Influence of Simulated Altitude on the Performance of Five Blood Glucose Meters

JEAN-FRANCOIS GAUTIER, MD
ANDRE XAVIER BIGARD, MD, PHD
PHILIPPE DOUCE, MD
ALAIN DUVALLET, MD
GERARD CATHELINEAU, MD

OBJECTIVE — To determine the reliability of five blood glucose meters (BGMs) at various simulated altitudes using a hypobaric chamber.

RESEARCH DESIGN AND METHODS — Blood glucose levels (ranged from 1.5 to 26.3 mmol/l, according to the reference method) were measured in 18 venous blood samples by each BGM at 200, 1,000, and every 500 m up to 4,000 m in a hypobaric chamber, where temperature and humidity were held constant.

RESULTS — Four BGMs underestimated and one overestimated blood glucose concentration while barometric pressure decreased. The average percent error varied in relation to simulated altitude from 0.26 ± 4.8% (SD) at 200 m to −28.9 ± 4.5% at 4,000 m (Glucometer 3; $P < 0.05$), from 28.4 ± 5.7 to 49.3 ± 5.9% (Accu-Chek Easy; $P < 0.05$), from −10.5 ± 2.6 to 19.8 ± 4.3% (Tracer; $P < 0.05$), from −5.5 ± 2.6 to −11.2 ± 3.0% (Reflolux; NS), and from 17.8 ± 4.3 to 14.8 ± 3.6% (One Touch; NS). The most accurate seemed to be the Reflolux, except for high blood glucose levels at simulated high altitudes. The One Touch II showed a good agreement, whatever the barometric pressure and the range of blood glucose concentrations. The highest underestimation was seen with the Glucometer 3.

CONCLUSIONS — Except for the Accu-Chek Easy, low barometric pressure underestimated the BGM results in comparison with measurements taken at simulated low altitudes. The lack of accuracy and consistency of performance >2,000 m should be known by diabetic patients practicing sports activities, such as trekking or skiing at high altitudes.

An important goal in IDDM treatment is to give patients the chance to live as normally as possible, remaining physically active and able to participate in different sports and leisure time activities. However, muscular exercise may induce hypoglycemia or worsen poor metabolic control (1,2). These risks may be avoided by decreasing insulin doses, adjusting the diet, and maintaining good metabolic control. Self blood glucose monitoring is mandatory to check adjustments of insulin dose and carbohydrate ingestion. Many blood glucose meters (BGMs) available for diabetic patients were found to be reliable and accurate at sea level (3,4). However, sports activities at high altitudes, such as trekking or skiing, usually entail long-lasting exercise in the cold and therefore require rigorous blood glucose monitoring. However, at high altitudes, capillary blood glucose monitoring may be unreliable because of changes in temperature, humidity, and barometric pressure (5–8). Because most BGMs are based on the glucose oxidase method, the altitude-linked decrease in partial pressure of oxygen may alter BGM performances. It has been shown that many BGMs underestimated blood glucose values at 2,244 m (6,800 feet) (6). The present study aimed at evaluating five BGMs currently used in Europe, at various levels of simulated altitude up to 4,000 m (12,120 feet) by steps of 500 m (1,515 feet).

RESEARCH DESIGN AND METHODS

Five BGM systems were evaluated in this study: Accu-Chek Easy, Reflolux SF, Tracer (Boehringer Mannheim, Indianapolis, IN), One Touch II (Lifescan, Milpitas, CA), and Glucometer 3 (Bayer Diagnostics, Ames, Elkhart, IN). These systems measure blood glucose using the colored chromogen produced by the glucose oxidase-peroxidase reaction. Identifying which BGMs overestimate low blood glucose values and which underestimate high values may be of great clinical importance. We therefore analyzed BGM performance in three ranges determined by the reference method: blood glucose levels <5.6 mmol/l, between 5.6 and 13.9 mmol/l, and >13.9 mmol/l (6). Venous blood samples were obtained from healthy Caucasian subjects who gave their free, informed, and written consent. Venous blood samples were enriched with glucose solutions so that blood glucose concentrations covered the hyperglycemic range. The hypoglycemic range blood samples were obtained after the intravenous regular insulin injection as described by Bonora et al. (9). Samples were collected into lithium heparin tubes, and glucose concentrations were immediately determined in duplicate by a reference method not dependent on the partial pressure of oxygen. Our method was a colorimetric method using ortho-toluidine (10). Blood glucose levels were assayed spectrophotometrically at 630 nm (coefficient of variation ~3%). We studied 18 samples with glucose concentrations ranging from 1.5 to 26 mmol/l, according to the reference method.

