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Original Research Article

Impact of weather conditions on the results of patch tests in the Tunisian central region

Aïcha Brahem*, Souheil Chatti, Olfa El Maalel, Wided Boughattas, Faten Debbabi, Néjib Mrizak

Department of Occupational Medicine, Farhat Hached University Hospital – 4002 Sousse, Tunisia

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***Correspondence:**
Dr. Aïcha Brahem,
E-mail: brahemaicha@yahoo.fr

ABSTRACT

Background: Several factors can influence the results of patch-tests (PT) such as individual and external factors especially climate ones. The aim of the study was to study the impact of meteorological parameters on patch-tests results.
Methods: This is a retrospective epidemiological study which concerned all patients of the Tunisian center, who consulted in the Dermato-Allergology Unit of Occupational Medicine Department of Farhat Hached University Hospital-Sousse (Tunisia) over a period of 5 years. All patients were tested by the European Standard Battery allergens (BSE). The eight allergens, most frequently encountered during the study period, were analyzed.
Correlation and regression tests were used to calculate the relation of the patch-tests results with temperature and absolute humidity.
Results: During the study period, 5560 patch-tests were analyzed. The results of these patch- tests for most allergens were not significantly influenced by external weather conditions. However, the irritant reactions for cobalt and colophony increased with the cold and dry climate. Some positive reactions to thiuram mix, cobalt and nickel were more frequent with humidity.
Conclusions: The results of this current study support those of the literature. The majority of reactions to patch- tests didn't seem to be influenced by weather conditions.

Keywords: Dermatitis, Allergic contact, Patch tests, Weather, Allergens

INTRODUCTION

The patch test was first devised by Jadassohn in 1895 and described in practical detail by Bloch in 1929. The immunological basis of the patch test is the type IV (cell mediated or delayed) hypersensitivity reaction. It remains the only practical method presently available for assessing cell medicated allergy.[1-3]

However, the validity and the accuracy of these tests are limited. Indeed, several factors can influence the results of skin tests such as individual factors and external factors especially climate ones.[4]

Several studies have shown that the reactivity of skin tests can be affected by seasonal variations and weather conditions.[5-9]

In fact, the increase in skin irritability which is observed in cold or dry conditions reveals sensitivity of the skin to weather conditions.[8-11] Skin irritability can interfere with patch tests during winter, perhaps giving false positive reactions.

The governorates of Sousse and Monastir are two coastal cities of Tunisian center. They belong to the semiarid bioclimatic stage with mild winters where maritime influences are pretty much felt.

The average annual temperature is 19.1 ° C with a range of 1.3 ° C and 42.5 ° C.

The aim of this study is to determine the impact of weather physical parameters of our region on the results of patch- tests.

METHODS

This is a retrospective study focused on all patients in the regions of Sousse and Monastir tested for allergens of the European Standard Battery (ESB) over a period of 05 years [January 2010- December 2014]. The patients were recruited at the Dermato-Allergology Unit of Occupational Medicine Department of the University Hospital Farhat Hached of Sousse.

Clinical data were collected and documented using a questionnaire. The analysis of the respective sensitizations was based on test readings at D2 following ICDRG (International Contact Dermatitis Research Group) criteria.[12]

The eight allergens, most frequently encountered during the study period, including nickel sulfate, potassium dichromate, cobalt, Peru balsam, colophony, thiuram mix, paraben mix and formaldehyde in water, were analyzed.

Meteorological data were collected from the metrology station located at 14.47 Km from Sousse on the URL: www.wunderground.com. Daily mean values were considered to provide sufficient temporal resolution.

Processing of meteorological data

For each patient, we calculated the average daily temperatures of the day of the application of the PT, the previous two days and the following 2 days (AT). Then, we linked this value with the date of the laying of the PT. We did the same to calculate the average relative humidity (ARH).

