Air pollution, weather variations and primary spontaneous pneumothorax

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ABSTRACT

Background Spontaneous pneumothoraces (SP) tend to occur in clusters which have been related to atmospheric pressure variations and thunderstorm insurgence. We examined the influence of standard meteorological parameter variations and concentrations of the major air pollutants on incidence of spontaneous pneumothorax (SP) in a highly developed industrial area (Turin, Italy).

Methods From October 2002 to December 2007, 591 SP patients were prospectively evaluated. For each day, standard weather parameters and concentration of air pollutants were recorded.

Results The total number of admissions for SP was 591. The number of days with admissions was 363, which represents the 19% of the total number of days in the study period (1918). Eighty-one percent of days with SP admissions were clusterized. Results of statistical analysis showed that the sequence of SP events was not random. There was relationship between SP and daily wind speed (WS) minimum, daily standard deviation of NO2, NO_2, CO_2 daily maximum and minimum, O_3 daily minimum, daily mean CO_2 ($p = 0.01$), daily NO_2 minimum ($p = 0.001$). Multiple regression analysis has shown relationship between number of SP admissions and increase of daily mean and minimum NO2 ($p = 0.001$), decrease of NO_2 standard deviation ($p = 0.01$), decrease of daily mean and minimum O_3 ($p = 0.01$), and of maximum of NO ($p = 0.001$), increase of daily O_3 standard deviation ($p = 0.05$). Daily decrement of standard deviation of temperature ($p = 0.01$) and increment of WS anomalies and minima ($p = 0.01$) were also significant.

Conclusions Meteorological parameters and atmospheric pollutants might explain cluster hospitalization.

KeyWords: Meteorological parameters; atmospheric pollutants; spontaneous pneumothorax; clustering; spectral analysis; bivariate and multiple regression.

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Although some studies hypothesize correlation of the development of spontaneous pneumothorax (SP) with the atmospheric pressure variations or thunderstorm insurgence, several other factors seem to have an important role in its insurgence. It has also been suggested that pneumothorax admissions occur in cluster (1, 2, 3, 4). Other investigators analyzed the influence of standard meteorological parameter variations on SP insurgence but only few studies, all at the limit of the statistical significance, showed positive outcomes (3, 4, 5, 6, 7, 8). This work focused on the correlation of SP with the meteorological variables and the concentrations of the major air pollutants in Turin, one of the European cities with the highest industrial density, where atmospheric particles (especially the PM10), ozone and nitrogen dioxide levels consistently exceed the legal threshold for urban areas. Due to the absence of previous studies linking SP to atmospheric chemical parameters, the results were compared with those of similar studies carried out in cases of asthma exacerbation (9, 10, 11, 12, 13).

Material and methods

Patients

The patients with documented SP included in this study came from the north-western area of Turin and were admitted at the two Hospitals of Azienda Sanitaria Locale Torino 2 between October 1st, 2002 and December 31st, 2007 (1918 days). When a patient call the emergency service (e.g. 118), he is normally transported to the hospital closer to his home; so in this study the patients came from the north-western area of Turin. The samples contained all admissions occurred in the period from October, 2002, to December, 2007. The list of patients with certified pneumothorax admitted in the two hospitals represented two samples which were compared in order to verify the homogeneity of the data, using a non-parametric tests Kolmogorov-Smirnov, with a significance level $p = 0.01$. Being the two populations comparable, SP events were assembled in a single time series. The total number of admissions was 591, and the number of days with admissions 363 (the 19% of the total).

No potential conflict of interest.

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Traumatic or secondary pneumothoraces were excluded. SP relapses were considered as new episodes of SP. SP episodes appeared frequent, severe and temporarily disabling: SP is a medical emergency and first aid intervention was rapid. Taking into consideration the short time available for the break-down of cellular structures, this study took into account only the variables recorded one day before SP occurrence, instead of assessing the performance of the variables in the preceding 3 to 4 days, as done by other investigators (2, 4, 6).

