

Pollutional and meteorological factors are closely related to complaints of non-allergic, non-infectious perennial rhinitis patients: a time series model

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Summary

Background Epidemiological studies in the past have focused on meteorological conditions, pollution and pollen and their relationship with symptoms of bronchial hyper-reactivity, however, there are no epidemiological studies which examine a wide range of such factors and determine their role in nasal hyper-reactivity.

Objective To investigate whether environmental factors can influence symptomatology in non-allergic non-infectious perennial rhinitis (NANIPER) patients, who suffer primarily from nasal hyper-reactivity symptoms.

Methods We studied 16 non-smoking NANIPER patients and seven non-smoking controls during a 218-day study period (March–October) by means of daily symptom scores and visual analogue scales for the subsets patency, secretions and sneezing, and compared them to seven primary factors which affected 'symptoms' and 10 secondary factors which affected primary factors only.

Results The mean symptom scores in the NANIPER and control groups were 2.17 and 0.13, respectively. In NANIPER, the highest correlations of primary factors with symptomatology were found for symptom scores and sneezing with minimum daytime temperature ($r = -0.62$ and -0.45 , respectively), ozone and NO concentrations. Patency and secretions were associated with minimum daytime temperature ($r = -0.39$ and 0.32 , respectively). Time series analysis, however, correcting for several confounders such as autocorrelated symptomatology, showed that minimum daytime temperature and daytime relative humidity made an independent contribution to symptoms. In the control group, correlations were much lower, though present. Time series analysis was not possible.

Conclusions We conclude that in a mild climate with relatively low levels of pollution, minor pollution and meteorological disturbances result in substantial changes in nasal reactivity symptoms in NANIPER patients, but not controls, irrespective of other factors such as allergy or infection.

Keywords rhinitis vasomotor, pollution, meteorological factors, computer simulation, time factors
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Introduction

Environmental factors can result in nasal symptoms in anyone, but in rhinitis sufferers in particular. Some studies have shown relationships between upper respiratory symptoms and black smoke in children [1,2]. Other studies stress the relationship with ozone [3]. Cold dry air results in severe reactions in the nasal mucosa in rhinitis sufferers [4], while warm moist air tends to ameliorate these symptoms [5]. Dryness too, is a potential irritant for the nasal mucosa exposing its sensory nerves. However the deposition of pollutants (SO_2 and NO_x) depends on water solubility [6]. In allergic rhinitis, air pollution agents can result in nasal blockage and potentiate sensibilization and airway inflammation with nasal blockage [7].

The rhinitis subgroup of NANIPER patients (non-allergic, non-infectious perennial rhinitis), suffers primarily from chronic ongoing nasal reactions to these environmental disturbances [8]. Symptoms include nasal problems such as sneezing, nasal blockage, runny nose, watery eyes and itchy nose. In these patients, there are no signs of allergy or inflammation of the nasal mucosa [9, 10]. Positive cold dry air provocation suggests the diagnosis, although no symptom or clinical feature exists to prove its presence [4]. Epidemiological studies in the past have focused on meteorological conditions, pollution and pollen and their relationship with symptoms of bronchial hyper-reactivity [11–15]. Despite pathophysiological similarities [16] and reports of poorer quality of life status in rhinitis patients compared to asthmatic patients [17], there are no epidemiological studies which examine a wide range of such factors and determine their role in nasal hyper-reactivity. This study therefore compares nasal symptomatology in NANIPER patients to daily fluctuations in a wide spectrum of air pollutants and meteorological factors.

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Materials and methods

Patients and controls

The nasal symptoms of 22 NANIPER patients and seven non-rhinitic controls were studied between 17 March and 20 October 1994 (218 days). Sixteen NANIPER patients and seven controls met all inclusion and exclusion criteria [4, 9] stated in Table 1. In short: patients suffered from moderate to severe complaints such as nasal obstruction, rhinorrhoea and/or sneezing for more than one year. Atopic rhinitis and nasal or paranasal sinus infection were excluded with rhinoscopy, serum RAST sampling and skin prick testing. Anatomical disorders affecting nasal function, pregnancy or lactation and/or systemic disorders were excluded. Medication affecting nasal function was not allowed. Patients and controls completed daily record charts for a minimum of 60 consecutive days. Weekly visual analogue scale (VAS) scores were also collected during this period. All the participants gave written informed consent.

