Measurement of electrical skin impedance of dermal-visceral zones as a diagnostic tool for disorders of the immune system

M Gerosa1†, E Zimlichman2†, D Ventura1, V Fanelli1, P Riboldi1 and PL Meroni1*
1Allergy, Clinical Immunology & Rheumatology Unit, Department of Internal Medicine, University of Milan, IRCCS Istituto Auxologico Italiano, Milan, Italy; and 2Department of Medicine ‘B’, Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel

Among complementary medicine approaches, diagnostic screening tools based on neuroreflexology have been recently developed. Such techniques are based on the rationale that measurement of electrical impedance of specific dermal zones might reflect the occurrence of pathological states in the corresponding internal organs or systems. Our objective was to evaluate the reliability of a neuroreflexology-based diagnostic test in diagnosing immune-mediated diseases in a blinded single centre study. Seventy-eight patients with immune-mediated diseases (38 patients with autoimmune diseases (AD), and 40 allergic patients) were included in the study. Thirty age and sex matched healthy subjects were also evaluated as a control group. All the patients and subjects underwent conventional medical history and physical examination. We evaluated a device manufactured by Medex Screen Ltd (Arad, Israel). The Medex Test analysis was carried out by a second physician who was blinded to the previous diagnosis. A high correlation between the formal clinical diagnosis and the results of the measurement of electrical skin impedance was reported, with a specificity of 93.3% and a sensitivity of 81.2%. Both sensitivity and specificity dropped when analysing the autoimmune and the allergic group separately, but remained significant for the autoimmune diseases. Degree of activity of the allergic disorders, or specific treatment, did not affect the diagnostic properties of the described device. The Medex Test neurophysiology based technique has the potential to serve as a diagnostic tool for immune based pathologies. Future studies will define this tool place in routine evaluation and potential screening ability. Lupus (2006) 15, 457–461.

Key words: allergic diseases; Medex screen; non-conventional medicine; skin impedance; systemic autoimmune diseases;

Introduction

Early timing of a diagnosis is important to start a prompt treatment before diseases become untreatable and to avoid permanent organ damage. This is particularly important in asymptomatic persons and for therapeutical approaches that act on pathogenic mechanisms, potentially able to block illness development. In this regard, the value of routine health examination of asymptomatic persons has been well established as part of a routine checkup.1,2 The identification of proper tests for preventive medicine is a matter of extensive research based on a systematic review of evidence of clinical effectiveness3.

Recently, a non-conventional diagnostic procedure based on the field of neurophysiology has been reported.4 This system is based on the analysis of the data obtained by measuring the skin electrical impedance of pre-determined dermal-visceral zones (DVZs) on the human body. The rationale behind the system is that single internal organs display corresponding representative zones on the trunk and on the limbs, whose physical parameters are strictly related with the presence of pathological processes. Thus, any pathological condition affecting an internal organ might induce electrophysiological changes in the corresponding DVZs.5,7

The first report on such a technique (Medex Screen diagnostic technique) described the results obtained by assessing patients referred to an Internal Medicine department service and suffering from a heterogeneous group of diseases. Overall 150 patients were evaluated and a good correlation between the formal clinical diagnosis and the results of the measurement of
electrical skin impedance was reported. In order to validate the new Medex Screen diagnostic technique in a well-defined Internal Medicine sub-specialty, we carried out a blinded study in patients suffering from immune-mediated diseases during conventional assessments in a day hospital setting.

Methods

The study was undertaken at the Allergy, Clinical Immunology and Rheumatology Unit of the Istituto Auxologico Italiano, Milan, Italy. We evaluated a device manufactured by Medex Screen Ltd (Arad, Israel). The major components of the Medex Test consists of a special skin impedance measurement device used to take various measurements of the DVZs of the human body (expressed as KOhm), which are then processed by the device software. Once the data are processed, the Medex device can determine if pathological states are present in the examined internal organs.

Study population

This was a blinded, single centre, retrospective and comparative study. Patients undergoing conventional immunological and allergological assessment were screened for potential participation in the study. The study group included patients with an established diagnosis of autoimmune disease (AD) or patients with an established allergic disorder.

