Clin Exp Allergy 2002; **32**:928–932

A double-blind, placebo-controlled study on the diagnostic accuracy of an electrodermal test in allergic subjects

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Summary

Background Many unconventional diagnostic procedures based on bioelectrical skin responses are presently widely used for allergic diseases, but rigorous experimental evaluations of their accuracy are still lacking.

Aim We assessed whether an electrodermal device can correctly diagnose respiratory allergy.

Methods The diagnostic accuracy of the electrodermal device was assessed in double-blind fashion in 72 allergic patients and 28 healthy volunteers. A random sequence of substances in sealed vials, including histamine, allergens, immunoglobulins at various dilutions and physiological saline, were tested in duplicate in each subject.

Results A wide variability of the measurements was found in most patients irrespective of their allergy status and of the substance tested. Allergic patients showed more negative skin electrical response at the second trial, compared to normal controls, independent of the tested substance. No significant difference in skin electrical response between allergens and negative controls could be detected.

Conclusion We conclude that the studied bioelectrical method, under blind testing, cannot correctly detect respiratory allergy.

Keywords allergy diagnosis, electrodermal test, unconventional medicine

Submitted 26 September 2001; revised 22 November 2001; accepted 26 January 2002

Introduction

At present, the diagnosis of IgE-mediated diseases relies on a number of standardized and validated procedures, including skin testing, RAST assay and allergen-specific challenge. Nevertheless, during the last 10 years many unconventional diagnostic procedures have been proposed and increasingly used [1, 2]. Those procedures based on electrical skin responses are probably the most common unconventional tests used to diagnose allergies. However, scientifically based research to support the efficacy of these procedures is still lacking.

Electrodermal tests are based on the hypothesis that the offending allergens can evoke measurable variations of the cutaneous electric potential at specific acupuncture points, which have a high electrical conductance [3–5]. Altered skin potentials at acupuncture points would indicate an 'electromagnetic perturbation' transferred by untolerated substances (even in sealed vials) to the patient. It is also claimed that electrodermal tests would be able to detect the effects or 'perturbations' induced on skin potentials by homeopathic remedies and preparations [4–7]. A variety of electrodermal devices (Dermatron®, DRIA®, Vega®) are commercialized and used [8–10].

The electrodermal method studied herein derives from the electroacupuncture according to Voll (EAV) and the classic German Vega Test [11,12]. The patient is included in an electric circuit crossed by a very low current. The current is supposed to be modulated by electromagnetic frequencies typical of the tested substances and therefore it would be possible to diagnose the effect of an 'incompatible' substance by measuring electrodermal changes. The perturbation of skin electric potentials does not require a direct contact, as it is evoked by a process of electromagnetic resonance. Therefore the measurement of skin potentials is non-invasive and does not expose the subject directly to sensitizing substances. Nevertheless, few rigorous scientific data are so far available to validate the procedure [13–15].

The aim of the present trial was to assess whether the electrodermal device (DBE204, Tekav S.r.l., Rovigo, Italy) is able to diagnose the presence of respiratory allergy in comparison with conventional procedures. The method was tested in double-blind fashion in both allergic and healthy subjects, using commercial allergenic extracts, histamine and physiological saline. According to the indications of the inventors of the device, the machine would be able to detect also the electrical perturbations induced by homeopathic preparations and inflammatory mediators. For this reason, homeopathic dilutions of the allergens IL-4, IgE and other classes of Ig have been included in the panel of tested substances.

Patients and methods

Study design

The electrodermal instrument was used in allergic and non-allergic subjects to assess whether it is capable of diagnosing

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allergy and of detecting the effect of homeopathic preparations. Allergens, histamine, immunoglobulins in different concentrations (some homeopathic) and a negative control (physiological saline) were tested in duplicate and in double-blind fashion in each subject. The homeopathic solutions employed in this study have been indicated by the manufacturer and by expert operators belonging to the team of Dr H. W. Schimmel, the inventor of the Vega test. The sequence of the substances tested (Table 1) was the same for each of the duplicate tests, but it was changed randomly from one subject to another. The same investigator performed all tests in the same room under the same conditions.

