

# Continuous glucose monitoring system: dawn period calibration does not change accuracy of the method

Sistema de monitorização contínua de glicose: calibração da madrugada não interfere na acurácia do método

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## ABSTRACT

**Introduction:** Continuous glucose monitoring system is a valuable instrument to measure glycemic control, which uses a retrospective calibration based upon 3 to 4 capillary glucose meter values inserted by the patient each day. **Objective:** We evaluated the interference of calibration during the dawn period in the system accuracy. **Methods:** The monitoring data were retrospectively divided into two groups: with (Group A) or without (Group B) the dawn period calibration (between 1:00 and 5:00 AM). Accuracy of the method was expressed by relative absolute difference. **Results:** Thirty-four continuous glucose monitoring data were evaluated comprising a total of 112 nights. A total of 289 paired readings were analyzed – 195 in Group A and 94 in Group B. We did not find a difference in relative absolute difference (RAD%) in any analyzed period of day by adding dawn calibration. **Conclusions:** These data suggest that dawn calibration does not alter accuracy of method. *Arq Bras Endocrinol Metab.* 2009;53(4):425-8.

## Keywords

*Diabetes mellitus*; glycemic control; hypoglycemia; continuous monitoring

## RESUMO

**Introdução:** O CGMS (sigla do inglês *continuous glucose monitoring system*) é um instrumento valioso no controle glicêmico e utiliza uma calibração por meio de 3 ou 4 medidas de glicemia capilar inseridas pelo paciente em cada dia do exame. **Objetivo:** Avaliar a interferência da calibração durante a madrugada na acurácia do sistema. **Métodos:** Os dados das monitorizações foram divididos retrospectivamente em dois grupos: com (Grupo A) ou sem (Grupo B) a calibração da madrugada (entre 1:00 e 5:00 AM). A acurácia do método foi mostrada pela diferença relativa absoluta (DRA%). **Resultados:** Trinta e quatro dados de monitorização foram avaliados em um total de 112 noites. Um total de 289 leituras pareadas foi analisado – 195 no Grupo A e 94 no Grupo B. Não foi encontrada diferença em DRA% em nenhum período do dia quando adicionada a calibração durante a madrugada. **Conclusões:** Esses dados sugerem que a calibração da madrugada não altera a acurácia do método. *Arq Bras Endocrinol Metab.* 2009;53(4):425-8.

## Descritores

Diabetes melito; controle glicêmico; hipoglicemia; monitorização contínua

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## INTRODUCTION

In the last years, the continuous glucose monitoring system (CGMS, Medtronic MiniMed, Northridge, CA) has arisen as a useful tool in glycemic evaluation of patients with diabetes, providing clinically relevant information for individuals with diabetes and their care providers (1,2). The CGMS uses a retrospective calibra-

tion based upon 3 to 4 capillary glucose meter values (CG) inserted by the patient each day, but there is no clear recommendation about the best time to perform CGMS sensor calibration (3,4).

Continuous glucose monitoring offers an opportunity to obtain detailed glucose control evaluation, especially during the overnight period, when the measurement of

CG by patients with diabetes is more difficult to obtain. The clinical practice has demonstrated that the number of blood glucose measurements during night-time is less frequent than desired to evaluate the adequacy of bedtime insulin dose, even when it is required by the care providers. Two recent studies (3,5) have suggested a reduction in the accuracy of the CGMS during night-time readings, with a tendency of lower values of interstitial glucose (IG) than CG. Moreover, DirectNet Study Group suggested that the sensor accuracy was much improved by calibrations when there was not a rapid rate of glucose change (3), for example, during the long fasting nocturnal period.

The present study was undertaken to evaluate the interference of CGMS calibration during the dawn period in the system accuracy.

## METHODS

All patients were followed up at the Hospital das Clínicas (HC), in São Paulo. The study protocol was approved by the ethics committee of the hospital, and informed consent was obtained from the patients or their guardians. From 2003 to 2006, CGMS data of 30 patients with type 1 and 2 diabetes, using intensive insulin therapy and presenting high levels of HbA1c and/or high frequency of hypoglycemia were retrospectively analyzed. CGMS sensors were inserted into the subcutaneous abdominal fat tissue. While wearing the CGMS, the patients were asked to perform, at least, four daily self monitoring of blood glucose (SMBG) tests by home glucose meter (Accu-Chek®; Roche®) and to enter these values into the CGMS for sensor calibration. Accuracy of the method was expressed by relative absolute difference (RAD%), calculated for each IG-CG pair:  $RAD\% = CG - IG / CG$  (6).

