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Brief Report

The OGTT is highly reproducible in Africans for the diagnosis of diabetes: Implications for treatment and protocol design

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ABSTRACT

Whether an OGTT reproducibly detects either type 2 diabetes (T2D) or prediabetes in Africans is unknown. Therefore, 131 Africans had two OGTT. Diagnostic reproducibility for T2D was excellent ($k = 0.84$), but only moderate for prediabetes ($k = 0.51$). A single OGTT positive for T2D may be sufficient to guide clinical care and inform epidemiologic study design. ClinicalTrials.gov Identifier: NCT00001853.

1. Introduction

As Africa has the highest global prevalence of people living with type 2 diabetes (T2D) who are undiagnosed, effective screening is essential for both clinical care and resource allocation [1]. As T2D is associated with poor outcomes from COVID-19, diagnosis of T2D has increased urgency [2]. Undiagnosed T2D in African countries is often attributed to a lack
of access to care [3]. However, failure of fasting plasma glucose (FPG) and HbA1c, to detect early T2D in Africans must be considered [3,4].

As early T2D in Africans often occurs with only a 2 h glucose (2 h-PG) $\geq$ 11.1 mmol/L, performance of an OGTT is pivotal [4,5]. Trust in OGTT results requires knowing whether OGTT results are reproducible. The only African study to assess OGTT diagnostic reproducibility was conducted in pregnant women [6]. Our goals were to determine in an African population the diagnostic reproducibility of the OGTT, primarily for the detection of T2D, and secondarily for prediabetes.

2. Materials and methods

OGTT (75 g dextrose) were performed after a 12 h fast, 11 ± 7 days apart in 131 African-born Blacks who self-identified as healthy and were living in America (age 40 ± 11 mean ± SD), range 20-65y, BMI 27.7 ± 4.5, range 19.3-39.5 kg/m², duration of United States residence 0.3–43 years. Participants denied a history of T2D or the use of medications or supplements which affect glucose tolerance. Prior to OGTT-1, routine blood tests which documented normal hemoglobin levels, liver, kidney and thyroid function were performed [7]. Glucose tolerance categories were based on International Diabetes Federation (IDF) glucose criteria [1]. The kappa-statistic was used to determine diagnostic reproducibility [8]. The study was approved by the NIH Institutional Review Board (Clinical Trials.gov Identifier: NCT00001853). Informed consent was obtained.

3. Results

For OGTT-1 and OGTT-2, prevalence of T2D was 23% (30/131) and 18% (23/131), respectively (Fig. 1). For prediabetes, prevalence was 24% (31/131) and 28% (37/131), respectively. For normal glucose tolerance (NGT), prevalence was 53% (70/131) and 54% (71/131), respectively. The coefficients of variation for FPG and 2h-PG were 3.7% and 10.6%, respectively.

Considering two outcomes (T2D or no-T2D), reproducibility for diagnosis of T2D was excellent ($\kappa$ = 0.84, 95% CI: 0.72, 0.95). All individuals who transitioned out of T2D on OGTT-1 were diagnosed with prediabetes on OGTT-2. Hence, everyone with T2D at OGTT-1 needed follow-up care.

Most individuals with T2D identified by 2 h-PG > 11.1 mmol/L would not have been detected if only FPG had been performed. At OGTT-1, thirty individuals had 2 h-PG > 11.1 mmol/L, but 23% (7/30) of those had normal fasting glucose (FPG < 5.6 mmol/L), 57% (17/30) had impaired fasting glucose (FPG ≥ 5.6 and < 7.0 mmol/L) and only 20% (6/30) met fasting glucose criteria for T2D (FPG ≥ 7.0 mmol/L).

In our secondary analysis, diagnostic reproducibility of prediabetes by OGTT was moderate ($\kappa$ = 0.51, 95% CI: 0.32, 0.69). Twenty-one individuals switched between NGT to prediabetes or prediabetes to NGT (Fig. 1). Eighteen of the 21 individuals who switched categories had FPG at OGTT-1 between 5.0 and 6.0 mmol/L. Overall, participants with FPG between 5.0 and 6.0 mmol/L had five times the odds of transitioning between NGT and prediabetes than those with FPG outside this range (OR 4.91, 95% CI: 1.34, 17.9, $P = 0.016$).

