

Comparative performance of lab tests and blood testing device to monitor glucose, total cholesterol and triacylglycerol in type 2 diabetic patients

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The performance of lab tests (LT) and blood testing devices (BTD) to monitor glycemia *vs.* glycosylated hemoglobin A1c (A1c) were compared. In addition, the performance of blood glucose, total cholesterol (TC) and triacylglycerol measured by LT and BTD were compared. All parameters were measured based on the same blood samples from overnight fasted type 2 diabetic patients (T2DP). Linear regression analysis was used for all comparisons. The results showed that A1c correlated better with LT-glucose ($r = 0.58$) than BTD-glucose ($r = 0.42$). Moreover, LT *vs.* BTD showed r values of 0.90, 0.82 and 0.92 for glucose, TC and triacylglycerol, respectively. It was concluded that the performance of LT-glucose was better than BTD-glucose. Moreover, since triacylglycerol and TC measured by BTD correlated better with LT compared to BTD-glucose *vs.* LT-glucose, the inclusion of BTD-TC and BTD-triacylglycerol for detecting and monitoring hyperlipidemia in T2DP should be considered.

Uniterms: Laboratory tests. Glycosylated hemoglobin. Glycemia. Total cholesterol. Triacylglycerol. Type 2 diabetes.

Comparou-se a performance de avaliação da glicemia através de dosagens laboratoriais (DL) ou dispositivo para teste de sangue capilar (DTSC) *vs.* hemoglobina glicada A1c (A1c). Comparou-se ainda a performance de avaliação da glicemia, colesterol total (CT) e triacilglicerol (DL *vs.* DTSC). Avaliou-se estes parâmetros a partir das mesmas amostras de sangue coletadas em pacientes diabéticos tipo 2 (PDT2) em jejum noturno, sendo as comparações realizadas através de análise de regressão linear. A A1c correlacionou-se melhor com a glicemia-DL ($r = 0,58$) em relação a glicemia-DTSC ($r = 0,42$). Comparou-se DL *vs.* DTSC obtendo-se $r = 0,90, 0,82$ e $0,92$ para glicemia, CT e triacilglicerol, respectivamente. Concluiu-se que houve melhor performance da glicose-DL em relação a glicose-DTSC. Além disso, considerando que o triacilglicerol e TC avaliados através de DTSC correlaciona-se melhor com DL em comparação a DTSC-glicose *vs.* DL-glicose, a inclusão de DTSC-TC e DTSC-triacilglicerol visando detectar e monitorar hiperlipidemia in PDT2 deve ser considerada.

Unitermos: Exames laboratoriais. Hemoglobina glicada. Glicemia. Colesterol total. Triacilglicerol. Diabetes tipo 2.

INTRODUCTION

Glycemic control is fundamental in the management of type 2 diabetes. The United Kingdom Prospective Diabetes Study (UKPDS), a prospective, randomized, controlled trial of intensive versus standard glycemic control in

type 2 diabetic patients, showed definitively that improved glycemic control is associated with significantly decreased rates of diabetic complications (UK Prospective diabetes study group (1998).

Moreover, epidemiological analyses of the UKPDS demonstrated a curvilinear relationship between glycosylated hemoglobin A1c and diabetic complications, suggesting that the majority of complications could be prevented by the implementation of good glycemic control (Stratton *et*

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al., 2000). This study also suggested that further lowering of glycated hemoglobin A1c from 7 to 6% was associated with significant reduction of diabetic complications. In agreement, the American Diabetes Association suggested glycated hemoglobin A1c of less than 7% to prevent chronic complications (American Diabetes Association, 2010).

However, in spite the fact that glycated hemoglobin A1c is considered the cornerstone of clinical management of diabetes, (American Diabetes Association, 2010) fasting glycemia is the most widely used lab test to evaluate the glycemic status of people with diabetes (Al-Lawati, Al-Lawati, 2007; Correr *et al.*, 2009; Silva *et al.*, 2004).

