Use of EZSCAN for detection of pre-diabetes and diabetes and comparison with standard screening methods

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Abstract

Objectives: Pre-diabetes is almost always a precursor to the development of type 2 diabetes. Comparison of EZSCAN with existing screening methods for detection of pre-diabetes and diabetes was done.

Settings and Design: Cross sectional epidemiological study.

Material and Methods: All cases underwent the EZSCAN test and had fasting plasma glucose (FBG), post-prandial plasma glucose (PPBG) and HbA1c level estimation. The results of EZSCAN were compared with fasting blood glucose, post-prandial blood glucose and HbA1c levels.

Statistical analysis used: Mean, Standard deviation, sensitivity, specificity, positive and negative predictive value.

Results: The sensitivity and specificity of EZSCAN when compared with FBG in diabetes was 87.2% and 87.2% respectively, for pre-diabetes 80.4% and 74.3% respectively and for non-diabetes 51.1% and 97.8% respectively. The sensitivity and specificity of EZSCAN when compared with PPBG in diabetes was 86.5% and 85.2% respectively, for pre-diabetes 76.9% and 72.6% respectively and for non-diabetes 52.8% and 98.9% respectively. The sensitivity and specificity of EZSCAN when compared with HbA1c in diabetes was 86% and 90.2% respectively, for pre-diabetes 87.8% and 71.4% respectively and for non-diabetes 46.3% and 98.8% respectively.

Conclusions: EZSCAN proved to be a sensitive, specific, easy to perform screening test for diabetes and pre-diabetes which can be performed in non fasting state. EZSCAN is a simple device that can be operated by non medical personnel in non-healthcare settings with minimal subject preparation.

Key-words: EZSCAN, diabetes, pre-diabetes.

Key messages: Type 2 diabetes often progress silently, without symptoms. Timely screening and early detection of diabetes and pre-diabetes will enable clinicians to intervene early in the course of the disease, preventing complications and adverse outcomes.

Introduction

Diabetes mellitus (DM) is a major healthcare problem affecting the whole world. Type 2 DM often progress silently, without developing clinical symptoms. It frequently remains undiagnosed until complications appear. As much as one third of cases may not be detected at all (1). At the same time, epidemiologic evidence suggest that complications are triggered at a much earlier stage of the disease than previously thought (2). For example, patients with impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), now commonly referred to as pre-diabetes, are exposed to an increased risk of cardiovascular disease and death (3). For a substantial number of patients, irreversible tissue damage (peripheral vascular disease, nephropathy, retinopathy, and peripheral neuropathy) have already set in at the time of diagnosis (4). The prevalence of type 2 DM is increasing and this appears to be greater in developing countries. The aetiology of this increase involve changes in diet, a higher fat intake, sedentary lifestyle, and decreased physical activity (5, 6). According to the ICMR-INDIAB national diabetes study, currently, there are an estimated 62.4 million individuals with diabetes in India (7).

Pre-diabetes indicates the state of a person born with genetic liability to diabetes from conception up to the stage when his glucose tolerance test (GTT) becomes abnormal. Therefore, pre-diabetes refers to a state and not a diagnosis.

There is a general agreement on the potential value

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of screening for diabetes and thus its early diagnosis (8). Screening for DM is recommended because, a large number of individuals who meet the current criteria for DM are asymptomatic and unaware that they have the disorder. Some individuals with type 2 DM have one or more diabetes-specific complications at the time of their diagnosis, and treatment of type 2 DM may favourably alter the natural history of DM.

The American Diabetes Association recommends screening all individuals more than 45 years every 3 years and screening individuals at an earlier age if they are overweight [body mass index (BMI) >25 kg/m²] and have one additional risk factor for DM. In those without risk factors for T2DM, testing should begin at 30-45 years of age. If test results are normal, repeat testing should be carried out at 3 to 5 year intervals.

EZ-SCAN is a new method for screening and assessment of early DM. The EZ-SCAN (Impeto Medical, Paris, France) is a patented device based on electrophysiological and electrochemistry principles which uses low level DC-induced reverse iontophoresis, together with chronoamperometry, to evaluate the behaviour of tissues in the body.

EZ-SCAN is basically SUDOSCAN and EZ-SCAN is the trade name given by the developers (Impeto Medical, Paris, France) because of ease of use. EZ-SCAN is non-invasive and provides immediate results, without any need for patient preparation, fasting or a blood draw. EZ-SCAN has demonstrated superior sensitivity and specificity ratings of 92% and 86%, respectively (9), with a variation coefficient of less than 5% (10).