4. Discussion

This investigation provides insight which could influence both diagnostic practice and epidemiologic survey design. As the reproducibility of the diagnosis of T2D by 2 h-PG ≥ 11.1 mmol/L was excellent, a single OGTT with a 2 h-PG ≥ 11.1 mmol/L could be considered diagnostic in both clinical settings and epidemiologic surveys. In contrast to the value of 2 h-PG, FPG ≥ 7.0 mmol/L detected only 20% of Africans with T2D. The low sensitivity of FPG as a diagnostic test for T2D in Africans needs widespread recognition.

Our secondary finding is that diagnosis of prediabetes by the OGTT is poorly reproducible. However, switching between NGT and prediabetes was highest if FPG at OGTT-1 was between 5.0 and 6.0 mmol/L.

4.1. Diagnosis of T2D by 2 h-PG ≥ 11.1 mmol/L

Currently two tests must be positive for the diagnosis of T2D [9]. As 2 h-PG ≥ 11.1 mmol/L was highly reproducible in the detection of T2D in African-born Blacks living in the United States, our study suggests a single OGTT with 2 h-PG ≥ 11.1 mmol/L could be considered diagnostic in both clinical care settings and epidemiologic evaluation of T2D prevalence. However, further verification by repeating this study in Africa would be valuable.

4.2. Diagnosis of T2D by FPG ≥ 7.0 mmol/L

FPG ≥ 7.0 mmol/L only occurred in 20% of participants with T2D based on 2 h-PG ≥ 11.1 mmol/L. FPG is often lower in African descent populations than whites [10]. Compared to whites, African descent populations have less hepatic fat, lower triglyceride concentrations, less hepatic glucose production, and greater hepatic insulin sensitivity [11,12]. These
population-based physiologic differences provide a rationale for designing prospective studies with power sufficient to determine the appropriate FPG threshold for the diagnosis of T2D in African descent populations.

As FPG performs poorly as a diagnostic test for asymptomatic T2D in Africans, the value of the cumbersome post-challenge glucose remains. To facilitate the conduct of an OGTT, there is a movement to transition from 2 h-OGTT to 1 h-OGTT [13]. As the 1 h-OGTT has been shown in several populations to provide a post-challenge assessment of glucose tolerance status, determining the 1 h-PG concentration predictive of 2 h-PG ≥ 11.1 mmol/L in Africans is worthy of investigation [13].

4.3. Fasting plasma glucose between 5.0 and 6.0 mmol/L

In our secondary analyses, we found that similar to other populations, OGTT reproducibility for the detection of prediabetes was unsatisfactory [14]. To understand why, we examined individuals who had FPG between 5.0 and 6.0 mmol/L and found that they were five times more likely to transition between NGT and prediabetes than individuals with FPG outside of this range. Therefore, low diagnostic reproducibility of prediabetes by the OGTT may be accounted for by frequent transitioning between NGT and prediabetes.

Identifying individuals who frequently transition between NGT and prediabetes is important. Duplicate OGTT performed in China found that individuals with one abnormal OGTT had a worse cardiovascular risk profile than individuals with two normal OGTT [15]. In a longitudinal study of Israeli soldiers, FPG between 5.0 and 6.0 mmol/L, carried a high risk for the future development of T2D [16]. Therefore, it would be valuable to perform prospective studies of Africans with FPG between 5.0 and 6.0 mmol/L to determine if they are at high risk for the development of both T2D and cardiovascular disease.

5. Conclusions

Based on duplicate OGTT studies in Africans, we have shown that an OGTT reproducibly detects T2D but not prediabetes. As FPG ≥ 7.0 mmol/L, was not found in 80% of those with T2D, appreciating that FPG is not a substitute for the OGTT is essential. In short, as the search for simpler alternatives continues, a single OGTT which detects T2D may be sufficient to guide diagnosis and provide data for population-based investigations.

Author Contributions

RJ, MB and AES did the literature search. CWD, LSM, STC and AES designed the study. CWD, LSM, STC and AES contributed to enrollment. CWD, LSM, STC and AES collected the data. RJ, AS, MB and AES analyzed the data. RJ and AES made the figures. RJ, MB and AES wrote the first draft. RJ, CWD, LSM, STC, RJ, AS, MB and AES provided critical rewrites of the manuscript.

Role of the funding source

None.

Prior presentation

This study was presented in abstract form at the American Diabetes Association Scientific Sessions in San Francisco, CA, June 2019.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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