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Continuous real-time monitoring and recording of glycemia during scuba diving: pilot study

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ABSTRACT

Introduction: Insulin-dependent diabetes has been considered a scuba diving contraindication. This is currently being reconsidered for well-controlled dia- betes. We developed a real-time continuous glucose monitor (CGM) to check glycemia, or blood glucose (BG), during diving, both for prospective studies and to increase diabetic diver safety, allowing for real-time control of glycemia and hypoglycemia pre- vention. To ensure CGM measurement accuracy we tested the method under hyperbaric conditions.

Materials and methods: Two experienced diabetic divers were studied during a one-week diving cruise. BG was monitored every five minutes on every dive, by a dedicated CGM, and values were visible to the divers throughout their dives. The mean of relative difference (MRD) between CGM and capillary blood glucose was calculated. Measurement accuracy was assessed according to ISO guideline 15197 and by Clarke Error Grid (CEG) analysis.

Results: Both divers showed gradual BG decrease during diving. Hyperbaric chamber accuracy tests showed two of 26 MRD values (7.7%) slightly exceed- ing the ISO-15197 allowed difference (5%). However, our data suggest that this discrepancy may have been an artefact.

Discussion: Our data (even limited to two subjects only) agree with the current literature showing that also in our investigated subjects diving does not imply significant risks of hypoglycemia. The use of a real-time CGM by diabetic divers during their dives can provide immediate information on BG values and trends, thus significantly improving diving safety. The accuracy tests comparing continuous glucose monitoring (CGM) and capillary blood glucose mea- surement (CBM) data recorded under hyperbaric conditions showed that data recorded under pressure are very close to the ISO-15197 and CEG acceptable limits.

Keywords: Scuba diving: Continuous glucose monitoring; Type 1 diabetes; Diabetes and sports; Insulin-dependent diabetes; Decompression sickness

INTRODUCTION

A frequent complication of insulin-dependent diabetes (IDD) is sudden hypoglycemia and a consequent sudden loss of consciousness. This is why IDD has been con- sidered a contraindication to scuba diving [1,2].

In 1993 and in 2007 Divers Alert Network (DAN) observed that a small percentage of DAN members were diabetic [3,4], some papers described diabetic divers [5,6] and Adolfsson, et al. estimated that about 1% of divers were using insulin treatment [7]. We reasoned that it is highly possible that the prevalence of individuals with diabetes in the diving community is similar to or the same as that in the general population, estimated to be 2.8% in 2000 and 4.4% in 2030 [8]. We can also speculate that some diabetic divers do not declare their condition when beginning their training and do not inform the diving center they make their dives with.

The absolute contraindication to diving for diabetics is currently being reconsidered [8,9], and the plasma glucose response has been investigated in selected groups of diabetic divers with well-controlled diabetes) [10,11]. The matter was also discussed during a work- shop, which resulted in the first guidelines for diabetics who engaged in recreational diving [12].

In 2004 DAN Europe cooperated in a pilot project (Submerged Diabetes), where interstitial glycemia values were recorded during diving and evaluated post-diving. Bonomo, et al. investigated 12 IDD divers who showed a gradual decrease of glucose values with no hypoglycemic episodes [13].

On the other hand, the accuracy of continuous glucose monitoring (CGM) during scuba diving has not been well investigated until now due to the difficulty in obtaining blood samples while diving [7].

This work aimed at developing a real-time CGM to check and record glycemia values and trends during diving. This could be used for prospective studies, and – perhaps more importantly – it could be used to in- crease the safety of diabetic divers helping to control glycemia levels in real time, thus preventing hypo- glycemia. Our data can also help to increase sports medicine knowledge and interest in this specific field.

A preliminary evaluation of accuracy of measurement by CGM in the hyperbaric environment and the effect of glucose ingestion during diving were also investigated.

MATERIALS AND METHODS

Subjects and dives

We studied two active, experienced and otherwise healthy diabetic divers (one male, one female) during a liveaboard dive week:

• N.B., a female, age 29, weight 53kg, height 157cm, BMI 21.5; and

• R.D., a male, age 36, weight 72kg, height 167cm, BMI 25.8.

Neither had historic or clinical evidence of arterial hypertension, cardiac, pulmonary or any other significant disease nor suffered from any diabetic complication such as retinal involvement, autonomic neuropathy or vascular diseases.

Neither subject declared previous decompression illness. Information about age, gender and standard anthropometric data such as height and weight were recorded and the BMI calculated. Heart rate and arterial blood pressure were monitored, recorded daily and their mean was calculated.

All divers respected their usual alimentary program and concluded a full week of intensive recreational diving, following the protocol already used for the Submerged Diabetes program [13] (Figure 1).