Daily record chart and visual analogue scale

Subjects registered nasal symptoms (scale 0–4; 0 = no symptoms) daily and VAS scores for the subsets patency (nasal obstruction), secretions (runny nose) and sneezing (scale 0–10 each; 0 = no complaints) weekly, by filling in a daily record chart (DRC). An average of ≥ 2 for one week within a period of 4 weeks was required as a symptom score in order to qualify for the study period. Compliance was checked on a weekly basis by examining DRC's of patients and controls during home visits or outpatient clinic visits. The average study period per patient was 75 days (ranging from 61–108 days). In the total observation period of 218 days, the number of subjects observed on any one day varied between one and 13.

Time-related symptomatology

In addition to the relationship between daily environmental factors and nasal symptoms registered the same day, we thought it was important to assess how long these effects last. Weather factors and amounts of air pollution were defined as the mean 24 h concentration for the day on which effects on health were measured (lag 0), for the two preceding days (lag 1, lag 2) and as the mean concentration for the preceding five days (mean 5 day lag).

Air pollution and weather data

Daily information on 29 air pollution and weather parameters (not shown) was available for analysis. In order to analyse the large number of variables systematically, we eliminated factors that were highly interrelated. This left 17 factors (Tables 2a and b).

We then elaborated a model on the basis of information from the literature. This model consisted of seven primary factors which were potentially directly related to nasal symptoms and 10 secondary factors which were considered to influence the primary factors and not the nasal symptoms directly. The primary factors were average daytime (6 AM–6 PM) minimum temperature, average daytime relative humidity and pollutional factors such as 24 h averages for SO₂, particulate matter (PM)-10, NO, ozone (O₃) and O_x [Fig. 1]. NO was selected in preference to NO₂ and NO_x because it had the lowest intercorrelations.

Statistical analysis

Bivariate Pearson correlation coefficients were calculated for primary factors and symptom scores, as well as primary factors

Table 1. Inclusion and exclusion criteria for NANIPER patients and controls

Inclusion criteria: NANIPER and controls

- Age between 16 and 65 years
- Negative skin prick test and negative RAST score
- Symptoms for more than 1 years (NANIPER only)
- NANIPER exacerbation group: moderate to severe nasal complaints on entry (subjective)
- NANIPER remission group: mild complaints on entry (subjective)

Exclusion criteria: NANIPER and controls

- The use of systemic or inhaled corticosteroids within the previous month
- The use of inhaled cromoglycates, astemizol or nedocromil sodium within the previous month
- Inability of the patient to stop taking medication affecting nasal function (e.g. xylometazoline)
- A serious and/or unstable disease and pregnancy or lactation
- Nasal surgery within the previous 3 months
- Significant anatomical abnormalities affecting nasal function
- Nasal polyps or a history of nasal polyps
- Nasal or paranasal sinus infection or abnormal sinus X-ray
- Abnormal laboratory results for:
 - In blood: Na, K, Ca, total protein, albumin, urea, creatinine, bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transpeptidase, haemoglobin, red blood cell count, plasma cell volume, mean corpuscular volume, platelets, total white blood cell count, lympho & monocytes, neutrophils, eosinophils, basophils
 - In urine: blood, protein and glucose
- Abnormal findings at physical examination
- Smoking
- Daily contact with physical or chemical irritants

Table 2a. Mean concentrations of ambient air pollutants and mean values of meteorological variables in The Hague, March–October 1994