These samples were evaluated using the five BGMs under local barometric pressure (BP ~765 mmHg, 200 m, 606 feet) and under hypoxic conditions in a hypobaric chamber from 1,000 m (3,030 feet; BP = 674 mmHg) to 4,000 m (12,120 feet; BP = 462 mmHg) by steps of 500 m (1,515 feet). Blood samples were maintained in ice during the sojourn in the hypobaric cham-

From the Department of Endocrinology, Saint-Louis Hospital, Paris; and the Department of Physiology, Institute of Aerospace Medicine, Brétigny sur Orge, France.
Address correspondence and reprint requests to J.-F. Gautier, MD, Service d'Endocrinologie, Hôpital Saint-Louis, 1 avenue Claude Vellefaux, 75475 Paris Cedex 10, France.
Received for publication 19 December 1995 and accepted in revised form 11 July 1996.
BGM, blood glucose meter; PE, percent error.

Downloaded from http://ada.silverchair.com/care/article-pdf/19/12/1430/445662/19-12-1430.pdf by guest on 09 April 2024

Table 1—*Linearity of the blood glucose data and estimation of the agreement between experimental and reference methods at each simulated altitude*

	Altitude							
m	150	1,000	1,500	2,000	2,500	3,000	3,500	4,000
feet	454	3,030	4,545	6,060	7,575	9,090	10,605	12,120
Accu-Chek Easy								
r	0.96	0.98	0.98	0.98	0.99	0.99	0.99	0.99
t	3.32	4.91	5.80	6.81	19.78	13.28	22.26	11.13
Bias	−2.33 ± 2.56	−2.50 ± 2.40	−2.79 ± 2.60	−3.12 ± 2.79	−3.19 ± 2.38	−3.26 ± 2.46	−3.78 ± 2.93	−3.67 ± 3.13
Glucometer 3								
r	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.98
t	−5.08	−6.35	−9.49	−5.82	−19.58	−18.33	−20.38	−17.56
Bias	0.70 ± 1.46	1.64 ± 1.99	2.24 ± 2.32	2.14 ± 1.99	3.12 ± 3.10	3.62 ± 3.63	4.06 ± 3.91	3.90 ± 3.44
One Touch II								
r	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.98
t	2.96	3.07	1.79*	2.60	−1.11*	−1.40*	−0.45*	−1.06*
Bias	−1.85 ± 2.18	−1.70 ± 1.75	1.56 ± 1.95	−1.65 ± 1.86	−0.79 ± 1.28	−0.56 ± 1.27	−0.87 ± 1.28	−0.96 ± 1.42
Reflolux SF								
r	0.99	0.99	0.99	0.99	0.99	0.97	0.98	0.99
t	0.85*	−2.05*	0.18*	−1.15*	−3.86	−4.42	−0.83*	−0.71*
Bias	0.26 ± 1.03	0.74 ± 0.85	0.48 ± 0.92	0.53 ± 0.77	1.37 ± 1.68	1.44 ± 2.32	0.70 ± 0.69	0.56 ± 0.48
Tracer								
r	0.97	0.97	0.98	0.98	0.99	0.99	0.99	0.98
t	−3.06	−3.85	−3.25	−4.76	−8.87	−10.90	−12.41	−10.12
Bias	0.84 ± 1.78	0.97 ± 1.73	1.25 ± 1.43	2.06 ± 1.90	2.55 ± 2.46	2.53 ± 2.69	2.15 ± 2.56	2.27 ± 2.89