Meteorological and air quality data

For each day of the analyzed period, following meteorological parameters and pollutant concentration data, measured in stations located close to the hospitals were recorded: atmospheric pressure P (hPa), temperature T (℃), relative humidity U (%), solar global radiation R (W/m^2), precipitation Pz (mm), average wind speed WS ($m\ s^{-1}$), gust wind speed WR ($m\ s^{-1}$), NO, NO_2, SO_2, PM10, C_6H_6, C_7H_8, O_3 ($\mu g\ m^{-3}$) and CO and CO_2 ($mg\ m^{-3}$). Average collecting time for the variables was 10 minutes for Pz and WS, 30 minutes for P, T, U and R, and 60 minutes for the others. Following parameters were calculated: mean, maximum and minimum daily values, daily standard deviations (σ), average daily anomalies (the daily mean value of each day minus the average of the daily mean value of that particular day in the other 5 years of the series), daily variations defined as (difference between the daily maximum and minimum values), +△ (difference between the maximum value of the day tth and the minimum value of the day (t-1)th) and△ (difference between the minimum value of the day tth and the maximum value of the day (t-1)th).

Statistical analysis

Clinicians hypothesized that SP patients were admitted in clusters (2, 4, 5, 6). In this study, a group of SP admissions was defined a cluster in accordance with a specific algorithm based on two "restrictive conditions" controlling the events aggregation or breakdown. For first restriction, only events separated by not more than 2 days between each other were considered as part of one cluster. For second restriction, clusters spreading over more than 4 consecutive days were subdivided into 2 or more clusters, in order to maintain the correlation of SP events with meteorological phenomena or with pollution events. Then, statistical analyses on the SP events time series, consisting on analyses of the distribution characteristics, spectral autocorrelation and spectral analysis, were carried out using MATLAB[1] with the aim to demonstrate the non-randomness of the admissions with the time. The clusterization of admissions suggested that meteorological or pollution conditions could play an important role in enhancing the SP development. Thus, those conditions were considered as independent samples, and analyzed using parametric (t-Student) and non-parametric (Kolmogorov-Smirnov and Wilcoxon) tests. Since there were not reasons to assume a causal relationship between the SP events, analyses using bivariate and multivariate regression techniques with software R[2] were performed. In this study, as the relationship between the data is non-linear, a method of generalized regression (GLM) was chosen, in which selected links were that of Poisson and Logistic one. The series of the daily mean, maximum and minimum values, daily σ, daily anomalies and△and ± △differences were analyzed with bivariate regression for each meteo-chemical parameter. The pairs of independent-dependent variables correlated were evaluated for the complete time series and for reduced series of cluster centroid-day, series of clustered days, and amended dichotomous series (containing only 0 and 1 values: "1" corresponding to the days with admissions, with the elimination of the single daily admissions, isolated in time, "0" corresponding to the days without admissions not occurring before or after an admission). The regression coefficients for each regression were considered significantly different from zero if there was a non-linear relationship between the response variable and the regressor, verified using a z-test under the hypothesis $\beta=0$ (regression coefficient equal to zero). Moreover, the model provided also the p-value of the regression and its degree of significance. To compare results of the Logistic and Poisson models, the R^2_{adj} corrected coefficient of determination (defined as the proportion of total variation of the dependent variable, explained by the independent variable and corrected for the number of variables and the number of pairs of measured data) was used. The basic model of multiple regressions was similar to that of bivariate regression, the only difference being in the number of predictor variables included in the model. The statistical analysis allowed assessing whether and how much the predictor variables of the model were able to estimate SP admissions. The meteo-chemical variables and the time series were the same used in the bivariate analysis. The regression coefficients were evaluated and their significance was assessed through a z-test; the adequacy of the regression model was established through the Akaike Information Criterion (AIC).

Results

Seasonal analysis and SP occurrence

There were 363 non-null events (days with SP admissions), with a maximum of 6 events in 4 different days. The events tended to

[1] *MATLAB ® is a high-level language and interactive environment that enables you to perform computationally intensive tasks faster than with traditional programming languages such as C, C++, and Fortran. http://www.mathworks.com/products/matlab/description1.html.*

[2] *R is a free software environment for statistical computing and graphics. It compiles and runs on a wide variety of UNIX platforms, Windows and MacOS. http://www.r-project.org/.*

group in the years 2003, 2004 and 2005. The summer showed the lowest number of events, while in the other seasons the events had approximately the same frequency. The monthly distribution of the events showed minima in July and November, and maxima in October and April. Thus, in this study, SP did not appear to be linked to specific monthly, seasonal and annual periodicities, as also founded by Bulajich B et al (4), Smit HJ et al and Alifano M et al (5, 6); on the contrary, Suarez-Varel MM et al reported a significant increase in admissions in May and December, a fall in January, and a higher frequency of SP events in spring (2).