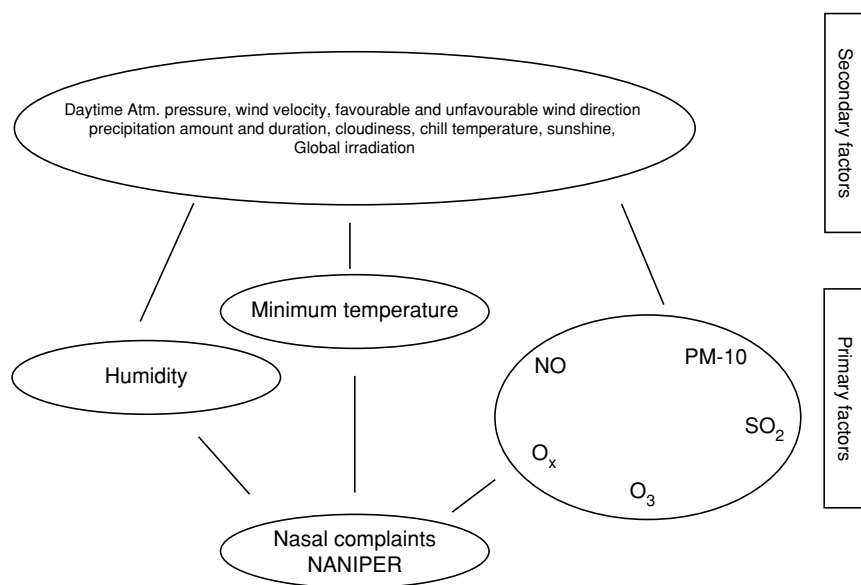
Primary Factors (abbreviation)	Description	Mean	Range	WHO Guidelines	EPA legislation 1997
Temp	Daytime average temperature (°C)	11.8	0–23		
Hum	Daytime average humidity (%)	66.0	36–98		
SO ₂	Sulphur dioxide, 24 h mean (µg/m ³)	8.0	1–37	125	365 (= 0.14 ppm)
PM-10	Particulate matter smaller than 10 µm 24 h mean (µg/m ³)	33.0	0–109	120	150
NO	Nitrogen monoxide, 24 h mean (µg/m ³)	6.0	0–302	np***	np***
O ₃	Ozone, 24 h mean ppb	50.0	2.5–72	120	235 (= 0.12 ppm)
O _x	Oxygen radicals, 24 h mean ppb	41.0	26–86	np	np

WHO = World Health Organisation; EPA = Environmental Protection Agency; np = not present. ***EPA guidelines for NO₂: annual arithmetic mean 100 µg/m³ or 0.053 ppm.

Table 2b. Mean concentrations of meteorological variables in The Hague, March–October 1994

Secondary factors	Description	Median	Range
Atmospheric Pressure	Average daytime, hPa	1017	987.1–1033.5
Wind velocity	Average daytime, Beaufort	3.5	2–7
Favourable wind direction	Daytime average, °†	313.2	276–358
Unfavourable wind direction	Daytime average, °†	183.2	138–210
Chill temperature	Daytime average, °C	8.0	–8.0–21
Global irradiation	J/cm ² per 24 h	1250	100–2800
Sunshine	h per day	5.0	0–15
Precipitation	mm per 24 h	0.0	0–33
Precipitation	h per 24 h	0.0	0–19
Cloudiness	Eights of 24 h	6	1–8

hPa = hecto Pascal; J/cm² = joules per cubic centimetre. °† = degrees from the North.

**Fig. 1.** Proposed model for the relationship between primary and secondary factors and nasal symptom scores in NANIPER.

Humidity, minimum temperature and several pollutants directly influence nasal symptomatology, while secondary factors react on primary factors only.

and VAS scores (SPSS-pc). Because a large number of comparisons were made, the levels of statistical significance, for these calculations only, were changed from $P = 0.05$ to $P = 0.01$. The symptom and VAS scores for a given day were calculated as the average of n individual symptom scores on that day. Due to an autocorrelation of these scores, correlation of lagged values were not considered. The multivariate ARIMA (autoregressive

integrated moving average) model was used for time series analysis in the NANIPER group to study time-related symptomatology and to predict which primary factors made a statistically significant contribution to the average nasal symptom scores on a given day, and to what extent. This average nasal symptom score on a given day was calculated for the subjects observed at that day. As the number of subjects varied between

1 and 13 from day to day, weighted analyses were performed using the square root of the number of subjects as the weighting. So variables were multiplied by the square root of the number of subjects over which the symptom score was averaged; the coefficient of this square root itself served as the constant in the model. In the model specification the autoregressive order was set at 2, and no differentiating or moving average was used. The explanatory environmental variables (air pollution and weather) were entered into the model simultaneously with no time lag, 1-day time lag, 2-day time lag or a mean 5-day time lag. Combinations of 'not time lagged' with variables at various time lags were also analysed. Variables which did not make a contribution to the model ($P > 0.2$) were eliminated by backward elimination. Secondary factors were added separately to this model. None of the secondary factors made a statistically significant contribution.