Data for bias are means ± SD. *r*, Pearson's correlaton coefficient of the linear relationship among glucose measurements using BGMs and the reference method; *t*, values calculated to compare the regression lines with the identity line; *, indicates that the regression line did not differ significantly from the identity line; bias is the difference between the methods.

ber. Each step was reached in 5 min, and measurements were carried out after 10 min, so that the total duration of each step was 20 min. Glucose measurements at each simulated altitude were compared to those obtained by the reference method under local barometric pressure. Before and three times during the sojourn in the hypobaric chamber, blood glucose concentrations were measured by the reference method under local barometric pressure to check the lack of drift over time. Before the testing session, the BGM systems were calibrated according to the manufacturer's recommendations. Blood was placed on the meter reagent strip using a graduated pipette. Coefficients of variation of each BGM were determined under local barometric pressure and averaged 5% (range 4.3% for the One Touch II to 5.7% for the Glucometer 3).

Statistical analysis assessed agreement between BGM determination of blood glucose and the reference method at each altitude. Measurement linearity was tested using Pearson's correlation coefficient (r). The estimated slope (b) of the regression line reflecting the relationship was compared with the slope of the identity line ($b = 1$) using a t test. In addition, the agreement between each BGM and the reference method was estimated after plotting the differences in blood glucose between the two methods against their mean (11). The mean of the differences represented the bias between the methods. This value ± 2 SD represented the limits of agreement for glucose measurement using the BGM system. Accuracy of each BGM system was estimated by calculating percent error (PE):

$$\text{PE}(\%) = \frac{\text{blood glucose (BGM)} - \text{blood glucose (reference)}}{\text{blood glucose (reference)}} \times 100\%$$

An analysis of variance (ANOVA) was used to analyze the effect of simulated altitude on measurement percent error. Scheffe's test was used for post hoc comparisons when needed.

RESULTS — Temperature and relative humidity during blood glucose measurements in the hypobaric chamber were 19.6 ± 0.6°C and 36.7 ± 4% (means ± SD), respectively. No significant difference in blood glucose measurements was observed over time using the reference method at local barometric pressure ($F = 0.22$, $P > 0.98$). All blood glucose measurements obtained from BGMs and the reference method were highly related (see r coefficients in Table 1). Decreased partial pressure of oxygen did not affect correlation coefficients.

Accu-Chek Easy

The regression lines representative of the relationship between blood glucose measurements using this sensor and the reference method significantly differed from the identity line at each altitude (Table 1). The bias estimated by the mean difference between the reference and the BGM system methods was markedly negative and increased with altitude (Table 1, Fig. 1). The limits of agreement were wide and increased as barometric pressure decreased (Fig. 1). As shown in Table 2, the Accu-Chek Easy overestimated blood glucose in all three measurement ranges.

Downloaded from http://ada.silverchair.com/care/article-pdf/19/12/1430/445662/19-12-1430.pdf by guest on 09 April 2024