Furthermore, in recent years a clear tendency for evaluating blood glucose, total cholesterol and triacylglycerol with blood testing devices has emerged (Laguna *et al.*, 2009; Nathan *et al.*, 2008; Cassani *et al.*, 2009; Pongwecharak, Treeranurat, 2010). However, the performance of these methods in comparison with classical lab tests is not yet well established.

In the present investigation, the performance of blood glucose measurements from lab tests and blood testing devices for glycated hemoglobin A1c levels was compared. Moreover, the performance of lab tests and blood testing devices was also compared for glucose, total cholesterol and triacylglycerol measurements.

PATIENTS AND METHODS

Written consent to participate in this investigation was obtained from each patient and the study was approved by the Ethics Committee of the State University of Maringá (COPEP - CAAE 0133-06).

Exclusion criteria were pregnancy, gestational diabetes, type 1 diabetes and other specific types of diabetes. Eligibility criteria were: age over 30 years, confirmed diagnosis of type 2 diabetes and use of at least one prescribed anti-diabetic drug.

The patients, recruited from a pharmacy school, were interviewed and information on medical history, socio-demographic characteristics, pharmacotherapeutic profile and lifestyle were collected. After the interview, blood pressure (BP) and body mass index (BMI) were evaluated. BP (mmHg) was measured as described elsewhere (Ferri *et al.*, 2006).

Immediately after the interview the patients received instructions for blood collection at a laboratory accredited by the Brazilian Society of Clinical Analysis.

Venous blood was collected from overnight fasted patients for analysis of glucose, total cholesterol and

triacylglycerol by a blood testing device (BTD) and lab tests (LT). In addition, glycated hemoglobin A1c was measured. All analyses were done from the same blood sample.

Immediately after blood collection, part of the fresh blood was immediately used to measure glycated hemoglobin A1c (Metus *et al.*, 1999), glucose, total cholesterol and triacylglycerol by BTD (Accutrend GCT[®] - Roche Company). The normal values of glycated hemoglobin A1c, glucose, total cholesterol and triacylglycerol were < 7%, 70-130 mg/dL, < 200 mg/dL and < 200 mg/dL, respectively.

Moreover, part of the blood was transferred to a tube containing sodium fluoride/EDTA, which was immediately centrifuged and the plasma separated to measure glucose (Bergmeyer, Bernt, 1974), total cholesterol (Allain *et al.*, 1974) and triacylglycerol (Bucolo, David, 1973) by LT. The normal values of blood glucose, total cholesterol and triacylglycerol were < 100 mg/dL, < 200 mg/dL, and < 150 mg/dL, respectively. These values were based in the position statement of the Clinical Practice Recommendation of the American Diabetes Association (2010).

Linear regression analysis using GraphPad Prism (version 5) was done to investigate the relationship between glycated hemoglobin A1c vs. glucose (LT), A1c vs. glucose (BTD), glucose (LT vs. BTD), total cholesterol (LT vs. BTD) and triacylglycerol (LT vs. BTD).

Some results were expressed as percentage (%) and others as mean \pm standard deviation (SD).

RESULTS

A total of 32 volunteers, 16 (50%) men and 16 (50%) women, were assessed. The values for all biochemical parameters did not differ between men and women (data not shown).

Among these patients, whose mean age was 57.8 ± 7.3 years ranging from 48 to 74 years, the time of diagnosis was 12.0 ± 9.0 years, ranging from 1 to 37 years.

Most patients had one or more comorbidities associated with diabetes, with a prevalence of hypertension (93.8%) and overweight or obesity (68.8%).

The value of glycated hemoglobin A1c, glucose (LT), glucose (BTD), total cholesterol (LT), total cholesterol (BTD), triacylglycerol (LT) and triacylglycerol (BTD) were $9.2 \pm 2.3\%$, 176.5 ± 56.3 mg/dL, 129.2 ± 44.2 mg/dL, 181.1 ± 36.9 mg/dL, 182.2 ± 21.8 mg/dL, 147.5 ± 88.0 mg/dL and 194.7 ± 90.0 mg/dL, respectively.

