Indoor nitrogen dioxide pollution
and respiratory symptoms of schoolchildren

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Summary. The influence of indoor nitrogen-dioxide exposure on respiratory symptoms of schoolchildren was investigated in a case-control study. The election method used was useful in obtaining symptomatic children, but insufficient in defining cases and controls without additional information. No relationship between indoor NO_2 and respiratory symptoms was found. Bias may have been present, especially because of the high mobility of the study population. Attempts to estimate historical exposure were inaccurate. Therefore the results do not exclude that an association between indoor NO_2 and respiratory symptoms exists.

Key words: Nitrogen dioxide – Indoor pollution – Respiratory symptoms

Introduction

Nitrogen-dioxide levels inside dwellings can exceed ambient levels due to the use of unvented gas appliances (Elkins et al. 1974; Melia et al. 1978; Boleij et al. 1982). Therefore several epidemiological studies have been performed, in which the influence of the use of unvented gas appliances on respiratory disease of children has been investigated (Melia et al. 1979; Keller et al. 1979; Speizer et al. 1980). The results of these studies were contradictory, possibly due to several limitations. Due to low prevalence of respiratory disease among children, it is necessary to study large population samples, which makes it difficult to obtain reliable estimates of individual exposure.

Consequently exposure to nitrogen dioxide was usually represented by cooking fuel (gas vs electric). Since there are more factors affecting nitrogen-dioxide levels (Spengler et al. 1983), this is probably not an accurate estimate of exposure.

Therefore we decided to study the influence of indoor nitrogen dioxide pollution on respiratory disease of primary choolchildren by using a case-control approach. An advantage of a case-control approach is that fewer children are necessary to obtain sufficient symptomatic children, compared to selection from the general population, so that actually measuring NO_2 inside the homes of the complete study population becomes feasible.

Materials and methods

Cases and controls were selected on the basis of the data of the School Health Service of the city of Rotterdam. At the age of six years all schoolchildren are examined by a number of physicians working for the School Health Service.

The results of this examination are registered on a standardized form. As cases, children were selected who were reported to suffer from bronchitis, asthma, frequent cough or colds and allergy. For each case, two controls were selected of the same sex and age and coming from the same school. Thus in the selection procedure, the presence or absence of gas appliances was not taken into account. Our assumption at the start of the investigation was that NO_2 exposure could not be characterized accurately by the cooking fuel. Therefore we decided to measure NO_2 directly.

The parents of all cases and of one control for each case were invited by letter to participate. For each control child whose parents returned a written refusal before the start of the field work, the second control child was invited to participate. Eighteen controls were thus replaced. Altogether, 360 children were invited to participate. Of these, 231 actually participated in the survey. There were 129 non responders, due to refusals (22 cases, 39 controls), unknown or incorrect addresses (13 cases, 20 controls), 3 times not at home (5 cases, 19 controls), miscellaneous reasons (3 cases, 8 controls). The responders were composed of 128 cases and 103 controls; there were 81 of the original pairs among them. All field workers in the survey were unaware of the child's case- or control-status at the time of the visit.

In each home of the study population, nitrogen dioxide weekly average levels were measured in the kitchen, living room and bedroom of the child, using duplicate Palmes diffusion tubes. Time-activity data of some children in the study were sampled using a time-activity sheet which was completed by the child's mother. The average time-activity pattern of these children was used to calculate time-weighted average NO_2 concentrations for each child in the study, using NO_2 data from each child's own home. In a questionnaire, information about the presence of gas appliances now and in the past was asked for. A historical nitrogen dioxide exposure could be estimated using the following procedure: the relationship between measured concentrations in the three rooms and presence of gas appliances (geyser, cooking device, heating system) was determined by multiple regression analysis; with the resulting regression coefficients and data on the presence of gas appliances in the past, historical exposure was estimated. In this way historical exposure is divided into a definite number of categories. Ambient levels were collected from a central monitoring site of the National Air Polluting Monitoring network. Standardized questions on respiratory symptoms were included in the questionnaire to obtain independent corroboration of the original case-control classification (Kerrebijn et al. 1975).

Finally the questionnaire contained questions about (potential) confounding factors. These were respiratory symptoms of parents, smoking of mother and others inside the house, humidity, presence of heating in bedroom of the child, presence of domestic animals, number of children, possession of own bedroom, social-economic status, parental education and age and sex of the child.