Analysis of the time series

Distribution of daily number of admissions was apparently similar to that of a Poisson distribution. The comparison of the frequencies of the SP event distribution and of those obtained with theoretical model of a Poisson distribution was evaluated with a χ^2 test, which demonstrated that frequencies of SP data did not fit with a Poisson distribution at the p = 0.01 significance level: the Poisson distribution possessed a fewer number of rare cases (number of daily events greater than 4) than the experimental series. Accordingly, these results seemed to demonstrate that series of SP events was not random. The temporal autocorrelation was studied by creating new series, in which a time lag was set varying from 1 to 100 days, which were compared with the original one. Coefficients of the Autocorrelation Function (ACF) were studied as function of time lags, taking into account the upper and lower values of confidence interval (Fig 1). All autocorrelation coefficients but one resulted significantly equal to zero (at the confidence level p = 0.01), and only that corresponding to a time lag of 5 days was significant. Therefore, this analysis suggested that there was a certain probability that two days with SP events are related to each other if they occurred within 5 days. This result was confirmed by spectral analysis, in which the power spectrum of sequence of data was estimated using the method of the non-parametric periodogram. The significance of the various peaks was tested by comparing each value of the spectral density with the spectra of white and red noise, the significant (at the level p 0.001) peaks corresponding to 2, 5 and 64 days (Fig 2). Through the method of cluster analysis, effective clustering of most of SP events was verified: considering a range between 2 subsequent admissions of 2 or more days, the 81% of the days with SP admissions was clusterized. Increasing this range to 3 days, the percentage of clusterization increased to 85% (88%) (4). Applying the same technique to series with a Poisson distribution and to synthetic series obtained by making a temporal rearrangement of SP events, the clustering percentages obtained were lower than those of the actual series; a test on the difference between a couple of distributions at the significant level of p = 0.01 confirmed that series of SP events was not similar to that of a Poisson distribution, and that the SP events were not distributed randomly.

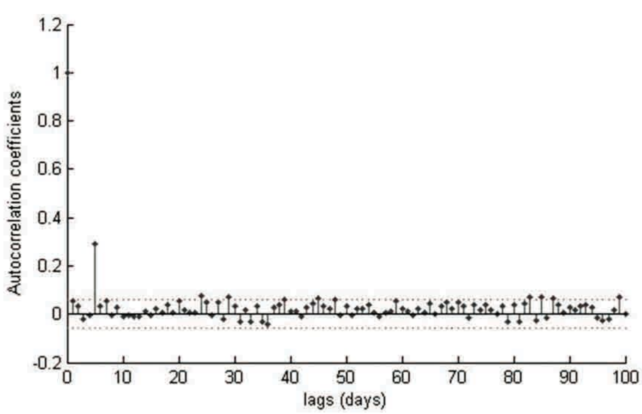

Fig.1 Autocorrelation plot. Coefficients of the Autocorrelation Function were studied as function of time lags, taking into account the upper and lower values of confidence interval. All autocorrelation coefficients but one resulted significantly equal to zero (at the confidence level p = 0.01), and only that corresponding to a time lag of 5 days was significant.

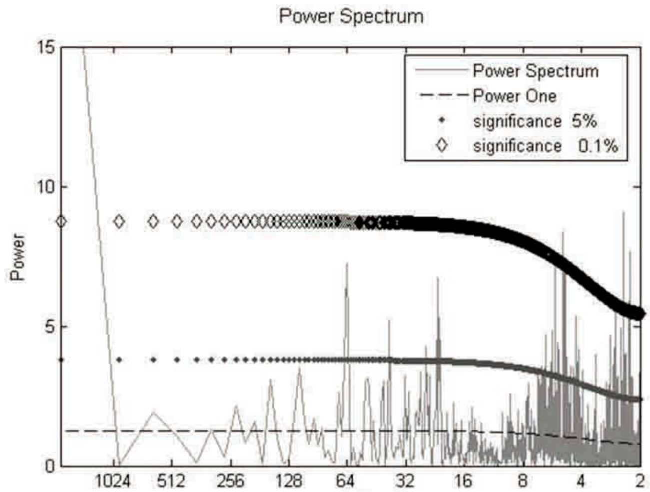

Fig.2 Power Spectrum with significance levels p =0.05 and p =0.001. These significances are relative to the power spectrum of a random dataset (assuming Gaussian "red noise").