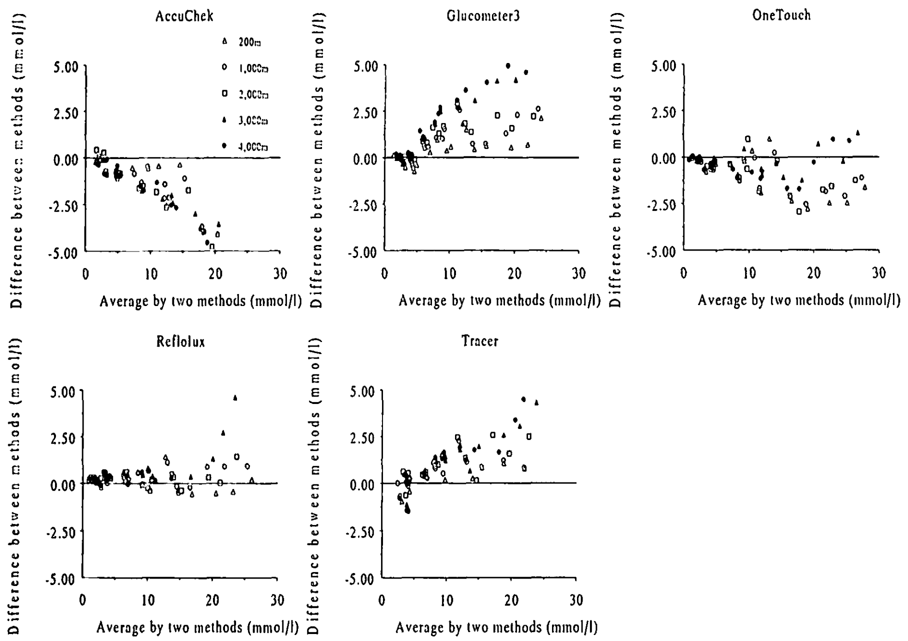

Figure 1—*Residual plot of the blood glucose results obtained using BGMs and the reference method. Difference between methods was the result using reference method minus result using BGM.*

This overestimation of blood glucose measurements slightly increased when barometric pressure decreased ($P < 0.05$). In addition, this sensor identified only three of the six high-glucose concentrations >3,000 m (7,575 feet).

Glucometer 3

At all altitudes, the regression lines of this BGM significantly differed from the identity line (Table 1). Above 1,500 m (4,545 feet), the bias was high, exceeding 2 mmol/l (Table 1, Fig. 1). The limits of agreement were wide for altitudes as low as 1,500 m (4,545 feet) (Table 1, Fig. 1). Except for glucose concentrations <5.6 mmol/l, this sensor underestimated blood glucose measurements. This increased when barometric pressure decreased ($P < 0.001$) and was >30% at 2,500 m (7,575 feet) for blood glucose levels >5.6 mmol/l (Table 2).

One Touch II

Except for low altitudes, the regression lines did not significantly differ from the

Table 2—*Percent error of the blood glucose measurements (mmol/l) determined at each simulated altitude*

	Altitude								Overall
m	150	1,000	1,500	2,000	2,500	3,000	3,500	4,000	effect
feet	454	3,030	4,545	6,060	7,575	9,090	10,605	12,120	of altitude
Accu-Chek Easy									
<5.6	26.56	28.68	17.60	28.90	30.11	30.96	45.54	49.87	NS
5.6–13.9	26.39	28.02	38.58	44.55	43.63	44.33	51.50	41.68	$P < 0.01$
>13.9	35.48	39.02	42.46	48.31	45.39	47.04	55.79	60.87	NS
All ranges	28.41	30.66	30.42	38.65	38 71	39.18	49.87	49.30	$P < 0.05$
Glucometer 3									
<5.6	18.77	11.59	4.95	3.19	1.90	1.98	−1.72	−6.72	$P < 0.05$
5.6–13.9	−12.73	−21.56	−24.64	−28.57	−33.58	−37.52	−38.90	−41.23	$P < 0.001$
>13.9	−10.51	−18.13	−26.54	−23.65	−31.11	−36.04	−44.62	−40.84	$P < 0.001$
All ranges	0.26	−8.65	−14.87	−15.63	−20.18	−23.06	−27.79	−28 91	$P < 0.001$
One Touch II									
<5.6	18.11	14.60	20.20	17.70	13.53	10.08	21.23	18.70	NS
5.6–13.9	16.44	16.77	20.82	15.01	16.83	12.12	14.69	20.29	NS
>13.9	18.51	17.19	13.73	18.98	4.54	3.29	5.83	6.25	NS
All ranges	17.76	16.15	18.09	17.36	11.33	8.28	13.87	14.77	NS
Reflolux SF									
<5.6	−4.95	−13.49	−16.25	−18.67	−18.66	−16.40	−22.70	−17.05	NS
5.6–13.9	−8.92	−7.54	−6.10	−3.42	−13.64	−9.98	−5.50	−5.65	NS
>13.9	0.05	−5.79	−2.46	−3.49	−10.78	−11.90	—	—	NS
All ranges	−5.45	−10.91	−9.63	−10.29	−15.70	−15.04	−14.26	−11.20	NS
Tracer									
<5.6	1.86	−0.75	−8.96	−18.51	−16.89	−12.41	−10.61	−7.32	NS
5.6–13.9	−16.28	−14.83	−17.38	−20.79	−25.21	−22.60	−18.19	−21.74	NS
>13.9	−12.05	−15.69	−15.19	−19.36	−22.16	−23.12	−24.05	−24.37	$P < 0.05$
All ranges	−10.46	−11.11	−14.60	−19.19	−21.39	−19.38	−19.08	−19.78	$P < 0.05$