Absolute humidity (AH) was calculated from temperature (T) and relative humidity (RH) using the following formula:

$$AH = (RH/100) \times SVP$$

SVP is the saturated vapor pressure average of the five days at a certain temperature T; it is derived from the following formula:[11]

$$SVP = C1 \times \exp(C2 \times T/(C3+T)$$

with C1, C2 and C3 three constants:

C1 = 6.11 (-50 ° C to 100 ° C)
C2 = 17.84 (-50 ° C to 0 ° C) or 17.08 (0 ° C to 100 ° C)
C3 = 245.43 (-50 ° C to 0 ° C) or 234.18 (0° C to 100° C)

The two physical variables (T and AH) were categorized into four levels of ordinal variables representing the respective quartile of the distribution. The ATs have been grouped into four intervals: $\leq$7.5, [7.5 to 15],]15 to 22] and >22 (°C) and The AHs in four ranges: $\leq$6.5, [6.5 to 11], [11 – 16] and >16 (mg/L).

For additional analysis, temperature and absolute humidity were also combined into a variable to have 16 theoretically possible values to address a possible interaction between the effects of T and AH and results of patch-test.[11]

Some combinations of temperature and humidity were not produced (this could be explained partly by the fact that a combination of high absolute humidity and a low temperature is not possible for physical reasons). Moreover, nine cells among sixteen will be considered.

Statistical analysis

Relative risk estimates for the results of PT associated with climate variables were calculated for the eight allergens of ESB. For the purpose of analysis several case-control studies were used. Readings of inconclusive reactions (+?), Irritant reactions (IR), weakly positive (+) and strongly positive reactions (++ / +++) were compared respectively with negative reactions (control group).

The results of PT of each considered allergen were used as dependent variable. Weather physical variables were used as independent variables. The highest levels of temperature, absolute humidity and the combination of both of them were respectively selected as the respective reference group. Confidence intervals were calculated by means of the profile likehood method.

A logistic regression analysis was conducted to examine the relationship between the different intervals of T, AH and those of the combined variable (T, AH) respectively, and the results of PT.

The T and AH were tested in separate models (marginally) in the four mentioned categories (+?, IR, +, ++ / +++). In addition, the nine relevant categories of cross T with AH were tested for each allergen in a combined variable. To examine the possible interaction effect between T and AH, each odds ratio (adjusted for age and gender) of a combination of variable T and AH was compared, respectively, with the two respective marginal odds ratio of T and the AH.

RESULTS

During the study period, 5560 patch-tests have been analyzed. The most frequent encountered allergens were cobalt, potassium dichromate and nickel sulphate.

The allergen which causes most strongly positive reactions ++/+++ was nickel sulfate (26%), followed by potassium dichromate (25%) and cobalt (10%). This order of allergens is reversed if the weakly reactions (+) were considered.

The allergen that gives the most irritant reactions was the cobalt (11% of total irritating reactions observed) and is also the first that generates inconclusive reactions (10.4% of total R +?), succeeded by lanolin and lactone mix (6.7% each).

Meteorological conditions considered in our study showed that temperature was ranged between 5° C and 36° C over the five years of our study. The coldest month was January with an average temperature of 11° C and the hottest month was the month of August with an average temperature of 28.5° C.

HA average over the five years was 14.87 mg/l with a range varying from 0.87 to 55.35 mg/l. The majority of tests were performed at moderate temperature and humidity in 50.6% and 49.5% of cases respectively.

The distribution of patch-tests according to the different temperature classes and absolute humidity is presented by Table 1. There was no statistically significant relationship between the different reactions to potassium dichromate and peru balsam with weather parameters.

Table 1: Distribution of patch–tests according to the different classes of temperature and absolute humidity.

Temperature (°C)	Absolute humidity (mg/L)				Total
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	504	-	-	-	504
[7.5–15]	1344	-	-	-	1344
[15–22]	304	1136	32	-	1472
>22	24	344	1240	632	2240
Total	2176	1480	1272	632	5560

Table 2: Odds ratio for ++/+++ reactions to thiuram mix associated with the different exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.15 (0.02 – 1.34)	-	-	-	0.26 (0.07 – 0.88)
[7.5–15]	0.52 (0.06 – 4.73)	-	-	-	0.88 (0.24 – 3.17)
[15–22]	0.49 (0.03 – 8.00)	0.36 (0.04 - 3.12)	-	-	0.65 (0.21 – 2.06)
>22	-	0.55 (0.03 – 9.06)	0.49 (0.05 – 4.43)	1.00 (réf)	-
Marginal estimation: absolute humidity	0.34 (0.04– 2.67)	0.39 (0.04 – 3.30)	0.50 (0.05 – 4.52)	-	1.00 (réf)