Results

Meteorological and pollution data

Tables 2a and b show means with standard errors and ranges of concentrations of ambient air pollutants and values of meteorological variables. Concentrations of pollutants in ambient air were relatively low, but varied widely from day to day. Available World Health Organisation guidelines and US Environmental Protection Agency legislation are stated here too.

Although selections of variables with the lowest interrelations had been made, the remaining seven primary factors were still interrelated. These interrelations were strongest for PM-10 with NO, and for ozone with NO ($r = 0.66$ and $r = 0.60$, respectively). These results are not shown.

Symptom scores

The mean symptom score for NANIPER patients was 2.17, as compared to 0.13 for the controls. For patients, symptom scores were inversely correlated with minimum daytime temperature (patients vs. controls: $r = -0.62$ vs. 0.26) see Fig. 2. This correlation was higher after a 1- or 2-day lag, reaching a maximum after a mean 5-day lag ($r = -0.70$).

Several pollutant concentrations correlated with symptom scores of the same day (ozone $r = -0.41$, NO $r = 0.32$). Here,

lagged symptom scores showed comparable correlation coefficients with day $t = 0$. For the other primary factors (PM-10, O₃, SO₂, and daytime relative humidity), coefficients did not exceed $r = 0.19$, see Table 3a.

In controls, the correlations were much lower, though present. High correlations were found between pollutants and symptom scores on the same day (ozone ($r = 0.28$) and NO ($r = 0.22$)), but here correlation coefficients increased with time lagged symptom scores and there was hardly any relation with minimal daytime temperature (Table 3b).

VAS scores

The mean VAS score was 3.89 for NANIPER patients vs. 0.32 for controls.

In NANIPER patients, pooled VAS scores and their subsets were strongly related to minimum daytime temperature, again with increasing correlations after a 1- or 2-day lag, with a maximum at the mean 5-day lag ($r = -0.63$). As stated earlier, coefficients of $P < 0.01$ were considered to be statistically significant. Here also NO and ozone were the highly correlated pollution factors. In particular, VAS scores for secretions and sneezing were closely related to ozone ($r = -0.48$ and $r = -0.50$, respectively) and NO ($r = 0.53$ and $r = 0.46$, respectively). Correlations with daytime relative humidity, SO₂, PM-10 and O₃ were low ($r < 0.25$). See Table 3a.

In controls, there was hardly any correlation between VAS scores and primary factors. see Table 3b.

Time series analysis and confounders

We considered all primary and secondary factors in their relation to daily symptom scores in order to achieve an optimum curve fit. The model was adapted as stated above.

Special attention was drawn to possible confounders such as the number of reporting patients per day, linear time trends, e.g. when registering nasal symptomatology for a longer period of time, and differences between the awareness of nasal symptomatology in weekends compared to weekdays. All of these possible confounders attained statistical significance. The model was corrected for these factors. During the study period, participants were asked not to take holidays or go abroad. Nor did participants take part in strenuous sport events. Furthermore, incidence rates for influenza A and B