Patients

The study included 100 patients. Seventy-two patients (39 female and 33 male, mean age 31.2 years, range 10 to 68) were suffering from allergic rhinitis and/or asthma, diagnosed according to international guidelines [16,17]. Their disease had lasted for at least 2 years and they had positive skin tests (mean wheal diameter 3 mm or more) and RAST (class II or higher) to one or more of the following allergens: Parietaria, grasses, cat dander, birch and mites. The remaining 28 subjects (20 female, 8 male, mean age 42.1 years, range 17 to 0), were healthy and had negative skin test and RAST. None of the patients suffered from skin disorders. Pregnant women or patients suffering from systemic immunological, metabolic or heart diseases were not admitted. All participants signed an informed consent at the enrolment.

Measurement of skin electrical response

The device DBE204 (Tekav S.r.l) measures the skin conductivity at acupuncture points. One of the two silver-plate electrodes is a cylinder with a large surface (about 50 cm^2) and has to be kept by the subject in his hand; the other electrode has a small contact area of about 10 mm^2 and delivers the current. While the subject holds the cylindrical electrode in the dominant hand, the operator delivers a direct current of 8 to 11 μA (approximately 1 V), for about 1 s by applying the stylus electrode with a slight pressure (100 to 150 g) at the chosen skin point. The body impedance between the skin point and the hand electrode is then measured; the value is shown on an arbitrary scale reading from 0 to 100 units. As there is a great variability of skin conductivity between individuals, due to a number of factors (skin thickness, humidity, blood flux), the instrument is calibrated before each series of measurements in each patient in a way that the index is set at approximately 80% of full scale. The setting-up procedure was recommended by the producers of the device and it is identically performed in routine clinical practice, except for blinding of the operator and the presence of an assistant.

Table 1. Substances tested in the trial

Vials*	Substance	Dilution† and manufacturer
1–4	*Parietaria* pollen	10.000 U/mL (Bayer) D6, D12, D30 (Boiron)
5–9	Grass pollen	10.000 U/mL (Bayer) D6, D12, D30, D200 (Boiron)
10–13	Birch pollen	10.000 U/mL (Bayer) D6, D12, D30 (Boiron)
14–18	*Dermatoph. Pter.*	10.000 U/mL (Bayer) D6, D12, D30, D200 (Staufen)
19–23	Cat dander	10.000 U/mL (Bayer) D6, D12, D30, D100 (Boiron)
24	IgA	D6 (Staufen)
25–26	IgG	D6, D30 (Staufen)
27–28	IgM	D6, D30 (Staufen)
29–32	IgE	D6, D30, D60, D200 (Staufen)
33–35	Histamine	1% (Bayer) D8, D200 (Staufen)
36	IL-4	D12 (Guna)
37–41	Physiological saline	

*The number of the vials in the table is for convenience and does not correspond to the random code assigned. †D stands for homoeopathic dilutions (serial 1/10 w/v dilutions and succession of starting material).

The vials containing the substances to be tested are put in a vial-holder, electrically connected to the hand electrode. After calibration, a measurement of skin conductivity index, in the absence of test vials, is performed in triplicate at the beginning of each one of the two series of measurements and the mean value of three consecutive measurements is taken as the reference baseline value. If the baseline value is < 75 or > 85, the calibration procedure is repeated. Skin conductivity is then measured in sequence for each of the substances placed in the vial-holder. A positive response is a decrease from the baseline measurement: the stronger the response, the lower the reading. The skin electrical response (SER) is defined as the difference of skin conductivity index between the measurement carried out with the test vial inserted into the vial-holder and the reference baseline value. Therefore, a positive reaction to the test is expected to give negative values of SER in this test.

Trial procedure

The operator was an experienced acupuncturist physician, who had attended a specific 1-year course for the use of the instrument, and had used the DBE204 device in her private practice for further 2 years under an expert's supervision.