Intrapair correlation coefficients of the matched pairs were calculated to investigate whether it was necessary to perform a matched analysis. For passive smoking, NO_2 concentrations in the kitchen, living room and bedroom intrapair correlations were not significant ($p > 0.10$). However, for time-weighted average NO_2 concentration, the intrapair correlation was

of borderline significance ($p = 0.05$). This indicates that a matched analysis would be somewhat more sensitive. However, performing a matched analysis would result in a considerable loss of data ($231 - 2 \times 81 = 69$ subjects). Therefore we decided on an unmatched analysis.

In the analysis, cases were defined as those who were symptomatic according to the questionnaire as well as the School Health Service Data. Controls were those who were non-symptomatic according to both classifications (cf. Results).

The first stage of the analysis involved simple Student's t-tests and cross-tabulations. Correction for confounders was achieved by a multiple regression analysis. In this analysis, the presence or absence of a specified symptom was included as a binary response variable, i.e. a dependent variable with only two possible values, absence (0) or presence (1) of the symptom. Two kinds of regression models were developed: one in which all measured concentrations were added to a model in which a number of confounders were already present; the other involved addition of one (measured or estimated) concentration to the model of confounders. In the latter case, regression coefficients were transformed into Odds-ratios and 90% confidence intervals of Odds-ratios were calculated (Kleinbaum and Kupper 1978). The Odds-ratio is an estimator of the relative risk, i.e. the chance for having a specified respiratory symptom at a certain NO_2 exposure, *relative* to the chance for having the symptom at one unit of NO_2 exposure less.

Results

In Table 1, measured nitrogen dioxide levels are presented. Levels inside the house are higher than ambient levels, especially in the kitchen. The coefficient of variation of the measurement was about 10% (based on duplicate samples). Indoor nitrogen dioxide levels were higher than levels in the USA, lower than in the UK and about the same as in another Dutch city and Japan (Goldstein et al. 1979; Keller et al. 1979; Elkins 1974; Nitta and Maeda 1982; Lebret et al. 1983).

The agreement between the original definition of cases and controls (on the basis of School Health Service data) and information from the questionnaire was satisfactory (Table 2). However, the agreement was not enough to use only the School Health Service (S.H.S.) information for classification as case or control. Our conclusion was therefore that the selection method used is useful in obtaining symptomatic children but not in defining cases and controls without additional information.

Figure 1 illustrates some of the difficulties if the present measured concentration is used as measure of exposure of the children. Only in 34% of the homes did no changes in gas appliances take place. This number may be specific for our population since it was concentrated in the older quarters of the city.

Table 1. Nitrogen dioxide, weekly average concentrations ($\mu g/m^3$) at different locations

Location	Arithmetic mean	Arithmetic SD	Geometric mean	Geometric SD	Range	Number
Kitchen	144.0	108.0	114.0	3.9	110–789	226
Living room	80.0	48.1	68.4	3.3	17–277	228
Bedroom	50.9	30.0	44.1	3.3	10–146	228
Ambient	45.0					

Table 2. Agreement between original definition of cases and controls and information from questionnaire

Number of symptoms according to questionnaire	Selected from School Health Service data	
	Case	Control
0	8	53
1	6	20
2	9	16
3	10	7
4	10	2
5	13	0
6	8	1
7	8	3
8	10	1
>9	46	0

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                         231 children (100%)
                                  |
              ┌───────────────────┴───────────────────┐
          ever moved                              never moved
          121 (52%)                                110 (48%)
              |                                         |
              |                    change in            |
              |                    gas appliances       |
              |                    32 (14%)             |
              |                        |                |
              └────────────┬───────────┘                |
                      total changes                     |
                       153 (66%)                        |
                           |                            |
              ┌────────────┴────────────┐               |
      exposure cannot          exposure can         no changes
      be estimated             be estimated          78 (34%)
      64 (28%)                 89 (38%)
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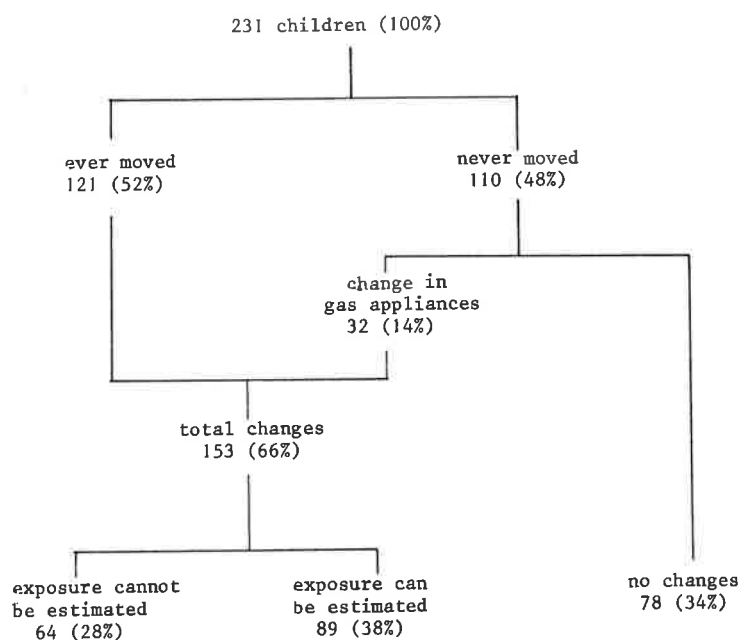
Fig. 1. Changes in the population affecting nitrogen dioxide levels