Before the diving week the diabetic divers received specific training about the CGM device, the correct insertion of the subcutaneous sensor in the abdominal region and the CGM calibration with capillary blood glucometer (CBG) every 12 hours, as recommended by Kropff, et al. regarding the accuracy of CGM [14].

Testing started no earlier than 24 hours after the in- sertion of the sensor in the abdominal region. This is because the accuracy of measurement improves sig- nificantly on Days 2 and 3 compared to Day 1, prob- ably due to a more stabilized environment around the sensor [7]. All divers made their planned dives without any restriction. All divers made a safety stop of five minutes at 5 meters of depth at the end of every dive.

In order to estimate decompression stress we cal- culated the inert gas supersaturation gradient factor (GF) and Hennessy and Hempleman exposure factor (EF) ($p\sqrt{t}$; where p is the absolute pressure and t is the total diving time) [16]. Differences in decompres- sion stress between the two subjects were evaluated.

Interstitial glycemia was monitored every five minutes during each dive through a subcutaneous sensor, (Figure 2, top) and a specially adapted CGM (Dexcom G4) device hosted in a waterproof case “dry box real time” (DBRT). This allowed divers to read their glucose values (BGs) at any time during the dive (Figure 2, bottom). Divers could continuously check their BG levels and trends. Data were recorded every five minutes starting one hour before and through one hour after the dive. Differences in BG values among pre- dive, during and post-dive recording were evaluated.

Diabetic divers kept the sensor in place 24 hours/day during the entire the dive week. During dives, sensors were kept under the diving wetsuit without any problems caused by water contact and pressure variations.

Evaluation of CGM accuracy by hyperbaric chamber ‘validation test’

To assure the correct measurement of interstitial glycemia values in a hyperbaric environment we had previously completed a comparison test between capillary blood glycemia values [17,18], measured by finger stick (Verio IQ) and subcutaneous interstitial glycemia values (Dexcom G4) in normobaric conditions and in a hyperbaric chamber.

This test was repeated three times. Measurements were made every five minutes for 45 minutes at the same time for both devices. Absolute differ- ences in CGM and CBG values were known to exist and expected to occur (CGM-CBM/capillary blood glucose measurement).

The mean of relative difference (MRD) between CGM and CBG was calculated as the mean of ([CGM-CBG] /CBG) * 100 [18]. A statistical analysis was conducted to evaluate the consistency of the absolute and relative difference between capillary blood glycemia values and subcutaneous interstitial glycemia values in the two different conditions. We evaluated the accuracy of our measurements according to the International Organization for Standardization (ISO guideline 15197) that suggests a maximum acceptable difference within 20% for glucose levels > 75mg/dL and within 15mg/dL for levels < 75mg/dL in at least 95% of the values compared [20].

We also analyzed our data by the Clarke Error Grid (CEG) analysis [21], which divides the difference between the two measurements in five zones and allows for 95% of the data in “Zone A” and 5% in “Zone B” to confirm the accuracy of data recorded with the tested device against the data referenced.

Evaluation of blood glucose response after ingestion of glucose containing beverages during diving

In a parallel session the female diver drank 88ml cranberry juice (sugar content 11.1g; Yoga San Lazzaro di Savena, Bologna, Italy) during diving whenever the monitored BG was approaching 70mg/dL with a downward trend.

The diver had undergone previous confined-water training for the "drinking during diving" procedure normally used in technical diving to prevent dehydration during prolonged dives.

Statistical analysis

Data are presented as the mean ± standard deviation (SD) for parametric data and median and range for non-parametric data. Differences in diving exposure factors (depth, diving time, GF and EF) between the two divers were investigated using the two-sample t- test and the Mann-Whitney U test, after the normality test (Kolmogorov-Smirnov) for parametric and non- parametric data respectively. The median of BG recorded pre-, during and post-dives were calculated and statistical differences were tested by non-parametric analysis of variance (Kruskal-Wallis test), after normality testing using the Kolmogorov-Smir- nov test).

Absolute difference in paired values of BG were calculated, and the relative difference were calculated as [CGM-CBG] /CBG) * 100. Difference between values obtained in normobaric and hyperbaric conditions were calculated by two-sample t-test after the Kolmogorov-Smirnov normality test.

The accuracy of CGM measurements during diving were also tested with respect to the ISO guideline 15197, which allows for a maximum difference within 20% for glucose levels > 75mg/dL and within 15mg/ dL for levels < 75 mg/dL in at least 95% of the values compared. Results of MRD were also evaluated by the Clarke Error Grid analysis, which allows 95% of the data in "Zone A" and 5% in "Zone B."

