among offspring. Mutual adjustment for maternal and paternal smoking clarified their associations with offspring's atopy. After adjustment for maternal smoking and all of the other measures, the odds ratio for atopy associated with paternal smoking increased with enhanced statistical significance. A non-statistically significant negative association between maternal smoking and offspring's atopy was observed after adjustment.

Evidence of effect modification through maternal smoking comes from the higher odds ratio for offspring's atopy associated with paternal smoking in families where the mother was a non-smoker. Analysis of paternal smoking in families without a smoking mother produced an odds ratio for offspring's allergy of 1.61 (1.09–2.37). After adjustment for the main effects the interaction of maternal and paternal smoking was not statistically significantly associated with atopy, with an odds ratio of 0.65 (0.27–1.50).

Another source of evidence for a positive association with smoke exposure comes from analysis of smokers in the same household other than parents. Although not statistically significant and underpowered (only 51 subjects reported sharing a household with a smoker other than their parents), this produced an odds ratio of 1.32 (0.69–2.54), similar in magnitude to paternal smoking.

Subject's age (birth cohort) was significantly associated with both likelihood of parental smoking (data not shown) and atopy and this potential confounding factor had a notable influence on associations of paternal smoking with allergy risk, somewhat increasing statistical significance. Among measures other than parental smoking, only subject's age and number of older siblings were observed to have a statistically significant association with atopy in the adjusted model.

Discussion

Using an objective measure of atopy – SPT – a statistically significant positive association was observed with paternal smoking during the subject's childhood. Maternal smoking was not positively associated with atopy in offspring. Adjustment for maternal smoking clarified that the positive association with paternal smoking may have been partly concealed by a modifying effect of maternal smoking, compounded by the

tendency of smokers to have smoking partners. Further evidence of this modifying effect comes from the stronger association of atopy with paternal smoking in families where the mother was a non-smoker. Variation in risk of allergy by maternal or paternal smoking may help to explain inconsistencies in previous research into passive tobacco smoke exposure in childhood and allergic sensitization.

This phenomenon could help explain variation by country. Passive smoking during infancy was associated to atopic sensitization in Estonia but not Sweden (2). In Estonia smoking prevalence is about two times higher among men (6), while more Swedish women smoke than men (5). The lower proportion of male smokers in Sweden may account for the reduced risk of allergic sensitization among infants with smoking parents. A recent Danish study (9) reported a negative association between passive tobacco smoke exposure in childhood and atopy defined by SPT. However, this study did not differentiate between maternal and paternal smoking so it is possible that the influence of maternal smoking concealed a positive association with passive exposure to tobacco smoke.

Perinatal and prenatal maternal smoking has been associated with reduced allergy risk (4) and one study (3) found this reduced risk among the whole sample, but not in a sample restricted to atopic mothers, suggesting complex mechanisms other than passive exposure to tobacco smoke, such as a differential effect of smoking on maternal immune function. If passive exposure to tobacco smoke in childhood increases the risk of allergic sensitization, but prenatal or perinatal maternal smoking decreases this risk through another mechanism, the conflicting effects of maternal smoking may lead to an overall reduction in association of maternal smoking with atopy, depending on the mother's smoking pattern. Also, just as maternal smoking may conceal a raised risk of allergic sensitization in offspring because of paternal smoking, paternal smoking may conceal a reduced risk associated with prenatal or perinatal maternal smoking. The positive association with paternal smoking reported here more plausibly reflects an increased risk of allergy associated with exposure to particulates, possibly explained by mechanisms such as the adjuvant effect proposed for diesel exhaust particles (10).

While avoidance of smoking by allergic mothers offers a potential explanation operating although inheritance, this cannot explain the positive association with paternal smoking. If

maternal smoking prior to, or during pregnancy is associated with a reduction in offspring's allergy risk, this may mask any increased risk associated with passive smoke exposure because of maternal smoking after birth. Although non-statistically significant, probably because of small numbers, the positive association with atopy for another individual (non-parent) smoking in the household found by our study lends further support to a causal rôle for passive exposure in childhood to tobacco smoke.

Through use of an objective measure of allergy – SPT – the possibility of reporting or diagnostic bias through exacerbation of symptoms by cigarette smoke exposure was eliminated. Information on parental smoking during the subject's childhood was collected by retrospective interview and this is a potential source of recall error. However the difference in association with atopy for maternal and paternal smoking, suggests that the findings are not driven by a systematic tendency for allergic individuals to have reported parental smoking.

We were able to adjust for potential confounding factors, independent risks and potential effect modifiers, including markers of material and cultural circumstances, to reduce the possibility that parental smoking is a marker for other exposures. The associations with parental smoking are not because of subjects' own smoking behaviour as this was not associated with atopy, nor did adjustment for this influence the association of parental smoking with atopy risk. Among all of the exposures, potential confounding factors and other measures, only paternal smoking during the subjects childhood remained as a risk for atopy in the adjusted model, while having more older siblings and older age at SPT (earlier birth cohort) are significantly protective. The only important factor potentially concealing a positive association of atopy with paternal smoking was effect modification associated with maternal smoking.

The results of this study are consistent with a putative causal role for early life passive tobacco

smoke exposure in increasing allergy risk. Future studies should take into account the possible modifying influence of maternal smoking that may operate through a mechanism other than passive tobacco smoke exposure, thus masking an allergenic effect of passive tobacco smoke exposure in childhood.

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