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Original Research

Visual Evoked Potential to Assess Retinopathy in Gestational Diabetes Mellitus

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ABSTRACT

Objective: We evaluated for early retinopathy using the visual evoked potential (VEP) in patients with gestational diabetes mellitus (GDM) and type 2 diabetes mellitus during pregnancy.
Methods: All patients with GDM and type 2 diabetes seen between June and October of 2014 were included in this cross-sectional, observational study. Patients with secondary diabetes, ocular or major illness were excluded from the study. VEP was recorded in both eyes to derive prominent positive peak latency (P100), amplitude and initial negative deflection (N75) latency. The data were compared with 10 gestational age-matched controls with normal glucose tolerance. Appropriate statistical methods were used for comparison among the 3 groups.
Results: The study participants (40 with GDM, 10 with type 2 diabetes, 10 with normal glucose tolerance) had a median (25th to 75th interquartile range) age of 26 (24.3, 30) years, a gestational age of 24.5 (21, 27) weeks and weights of 66.8 (63.4, 71.5) kg. The P100 latencies were comparable among the 3 groups (p=0.0577). However, patients with any diabetes (GDM and type 2 diabetes) had prolonged P100 latencies (p=0.0139) and low P100 amplitudes (p=0.0391) in comparison to controls. P100 latency showed a direct correlation with hyperglycemia (p=0.0118).
Conclusions: Our data showed that VEP abnormalities are detectable even in the short-term hyperglycemia of GDM and type 2 diabetes.

Mots clés :
examen du fond d'œil
diabète sucré gestationnel
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RÉSUMÉ

Objectif : Nous avons évalué la rétinopathie de stade précoce à l'aide des potentiels évoqués visuels (PEV) chez les patientes souffrant du diabète sucré gestationnel (DSG) et du diabète sucré de type 2 durant la grossesse.
Méthodes : Nous avons inclus à l'étude observationnelle transversale toutes les patientes souffrant du DSG et du diabète de type 2 vues entre juin et octobre 2014. Nous avons exclu de l'étude les patientes souffrant d'un diabète secondaire, d'une maladie oculaire ou d'une maladie grave. Nous avons effectué l'enregistrement des PEV dans les deux yeux pour extraire la latence du pic positif de culmination (P100), l'amplitude et la latence de déflexion négative initiale (N75). Nous avons comparé les données avec celle des 10 témoins enceintes appariées selon l'âge qui ont une tolérance normale au glucose. Nous avons utilisé les méthodes statistiques appropriées pour comparer les 3 groupes.
Résultats : Les participantes à l'étude (40 souffrant du DSG, 10 souffrant du diabète de type 2, 10 ayant une tolérance normale au glucose) avaient un âge médian (écart interquartile entre 25e et 75e) de 26 (24.3, 30) ans, un âge gestationnel de 24.5 (21, 27) semaines et un poids de 66.8 (63.4, 71.5) kg. Les latences de l'onde P100 ont été comparables entre les 3 groupes (p=0.0577). Cependant, les patientes souffrant de l'un des diabètes (DSG+diabète de type 2) montraient un allongement de la latence de l'onde P100 (p=0.0139) et une faible amplitude de l'onde P100 (p=0.0391) comparativement aux témoins. Nous avons observé une corrélation directe entre la latence de l'onde P100 et l'hyperglycémie (p=0.0118).
Conclusions : Nos données ont montré que les anomalies observées dans les PEV sont détectables même lors de l'hyperglycémie de courte durée du DSG et du diabète de type 2.

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Introduction

Gestational diabetes (GDM) is defined as the glucose intolerance that is identified for the first time during pregnancy. The prevalence of GDM is increasing across the world due to advancing ages of pregnancies and revised criteria that have lower cut-off values given by the American Diabetes Association (1,2). GDM presents typically in the second trimester and contributes to morbidity and adverse outcomes during pregnancy. GDM increases the risk for future type 2 diabetes mellitus, and a previous study estimated this risk to be in excess of 20% after 9 years of follow up (3). The progression of GDM is influenced by many factors, including obesity, family history and physical activity. Many patients with type 2 diabetes have prolonged asymptomatic phases, and early detection of the disease is essential to prevent the possible complications (4). The hyperglycemia in type 2 diabetes is associated with an increased risk for microvascular complications, including neuropathy, nephropathy and retinopathy.

Diabetic retinopathy is the most common cause of blindness across the world. More than 20% of patients with type 2 diabetes have retinopathy at the onset, and the recommendation is to screen these individuals at the time of diagnosis and annually thereafter (2,5). Pregnancy has been associated with increased progression of retinopathy in patients with diabetes (6). However, no formal guidelines exist regarding the screening of patients with GDM for retinopathy. The functional changes in the fundus precede the structural alterations but are appreciated only by visual evoked potential (VEP) testing and not by conventional ophthalmoscopy (7). Assessment of VEP helps in the identification of the retinal ganglion cell damage that remains undiagnosed by ophthalmoscopy (8).