The number (%) of patients with altered values for glycated hemoglobin A1c, glucose (LT), glucose (BTD), total cholesterol (LT), total cholesterol (BTD), triacyl-

glycerol (LT) and triacylglycerol (BTD) were 25 (78.1%), 24 (75.0%), 14 (43.8%), 9 (32%), 4 (14.3%), 10 (33.3%) and 13 (41.9%), respectively (Table I).

As can be seen in Figure 1A and 1B, glycated hemoglobin A1c correlated better with glucose measu-

red by LT ($r = 0.58$) than BTD ($r = 0.42$). On the other hand, the comparison of LT and BTD show r values of 0.90, 0.82, 0.92 and glucose (Figure 2A), total cholesterol (Figure 2B) and triacylglycerol (Figure 2C), respectively.

TABLE I - Individual and mean (M) \pm standard deviation (SD) of glycated hemoglobin A1c (A1c), blood, glucose (GLU), total cholesterol (TC) and triacylglycerol (TG). GLU, TC and TG were measured by Lab test (LT) and blood testing device (BTD). A1c was expressed as % and all other parameters were expressed as mg/dL. Blood was collected from overnight fasted type 2 diabetic patients. nd: not determined

Patient	A1c	GLU – LT	GLU-BTD	TC – LT	TC-BTD	TG – LT	TG – BTD
1	8.4	156	88	166	150	192	229
2	8.2	192	158	237	193	224	267
3	9.9	188	117	107	167	88	143
4	9.5	180	98	172	193	322	246
5	10.3	169	103	170	174	93	146
6	12.8	229	158	202	196	202	255
7	7.5	168	144	202	190	130	192
8	9.6	264	196	172	180	206	292
9	9.6	196	169	142	169	192	193
10	11.6	252	179	210	200	95	138
11	12.4	266	216	218	223	122	177
12	8.7	229	146	nd	nd	nd	101
13	10.6	137	77	182	168	103	156
14	6.4	113	94	nd	nd	127	203
15	7.2	164	110	nd	nd	110	208
16	6.4	103	83	116	168	68	120
17	7.5	121	101	180	171	46	89
18	6.8	92	73	171	165	108	97
19	11.5	219	175	175	180	471	548
20	11.6	301	234	174	169	132	198
21	7.4	126	130	151	157	64	101
22	9.1	212	171	152	165	135	198
23	9.4	184	145	198	175	160	221
24	7.0	173	134	181	175	115	171
25	6.9	148	97	196	185	88	138
26	8.7	51	53	202	200	37	88
27	7.2	156	107	207	199	119	183
28	14.1	173	87	286	250	nd	nd
29	13.9	155	114	132	160	91	134
30	6.8	126	91	nd	nd	143	213
31	12.2	258	176	215	213	192	269
32	6.3	148	111	157	168	250	322
M	9.2	176.5	129.2	181.1	182.2	147.5	194.7
SD	2.3	56.3	44.2	36.9	21.8	88.0	92.0