Diagnosis of the different AD was done according to well established criteria. Systemic lupus erythematosus (SLE) patients were classified according to Hochberg; undifferentiated connective tissue diseases patients were classified as reported; primary Sjögren syndrome according to Vitali et al.; scleroderma patients according to Lonzetti et al.; patients with systemic vasculitis according to Janette et al.; rheumatoid arthritis (RA) patients according to Arnett et al.

Among atopic oculo-rhinitis patients one was suffering from severe-intermittent form, 19 out of 29 from mild-intermittent form, eight out of 29 from mild-persistent form and one from severe-persistent form. The classification was performed according to the international criteria. Six out of 29 oculo-rhinitis patients also suffered from asthma diagnosed according to international guidelines. Four patients were classified as atopic contact dermatitis. Two additional patients were suffering from food allergy and five from drug allergy.

Age and sex matched normal healthy subjects have been included as control group; all of them were randomly chosen from patients’ chaperons and hospital personnel and have been subjected to a medical screening questionnaire and physical examination to rule out any immune pathological condition.

Exclusion criteria were represented by local skin damage in the evaluated areas, patients with missing limbs and pregnant women. All the patients and the controls were asked to sign an informed consent and the study was approved by the ethical committee of the Istituto Auxologico Italiano.

Patient examination and evaluation

Patients with immune-mediated diseases and healthy subjects were subjected to a medical examination by authorized Clinical Immunologists before the Medex Test. A pre-study case report form for everyone was recorded with medical information including main current diseases, current medical therapy, relevant past medical history and clinically significant abnormalities of all body systems.

Technicians that were trained by Medex Screen personnel performed the Medex Test measurement. Before testing, the DVZs are cleaned with 70% ethyl alcohol solution to avoid possible effects of sebum or humidity on the skin, which could affect the test. Measurements were carried out by using the skin electrode on 24 predetermined zones on the hands and feet. Each measurement was repeated twice. First, a baseline measurement was performed; the recorded values were considered to be normative values for the individual. Second, trans-cutaneous electrical stimulation of other specific skin areas was performed. The response of these areas is supposed to be different between normal and abnormal conditions. A second measurement was performed, and any differences were recorded and analysed in comparison to the first set of values. The measurements were performed with an electrical current of 20 μA (voltage of 5 V). This very low electric current, is safe and does not display any damage to the skin during the short time of testing. A software program processes the collected information with the help of previously built correlative algorithm, and produces an output of suggested diagnosis, among them – immune pathologies.

The Medex Test testing technical personnel were unaware of the patient’s diagnoses. The results of Medex Test assessment have been compared to data from the conventionally accepted tests and the patients’ charts, in order to determine the accuracy of Medex Test device.

Software analysis was done at the Medex Screen Company’s headquarters by a second investigator that was blinded to the medical charts and physical examination details. The diagnosis made by the Medex software was printed as a written report. A third investigator, also blinded to the actual process conducted previously, compared the actual ‘conventional’ diagnosis and the
Medex device output, as described under the statistical analysis section below.

Statistical analysis

Statistical analysis was conducted using the SPSS for Windows 10.0 program. The Medex Test diagnosis was statistically compared to the results obtained from the conventional diagnosis methods. The statistical analysis estimated agreement between the Medex Test diagnosis and the results of the conventional diagnostic examinations. A standard measure of agreement (Cohen-Kappa) between two binary variables was estimated. In addition, all measures of agreement (sensitivity, specificity, positive and negative predictive values) for the Medex Test diagnosis were calculated using the conventional diagnosis as the gold standard. Significance was measured using the t-test for independent samples. In order to analyse the affect of treatment and disease activity on the test results, we performed linear regression models were the result of the Medex Test was considered the dependent variable. P-values < 0.01 were considered significant.

Results

Overall, 108 participants were included in the study, 78 were female and 30 males. Of these, 38 were patients with systemic AD, 40 were patients with an allergic disorder and 30 participants served as age and sex matched controls. Description of the specific pathologies is detailed in Table 1. Average age of all participants was 40.5 ± 14.8 years.