Patients always performed SMBG calibration measures at night and, while fasting, during the exam days. The monitoring data were retrospectively divided into two groups: with (Group A) or without (Group B) the dawn period calibration (between 1:00 and 5:00 AM). A total of 289 paired readings were analyzed, 195 in Group A and 94 in Group B. Differences in the accuracy in the morning period in relation to the night period between Groups A and B were studied. Clinical data of patients are showed in table 1.

The Pearson correlation coefficient ( $r$ ) between CG and IG of Groups A and B was determined by linear regression. *T*-Student test was performed to compare the RAD% of Groups A and B.

**Table 1.** Characteristics of patients

Group	A	B	p-value
n	14	16	
Male (%)	25%	21,4%	
Age	26,4 ± 9,1	31,6 ± 15,9	0,32
Diagnosis (years)	14,7 ± 9,2	13,5 ± 8,0	0,73
DM1	100%	85,7%	
HbA1c (%)	7,12 ± 0,8	9,11 ± 0,8	< 0,0001
Complications	25,0%	35,7%	
Microalbuminuria	8,3%	28,5%	
Retinopathy	25,0%	28,5%	
Nephropathy	0,0%	14,2%	
Neuropathy	8,3%	7,1%	

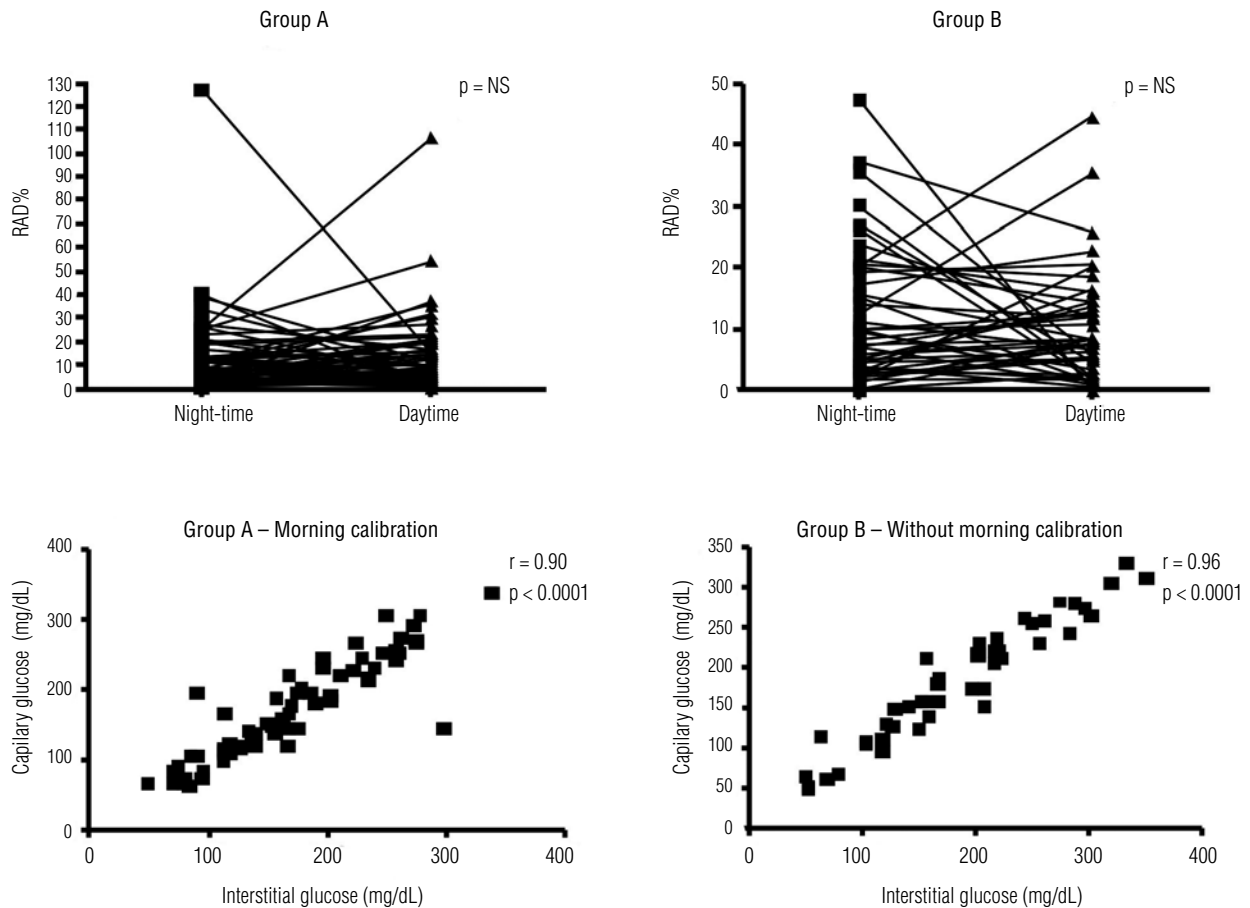
## RESULTS

The 30 diabetic patients who participated in the study had a median age of 24.5 years (range 14 to 63 years); median time since diagnosis of 14.5 years (range 3 to 31 years) and median HbA1c of 8.2% (range 5.6 to 11.2%). Twenty-four patients were female. Thirty-four continuous glucose monitoring data were evaluated comprising a total of 112 nights. Thirty percent of patients (8/30) had hypoglycemia during the evaluated nights, with a median duration of 200 minutes (range 30 to 500 minutes).

We identified an adequate correlation between CG and IG in both Groups A and B with Pearson coefficient ( $r$ ) of 0.91 ( $p < 0.0001$ ) and 0.96 ( $p < 0.0001$ ), respectively. There was no difference in median fasting RAD% among Groups A and B (7.4 *versus* 7.8%;  $p = 0.73$ ); neither difference was seen in night-fasting RAD% variation between the two groups (-0.34 *versus* +1.91%;  $p = 0.75$ ) (Figure 1). The mean RAD% of Group A was  $12 \pm 9.4$  and, of Group B, it was  $11 \pm 7.7$ , with no difference between them.