Data are %.

Downloaded from http://ada.silverchair.com/care/article-pdf/19/12/1430/445662/19-12-1430.pdf by guest on 09 April 2024

identity line (Table 1). The bias was <1 mmol/l above 2,000 m (6,060 feet; Table 1). As shown in Fig. 1, the degree of agreement of this system was acceptable at altitudes exceeding 2,000 m (6,060 feet) and up to 3,500 m (10,605 feet). The sensor overestimated blood glucose values throughout all ranges (Table 2). Interestingly, despite the lack of statistical significance, the accuracy of this system tended to increase for higher blood glucose levels (>13.9 mmol/l) as altitude increased.

Reflolux SF

As shown in Table 1, the regression lines did not significantly differ from the identity line up to 2,000 m (6,060 feet). The bias remained small up to 2,000 m (6,060 feet; Table 1, Fig. 1). The limits of agreement estimated from Fig. 1 were narrow, suggesting that the use of this sensor for blood glucose measurements is acceptable at intermediate altitudes (<3,000 m, 9,090 feet). The Reflolux SF slightly underestimated the blood glucose values in all ranges (Table 2). This tended to increase as altitude increased when measuring glucose concentrations <5.6 mmol/l. Moreover, this sensor did not identify most of the high blood glucose levels >3,000 m (7,575 feet).

Tracer

As with Glucometer 3, the Tracer regression lines significantly differed from the identity line at each altitude level (Table 1). The bias was >2 mmol/l as low as 2,000 m (6,060 feet; Table 1). The limits of agreement were wide and the system performances decreased with barometric pressure (Fig. 1). This BGM system underestimated whole blood glucose when measuring blood glucose levels >5.6 mmol/l (Table 2). The measurement of percent error increased when barometric pressure decreased ($P < 0.05$).

CONCLUSIONS — This study was designed to assess the specific effect of oxygen partial pressure decrease on BGM system performance. High altitude is mainly characterized by a decrease in partial pressure of oxygen, ambient temperature, and relative humidity. Deviations in blood glucose concentrations using BGMs at high altitudes could result from errors due to one or more of these factors (6). An increase in hematocrit, a factor known to alter the measurements of blood glucose with BGMs, may also occur in subjects chronically exposed to high altitude (12). In the present study, only partial oxygen pressure was progressively decreased to simulate altitude, ambient temperature, and relative humidity remaining constant, while hematocrit did not change over time. This suggests that changes in local barometric pressure contribute to loss of BGM system performance at high altitudes. The BGMs evaluated in our study measure blood glucose using glucose oxidase-peroxidase chromogen reaction reflectance analysis. It has been postulated that decreasing partial oxygen pressure alters the second phase of the chromogen reaction and leads to true blood glucose values underestimation (5), while increasing atmospheric pressure overestimates blood glucose concentrations (13). The overestimation of the Accu-Chek Easy, which rose with altitude, could also be explained by the specific chromogen reaction used in this sensor.