Forty-one opaque vials, containing different substances at different dilutions (as detailed in Table 1), were coded and numbered by an independent investigator. Prior to beginning each test on each subject, the vials were mixed according to a computer-generated random sequence. The operator (who performed the measurement), the assistant (who inserted the sequence of vials into the device) and the patient were blinded to the content of the vials. Moreover, both the tester and the assistant did not know whether the subject was allergic or not. The tested skin point was the lateral side of the fifth finger. Testing of SER with the 41 vials was performed in duplicate in each patient, with the same sequence of vials. The two measurements were separated by a 5-min interval, during which the patient stayed out of the testing room and washed her/his hands without soap. During the test, patients did not wear battery-powered watches, and no electronic device was functioning in the room. Fluorescent bulbs lightened the room. At the end of the study the code was broken and the results were evaluated statistically.

Statistical analysis

The Mann–Whitney rank sum test was used for analysis of non-parametrically distributed data. The statistical analysis was performed using a computer program (SigmaStat 2.0, SPSS). Data were expressed as mean ± SD. $P < 0.05$ was considered statistically significant.

Results

We observed a high variability between individuals: some subjects gave consistently stable measurements with little variation (1 to 3 scale units), while others produced highly dispersed measurements, with oscillations up to 5 to 10 scale units. Figure 1 shows three examples of sequences of measurements from a 'stable' subject, from a very 'unstable' subject and from an intermediate case, respectively. The variability of the measurements was an intrinsic characteristic of the subject, as subjects who gave unstable values in the first trial did the same in the second trial. However, there was no reproducibility of observations with the same stimulus in the same individual. In general, we observed that during measurement trial, the index of conductivity showed a decreasing trend, so that SER tended to have more negative value, independent of the type of vial that was inserted into the circuit. By looking at individual sequences of measurements, it was impossible to distinguish allergic patients from controls. The only evidence was that the decrease of conductivity was remarkable in many allergic patients during the second trial.

There was no relation between skin conductivity changes and the type of substance contained in the vial, because either sudden decrease or increase of SER was observed both when physiological saline or allergens to which patients were sensitized were inserted into the machine. Due to the great number of data and the high variance of measurements, statistical analysis was possible only on the mean values of the two groups of subjects. For simplicity and in order to increase the number of tests, the reactions to the same substance have been grouped irrespective of the concentration/dilution. Table 2 reports the mean value $\pm$ SD of the SER of the two subject populations to the indicated compounds as assessed by DBE204 in two separate trials. Prick + and Prick – indicate the presence or absence of allergy. Table 2(a) shows that in allergic patients all the tested vials but histamine yielded slightly negative values, but the differences were not significant with respect to physiological saline, probably because the measurements were quite variable, as shown by high SD values. In Table 2(b), reporting the data of the second trial, all the values were more negative than in the first trial, but also in this case the variation between measurements was high and the differences were not significant with