Table 1 Diagnosis of the patients included in the study

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic autoimmune diseases (SAD)</td>
<td></td>
</tr>
<tr>
<td>Scleroderma (systemic + limited)</td>
<td>9</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>7</td>
</tr>
<tr>
<td>Undifferentiated connective tissue disease</td>
<td>6</td>
</tr>
<tr>
<td>Churg-Strauss</td>
<td>3</td>
</tr>
<tr>
<td>ANCA positive systemic vasculitis</td>
<td>2</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>2</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>1</td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
<td>1</td>
</tr>
<tr>
<td>Autoimmune pericarditis</td>
<td>1</td>
</tr>
<tr>
<td>Sjögren syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Anti-phospholipid syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Discoid lupus</td>
<td>1</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>1</td>
</tr>
<tr>
<td>Adult Still’s disease</td>
<td>1</td>
</tr>
<tr>
<td>Autoimmune polyendocrinopathy</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
</tr>
<tr>
<td>Allergic disorders</td>
<td></td>
</tr>
<tr>
<td>Atopic oculo-rhinitis</td>
<td>29</td>
</tr>
<tr>
<td>Atopic contact dermatitis</td>
<td>4</td>
</tr>
<tr>
<td>Severe food allergy</td>
<td>2</td>
</tr>
<tr>
<td>Severe drug allergy</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 2  Sensitivity and specificity of the Medex Test method to predict diagnosis, compared to conventional established diagnosis

<table>
<thead>
<tr>
<th>Study group</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Kappa*</th>
<th>P**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic autoimmune diseases (AD)</td>
<td>81.2%</td>
<td>93.3%</td>
<td>0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergy disorders</td>
<td>69.2%</td>
<td>42.1%</td>
<td>0.09</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Cohen-Kappa is the measure of agreement. Kappa equals 0 when the agreement equals that expected by chance.
**Significance was measured using the t-test for independent samples.

In the systemic AD patient group, all patients were under medical treatment at the time of examination (including either non-steroidal anti-inflammatory drugs, steroids or other immunosuppressant drugs). In the allergy disorder patient group 12 patients had manifestations of an active allergic disorder of which eight patients were treated for (with local corticosteroids, anti-histamins or with specific immunotherapy).

Medex Screen diagnostic technique displays a very good specificity (93.3%) as well as a good sensitivity (81.2%) in recognizing pathological disorders of the immune system (AD and allergy). The overall Cohen-Kappa value is 0.65. When analyzing both groups separately, specificity drops in the AD group (58.8%) and sensitivity rises (91.5%) with a smaller Kappa value (0.47), while in the allergy disorder group both specificity and sensitivity drop (42.1% and 69.2%, respectively) with a non-significant Kappa value of 0.09. Table 2 reports the sensitivity, specificity of the Medex test as well as the Cohen-Kappa values and the significance.

In a linear regression model where the existence of an allergic disorder and the activity of the disease served as independent variables and the result of the Medex Test considered the dependent variable, both independent variables were not significant in the model (P = 0.73 for the disease activity variable). This indicates that for the allergy patients, the activity of the disease did not affect the result of the Medex Test.

In a second linear regression model, the occurrence of the disease (both allergic and autoimmune disorders) and the treatment of the patient (treated versus non-treated) served as independent variables while the Medex Test result was considered the dependent variable. Treatment of the patient was found to be non-significant in the model (P = 0.17).

Discussion

As complementary medicine is gaining momentum with increasing numbers of people seeking non-conventional therapies, new screening techniques are also being developed. One of them is based on the
selection and analysis of data obtained from measuring the skin’s electrical impedance of predetermined DVZ on the human body. It is still considered as ‘complementary’ medicine, and has just recently become the subject of conventional scientific research. Actually, one study demonstrated the device ability to diagnose common disorders such as respiratory, cardiovascular and gastrointestinal pathologies in an internal medicine department setting.4 Another recent study demonstrated the ability of Medex Test to detect with high accuracy the presence of liver disorders and to determine the necro-inflammatory grade (Lurie Y, Landau D, Kanevsky A, et al. Medex Test, a novel modality for liver disease diagnosis – a pilot study. Unpublished data).