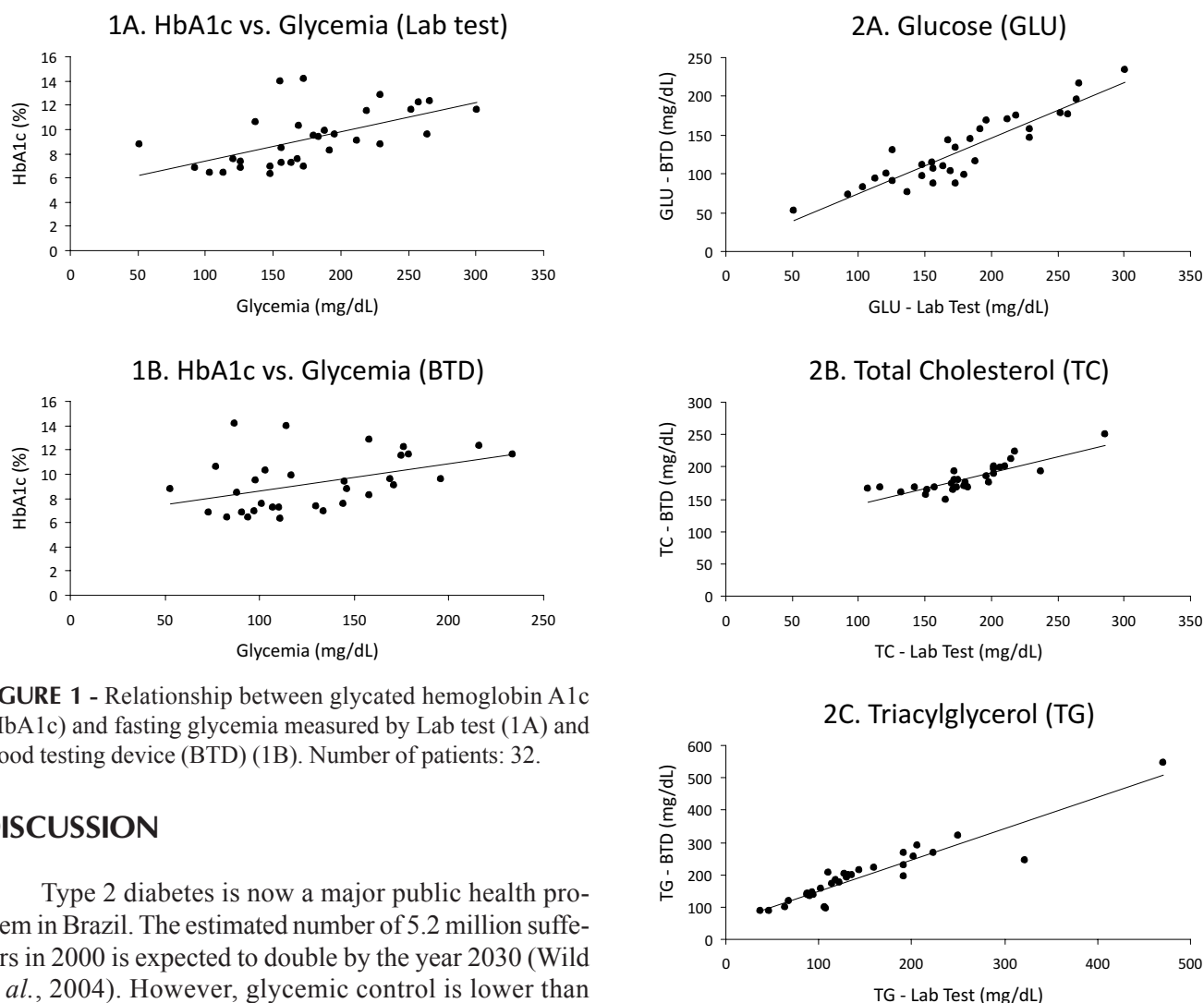


FIGURE 1 - Relationship between glycated hemoglobin A1c (HbA1c) and fasting glycemia measured by Lab test (1A) and blood testing device (BTD) (1B). Number of patients: 32.

DISCUSSION

Type 2 diabetes is now a major public health problem in Brazil. The estimated number of 5.2 million sufferers in 2000 is expected to double by the year 2030 (Wild *et al.*, 2004). However, glycemic control is lower than 50% (Gomes *et al.*, 2006; Assunção, Santos, Valle, 2005), which inevitably contributes to the increasing occurrence of chronic complications in type 2 diabetic patients.