Overall, four out of five BGMs underestimated blood glucose measurement, while Reflolux seemed more accurate. At high altitudes, however, this sensor did not identify most blood glucose levels >13.9 mmol/l. The BGM showing the best agreement was the One Touch II, whatever the altitude and range of blood glucose concentrations. Up to 1,500 m, the Glucometer 3 showed good accuracy and agreement.

Patients living in or exposed to high altitude should be aware of low barometric pressure effects on each BGM's performance. It has been recently proposed that blood glucose monitoring devices using a non–oxygen-dependent hexokinase reaction gave readings unaltered by changes in barometric pressure (13) and could be recommended for these patients.

Acknowledgments — We gratefully acknowledge Boehringer Mannheim, Lifescan, and Bayer Diagnostics for supplying the equipment, and Boehringer Mannheim for financial support for this investigation. We thank Françoise Lienhard, Danièle Merino, and Dominique Bonneaut for their skilled technical assistance.

This study was presented in part and in abstract form at the 15th Annual Meeting of the International Diabetes Federation, Kobe, Japan, November 6–11, 1994.

References

1. Berger M, Berchtold P, Cüppers HJ, Drost H, Kley HK, Müller WA, Wiegelmann W, Zimmermann-Telschow H, Gries FA, Krüskemper HL, Zimmermann H: Metabolic and hormonal effects of muscular exercise in juvenile type diabetics. *Diabetologia* 13:355–365, 1977
2. Horton ES: Role and management of exercise in diabetes mellitus. *Diabetes Care* 11:201–211, 1988
3. Gifford-Jorgensen RA, Borchert J, Hassanein R, Tilzer L, Eaks GA, Moore WV: Comparison of five glucose meters for self-monitoring of blood glucose by diabetic patients. *Diabetes Care* 9:70–76, 1986
4. Moberg E, Lundblad S, Lins PE, Adamson U: How accurate are home blood-glucose meters with special respect to the low glycemic range? *Diabetes Res Clin Pract* 19:239–243, 1993
5. Barnett C, Ryan F, Ballonoff L: Effect of altitude on the Self Monitoring of Blood Glucose (SMBG) (Abstract). *Diabetes* 36 (Suppl.):117A, 1987
6. Giordano BP, Trash W, Hollenbaugh L, Dube WP: Performance of seven blood glucose testing systems at high altitude. *Diabetes Educ* 15:444–448, 1989
7. Gautier JF, Duvallet A, Rieu M, Cathelineau G: Effet de l'altitude sur la mesure de la glycémie capillaire par un lecteur glycémique (Glucometer 3, Ames) (Abstract). *Diabete Metab* 20 (Suppl.):A35, 1994
8. Gregory M, Ryan F, Barnett JC, Youtz T: Altitude and relative humidity influence results produced by glucose meters using dry reagent strips (Abstract). *Clin Chem* 34:1312, 1988
9. Bonora E, Moghetti P, Zancanaro C, Cigolini M, Querena M, Cacciatori V, Corgnati A, Muggeo M: Estimates of in vivo insulin action in man: comparison of insulin tolerance tests with euglycemic and hyperglycemic glucose clamp studies. *J Clin Endocrinol Metab* 68:374–378, 1989
10. Hyvärinen A, Nikkilä EA: Specific determination of blood glucose with o-toluidine. *Clin Chim Acta* 7:140–143, 1962
11. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 8:307–310, 1986
12. Barreau PB, Buttery JE: Effect of hematocrit concentration on blood glucose value determined on Glucometer II. *Diabetes Care* 11:116–118, 1988
13. Piepmeier EH, Hammett-Stabler C, Price ME, Kemper GB, Davis MG: Atmospheric pressure effects on glucose monitoring devices (Letter). *Diabetes Care* 18:423–424, 1995

Downloaded from http://ada.silverchair.com/care/article-pdf/19/12/1430/445662/19-12-1430.pdf by guest on 09 April 2024