In this study we set out to explore the efficacy of this diagnostic/screening tool using conventional evidence-based medicine techniques, specifically for immunemediated diseases. As we analysed the data presented here, we found a high correlation when comparing the results of the Medex Test to the conventional clinical diagnosis for all immune pathologies (both autoimmune and allergic disorders). However, the Medex diagnostic tool was not able to differentiate effectively between the two subgroups, as both sensitivity and specificity dropped under statistical significance when analysing the allergic group separately. We also found that degree of activity of the allergic disorders, or specific treatment, did not affect the diagnostic properties of the described device.

Early diagnosis of diseases, preferably in the preclinical stages, is the basic rationale beyond screening tests for asymptomatic individuals. It is now common practice among health professionals to recommend routine testing as effective preventive medicine, with the intention that early diagnosis and treatment of illness will lead to improved prognosis. Presumably, this is also true for autoimmune disorders, specifically systemic autoimmune diseases, as recent evidence have shown that some of these disorders can be diagnosed in the preclinical stage.21,22 Such is the case with inflammatory bowel disease were auto antibodies (anti-Saccharomyces cerevisiae mannan antibodies (ASCA) in Crohn’s disease (CD) and perinuclear anti-neutrophil cytoplasm antibodies (pANCA) in ulcerative colitis (UC)) are present in patient sera before the emergence of overt clinical manifestations.23 It has been recently found that antibodies are present in the sera of patients long before the clinical manifestation of SLE. In a study by Arbuckle et al.24 – 88% of patients who eventually developed SLE – at least one of the autoantibodies tested was present, a mean of 3.3 years before the diagnosis. Further evidence has shown similar conclusions for many other autoimmune disorders such as autoimmune thyroid disease,25 hepatic disease26 and RA.27 This has recently raised the issue and the debate concerning the need for screening of autoimmune disorders as the benefits of screening for such antibodies in the general or at risk population has not yet been established.

In our present study, the overall accuracy of the Medex device to identify autoimmune pathologies is surprisingly high. Just as a comparison, commonly used autoantibodies, such as anti double-stranded DNA and rheumatoid factor, carry 70% sensitivity and 94% specificity for SLE,28 and 50–90% sensitivity and 80–90% specificity for RA, respectively.29 When compared to sensitivity and specificity of most autoantibodies used to diagnose AD, the sensitivity and specificity of the Medex test can lead to the conclusion that this test is suitable for use as a diagnostic tool, and perhaps even a screening tool for immune pathologies.

However, our results also show that the technique described was unable to differentiate between autoimmune and allergic disorders. Since the mechanism and the physiology of this method is not well established scientifically, we can only speculate on the reason. Although both autoimmune and allergic diseases are disorders mediated by the immune system, different specific effector mechanisms are involved in the two conditions. Such a difference might be responsible for the different sensitivity displayed by the test. Better knowledge of the mechanisms behind the test itself might help in understanding the discrepancies and to further validate the system.

One of the limitations of our study is the fact that we assumed that the control or the allergy disorder patients indeed did not have an undiagnosed AD and have not performed any diagnostic tests to rule out a sub-clinical autoimmune disorder (ie, autoantibody screening). Thus, theoretically, one of our false positives might have had an undiagnosed AD.

We consider this a preliminary study aimed at evaluating the potential of this unexplored (by conventional scientific methods) technique. We feel that the results presented here, and the results published earlier4 merit further research aimed at better understanding of the physiologic mechanism, and further evaluation of this tool’s potential.

If indeed this technique will be further validated as either a diagnostic and/or a screening tool, one cannot overlook its potential advantages. The test itself is very safe, with no potential unwanted side effects. Furthermore, it is relatively inexpensive, easily operated and accessible.

However, we wish to point out that at this point, this method cannot replace formal physical examination or other well-established diagnostic tests or devices, and believe that ultimately it will be used as a practical
application in conjunction with other well established clinical and laboratory diagnostic tools.

References

3 Lawrence RS, Mickalide AD. Preventive services in clinical practice: designing the periodic health examination. JAMA 1987; 257: 2205–2207.