Since, in principle, exposure in the past has to be known, these data stress the desirability of a method of estimating historical exposure, since otherwise, mis-classifications will occur. Table 3 shows the results of the multiple regression analysis, in which $\log_{10} NO_2$ was the dependent variable and gas appliances were the independent variables. These data indicate that only for the kitchen concentration a moderate explanation of variance possible. This is in agreement

Table 3. Explanation of measured nitrogen dioxide levels by presence of gas appliances, using multiple regression analysis

Conc. (10 log) $\mu g/m^3$	Model	C[a]	B[b] Un-vented geyser	B[b] Vented geyser	B[b] Cooking fuel gas	B[b] Gas heating system	B[b] Ven-tilation hood	R[2c] (%)
Kitchen	1[d]	1.322	0.442	0.092	1.38	0.127	N.S.[e]	57
	2	1.823	0.441					51
Living room	1	1.365	0.258	0.100	0.124	0.088	−0.062	36
	2	1.694	0.255					28
Bedroom	1	1.514	0.247	N.S.	N.S.	N.S.	N.S.	25
	2	1.514	0.247					25

[a] C = constant value in regression analysis
[b] B = regression coefficient
[c] R^2 = percentage of variance of dependent variable explained by the model
[d] 1 = Stepwise-procedure, all 5 independent variables eligible for incorporation into the model
2 = model with unvented geyser only
[e] N.S. = not significant, $p > 0.10$

Table 4. Arithmetic mean nitrogen dioxide levels ($\mu g/m^3$) for cases and controls, unadjusted for confounders

Dependent variable	Kitchen conc.		Living room conc.		Bedroom conc.		TWA[a]	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Cough 3 months	137	148	89	80	55	46[c]	68	59[d]
Breathlessness·	135	148	74	80	48	46	59	59
Wheezing	152	148	78	80	49	46	63	59
Bronchitis	148	148	76	80	48	46	59	59
Asthma	141	148	89	80	51	46	67	59
Symptom-comb. 1[b]	139	133	78	72	51	48	63	59
Symptom-comb. 5[b]	146	133	82	72	49	48	63	59

[a] TWA = average exposure in kitchen, living room, bedroom taking into account time spent in these locations
[b] S.C.1 = cases: at least one of the most severe symptoms asthma, 3-month cough, attacks of breathlessness with wheezing; controls; none of severe symptoms and fewer than two less severe symptoms. S.C. 5 = cases: one or more symptoms according to questionnaire; controls: no symptoms
[c] Student's t-test, $p < 0.05$
[d] Student's t-test, $p < 0.10$

Table 5. Relationship between respiratory symptoms and measured nitrogen dioxide levels, adjusted for a number of confounders[a]

Dependent variable	OR-kitchen conc.[b] (90% conf. limits)	OR-living room conc. (90% conf. limits)	OR-bedroom conc. (90% conf. limits)	n_1[c]	n_2[d]
Cough 3 months	0.60 (0.12–3.0)	1.97 (0.24–16.2)	7.5 (0.84–58)	48	24
Breathlessness	1.05 (0.31–3.5)	1.15 (0.23– 1.7)	1.05 (0.23–15.0)	48	59
Wheezing	1.45 (0.50–4.0)	1.57 (0.38– 6.2)	1.45 (0.37– 5.5)	48	76
Bronchitis	1.16 (0.40–3.5)	0.92 (0.20– 4.2)	1.24 (0.30– 5.1)	48	71
Asthma	1.29 (0.40–5.4)	5.83 (0.70–34.9)	2.68 (0.4 –16.2)	48	32
Symptom-comb. 1	1.87 (0.70–1.6)	1.93 (0.50– 7.3)	1.65 (0.4 – 6.2)	77	72
Symptom-comb. 5	1.29 (0.50–3.3)	1.60 (0.50– 5.70)	0.55 (0.2 – 1.8)	80	90