Table 3: Odds ratios for (+?/IR) reaction to cobalt associated with the different exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.37 (0.03 – 4. 18)	-	-	-	0.42 (0.07 – 2.36)
[7.5–15]	0.18 (0.02 – 1.47)	-	-	-	0.21 (0.06 – 0.68)
[15–22]	0.39 (0.02 – 6.56)	0.15 (0.02 – 1.18)		-	0.20 (0.06 – 0.64)
>22			0.65 (0.06 – 6.34)	1.00 (réf)	
Marginal estimation: absolute humidity	0.23 (0.03 – 1.81)	0.20 (0.02 – 1.59)	0.66 (0.06 – 6.52)		1.00 (réf)

Concerning, the thiuram mix, marginal evaluations have shown that strongly positive reactions (++/+++) were increased with AH (Table 2). However, the irritant and inconclusive reactions to cobalt were appeared to increase with low temperatures (Table 3).

Marginal estimation of absolute humidity showed that the strongly positive reactions (++ / +++) to cobalt were the most frequent as the weather is humid (Table 4).

The various reactions (strongly and weakly positive) to colophony were not influenced by the different considered weather factors (T° and AH). However irritant and inconclusive reactions to colophony increased with the dry climate (Table 5).

The strongly and weakly positive reactions to paraben mix occurred three times during the dry climate. Concerning inconclusive and irritant reactions to paraben

mix, the only association was seen with the temperature and the combined variable (T/AH) (Table 6).

Table 4: Odds ratios for (++/+++) reactions to cobalt associated with the different exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.29 (0.05 – 1. 58)	-	-	-	0.42 (0.14 – 1.28)
[7.5–15]	0.31 (0.07 – 1.41)	-	-	-	0.44 (0.18 – 1.04)
[15–22]	0.26 (0.04 – 1.67)	0.29 (0.06 – 1.39)	-	-	0.42 (0.18 – 0.99)
>22	-	1.04 (0.09 – 11.85)	0.55 (0.11 – 2.74)	1.00 (réf)	-
Marginal estimation: absolute humidity	0.30 (0.07– 1.33)	0.36 (0.08 - 1.68)	0.57 (0.11 – 2.82)	-	1.00 (réf)

Table 5: Odds ratios for (+?/IR) reactions to colophony in relation with the different exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.41 (0.04 – 4. 67)	-	-	-	0.58 (0.11 – 3.05)
[7.5–15]	2.12 (0.13 – 34.35)	-	-	-	2.96 (0.34 – 25.62)
[15–22]	0.49 (0.03 – 8.11)	0.59 (0.06 – 5.83)	0.04 (0.00 – 0.80)	-	0.65 (0.18 – 2.27)
>22	-	-	0.49 (0.05 – 4.46)	1.00 (réf)	
Marginal estimation : absolute humidity	0.87 (0.09– 7.90)	0.78 (0.08 – 7.68)	0.40 (0.04 – 3.48)	-	1.00 (réf)

Table 6: Odds ratios for (+?/IR) reactions to paraben mix associated with the different exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	1.27 (0. 20 – 7.85)	-	-	-	0.81 (0.16 – 4.02)
[7.5–15]	1.33 (0.31 – 5.73)	-	-	-	0.85 (0.27 – 2.74)
[15–22]	-	1.40 (0.30 – 6.45)	-	-	1.17 (0.34 – 4.07)
>22	-	-	1.52 (0.33 – 6.97)	1.00 (réf)	-
Marginal estimation: absolute humidity	1.55 (0.39 – 6.16)	1.83 (0.40 – 8.40)	1.56 (0.34 – 7.16)	-	1.00 (réf)

The strongly and weakly positive reactions to paraben mix occurred three times during the dry climate. Concerning inconclusive and irritant reactions to paraben mix, the only association was seen with the temperature and the combined variable (T/AH) (Table 6).