Furthermore, type 2 diabetes is normally asymptomatic, but if the disease is not adequately treated a range of chronic complications can result in reduced quality of life and premature death (Assunção, Santos, Valle, 2005).

Therefore, monitoring the treatment of type 2 diabetes has important implications for individual health and public health policy and for this purpose fasting glycemia is the most commonly used exam (Silva, Bazotte, 2010; Pimentel *et al.*, 2010). Moreover, considering the high risk of cardiovascular disease, the control of blood lipid profile must be considered (Colagiuri, 2010).

Our results showed that the majority of the patients did not exhibit suitable control of glycemia and lipid profile (Table I). These results are in line with the findings of several other studies, in which the majority of type 2 diabetic patients exhibited poor blood glucose and lipid

FIGURE 2 - Relationship between lab test and blood testing device (BTD) for glycemia (2A), total cholesterol (2B) and triacylglycerol (2C). Number of patients: 32.

control (Kemp *et al.*, 2005; Saydah, Fradkin, Cowie, 2004; McFarlane *et al.*, 2002; Grant, Buse, Meigs, 2005; Silva, Bazotte, 2010).

Linear regression analysis to investigate the relationship between glycated hemoglobin A1c vs. fasting glycemia (LT and BTD) revealed that glycated hemoglobin A1c correlated better with LT than with BTD (Figure 1A, B). Furthermore, in the case of patients 1, 4, 13, 26 and 28 (Table I), fasting glycemia obtained by BTD, i.e., ≤ 100 mg/dL, could yield misleading information of good glycemic control since results contrasted with the elevated values of glycated hemoglobin A1c. For LT, this problem is limited to patient 26 (Table I). Therefore, in spite of the fact that glycemia measured by BTD has become faster and more accurate over the past 3 decades and now allows

for better glycemic control by diabetics than in the past, this test is no substitute for fasting glycemia values obtained by lab tests.

There is consensus on continuous monitoring of lipid profile in type 2 diabetes. This question acquires greater relevance considering that diabetes is a significant cardiovascular risk and given that blood lipid targets are not attained by the majority of type 2 diabetic patients (Gomes *et al.*, 2006; Grant, Buse, Meigs, 2005; Silva, Bazotte, 2010). In this context, our results showed that, in spite of the fact that BTM for measuring total cholesterol and triacylglycerol were introduced into clinical practice later than glycemia, they show good correlation with laboratory results. In the specific case of triacylglycerol, the *r* value (*r* = 0.92) for comparison of BTM vs. LT was higher than that obtained for glucose (*r* = 0.90).

CONCLUSION

Congruent with the well-established role of BTM in the detection and self-monitoring of glycemia, the Brazilian Government approved RDC 44/ANVISA (Resolução da Diretoria Colegiada, 2009) in which capillary glycemia was established as a pharmaceutical service care for diabetes screening and glucose monitoring. However, considering that glycated hemoglobin A1c correlated better with LT than BTM, device tests are no substitute for the fasting glycemia values obtained by lab tests. Finally, since BTM-TC and BTM-triacylglycerol showed good correlation with LT, the inclusion of BTM-TC and BTM-triacylglycerol in the detection and monitoring of hyperlipidemia in T2DM should be considered.

Finally, any analysis of the results must consider the limited number of patients investigated, i.e., 32 volunteers. However, this limitation was overcome, partly at least, by the fact that all biochemical parameters were evaluated based on the same blood sample. This experimental approach, in which each patient served as their own control, rules out the interference of several factors such as age, duration of diabetes, gender, BMI and variability owing to blood collection on different days. However, future studies involving a higher number of patients are necessary to confirm the conclusions of this study.

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Conflict of Interest

The authors declare that they have no proprietary, financial, professional, or other personal interest that may influence the conclusions of this study.

Statement

I hereby confirm that all patients/personal identifiers have been removed or masked to ensure the patient/person(s) described are not identifiable and cannot be identified through the details of the study.

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