## DISCUSSION

CGMS allows continuous evaluation of glucose levels due to strictly correlation between IG and CG (7). Therefore, it could help handling patients with diabetes, mainly using multiple doses of insulin, in association with HbA1c and SMBG (8,9). There is a recommendation to perform at least 3 to 4 calibrations/day, during continuous glucose monitoring. Studies observed that the accuracy of CGMS is higher when more calibrations values are performed (10). We did not find a difference in RAD% in any analyzed period of day by adding dawn calibration.



**Figure 1.** Night-fasting RAD% variation in Groups A and B; correlation between CG and IG in both groups.

One of the most important indications of CGMS is the evaluation of hypoglycemia, especially asymptomatic episodes in the dawn period (11). In the presented study, 1/3 of the patients presented hypoglycemia during sleep. However, it has been noted that accuracy during this period is decreased, as well as in hypoglycemic episodes (3,5). In addition, hypoglycemia can be overestimated during the dawn period, due to physiologic differences in glucose uptake, utilization, and elimination in blood, interstitial space, and cells or a change in bioactivity of sensor (10,12). Furthermore, rapid changes in plasma glucose may not be followed by IG variation of the same degree and speed (13). In our study, we did not find an increased accuracy between CG and IG in the morning measurements of Group A (with dawn calibration) when compared with Group B, using relative absolute difference (RAD%). We also did not observe statistical difference between CG and IG fasting values of both groups.

In their study, Guerci and cols. (14) compared CGMS accuracy with CG and blood sample glu-

cose. Coefficients of correlation ranged from 0.87 to 0.92, and the mean absolute error ranged from 12.8 to 15.7%. Only 39% of the CGMS values satisfied the American Diabetes Association (ADA) precision criteria to within  $\pm 10\%$ , and 19% of these values satisfied the future ADA precision criteria of accuracy to within 5%. Although the accuracy of CGMS can be improved, we observed an adequate correlation between CG and IG in our study, therefore we could evaluate glucose control during night-time.

These data suggest that dawn calibration does not alter accuracy of CGMS and it implies a more comfortable exam without the recommendation to perform a dawn period calibration.

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