The strongly positive reactions to formaldehyde (+++/++) did not follow a logical pattern with climate parameters. However, the weakly positive reactions were more frequent as the climate was drier. Inconclusive and irritant reactions occurred more when the weather is warmer (Table 7).

Table 7: Odds ratios for (+?/IR) reactions to formaldehyde.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.40 (0. 03 – 4.55)	-	-	-	0.44 (0.08 – 2.48)
[7.5–15]	1.11 (0.09 – 12.45)	-	-	-	1.22 (0.22 – 6.77)
[15–22]	0.47 (0.03 – 7.77)			-	2.60 (0.29 – 23.51)
>22	-	-	0.66 (0.07 – 6.52)	1.00 (réf)	-
Marginal estimation: absolute humidity	0.71 (0.08 – 6.16)	-	0.67 (0.07 – 6.61)	-	1.00 (réf)

Table 8: Odds ratios for (++/+++) reactions to nickel associated with the various exposure classes.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.44 (0. 16 – 1.22)	-	-	-	0.51 (0.24 – 1.10)
[7.5–15]	0.46 (0.19 – 1.11)	-	-	-	0.54 (0.31 – 0.94)
[15–22]	0.33 (0.11 – 0.97)	0.42 (0.17 – 1.03)	-	-	0.48 (0.28 – 0.82)
>22	0.10 (0.01 – 1.83)	1.37 (0.33 –5.61)	0.7 (0.30 – 1.89)	1.00 (réf)	-
Marginal estimation: absolute humidity	0.42 (0.18 – 0.98)	0.52 (0.22 – 1.24)	0.78 (0.31 – 1.95)	-	1.00 (réf)

Table 9: odds ratios for (IR/+?) to nickel associated with the weather parameters.

Temperature (°C)	Absolute humidity (mg/l)				Marginal estimation: temperature
	≤6.5	[6.5–11]	[11–16]	>16	
≤7.5	0.51 (0. 11 – 2.42)	-	-	-	0.34 (0.09 – 1.21)
[7.5–15]	1.14 (0. 26 – 4.94)	-	-	-	0.75 (0.23 – 2.43)
[15–22]		1. 65 (0.32 – 8.39)		-	1.40 (0.36 – 5.51)
>22	0.44 (0.01 – 0.89)		1.94 (0.38 – 9.87)	1.00 (réf)	
Marginal estimation: absolute humidity	0.91 (0.24 – 3.41)	2.23 (0.44 – 11.36)	2.00 (0.39– 10.17)		1.00 (réf)

Marginal estimations have shown that the probability of strongly positive reactions to nickel increased with absolute humidity as shown in Tables 8 and 9. Concerning the weakly, inconclusive and irritant reactions to Nickel, they increased with hot and humid climate.

DISCUSSION

In order to highlight the effect of climate on the results of PT, we have chosen to consider the average of temperature and absolute humidity during 5 days (the day of the application of the PT. 2 days before and 2 days after) by analogy to the Uter et al study.[13]

Similarly to other studies, absolute humidity (AH) has been preferred to relative humidity (RH), to analyze the association with skin irritation.[10,14]

The possibility of insufficient spatial resolution of weather stations in relation to the sites where participants worked, lived and were examined was assessed. Moreover, this study did not take into account the extent of outdoor activities and exposure to air conditioning that could change the climate for the individual.[15]

Besides, another limit of our study was the small sample size which can impact the productivity of results. The influence of climate on PT results is controversial. Some studies have shown an association between climate and responsiveness of patch- tests, with increased reactivity during cold seasons and its decrease during the warmer seasons.[5,6]

The mechanism by which low humidity and low temperature contribute to irritant damage of the skin is less well understood. Previous investigations have shown an association between skin chapping, extensibility, of isolated stratum corneum, resistance to tearing and temperature and/or humidity, respectively.[11] However, other studies have found no effect of climate on the results of the PT.[17,18]

The results of this study showed that, in the case of potassium dichromate, peru balsam and colophony, different types of allergic reactions weak or strong were not influenced by different temperature classes, absolute humidity or the combined variable (t°, AH).