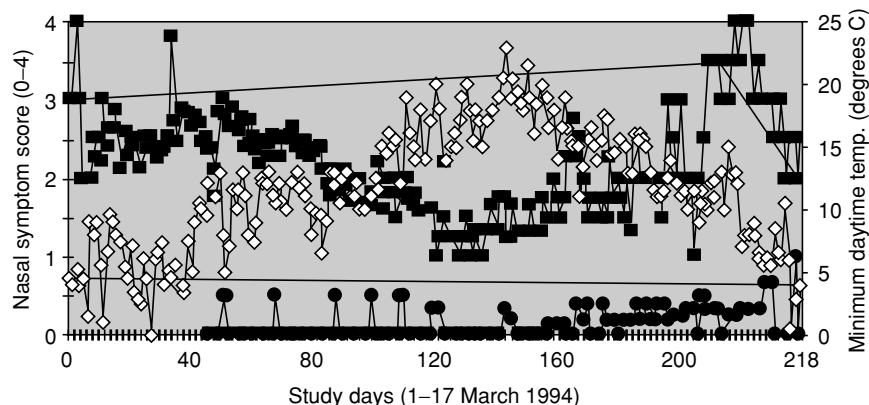


Fig. 2. Example of the relationship between primary factor and nasal symptom scores. Minimum daytime temperatures vs. nasal symptom scores in NANIPER ($r = -0.62$) and in controls ($r = -0.26$). ■: symptom scores in NANIPER patients; ●: symptom scores in controls; ◇: temperature.

Table 3a. Pearson correlation coefficients between primary factors and symptom scores or VAS scores in NANIPER patients

Primary factor	Temp.	Hum.	SO ₂	PM-10	NO	Ozone	O _x
Complete lag 0	−0.62**	0.10	0.10	−0.007	0.26**	−0.35**	−0.16
lag 1	−0.63**	0.10	0.15	−0.007	0.23**	−0.34**	−0.15
lag 2	−0.65**	0.10	0.17*	0.046	0.28**	−0.37**	−0.15
5 days mean	−0.70**	0.11	0.19*	0.034	0.32**	−0.41**	−0.17
VAS total lag 0	−0.48**	0.18	0.10	0.049	0.37**	−0.29*	−0.085
lag 1	−0.50**	−0.027	0.14	0.25*	0.42**	−0.37**	−0.096
lag 2	−0.49**	0.057	0.33*	0.10	0.45**	−0.45**	−0.16
5 days mean	−0.63**	0.13	0.27*	0.052	0.53**	−0.55**	−0.24
VAS pa. lag 0	−0.39**	0.10	0.21*	−0.079	0.24*	−0.15	−0.049
lag 1	−0.44**	0.19	0.11	0.12	0.28*	−0.31*	−0.092
lag 2	−0.42**	0.069	0.14	0.0029	0.24*	−0.26*	−0.12
5 days mean	−0.59**	0.024	0.22**	−0.029	0.33**	−0.39**	−0.19
VAS se. lag 0	−0.32**	0.14	0.023	0.092	0.26*	−0.21	−0.039
lag 1	−0.32**	0.052	0.15	0.23*	0.34*	−0.30*	−0.077
lag 2	−0.32**	0.063	0.38**	0.11	0.43**	−0.41**	−0.0876
5 days mean	−0.42**	0.16	0.25*	0.081	0.46**	−0.50**	−0.21
VAS sn. lag 0	−0.45**	0.20	0.029	0.098	0.39**	−0.34**	−0.12
lag 1	−0.45**	0.063	0.082	0.25*	0.39**	−0.28**	−0.06
lag 2	−0.45**	0.0043	0.25*	0.12	0.40**	−0.39**	−0.17
5 days mean	−0.60**	0.14	0.20**	0.086	0.53**	−0.48**	−0.20

Temp. = minimum temperature daytime average; hum. = humidity daytime average; VAS total = average VAS scores for the three subsets; VAS pa. = VAS score for patency; VAS se. = VAS score for secretions; VAS sn. = VAS scores for sneezing. * $P < 0.05$; ** $P < 0.01$. Numbers in bold: $r > 0.4$.