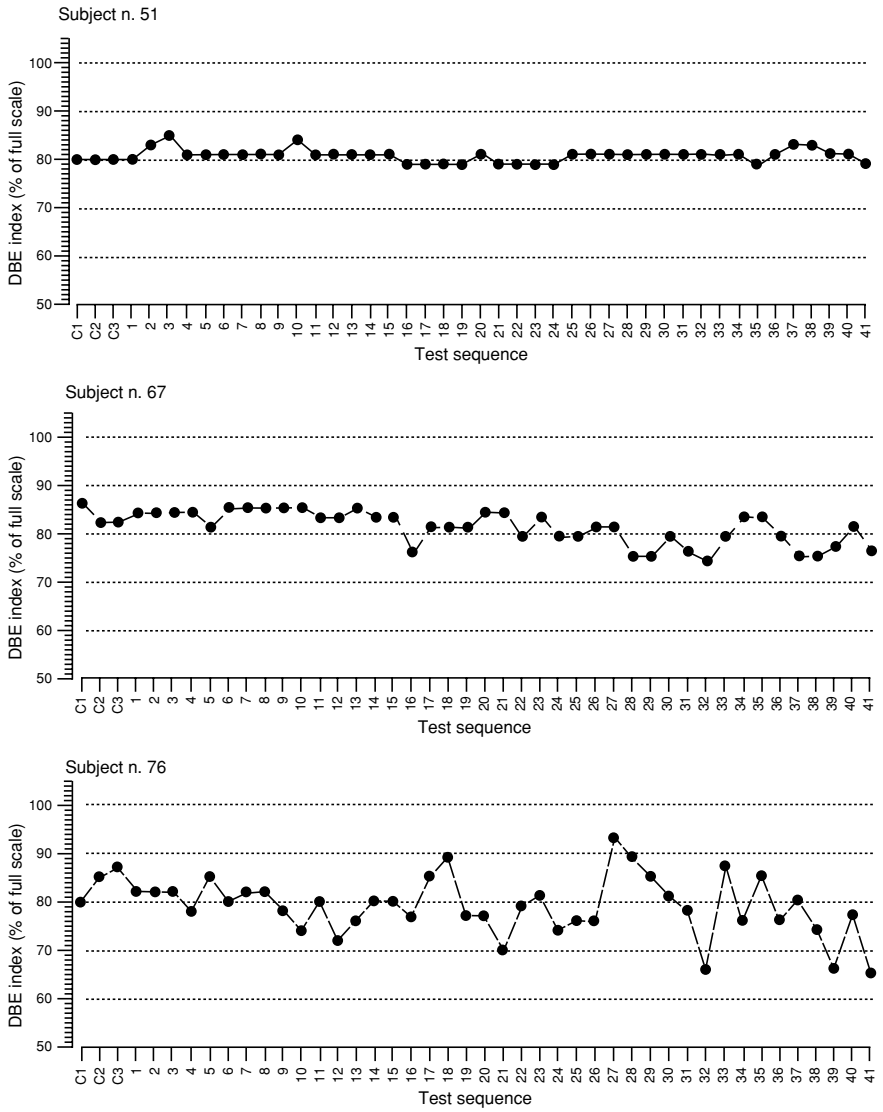

Fig. 1. Three sequences of electrodermal testing in allergic patients. Vials with the compounds indicated in 'Methods' section are randomly inserted into the vial-holder and skin electrical conductivity is immediately recorded.

Table 2. Skin electric responses of allergic patients and controls to indicated compounds

	Saline	Prick+	Prick−	Histamine	IgG	IgM	IgA	IgE	IL-4
2a. Allergic patients first trial									
Mean	−0.24	−0.39	−0.29	0.02	−0.32	−0.47	−0.90	−0.51	0.36
SD	4.40	4.41	4.19	4.50	5.09	5.33	7.12	4.41	3.95
P (vs. saline)	–	0.82	0.98	0.81	0.64	0.49	0.88	0.81	0.69
P (Prick ±)		0.74							
2b. Allergic patients second trial									
Mean	−3.31	−2.58	−3.05	−2.93	−3.14	−2.95	−4.22	−3.08	−4.07
SD	4.25	4.10	4.50	5.58	5.09	5.33	6.97	5.08	6.87
P (vs. saline)	–	0.63	0.74	0.35	0.70	0.36	0.61	0.69	0.80
P (Prick ±)		0.60							
P (2A/2B)	< 0.001								
2c. Control subjects first trial									
Mean	−1.91	–	−1.89	−2.68	−1.36	−2.66	−2.82	−2.67	−2.39
SD	4.68	–	4.91	5.68	6.04	5.47	7.36	5.40	6.16
P (vs. saline)	–	–	0.89	0.46	0.85	0.48	0.84	0.58	0.65
2d. Control subjects second trial									
Mean	−1.66	–	−2.14	−2.52	−2.34	−2.13	−4.29	−2.46	−3.11
SD	6.25	–	5.22	5.10	5.44	4.80	8.54	5.05	8.02
P (vs. saline)	–	–	0.74	0.89	0.49	0.97	0.17	0.68	0.70
P (2C/2D)	0.89								