EZ-SCAN working principle

Sympathetic innervation of eccrine sweat glands is progressively reduced at an early stage in the evolution of diabetes. This alteration of autonomous control of sweat glands causes a durable shift in the ionic balance of sweat conducts, which is independent from temperature and physical exercise.

Reverse iontophoresis, the process carried out by EZ-SCAN, extracts ions from the sweat which is secreted by sympathetically controlled sweat glands. The extracted sweat creates a current when it encounters specific sensors such as nickel electrodes. The current produced is proportional to the chloride concentration that reacts specifically with the nickel electrodes at a low DC stimuli. A time/ampere curve is recorded for each derivation. The conductance, expressed as micro-Siemens (mSi) is the ratio between the current generated and the constant DC stimulus. The measurement of the conductance is done by chronoamperometry (EZ-SCAN) and graphically displayed on a standard PC computer. Higher readings in mSi indicate a lower risk of any abnormality. According to the conductance measured on forehead, hands and feet,

an EZSCAN score is calculated and results are displayed using a risk score with a colour index.

- Green (0-25%): no risk

- Yellow (26-50%): moderate risk / pre-diabetes

- Orange-red (51-100%): high risk / diabetes with or without complications

Material and methods

The present study was conducted at M.L.N. Medical College, Allahabad and its associated hospital SRN hospital/ Nazareth hospital, Allahabad during a period from July 2013 to July 2014.

Subjects aged more than 18 years were selected from the patients who attended medicine outpatient department or were admitted in department of medicine in SRN hospital/ Nazareth hospital. Patients with a first degree relative with DM and with risk factors for developing DM were included in the study. Risk factors included hypertension (140/90 mmHg), high-density lipoprotein cholesterol level <35 mg/dL and/or a triglyceride level >250 mg/dL, physical inactivity, polycystic ovary syndrome, delivery of a baby weighing >4 kg, having been diagnosed with gestational DM, IGT, IFG on previous testing or having other clinical conditions associated with insulin resistance (eg, acanthosis nigricans).

Exclusion criteria

Known cases of DM and persons taking drugs that affect blood glucose levels.

All cases underwent the EZSCAN test and had their FPG, PPPG and HbA1c level estimated. The results of EZSCAN were compared with FBG, PPPG and HbA1c levels. The data were analysed and assessed with appropriate statistical methods within different groups.

Criteria for diagnosis of pre-diabetes:

- IFG = fasting plasma glucose 100 mg/dL to 125 mg/dL

- IGT = 2-h plasma glucose 140 mg/dL to 199 mg/dL

- HbA1c-5.7 to 6.4%

Criteria for diagnosis of DM:
- Fasting plasma glucose ≥ 126 mg/dL
- 2 hour plasma glucose ≥ 200 mg/dL
- HbA1c ≥ 6.5%

Results

Out of the total 125 patients included in the study there were 66 males and 59 females. The mean age was 50±14 years. Each patient was categorized as a pre-diabetes, DM, and non-diabetes on the basis of FBG, PPBG and HbA1c. Finally each category was compared with EZSCAN.

The sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) of EZSCAN in relation to FBG, PPBG and HBA1c in DM are depicted in tables 1-3.

Table 1. Association of EZSCAN with fasting blood glucose

EZ-Scan Results	Diabetes status based on FBG					
	D		PD		ND	
D	34	87.2%	8	15.7%	3	8.6%
PD	5	12.8%	41	80.4%	14	40.0%
ND	0	0%	2	3.9%	18	51.4%
Sensitivity	87.2		80.4		51.4	
Specificity	87.2		74.3		97.8	
PPV	75.6		68.3		90.0	
NPV	93.8		84.6		83.8	

D (Diabetes), PD (Pre-diabetes), ND (Non-diabetes)

Table 2. Association between EZSCAN and PPBG

EZ-Scan Results	Diabetes status based on PPBG					
	D		PD		ND	
D	32	86.5%	11	21.2%	2	5.6%
PD	5	13.5%	40	76.9%	15	41.7%
ND	0	0%	1	1.9%	19	52.8%
Sensitivity	86.5		76.9		52.8	
Specificity	85.2		72.6		98.9	
PPV	71.1		66.7		95.0	
NPV	93.0		81.5		83.8	

PD (Pre-diabetes), D (Diabetes), ND (Non-diabetes)

