Evaluation of High Speed Laser Doppler Imaging Technology to Measure Skin Prick Tests in Daily Allergologic Practice

Abstract Nr. 789

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Abstract

Rationale

Skin prick tests (SPT) are commonly used in daily allergologic practice to evaluate skin reactivity to various allergens. The current visual evaluation of SPT is observer dependent. To evaluate an objective measurement of skin reactivity to SPT, we compared the classical visual reading (CVR) with a method of high speed laser Doppler imaging (HS-LDI).

Methods

First, SPT, including positive and negative controls, birch and grass pollen extracts (Stallergènes, France), were applied to 20 volunteers (10 atopics, 10 non atopics) to determine tests caracteristics (cut-off, optimal reading time and allergen concentration). Then 30 atopic patients were tested, with optimal allergen concentration and time window, with birch and grass pollen extracts and skin reactivity was measured with CVR and HS-LDI.

Results

The optimal concentration was 1/1 whereas the optimal time window for the lecture of SPT with HS-LDI was at a time window of 5-10 minutes for histamine and at a time window of 12.5-17.5 min. for allergens. The sensitivity of CVR was 96% and of HS-LDI 100%, whereas the specificity of CVR was 91% and of HS-LDI 83%.

Conclusions

The lecture of SPT with HS-LDI proved to be a simple and more sensitive but less specific method than CVR. Its future application could be the lecture of SPT in patients showing borderline results with CVR and in clinical trials where an objective method of reading of SPT is needed.

Fig. 1: photographs of the high-speed laser Doppler imaging system (HS-LDI) used

Introduction

Prick-tests are currently used in daily allergology practice to evaluate hypersensitivity to respiratory allergens, foods and drugs. A positive reaction elicites a wheal and flare reaction and the evaluation of these prick tests takes into account the diameter of the wheal reaction appearing 15 min. after the prick test has been done. Because there is a considerable interindividual variability of these prick tests, an objective method to measure prick tests would be very useful. There is also a lack of sensitivity of certain tests and at least a part of this lack of sensitivity could be in relation with weak tests that are negative with classical visual lecture.

Laser Doppler imaging is a new technique of medical imaging developed to obtain a imaging of the microcirculation in biologic tissues. The device used in this study uses a newly developed high-speed Laser Doppler imaging system (HS-LDI) which allows to obtain high-speed imaging in a very short time (10 seconds).

We applied this technique on 50 volunteers and patients to evaluate its sensitivity, it's specificity and it's global usefulness in daily clinical practice.

Material and methods

Laser Doppler imaging system

We used a new medical imaging system [1] developed for imaging of microcirculation in human skin. The measurement principle of this device is based on a laser Doppler imaging technique where the laser light scattered by moving blood cells obtains a Doppler-shift which is proportional to the speed of the moving particle. The detectors of the system allows to measure the Doppler signal from thousands of object points simultaneously. After an appropriate signal processing based on the Fast Fourier Transformation (FFT) algorithm, a 2D image of the blood flow is reconstructed. Both the acquisition and processing procedures take about one second. In 10 seconds, the system allows to obtain high-speed images of high quality and resolution. Thus it allows obtaining images much faster than usual Laser Doppler scanners which need 5-10 minutes for obtaining a single image of a standard resolution.

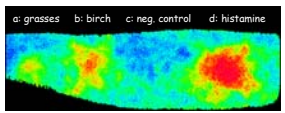
Measurement method

The obtained 2D images of blood flow evaluates the flare reaction induced by SPTs. The flow map obtained before the prick test is subtracted form the one obtained after. The remaining non-zero pixels show the area where the blood flow is increased compared to the normal state.

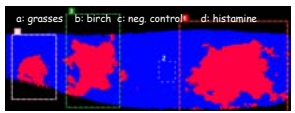
For the data analysis we used two parameters, total number of non-zero pixels in the "prick-zone" Npix (area), and Flow power Peff (flow), which is a parameter found from the formula:

$$P_{eff} = k\sum_{i=1}^{N} \Delta r_i P(\Delta r_i)$$

Δr_i is the distance between the geometrical center of the erythema spot and i^{th} pixel, $P(\Delta r_i)$ is the flow value in i^{th} pixel and k is an arbitrary coefficient (>0, <1) used to avoid too large numbers for the representation of the results. Effectively, the Peff takes into account both parameters of the flare reaction: the size of the flare reaction and the flow values in the zone.