Meteo-chemical features of pneumothorax and non-pneumothorax days

For each meteo-chemical variable, the contributions referred to SP days and non-SP days were considered separately. SP and non-SP series were constructed with the help of a dichotomous modified series, in order to clean up the series by removing SP cases that could be affected by non-SP cases, and vice versa. Concerning the meteorological parameters, the following series of SP and non-SP resulted significantly different at the level of confidence p = 0.05: △U- (Wilcoxon test) and WS minimum (t-Student and Wilcoxon tests). At p = 0.01 confidence level, all couples of series resulted significantly equal. Series of pollutant concentrations were analyzed in the same way, showing that, at p = 0.05 confidence level, the following series of SP and non-SP resulted significantly different: CO minimum and NO_2 minimum (t-Student and Wilcoxon tests), △and σ of C_6H_6 (Kolmogorov-Smirnov and Wilcoxon tests), and O_3 minimum (Wilcoxon test).

Bivariate and multivariate regression analysis

The non-linear bivariate regression showed many coefficients significantly different from zero, particularly for atmospheric pollutants and for the complete and the dichotomous modified series. The non-linear model showing the greatest value of R^2_{adj} corrected was the logistic one. Significant predictors of meteorological variables according to logistic model were (Table 1): at confidence level p = 0.01, daily WS minimum (complete and dichotomous modified series); at confidence level p = 0.05, P maximum (dichotomous modified series), daily anomalies of T (dichotomous modified series) and △-U (dichotomous modified series). Thus, although some authors argued that sudden changes in pressure can be an important cause for occurrence of SP (Scott GT et al reported that only one patient with SP out of 4 in their series was exposed to significant pressure variations in the 4 days prior to admission in hospital (1)), in this study, correlation between pressure variations and SP was not substantiated, indicating that probably there are other causative factors leading to a SP event[3]. Moreover, in this setting, relative humidity and temperature were not clearly linked to SP events, contradicting findings by Bulajich B et al and Smit HJ et al showing a slight temperature increase in the days preceding the admissions[4] (4, 5). Significant predictors of atmospheric pollutants according to logistic model were (Table 1): daily NO2 minimum (full and dichotomous modified series) at p = 0.001 confidence level, daily σ and △NO_2, CO_2 daily maximum and minimum, O_3 daily minimum (dichotomous modified series), daily mean CO_2 (complete series) at p = 0.01 confidence level, and daily and mean NO_2 (complete series) at p = 0.05 confidence level. The study of Celenza A et al outlined the correlation between thunderstorms and asthma exacerbations (9). Since asthma and SP are characterized by similar inflammatory broncho-alveolar changes, it is possible that there could be similarities also between the factors triggering the respective episodes. In addition to viral infections and cigarettes smoke, already recognized to cause SP, other conditions, such as high concentration of pollutants or continued exposure to allergens, should be also taken into account. For this reason, in the present study a multiple regression analysis, taking into account meteorological and chemical (pollutants) variable together, was carried out. Logistic model provided best results (according with AIC criterion). By calculating regression between logistic variable (stepwise - regression) of SP admissions versus meteorological variables, the output of the model indicated as significant regressors the coefficient of daily minimum wind speed (p = 0.01) and temperature (p = 0.05). In addition, model yielded a positive coefficient in the first case and a negative one in the second. The same regression analyses were repeated considering the pollutants series. The highly significant predictors (p = 0.001) were the daily mean and maximum O_3 and the daily minimum NO_2 and, with a lesser significance (p = 0.01), the daily mean PM10 and the NO daily maximum and minimum. At confidence level of p = 0.05, the coefficients related to the daily maximum PM10 and CO_2 and to daily σNO_2 were significant. As a further step, two models where the regressor variables were both meteorological and chemical (Table 2) was built. In the first, only the daily mean values, σ and anomalies were considered, whereas, in the second, daily maximum and minimum values were included. Regression analysis showed a relationship between number of SP admissions and increase of daily mean and minimum NO_2 (p = 0.001), decrease of σNO_2 (p = 0.01), decrease of daily mean, minimum O_3 (p = 0.01) and maximum NO (p = 0.001), and increase of daily σO_3 (p = 0.05). The maximum daily CO_2 concentration showed a significant and positive coefficient (p = 0.05). The daily decrement of σT (p = 0.01) and increment of daily σR (p = 0.05) were also significant. Finally, analysis also revealed that increment of WS anomalies and minima (p = 0.01) and decrease of its σ (p = 0.05) could contribute to SP onset.