Table 3b. Pearson correlation coefficients between primary factors and symptom scores or VAS scores in controls

Primary factor	Temp.	Hum.	SO ₂	PM-10	NO	Ozone	O _x
Complete lag 0	−0.26**	0.10	0.12	0.054	0.22**	−0.28**	−0.14
lag 1	−0.25**	0.19	0.15	0.054	0.20*	−0.32**	−0.21*
lag 2	−0.19*	0.28*	0.18*	−0.0047	0.25**	−0.39**	−0.24*
5 days mean	−0.31**	0.28*	0.21*	0.028	0.43**	−0.51**	−0.29*
VAS total lag 0	−0.21	0.044	0.094	0.062	0.37	−0.18	−0.031
lag 1	−0.20	0.028	0.065	0.015	0.032	−0.042	−0.045
lag 2	−0.22	0.029	0.12	−0.14	0.046	−0.15	−0.13
5 days mean	−0.29*	0.071	0.20*	−0.025	0.15	−0.32*	−0.13
VAS pa. lag 0	−0.15	−0.034	0.042	0.028	−0.0033	−0.13	−0.020
lag 1	−0.14	0.019	0.040	0.0023	−0.036	−0.12	−0.062
lag 2	−0.18	−0.13	0.21*	0.066	0.11	−0.19	−0.12
5 days mean	−0.24*	−0.012	0.23*	0.071	0.091	−0.28*	−0.048
VAS se. lag 0	−0.14	−0.013	0.017	0.085	0.033	−0.019	0.072
lag 1	−0.034	0.12	−0.093	0.018	−0.0035	0.12	0.027
lag 2	−0.070	0.20	−0.0097	−0.074	−0.017	0.0002	−0.052
5 days mean	−0.18	0.10	−0.043	−0.031	0.10	−0.13	−0.048
VAS sn. lag 0	−0.15	0.17	0.089	0.034	0.10	−0.18	−0.072
lag 1	−0.24	0.0002	0.065	0.0066	0.078	0.038	0.003
lag 2	−0.17	0.051	−0.0082	−0.15	0.070	0.022	0.028
5 days mean	−0.19	0.12	−0.050	−0.050	0.13	−0.17	−0.092

Temp. = minimum temperature daytime average; Hum. = humidity daytime average; VAS total = average VAS scores for the three subsets; VAS pa. = VAS score for patency; VAS se. = VAS score for secretions; VAS sn. = VAS scores for sneezing. * $P < 0.05$; ** $P < 0.01$. Numbers in bold: $r > 0.4$.

epidemics were not raised and remained below the standard of 5/10 000 inhabitants/week.

Finally, after all confounders were taken into account and remaining primary factors with their optimal time lagged symptom score relationships were introduced, the second order autoregressive ARIMA (200) model below was the result, describing

symptom scores of NANIPER patients during the study period (also see Table 4):

$$\begin{aligned} \text{Comp}(t) = & 2.46* \text{nd}(t) + 0.53* \text{AR}(1) + 0.33* \text{AR}(2) + 0.12* \\ & \text{weekend} + 0.022* (\text{temp} - 1) + (-0.0093)* (\text{Ox} - 1) + (-0.0069)* \\ & \text{daynum} + (-0.0058)* \text{SO}_2 - 1 + (-0.041)* \text{O}_3 - 1 + (-0.0035)* \\ & (\text{PM} - 10 - 1) + 0.0028* \text{NO} \\ & \text{comp}(t) = \text{symptom score at day } t_1 \end{aligned}$$

Table 4. Estimated variables in multivariate ARIMA (200) modelling. Primary factors and confounders are related to symptom scores with 0,1 or 2, daytime lag or 5 days average lag. Variables ($\pm$ SE) normalized by square root weighting