Table 3. Association between EZSCAN and HbA1c

EZ-Scan Results	Diabetes status based on HbA1c					
	D		PD		ND	
D	37	86.0%	5	12.2%	3	7.3%
PD	5	11.6%	36	87.8%	19	46.3%
ND	1	2.3%	0	0%	19	46.3%
Sensitivity	86.0		87.8		46.3	
Specificity	90.2		71.4		98.8	
PPV	82.2		60.0		95.0	
NPV	92.5		92.3		79.0	

PD (Pre-diabetes), D (Diabetes), ND (Non-diabetes)

In this study EZSCAN best co-related with HbA1c. The sensitivity and specificity for diabetes were 86 and 90.2 percent respectively and sensitivity and specificity for pre-diabetes were 87.8 and 71.4 percent respectively.

Discussion

This study demonstrates that EZSCAN, as a screening tool, had an acceptable accuracy for the diagnosis of pre-diabetes and DM.

To the best of our knowledge, only 5 published studies have investigated the accuracy of EZSCAN for the diagnosis of impaired glucose metabolism. In 212 subjects recruited in India by Ramachandran et al (11), the sensitivity of EZSCAN was 75% to detect DM, 70% for IGT and 84% for normal glucose tolerance with Metabolic syndrome (NGT with MetS) at a threshold of 50%. In our study when EZSCAN was compared with FBG, the sensitivity for detection of DM was 87.2% and specificity 87.2%. The sensitivity for detection of pre-diabetes was 80.4 percent and specificity 70.4%.

In the Chinese study done by Sheng et al (12) where the EZSCAN diabetes index of 40 was used as the threshold for the diagnosis of DM in all subjects, the sensitivity and specificity were 85 and 64 percent respectively. In our study when EZSCAN was compared with FBG, PPBG and HbA1c for detection of diabetes it showed sensitivities and specificities of 87.2 and 87.2%, 86.5 and 85.2% and 86.0 and 90.2% respectively.

Chen et al evaluated the performance of EZSCAN as a screening tool for impaired glucose metabolism (IGM), including impaired glucose tolerance, impaired fasting glucose and undiagnosed diabetes in a Chinese population (13). Their cut-off point of EZSCAN for IGM detection was 40% with a sensitivity of 80% and a specificity of 72%. In our study we used cut-off points as 25-49% for pre-diabetes. For detection for pre-diabetes, EZSCAN showed sensitivity and specificity of 80.4 and 74.3 percent when compared with FBS, 76.9 and 72.6 percent when compared with PPBG and 87.8 and 71.4 percent when compared with HbA1c.

Yang et al (14) using an EZSCAN value higher than 30% as cut-off point, provided reasonable sensitivities (70.3-83.7%) to detect dysglycaemia not only in the total population regardless of sex but also in individuals with high risk of developing diabetes. In our study subjects with an EZSCAN score more than 25% who were considered as pre-diabetes, should be further advised for life style modification for prevention of DM and related complications.

Peter eh schwaz (15) used a cut-off value of 50% on its scale had 75% sensitivity to detect diabetes, 70% for

IGT and 84% for NGT with metabolic syndrome. In our study EZSCAN score more than 25-49% considered as pre-diabetes and ≥50 considered as DM.

Taking the results of the previous studies and this research together, EZSCAN seemed to have consistent and constant sensitivity but divergent and variable specificity across populations.

The heterogeneous specificity might be attributable to the differences in characteristics of participants between these studies. In our study sensitivity for non-diabetes were low because of early detection of pre-diabetes in comparison to standard screening methods. In early stages of disease blood glucose level does not correctly reflect disease burden because of initial hyperinsulinemic phase to overcome excess glucose in blood and maintain the normal blood glucose level.

Nonetheless, our study had a small sample size and a cross-sectional design. A larger prospective study may be required.

Limitations of the study

EZSCAN may give false positive results for elderly age groups – age may be considered as a confounding factor.

Implications

The EZSCAN technique proved to be a sensitive, specific, easy to perform screening test for diabetes and pre-diabetes which can be performed in non fasting state.

EZSCAN seems to be a simple device that can be operated by non medical personnel in non-healthcare settings with minimal subject preparation.

Keeping the rising trend of diabetes and pre-diabetes in mind, EZSCAN can be used for mass screening of the population on a large scale.

Future research

To develop a study which will facilitate further longitudinal follow up of patients diagnosed as pre-diabetics by EZSCAN with standard screening method and OGTT.

Regional/ ethnic cut off value for detection of pre diabetes and diabetes by EZSCAN.

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