Discussion

SP is a medical emergency and first aid intervention is rapid; for these reasons, this study took into account only the variables recorded one day before the pneumothorax occurrence, instead of assessing the performance of the variables in 3 - 4 previous days (as has been done in the study of Alifano M et al (6), Suarez-Varel MM et al and Bulajich B et al (2,4)). This approach, due to the short time for the breaking of the cellular structures, seems to be better. The analysis of monthly, seasonal and annual distributions had not found significant correlations between the insurgence of pneumothorax and specific time periods. The season with the low-

[3] *There is also another reason to support this finding: as atmospheric pressure decreases with the increasing quote (approximately 1 hPa every 10 m at the sea level), the typical daily pressure variations recorded in a place (1–2 hPa) are corresponding to quote variations of 10–20 m, which can be usually experienced by a person rising at the 3rd–6th floor of a building. And people living in hilly areas (some 200–300 m above urban areas) will experience pressure variations much higher than the typical meteorological variations. As there is not any evidence of an anomalous number of SP cases corresponding to people taking lifts or living in the hills, it is possible to deduce that pressure variations cannot be considered a relevant factor triggering a SP event.*

[4] *In common life, sometimes persons are exposed to abrupt temperature variations very high (entering in a place with strong air conditioning during summertime, or in a place heated during wintertime, or in a sauna) that exceed the usual temperature variations caused by meteorological factors, but there is not any evidence of an anomalous number of SP events correlated with the above mentioned temperature variations, which supports the conclusions that temperature variations does not influence SP events.*

er number of admissions was the summer, and the monthly distribution suggested a preponderance of admissions during October and December. Among the papers analyzed, that published by Suarez-Varel et al have reported a significant increase in admissions in May and December, and a fall in January (2); the seasonal analysis of this paper has also reported a higher frequency of pneumothorax events in the spring. On the contrary, other papers have not found significant differences in the seasonal and monthly distribution of admissions (4, 5, 6). A first clinical investigation revealed that the admissions tend to occur in clusters. These results are in agreement with previous analyses (2, 4, 5, 6). The fact that the admissions are clustered suggested the hypothesis that the meteorological conditions (or some related factors) could play an important role in the mechanism that leads to the development of pneumothorax. The results of the autocorrelation and spectral analyses had confirmed those obtained with the cluster analysis: the admissions tend to aggregate temporally. This behavior could be due to the hazard but, as there is not any reason to suppose this fact, an analysis had been performed to check the dependence from some meteorological and chemical variables. Some authors argue that sudden changes in pressure can be an important cause for the occurrence of pneumothorax. In this study, results that could provide a link be-

Table 1 Bivariate regression. The meteorological and pollutant data represent the independent variable while pneumothorax cases represent the dependent variable. Series: series of pneumothorax cases ('1' complete series, '2' series of the cluster centroids, '3' series of the clusterized days, '4' dichotomous modified series). Significance: significance level of regression coefficients (' ' p = 0.1, '.' p = 0.05, '*' p = 0.01, '**' p = 0.001, '***' p = 0). Sign: positive or negative sign of regression coefficients.

Variable	Series	Regression Logistic		Regression Poisson	
		Significance	Sign	Significance	Sign
P_{med}	(2)			.	+
P_{min}	(2)			.	+
P_{max}	(4)	.	-		
$P_{anomaly}$	(1)			.	+
T_{σ}	(1)			.	+
T_{anom}	(1)			.	+
T_{anom}	(4)	.	+	.	+
$\triangle T$	(1)			.	+
$\triangle U$	(1)			.	-
$\triangle U_{-}$	(1)			*	-
$\triangle U_{-}$	(4)	.	-	.	-
WS_{med}	(2)			.	+
WS_{min}	(1)	*	+	.	+
WS_{min}	(4)	*	+	.	+
WS_{anom}	(1)			.	+
NO_{2med}	(1)	.	+		
NO_{2min}	(1)	**	+	**	+
NO_{2min}	(4)	**	+	*	+
$NO_{2\sigma}$	(1)	*	-	***	-
$NO_{2\sigma}$	(4)	*	-	**	-
$\triangle NO_2$	(1)	.	-	**	-
$\triangle NO_2$	(4)	*	-	*	-
CO_{2med}	(1)	*	+		
CO_{2max}	(1)	*	+	.	+
CO_{2max}	(4)	*	+	.	+
CO_{2mi}	(1)	*	+	*	+
O_{2min}	(4)	*	+	.	+
O_{3max}	(2)			.	-
O_{3min}	(1)	*	-	*	-
O_{3min}	(4)	*	-	*	-
$O_{3\sigma}$	(1)			*	+
$O_{3\sigma}$	(2)			*	+
$\triangle O_3$	(1)			.	+
$\triangle O_3$	(2)			*	+

Abbreviations: pressure (P), temperature (T), relative humidity (U), average wind speed (WS).