RESULTS

The two diabetic subjects, one male and one female, were investigated during an intensive scuba diving period (18 dives for the female and 10 for the male):

• N.B. – female, age 29, weight 53 Kg, height 157 cm, BMI 21.5); and

• R.D. – male, 36 years, weight 72 Kg, height 167 cm, BMI 25.8).

Mean physiological data during the diving week:

N.B. – heart rate 78 beats·min-1 (+/-9.5); diastolic BP 74 mmHg (+/- 8.4); systolic BP 139 mmHg (+/- 25.0); and

R.D. – heart rate 76 beats·min-1 (+/- 9.2); diastolic BP 73 mmHg (+/- 6.9); systolic BP 133 mmHg (+/-15.5).

We did not find any difference in diving exposure factors (depth, diving time, GF and EF) between the two divers (Table 1). Both divers showed a gradual decrease in BG during diving; the decrease was statistically significant for the male:

• median pre-diving 184.0 range 75-27mg/dL and median diving 140 range 70-264mg/dL $p<0.001$

but not statistically significant for the female:

• median pre-diving 171.0 range 69-324mg/dL and median diving 152.5 range 70-329mg/dL $p=0.3$).

Table 1 shows the complete results including post- diving data.

Occasional low BG values were observed during diving (+/-70mg/dL) without any symptoms of hypoglycemia.

CGM accuracy evaluation

As expected, we found a statistically significant absolute difference in measurements made by finger stick (Verio IQ) vs. values obtained at the same time by the CGM Dexcom G4 device in both test conditions (normobaric $p=0.0001$ and hyperbaric $p=0.0002$). The differences between the two different environ- mental conditions were not statistically significant: $p=0.36$ (normobaric conditions 9.05 +/- 7.6mg/dL; hyperbaric conditions 12.5 +/- 14.7 mg/dL).

No statistical difference was found for MRD in the two different conditions: $p=0.26$ (normobaric condition 7.03+/- 6.5 %; hyperbaric condition 9.8 +/- 10.6 %). The accuracy tests made in the hyperbaric chamber showed two out of 26 MRD glucose values (7.7%) exceeding the 5%

difference allowed by ISO guideline 15197 as the maximum difference acceptable in at least 95% of the compared values. These two MRD readings were caused by an unexpected sudden decrease of capillary measurement values with respect to the previous and successive values measured with this device. In both instances the “apparent” irregular measurement occurred when the hyperbaric chamber was approaching atmospheric level (surface). The Clarke Error Grid analysis returned similar results showing 92.3% of the values in Zone A and 7.7 % in Zone B (Figure 3).

Evaluation of blood glucose response

We found a statistically significant increase in BG (p=0.001) when the diver drank fluid cranberry juice during diving (Figure 4). Divers regularly checked their BG during diving using their CGM; no failure of the sensor occurred during the entire diving week and up to 40 meters’ depth.

DISCUSSION

Several papers have shown modest changes in BG during diving and no additional diving risks in well-controlled IDD. Our data (even if limited to two subjects only) agree with the current literature and confirm that diving does not imply significant risks of hypoglycemia, even if continuous monitoring shows a progressive BG decrease as reported by Bonomo, et al [14]. On the other hand, very low BG values (+/- 70mg/dL) were occasionally reported. This is quite important, as continuous BG monitoring can help in preventing, understanding and correcting any hypoglycemia-related problem during diving. This is additionally valuable considering that such problems can be confused with other diving-related symptoms such as nitrogen narcosis, for instance.

The use of a real-time CGM system by diabetic divers can help solve the problem of low blood sugar levels during a dive by providing the divers with immediate information on BG values and trends, with a significant increase in diving safety. We can imagine a not-unrealistic future when the dive buddy can check the buddy-diver's BG through a second wireless receiver-monitor.

The CGM system can be an important additional safety tool for properly trained diabetic divers. The accuracy tests, comparing CGM and CBM data recorded in hyperbaric condition showed that data recorded under pressure are close to the limit suggested by the ISO 15197 guideline and by the Clarke Error Grid analysis.

LIMITATIONS

This manuscript represents a pilot test; further investigations are needed to confirm our preliminary results. For instance, an important limitation in our accuracy test is the low number of measurements. In fact, with 26 recorded data available, only one measurement can fall out of the indicated range according to the ISO 15197 guidelines and the Clarke Error Grid, and just one more is sufficient to exceed the acceptable limit. In our case, both measurements exceeding the acceptable limits occurred during the last phase of decompression of the hyperbaric chamber and coincided with an odd CBM value, not consistent with the immediately preceding and following measurements. This suggests the possibility that the CBM device (control device) incurred unexpected technical problems in this phase where we have the maximum gradient of gas expansion. If we exclude these two "odd" results, the accuracy of measurement respects both the ISO 15197 guideline and the Clarke Error Grid and no MRD exceeds the cut-off of 20%.