respect to the mean value of physiological saline. The difference between the first and second trial was highly significant in all tested vials (only the *P*-value of physiological saline is reported). Table 2(c) shows that also in the control group the measurements of skin conductivity were slightly reduced with all the test vials, without any significant difference with respect to physiological saline. Also in the control group, high variance of measurements was noted using all test vials. The second trial in the control group gave results very similar to the first one (Table 2d). A separate analysis was carried out on the three different concentrations/dilutions of histamine, but also in this case no significant differences were found with respect to the mean value of physiological saline.

Discussion

Electrodermal instruments have been widely used throughout the world for at least 40 years and they are presently manufactured in many countries, including Germany, Japan, China, France, Russia, Korea, the United States of America and Italy [1]. Many non-health professionals and also some doctors believe that electrodermal devices are valuable diagnostic tools because of their safety, non-invasive nature and simplicity; the use of unconventional medicine techniques is therefore largely increasing [1, 2, 18, 19]. Nevertheless, only a few rigorous studies have investigated double-blindly these procedures [13–15], with controversial results.

The main object of this investigation was to assess whether the inclusion in the device of a vial containing allergens can be revealed, in allergic subjects, by a change in SER. To test this hypothesis we used a double-blind procedure, where the operator was not aware of the allergic/healthy status of the tested subject and where neither the operator not the tested subject knew the content of each vial. Using this procedure we found no change in the SER of allergic patients in the presence of the offending allergen. Moreover, SERs of allergic patients were superimposable on those of healthy subjects, at least in the first session of measurements. This disproves that this machine can have, under rigorous conditions, a reliable diagnostic value for respiratory allergies. Our data are in agreement with those of Lewith and colleagues [15] who carried out a similar, although more simplified, study on a small sample of volunteers. In addition we tried to assess, under the same experimental conditions, whether the machine is able to detect the presence of homeopathic preparations and some inflammatory mediators. Also in this case, the electrodermal device failed to produce positive results.

It is of notice that the highly dispersed results and the variations of two subsequent measurements in the same subject, indicate a poor reproducibility of the method. Possible reasons for explaining the failure of this trial may be the influence of multiple and repeated testing, the role of the material of the electrodes and the influence of the operator himself; in fact all authors working in this field agree that in electrodermal testing the operator skill is essential. Another main problem is the fact that measurement of skin conductivity is largely influenced by the extent of pressure of the stylus, which is, in turn, influenced by conscious and unconscious factors related to the operator. It has been shown that when two investigators measure the conductivity of the skin in the same conditions, the values found often differ [20]. In this study all measurements were performed by the same trained operator in invariant conditions, but very stable measurements in some cases and highly variable data in others were obtained; therefore the variability may be due to an intrinsic difference among individuals. In any case, all the considerations mentioned above further confirm that this kind of measurement is affected by a too great number of unknown

variables. Finally, since the drop of SER between measurements in the same patient was significantly greater in the allergic population than in the controls, we should conclude that this lability of electrodermal skin conductivity index is somehow associated with the pathological status.

It is important to consider that there are a number of electronic devices enabling measurement of skin potentials and that there are many different technical and theoretical differences between them [21]. Indeed, recently, the measure of electropotentials has been proposed as a valuable diagnostic modality for breast cancer [22]. Therefore, the results of the present investigation cannot be extended to the whole field of new bioelectronic techniques, which remains open to further studies and developments. In view of the wide range of unconventional medicines [1, 2, 19], those who manufacture or use electrodermal instruments should always refer to rigorous well-controlled data before claiming for the efficacy of the method.

Acknowledgements

We thank Dr M. Kofler (Monguelfo, Italy) for his assistance in the project of this study, Dr G. Andrioli for statistical analysis and Dr H. W. Schimmel (Baden-Baden, Germany) for his suggestions in the discussion of the results.

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