Similarly to other studies carried out in Austria. Denmark. Greece. Belgium and Germany in which there was no statistically significant associations between the results of PT and weather factors.[7,16,18] The results of the PT are relatively stable for most allergens under the weather conditions of Central Europe. at least for strongly or weakly positive results.[13]

In the study of Hägewald, most examined occupational allergens revealed no correlation between weather conditions and allergic and irritant reactions to patch tests, including allergens from the family of plastics (epoxy resin, colophony, resin-formaldehyde), and the vulcanization accelerators and rubber additives.[19]

In this present study, there was an increase in irritant and inconclusive reactions to cobalt in cold climate and colophony in dry climate. The weakly positive reactions increased with the dry climate for the paraben mix and formaldehyde. These results may be explained by a probable relationship between dry / cold air and irritative reactions to patch testing.[15]

Indeed, Uter et al showed that cold and dry weather reveals the subjective signs of irritation: itching, feeling of tension and dryness, and burning sensation.[11]

In the study of Hägewald on 61435 patients (1993-2001), irritant and inconclusive reactions increased during cold and arid conditions for potassium dichromate, nickel and cobalt as well as weakly positive reactions to the last two allergens.[20] The weakly positive reactions could be attributed to the fact that some allergens are simultaneously marginal irritants and contact allergens.[15]

Similarly, Uter et al noted that the reactions irritant and inconclusive reactions were observed more frequently in dry and cold conditions for a lot of allergens.[13] This can be partly explained by the fact that the epidermal barrier function, weakened under these environmental conditions, makes the skin more susceptible to the irritating effect that can have more allergens in the conditions of PT. This was more marked for the inconclusive reactions to formaldehyde and Kathon CG. Allergen preparations based on water are most affected by climate change than those based on paraffin.[13]

Paraffin seems to protect the epidermal barrier function against the dry and cold weather. This finding seems to be consistent with the study of Hägewald.[20]

Recently, the effect of the season on epidermal lipids which is essential for the homeostasis of the barrier has been demonstrated: fatty acids of the stratum corneum, the levels of ceramide and cholesterol were significantly lower in winter especially at the exposed areas.[21] This has the effect of weakening the epidermal barrier function and increasing the irritability of the skin during cold dry season.

Volunteers have set their hands to cold and dry wind for three hours daily. They found visible alterations (erythema, fine cracks, peeling), a decrease of the surface lipids and enzymes and a decrease in skin elasticity after 4 to 5 days.[22]

It was noted that the characteristics of the skin vary with humidity. The severity of skin disorders increases in winter, and low humidity is implicated in this problem.[23] The skin moisturizing can protect against the aggressive weather conditions.[24]

The penetration of antigens across the epidermal stratum corneum is increased in a low relative humidity in relation with a barrier function alteration.[25]

In this study, inconclusive reactions to formaldehyde and nickel increased with warm weather. Indeed, it was shown that high temperature can be irritant for skin.[26] In the present study, strongly positive reactions to cobalt, nickel and thiuram mix increased with moisture, unlike weakly and strongly positive reactions to paraben mix that increased in dry climate.

Grunewald et al have shown that the major cause of occupational dermatitis is working in a damp place that generates alkalinization of the skin which is responsible for an exhaustion of the buffer system.[27]

Hosoi et al demonstrated experimentally that hypersensitivity contact reactions in a mouse model were remarkable during sensitization and elicitation phases, during low relative humidity (10%).[28] These reactions are probably related to the increase of the epidermal Langerhans cells according Prosch and Brasch, as well as to the increase of IL-12 and IgG by Ashida et al.[29,30] Furthermore, the loss of trans-epidermal water is reduced during these weather conditions. The potential variability of patch tests may be due to irritation, changes in skin barrier function, or to changes in immunological function caused by weather changes.[30]

CONCLUSION

An overall some irritative and inconclusive reactions increased with cold and dry climate. Some highly positive reactions are more common with moisture. For the most part, patch testing for most ESB allergens are not significantly influenced by external conditions during the test. Thus the validity of patch testing does not largely seem to be compromised by ambient meteorological conditions.

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