[a] Confounders in model: bedroom heating, mother smoking, home humidity, parental education, parental respiratory symptoms, age and sex of child
[b] OR = Odds-ratio, i.e. relative risk due to an increase of the 10 log NO_2 concentration with one unit
[c] n_1 = number of controls
[d] n_2 = number of cases

Table 6. Relationship between respiratory symptoms and estimated historical nitrogen dioxide exposure, adjusted for a number of confounders[a]

Dependent variable	OR[b]-EH4[b] (90% conf. lim.)	n_1	n_2	OR[b]-EH8[b] (90% conf.lim.)	n_1	n_2
Cough 3 months	0.05 (0.00–0.57)	50	24	0.09 (0.04–15.7)	38	18
Breathlessness	0.59 (0.09–3.7)	50	60	0.86 (0.07–10.6)	38	43
Wheezing	0.75 (0.10–4.1)	50	76	0.94 (0.07– 4.8)	38	56
Bronchitis	0.53 (0.10–2.9)	50	82	1.57 (0.20–14.0)	38	61
Asthma	0.40 (0.09–3.0)	50	33	0.16 (0.01– 4.3)	38	21
Symptom-comb. 1	0.74 (0.10–3.0)	78	73	0.65 (0.20– 3.3)	60	52
Symptom-comb. 5	0.44 (0.10–1.8)	81	90	0.47 (0.09– 2.8)	62	67

[a] Confounders in model: bedroom heating, mother smoking, home humidity, parental education, parental respiratory symptoms, age and sex of child
[b] OR = Odds-ratio, i.e. relative risk due to an increase of the 10 log NO_2 concentration with one unit
[c] EH4 = estimated historical exposure over last four years
[d] EH8 = estimated historical exposure over whole life of child

with other investigations performed in the Netherlands (Lebret et al. 1983). Therefore it was decided to estimate historical exposure in the kitchen only. Exposure of 28% of the population (Fig. 1) could not be estimated because questions about the former house were asked only if the family had moved less than four years ago. Table 4 shows arithmetic mean, nitrogen dioxide concentrations for cases and controls for some of the symptoms investigated. Virtually none of the tested differences was statistically significant. In addition, there was no trend in the data; in some comparisons, NO_2 concentrations were higher in the homes of controls, in others they were higher in the homes of cases. The results of the multivariate analysis are shown in Tables 5 and 6. The Odds-ratios were all adjusted for parents' respiratory symptoms, indoor humidity, parental education, bedroom heating, numbers of cigarettes smoked by the mother and age and sex of the child. None of the Odds-ratios were significantly different from unity. The Odds-ratios for concentrations, measured in 1982, however, were mostly slightly above unity. This could be interpreted as a trend in the expected direction (Table 5). Most Odds-ratios for historical exposure were, on the contrary, below unity, which suggests the opposite. There is, however, reason to believe that historical exposure, estimated in this way, is too inaccurate to be of much use (cf. also Remijn et al. 1984).

Discussion

No difference in indoor nitrogen-dioxide levels could be established between cases and controls.

Selection bias may have occurred. There are weak indications that some people refused to participate because they did not have any gas appliances in their homes (which was mentioned in the information letter). Since more controls than cases refused to participate, the average nitrogen dioxide level of the controls may have been high compared to the general population of eligible controls.

Another problem is the fact that many changes in factors affecting nitrogen dioxide had occurred. Estimation of a historical exposure most probably was not very accurate, since present nitrogen dioxide levels could not be well predicted by the presence of gas appliances. This also shows that by characterizing exposure by the type of cooking fuel (gas vs electric) many misclassifications of exposure will occur.

Our conclusion is that the present study does not suport an association between indoor NO_2 exposure and respiratory symptoms in schoolchildren. Due to the exposure classification problems mentioned above, it cannot reject the possibility of an association either.

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