Time factor	No time lag coefficient ($\pm$ SE)	One day time lag coefficient ($\pm$ SE)	two days time coefficient ($\pm$ SE)	Five days average lag coefficient ($\pm$ SE)
ND	3.10* ($\pm$ 0.25)	2.51* ($\pm$ 0.29)	2.82* ($\pm$ 0.25)	3.06* ($\pm$ 0.62)
AR(1)	0.47* ($\pm$ 0.069)	0.52* ($\pm$ 0.069)	0.48* ($\pm$ 0.070)	0.42* ($\pm$ 0.066)
AR(2)	0.33* ($\pm$ 0.067)	0.33* ($\pm$ 0.070)	0.32* ($\pm$ 0.073)	0.30* ($\pm$ 0.067)
Weekend	0.12* ($\pm$ 0.039)	0.097* ($\pm$ 0.038)	0.13* ($\pm$ 0.039)	0.12* ($\pm$ 0.037)
Daynum	-0.0052* ($\pm$ 0.0020)	-0.0068* ($\pm$ 0.0026)	-0.0038* ($\pm$ 0.0021)	-0.0036* ($\pm$ 0.0022)
Temp.	-0.0058 ($\pm$ 0.011)	0.024* ($\pm$ 0.011)	-0.024* ($\pm$ 0.011)	-0.029 ($\pm$ 0.026)
Humidity	-0.0032* ($\pm$ 0.0015)	-0.00055 ($\pm$ 0.0014)	0.00083 ($\pm$ 0.0015)	0.0030 ($\pm$ 0.0054)
SO ₂	-0.0053 ($\pm$ 0.0047)	-0.0082 ($\pm$ 0.0046)	0.0049 ($\pm$ 0.0046)	-0.020 ($\pm$ 0.015)
PM-10	0.00016 ($\pm$ 0.0018)	-0.0039* ($\pm$ 0.0017)	0.0034* ($\pm$ 0.0018)	0.0039 ($\pm$ 0.0062)
NO	0.0045 ($\pm$ 0.0027)	0.0056* ($\pm$ 0.0027)	-0.0050 ($\pm$ 0.0020)	0.0036 ($\pm$ 0.0073)
Ozone	-0.00052 ($\pm$ 0.0020)	-0.0024 ($\pm$ 0.0020)	0.0014 ($\pm$ 0.0020)	-0.0052 ($\pm$ 0.0078)
O _x	-0.0038 ($\pm$ 0.0042)	0.0063 ($\pm$ 0.0041)	-0.0069 ($\pm$ 0.0042)	-0.0043 ($\pm$ 0.014)

ND=number of subjects reporting per day; AR(1) and AR(2) = autoregressive factors first and second order; Weekend=weekend days; Daynum=linear time trend; * $P < 0.05$.

nd(t)=number of reporting patients per day, $P < 0.000001$
 AR(1), AR(2)=autoregressive factors 1st and 2nd order, respectively, $P < 0.000001$ and $P < 0.000004$, respectively
 weekend = symptom scores on weekend days $P = 0.0041$
 temp ($t-1$) = minimum daytime temperature ($^{\circ}\text{C}$) on day ($t-1$), $P = 0.045$
 daynum = linear time trend, $P = 0.0074$
 SO₂₋₁ = SO₂ concentration in ambient air on day ($t = -1$) ($\mu\text{g}/\text{m}^3$), $P = 0.16$
 O₃₋₁ = O₃ concentration in ambient air on day ($t = -1$) (ppb), $P = 0.028$
 O_{x-1} = O_x concentration in ambient air on day ($t = -1$) (ppb), $P = 0.027$
 PM-10-1 = PM-10 concentration in ambient air on day ($t = -1$), $P = 0.041$
 NO = NO concentration in ambient air on day ($t = 0$) ($\mu\text{g}/\text{m}^3$), $P = 0.078$

NB: All variables are normalized by taking the square root of the values.

Nasal symptom scores of NANIPER patients were affected the most by daytime relative humidity and minimum daytime temperature according to the model above. Of all primary and secondary factors, minimum daytime temperature ($P = 0.045$), O₃ concentration ($P = 0.028$), O_x concentration ($P = 0.027$) and PM-10 concentration ($P = 0.041$) made a statistically significant contribution to the determination of the final nasal symptom score. NO and SO₂ concentration were just below significance level ($P = 0.07$ and 0.16) in this model. Daytime average humidity did not contribute to symptom scores in any model and was therefore omitted ($P = 0.78$).

It should be pointed out that introducing the factors NO or SO₂ to the model with other time lags resulted in significant contributions of these factors at the expense of two or more other primary factors. The model above was therefore considered to be the most appropriate because it used the largest number of explanatory factors available for describing symptom scores. Time series analysis was not possible for the controls since no model could be fitted.

