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Original article

A new simple method for assessing sudomotor function: Relevance in type 2 diabetes

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Abstract

Aim. – The current sudomotor function tests are too time-consuming to be used for diabetic patients in daily practice. EZSCAN is a new, patented technology that measures electrochemical skin conductance (ESC) through reverse iontophoresis and chronoamperometry. The aim of the present study was to assess the sensitivity, specificity and reproducibility of the method in type 2 diabetic patients in comparison to control subjects with no risk of diabetes.

Methods. – A total of 133 type 2 diabetic patients and 41 control subjects were tested. Participants placed their hands and feet on nickel electrodes, and an incremental low direct current was applied to the anode for 2 min. ESC was calculated from the resulting voltage and generated current. ESC diagnostic accuracy was analyzed by ROC curve modeling, and reproducibility was assessed using Bland–Altman analysis.

Results. – The ESC of hands and feet was significantly reduced in diabetic patients (53 ± 16 μSi and 67 ± 14 μSi, respectively) compared with control subjects (68 ± 16 μSi and 80 ± 7 μSi, respectively; $P < 0.0001$). ESC values had a sensitivity of 75% and specificity of 100%, with an area under the ROC curve of 0.88 at a threshold of 50% on the EZSCAN scale. Coefficients of variation in hand and foot measurements were 15 and 7%, respectively.

Conclusion. – The good sensitivity, specificity and reproducibility of EZSCAN make it a feasible alternative for assessing sudomotor dysfunction, a clinical manifestation of autonomic neuropathy in diabetic patients. The test takes < 3 min to perform, and requires neither special patient preparation nor medical personnel training.

Keywords: Type 2 diabetes; Sudomotor function; Electrochemical skin conductance; Autonomic nervous system; EZSCAN

Résumé

Une nouvelle méthode simple pour évaluer la function sudomotrice : intérêt dans le diabète de type 2.

Objectif. – Les tests destinés à évaluer la fonction sudorale sont trop longs pour pouvoir être utilisés en pratique courante chez le diabétique. EZSCAN est une nouvelle méthode brevetée qui mesure la conductance éléctrochimique de la peau (CEP) en utilisant l'iontophorèse inverse et la chronoampéromètrie. Le but de l'étude était d'évaluer la sensibilité, la spécificité et la reproductivité de la méthode utilisée chez des diabétiques de type 2 comparativement à des non-diabétiques.

Méthodes. – Cent trente trois patients DT2 et 41 sujets témoins on été testés. Il était demandé aux participants de placer leurs mains et leurs pieds sur des électrodes de nickel et un faible courant continu était appliqué sur l'anode durant 2 min. La CEP est calculée à partir de la tension résultante et du courant généré. La performance diagnostic de EZSCAN a été analysée au moyen d'une courbe ROC. La reproductibilité a été évaluée par un test de Bland et Altman.

Résultats. – La conductance électrochimique des mains et des pieds étaient significativement diminuées chez les patients DT2 (53 ± 16 et 67 ± 14 μSi, respectivement) par comparaison aux sujets témoins (68 ± 16 et 80 ± 7 μSi, $P < 0{,}0001$). La sensibilité et la spécificité de la mesure de la conductance électrochimique étaient respectivement de 75 et 100 % avec une aire sous la courbe de 0,88 en se fondant sur le seuil de 50 % sur l'échelle EZSCAN. Les coefficients de variations pour les mains et pour les pieds chez les patients DT2 étaient respectivement de 15 et 7 %.

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Conclusion. – La bonne sensibilité, spécificité et reproductibilité de EZSCAN en font une alternative crédible pour évaluer les perturbations de la fonction sudorale, manifestation clinique de la neuropathie du système végétatif chez les patients diabétiques. Ce test ne requiert ni préparation spéciale, ni entraînement du personnel médical et nécessite pour la mesure moins de trois minutes.