Table 2 Multiple regression. The meteorological and pollutant data represent the independent variable while pneumothorax cases represent the dependent variable (complete series). Significance: significance level of regression coefficients (' ' p = 0.1, '.' p = 0.05, '*' p = 0.01, '**' p = 0.001, '***' p = 0). Sign: positive or negative sign of regression coefficients.

Variable	Regression Logistic		Regression Poisson	
	Significance	Sign	Significance	Sign
T_{max}			***	-
T_{min}			***	+
T_{σ}	*	-	**	-
T_{anom}			*	-
U_{min}			*	-
U_{anom}			.	-
R_{σ}	.	+	.	+
WS_{max}			.	-
WS_{min}			*	+
WS_{σ}	.	+	**	+
WS_{anom}	*	+	*	+
NO_{2med}	**	+	***	+
NO_{2max}			*	-
NO_{2min}	**	+	***	+
$NO_{2\sigma}$	*	-	***	-
NOmax	**	-		
$CO2_{max}$	.	+	*	+
$CO_{2\sigma}$			*	+
C_6H_{6min}			*	-
O_{3med}	*	-		
O_{3max}			***	+
O_{3min}	*	-	**	-
$O_{3\sigma}$	***	+	***	+

Abbreviations: pressure (P), temperature (T), relative humidity (U), average wind speed (WS).

tween the pneumothorax events and pressure variations had not been founded. It could be expected that the influence of significant atmospheric pressure variations could be more efficient in a period of long exposure, but the study of Scott GC et al reported that only one patient over 4 was exposed to significant pressure variations in the 4 days prior to the admission in hospital (1). This does not mean that a sudden change of atmospheric pressure does not lead to a pneumothorax event, but indicates that probably there are other factors, whose influence cannot be evinced with this kind of analyses. The temperature did not reveal clear links with the pneumothorax events: at the increasing of the events, there was been a decrease in daily anomalies and in the standard deviations (for the bivariate regression). In the study of Smith HJ et al (5), a slight increase in temperature has been observed in the days preceding the admissions, and also the study published by Bulajich B et al confirms this hypothesis (4). The relative humidity showed a small difference between the minimum of a day and the maximum of the previous day, both in the cases of pneumothorax and non-pneumothorax events, and the bivariate regression analysis had confirmed the existence of a relationship between the admissions and different sets of variables correlated to the humidity. In the study of Smith HJ et al (5), the correlation between the pneumothorax events and the occurrence of thunderstorms (when there are rapid variations of the meteorological variables) on the day preceding the admission has been shown. But, at a matter of fact, in this paper, the results have indicated that the only significant meteorological variable correlated with the pneumothorax onset is the minimum wind speed. Often the conclusions of the papers on pneumothorax occurrence were not homogeneous, and the comparisons between different approaches are difficult because the definitions of the assumptions are also different. Moreover, many studies involving few patients and generally involve countries with different climatic conditions. In the study of Celenza A et al, the correlation between thunderstorms and cases of asthma reinforcements has been reported (9). Because asthma, with respect to pneumothorax, is characterized by similar inflammation, it is possible that there could be similarities also between the factors that could trigger the crisis of pneumothorax and asthma. Although viral infections and smoke cigarettes are recognized as factors able to unleash the pneumothorax, also many other factors, including pollutants concentrations or exposures to allergic substances should be taken into account. The results of the mentioned study, with regard to atmospheric pollutants, has led to the same meteorological phases resulted unfavorable for the pneumothorax cases already reported in Bulajich B et al (4). As said before, asthma and pneumothorax share common patho-physiological mechanisms. For this reason, in the present study a multiple regression analysis, taking into account the meteorological and chemical (pollutants) variable together, was carried out.

Conclusions

Statistical analysis of the SP events collected at Turin, Italy, during 5 years showed that most of them were clusterized, supporting thus the idea that there could be a triggering factor enhancing the insurgence of SP. The series of SP events and meteo-chemical observations were thus analyzed using non-linear bivariate and multiple regressions. Occurrence of SP appears to be significantly facilitated by higher and less dispersed values of daily mean NO_2, by lower and more dispersed values of O_3, and by less dispersed temperature and wind speed values. Other correlations, as those with large CO_2 maxima and during cold and windy days, appeared less significant.

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