Discussion

In this study daily symptom data were collected on nasal hyper-reactivity in subjects with non-allergic, non-infectious perennial rhinitis (NANIPER) and controls in order to assess the impact of two conditions: (a) air pollution and (b) weather conditions. We found that although measures of two kinds of air pollution and temperature correlated with nasal symptoms bivariately – in particular in NANIPER patients – nearly all five measured air pollutants and temperature were significantly related to nasal symptoms in time series models that adjusted for both conditions simultaneously.

The fact that not all five pollutants had significant relations with nasal symptom scores could be due to the relatively small group studied.

In order to establish an explanatory model for environmental effects on symptomatology in NANIPER patients, the 29 collected variables were restricted to seven primary factors and 10 secondary factors. We considered the correlation of variables and known pathophysiological mechanisms of rhinitis, together with the small amount of information available from epidemiological studies of lower airway reactivity which also address upper respiratory symptoms [1, 2].

Primary factors were those which were considered to have a direct effect on nasal symptomatology, while secondary factors were considered to influence primary factors. [Fig. 1].

In NANIPER, minimum daytime temperature resulted in the highest bivariate correlation coefficients with complaint scores by far, while this observation was absent in controls. Bivariate correlation coefficients for ozone and NO were high too, both in NANIPER and controls. The same factors were identified by Pönkä reviewing asthma attack admissions [13]. In lower airways, PM-10 and SO₂ are the main distressing pollutants [1, 2, 18, 19]. It must be pointed out that correlation coefficients almost invariably increased with lagged symptom scores and nearly always peaked after a mean 5-day lag, indicating autocorrelation. Time series analysis was therefore necessary to correct for autocorrelation and other confounders such as

differences in symptomatology between weekends and weekdays and a linear time trend. Due to the risk of an influenza epidemic, we excluded the period November–February from our study period (this is the coldest period of the year in the Netherlands). In retrospect, this was not necessary. Concentrations of pollutants in ambient air were low in this study compared to those stated in some articles [1, 13, 20] and comparable to those found by others [2, 12, 21]. Due to the prevailing westerly wind, little air pollution from the large concentration of petrochemical industries in the port of Rotterdam 25 km south from The Hague was measured. Favourable (north-westerly) and unfavourable (southerly) winds were taken into account, but they did not influence nasal symptoms significantly. Several studies have focused on indoor and outdoor pollutants and their effect on the upper respiratory tract. Along with cigarette smoke, indoor air pollutants such as formaldehyde, cadmium and ammonium or sulphate ions have been shown to alter mucociliary function and increase nasal airway resistance [6]. Ozone has been shown to result in neutrophilic influx and increased surface integrin expression in nasal lavages [22]. In an area with high pollution levels, epithelial lesions with dysplasia and p53 mutations were found in nasal biopsies [23].

Gielen [2] found a statistically significant relation between ozone and upper respiratory symptoms (lag = 0) and black smoke (lag = mean 5 day). Several studies, mostly in healthy school children [18, 24] and non-smoking adults [25] have demonstrated a clear increase of 2.7–6.9% in upper respiratory symptoms per 10 µm/m³ PM-10. When comparing correlation coefficients of VAS scores (overall or subsets) with pollution and weather parameters to those of nasal complaint scores, a similar pattern can be seen. The sneezing subset had the highest coefficients. This is compatible with earlier research studies pointing to the axon reflex as a pathophysiological mechanism underlying nasal hyper-reactivity in NANIPER (Braat J et al.: paper submitted). We conclude that in a mild sea climate with comparatively little pollution and little variability in meteorological factors, NANIPER subjects remain sensitive to minor fluctuations in meteorological and pollution factors, more so than controls. In particular, cold resulted in an increase in symptomatology of nasal hyper-reactivity. However, ozone (sun radiation), oxygen radicals (traffic) and particulate matter smaller than 10 µm (shoot from, e.g. combustion engines) were significantly related to symptom scores, particularly sneezing. Humidity was not an important factor. For the present, until the precise mechanism of the hyper-reactive nasal mucosa has been elucidated, this knowledge may help when advising NANIPER patients how to cope with their nasal disorder.

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