Mots clés : Diabète de type 2 ; Fonction sudomotrice ; Conductance électrochimique de la peau ; Système nerveux autonome ; EZSCAN

1. Introduction

Diabetes mellitus (DM) is one of the most common metabolic disorders in nearly all countries around the world. The global burden of DM in adults was estimated to be around 246 million in 2007 [1], and it is now also estimated that the global prevalence among adults will increase from 6.4% in 2010 to 7.7% by 2030 [2]. The diabetes epidemic is accelerating in the developing world, with an increasing proportion of affected individuals being in the younger age groups [2]. This is likely to increase the disease burden even further because of chronic diabetic complications such as neuropathy. Diabetic autonomic neuropathy (DAN) is a common multifactorial disease with a prevalence ranging from 7.7 to 90%, depending on the tests used, populations examined, and type and stage of disease [3]. Risk factors for the development of DAN include diabetes duration, age and long-term poor glycaemic control. Its major clinical manifestations include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis and sudomotor dysfunction. The clinical diagnostic signs are often silent or difficult to assess routinely, even in patients with peripheral neuropathy, and some studies suggest that small fibres may be injured early in the course of DM and particularly affect sudomotor function [4,5]. As DM can remain asymptomatic for years, the screening, and thus, the diagnosis of neuropathy may be delayed, whereas its early detection could result in appropriate interventions, thereby reducing the incidence of complications such as diabetic foot [6].

Sudomotor function can be assessed through various tests. The quantitative sudomotor axon reflex test (QSART) is the most commonly used, as it is considered to be the most accurate and sensitive [7,8]. This test measures sweat output in a reproducible and dynamic way (after simultaneous axon reflex stimulation), and relies on iontophoresis of quantified acetylcholine [7]. However, it also requires a high level of clinical expertise to perform and specialist facilities, and is too time-consuming for daily practice.

The aim of the present study of type 2 diabetic patients and healthy control subjects was to assess the sensitivity, specificity and reproducibility of EZSCAN, a new, noninvasive and quick method for the precise evaluation of sweat-gland function through electrochemical skin conductance (ESC) measurement.

2. Methods

2.1. Study population

The present study included 133 type 2 diabetic patients (mean age: 58.9 ± 12.1 years; mean diabetes duration: 14 ± 10 years; 28% with nephropathy, 11% with retinopathy, 7% with peripheral neuropathy and 9% with cardiovascular complications; none using beta-blockers or angiotensin-converting enzyme [ACE] inhibitors) who had attended diabetes consultations at Bégin Hospital, and 41 healthy volunteers (mean age: 25.5 ± 6.4 years; no known risk of diabetes) living in Saumur. Approvals for the study protocol, subject information sheet and the consent form were obtained from the relevant ethics committee.

The main inclusion criteria applied to the control subjects, who had to have no risk factors for diabetes (age < 45 years, frequent physical activity, no first-degree relative with diabetes) and fasting plasma glucose (FPG) levels < 7 mmol/L. Criteria for diabetic patients were: diabetes consultation resulting in a diagnosis of type 2 diabetes; and the use of at least one oral medication for diabetes management. Written informed consent was obtained from all study participants.

2.2. Measurement of electrochemical skin conductance

The new EZSCAN device is designed to perform a precise evaluation of sweat-gland function through measurement of sweat chloride concentrations using reverse iontophoresis and chronoamperometry [9,10]. Two sets of large-area nickel electrodes are used as an anode and a cathode, and a direct-current (DC) incremental voltage ≤ 4 V is applied to the anode. This DC generates voltage to the cathode, and a current between the anode and cathode that is proportional to chloride concentration and measurable by chronoamperometry.

The apparatus consists of two sets of electrodes each for both hands and feet, as well as a headband device for the forehead, all of which are connected to a computer for recording and data management (Fig. 1). The sites for electrodes were chosen because of their high density of sweat glands. For the test, the patient places his hands and feet on the electrodes, and places the headband electrodes on his forehead. The patient is then required to stand still for 2 min. During the test, six combinations of 15 different low DC voltages are applied.

The ESC (measured in μSi), the ratio of the current measured over the constant power applied, is calculated for the forehead (left and right), the hands (left and right) and the feet (left and right). These measurements are displayed instantaneously in the form of a graphic representation that allows quick intuitive interpretation, using a standard personal computer (PC). Detailed results are provided in alphanumeric format. Higher μSi readings indicate lower risk of abnormality. A scale (0–100%) calculated with an algorithm is displayed, using different color codes, on the device screen to make interpretation easier. A positive response is defined as a reading that is > 50% on the scale. The cutoff point for the method was evaluated using a