VEP is a method of evaluating the visual pathways, including the brain, by recording the evoked response using a surface electrode over the occipital lobes. The VEP waveform consists of an initial negative deflection (N75), a prominent positive peak (P100) and a later negative deflection (N145) (9). A normal response to a stimulus is a positive peak after a latency of 100 ms, also known as P100. The latency and peak-to-peak amplitude are measured to compare the normal and abnormal visual pathways. Alterations in the VEP have been documented in early stages of diabetic retinopathy, but the same has not been studied in GDM (10,11). Hence, we conducted this pilot study to study the changes in VEP in patients with GDM and compared the same with patients who had type 2 diabetes.

Methods

This was a cross-sectional, observational study conducted at a tertiary care referral hospital located in North India. The participants were recruited from the antenatal clinic of our hospital and included referrals to the endocrinology department for management of diabetes. Serial patients with diagnoses of GDM and type 2 diabetes who were seen between June 2014 and October 2014 were included in the study. All patients with diagnoses of type 2 diabetes who had received prescriptions for oral hypoglycemic agents or insulin) for at least 1 year's duration were included. We excluded patients with any major illnesses, ocular ailments, surgeries or diabetic ketoacidosis in the past 6 months, use of glucocorticoids, and diagnoses of type 1 diabetes or secondary diabetes (secondary to endocrine or pancreatic disorders and drugs such as glucocorticoids). Pregnancy is known to worsen retinopathy in type 1 diabetes; hence, we excluded that group from the study (6). The control group was derived from the patients attending the antenatal clinic who were free from any systemic illness and had normal glucose tolerance (NGT) tests. VEP abnormalities were evaluated extensively in subjects with type 2 diabetes but rarely in patients with GDM. Hence, we planned to include the same number of controls, matching the number of the group with type 2 diabetes. This would give us a fair estimate of comparison between the retinopathy in patients with type 2 diabetes and normal glycemic profiles. All the study participants were divided into 3 groups for the analysis: group 1 (GDM), group 2 (type 2 diabetes) and group 3 (NGT).

Clinical data were collected from all the participants, including demographic details, such as age, gestational age, parity, family history of diabetes and duration of type 2 diabetes (in group 2 only). Details of the therapy prescribed were noted, including diet control alone, diet plus metformin or use of insulin. All the participants except group 2 (type 2 diabetes) were subjected to the 75 gm, 2-hour glucose tolerance test. We used the American Diabetes Association recommendations for the diagnosis of GDM (2). Fasting and the 2-hour postmeal blood glucose values were obtained from the patients with type 2 diabetes.

The VEP was recorded using the Scorpio System (Allengers Medical System, Chandigarh, India) connected to an amplifier for storing and summating the waves. We used the Scorpio System, because previous researchers used the same system for studying the normal values in the population from this part of the country (12). The VEP was evaluated by the voltage changes generated following application of a patterned stimulus to the visual system. The procedure was done according to the guidelines issued by the International Society of Clinical Electrophysiology of Vision (13). The VEP was recorded individually in each eye, and the average reading was taken for the study's purposes. We recorded the latency for P100 and N75 waves in milliseconds and the amplitude of P100 wave in microvolts. The local ethics committee approved the study protocol, and all patients provided written informed consent.

Data are presented as median (interquartile ranges) or numbers (%). Categorical variables were compared by using the Fisher exact test, and continuous variables were analyzed by the Kruskal-Wallis test. The Spearman correlation was used to study the associations with vitamin D and other clinical parameters. The Mann-Whitney test was used when the study population was divided into 2 groups: with diabetes (group A) and without diabetes (group B). A 2-tailed p value of less than 0.05 was considered significant for all the tests. The statistical analysis and graph generation was done using the GraphPad Prism Software, v. 6 (Graph Pad Software, San Diego, California, USA).

Results

The study participants (40 GDM, 10 type 2 diabetes, 10 NGT) had a median (25th to 75th interquartile range) age of 26 (24.3 to 30) years, a gestational age of 24.5 (21 to 27) weeks and weights of 66.8 (63.4 to 71.5) kg. The baseline parameters and detailed comparison among the 3 groups is given in Table 1. Briefly, the results show that the patients with type 2 diabetes were older than those in the other groups. The majority of the participants required dietary intervention along with metformin for the control of blood glucose levels. P100 latency was 96.6 (92.3, 102) in group 1, 96.7 (96, 99.9) in group 2 and 90.9 (85.5, 95.5) in controls. The P100 latency showed a trend toward significance (p=0.0577), and none of the VEP parameters differed significantly among the groups.

Correlation analyses in the entire study population revealed that the P100 latency showed a linear association with 2-hour blood glucose levels after glucose tolerance tests, as shown in Figure 1 (p=0.0118). However, the same finding was not observed with the fasting (p=0.1229) or 1-hour (p=0.4338) values. The P100 latency in patients with any glucose intolerance (96.7, 93.7, 101) (group A) was higher in comparison to the controls (90.9, 85.5, 95.5), as shown in the Figure 2 (p=0.0194). The comparison of VEP parameters between patients with glycemic intolerance and controls is given