A. Original blood flow distribution map



B. Flow distribution after the background substraction

Figure 2: A typical laser Doppler image of the volar side of the forearm of a patient with a positive reaction to birch and grasses. Fig. 1A shows the original image, whereas fibure 2B shows the figure after substraction of the background

Skin prick tests

In the first part of the study, histamine (Stallergènes, France, 10 mg/ml) was used at a concentration of 10 mg/ml (1:1), 2.5 mg/ml (1:4), 0.625 mg/ml (1:16), 0.312 mg/ml (1:32) and 0.156 mg/ml (1:64). NaCl 0.9% (Stallergènes, France) was used as a negative control, birch and grass pollen extract (Stallergènes, France) was used at the standard concentration (1:1) and at different dilutions (1:4, 1:16, 1:32, 1:64). The measures of the SPTs were done every 2.5 minutes until 20 min. after application of the SPTs. The goal of the first part of this study was to evaluate the optimal measurement time after after the prick test, the optimal concentration o the allergens used and the cut-off value.

Ref. 1) Serov A, Lasser T. High-speed laser Doppler perfusion imaging using an integrating CMOS image sensor. Optics Express 2005; 13: 6416-6428

Results

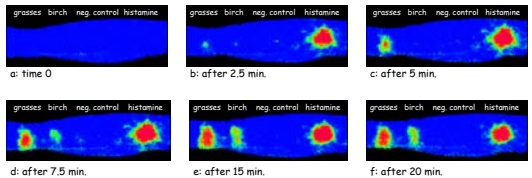


Fig. 3: typical time evolution of the skin response evaluated by HS-LDI

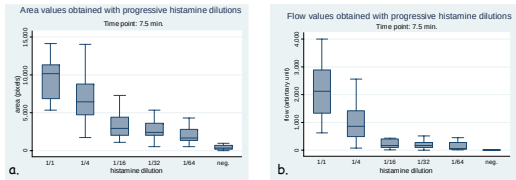


Fig. 4: area (a) and flow (b) values for histamine at 7.5 min. Concentration of 1/1 is most distinctive. This is also true for birch and grass pollens (data not shown)

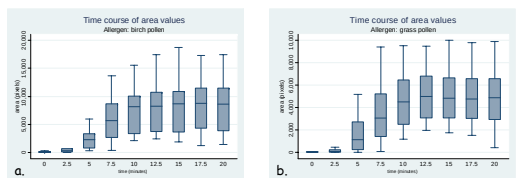


Fig. 5: time course of values of area for birch (a) and grass (b) pollens (1/1). The maximum is reached at a time window of 12.5-17.5 min.

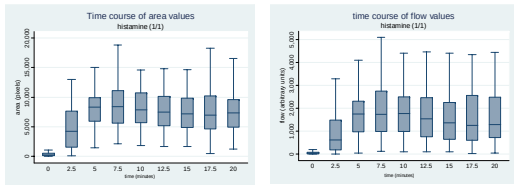


Fig. 6: time course of values of area for histamine (1/1). The maximum is reached at a time window of 5-10 min.

The cut-off values for HS-LDI were determined on 20 volunteers (10 non-atopics, 10 atopics) as follows:

cut-off = mean of neg. controls values + 3 SD

cut-off for the parameter "area": 1400 pixels
cut-off for the parameter "flow": 35 a.u. (arbitrary unit)

Application of lecture of SPT with HS-LDI on 30 patients with allergic rhinitis to grass and/or birch pollen

Table 1: Test characteristics of lecture of SPT with CVL and HS-LDI with regards to the diagnosis of allergic rhinitis to grass and/or birch pollen

Test characteristics	CVL	HS-LDI
Sensitivity	96 %	100 %
Specificity	91 %	83 %
PPV (positive predictive value)	96 %	92 %
NPV (negative predictive value)	91 %	100 %

Conclusions

The lecture of SPT with HS-LDI proved to be a simple and more sensitive but less specific method than CVR. HS-LDI may find future application in the lecture of SPT in patients with borderline results by CVR and in clinical trials where an objective methodology for SPT reading is needed. Further evaluation in a larger study is warranted.

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