We believe that CGM measurement during diving can be very helpful for diabetic divers even if further investigation is need to confirm the accuracy of the technique. Our data are encouraging in this respect. A specific aspect of our investigation modality is that divers conduct their planned dives without any imposed restrictions, thus allowing us to study “real diving” as opposed to “laboratory diving.”

Our findings agree with those of Bonomo, et al. regarding the similarity between the progressive BG decrease during diving and other aerobic activities, with no apparent interference by the underwater environment, and confirm Bonomo’s conclusion that scuba diving by well-controlled IDD divers can be considered safe, provided that diabetic divers know and respect specific hypoglycemia prevention protocols.

Furthermore, the possibility of drinking glucose beverages underwater represents an additional safety measure in case of near-hypoglycemic BG values during diving. That, together with the possibility of monitoring BG during diving, could eventually overcome the “resistance” of medical practitioners to “clear” IDD patients for scuba diving, while providing them with additional motivation for better manage- ment of their diabetic condition. A study aimed at investigating these aspects on a more significant number of diabetic divers is already in progress.

CONCLUSION

A real-time continuous glucose monitoring system used by diabetic divers during diving can provide immediate information on blood glucose values and trend, with a significant increase in diving safety and with an increase of sports medicine knowledge and interest in this specific field.

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Conflict of interest statement

The authors have declared that no competing financial interests exist.

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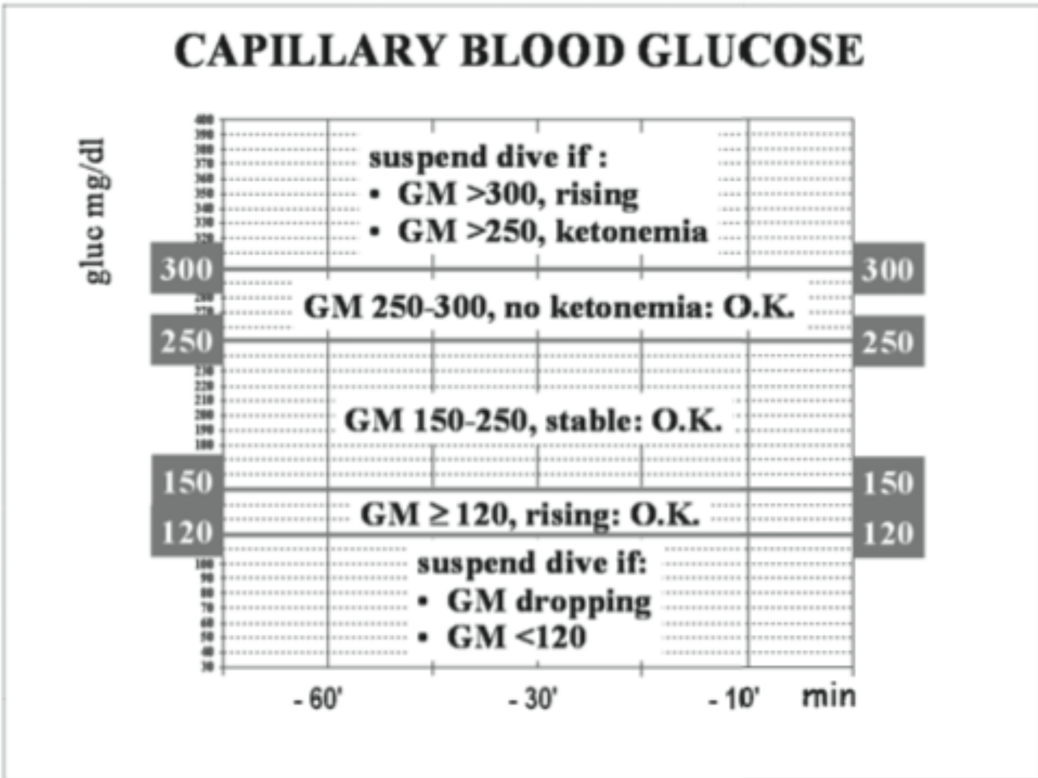

Figure 1: Both divers respected their usual alimentary program and concluded a full week of intensive recreational diving following the protocol already used for the Submerged Diabetes study, allowing or forbidding diving according to the guideline shown in this figure.

Figure 2: Interstitial glycemia was monitored by a special CGM (Dexcom G4), through a subcutaneous sensor (upper). The glycemia value was shown on the G4 monitor display, kept in a waterproof case, through a glass screen (lower).

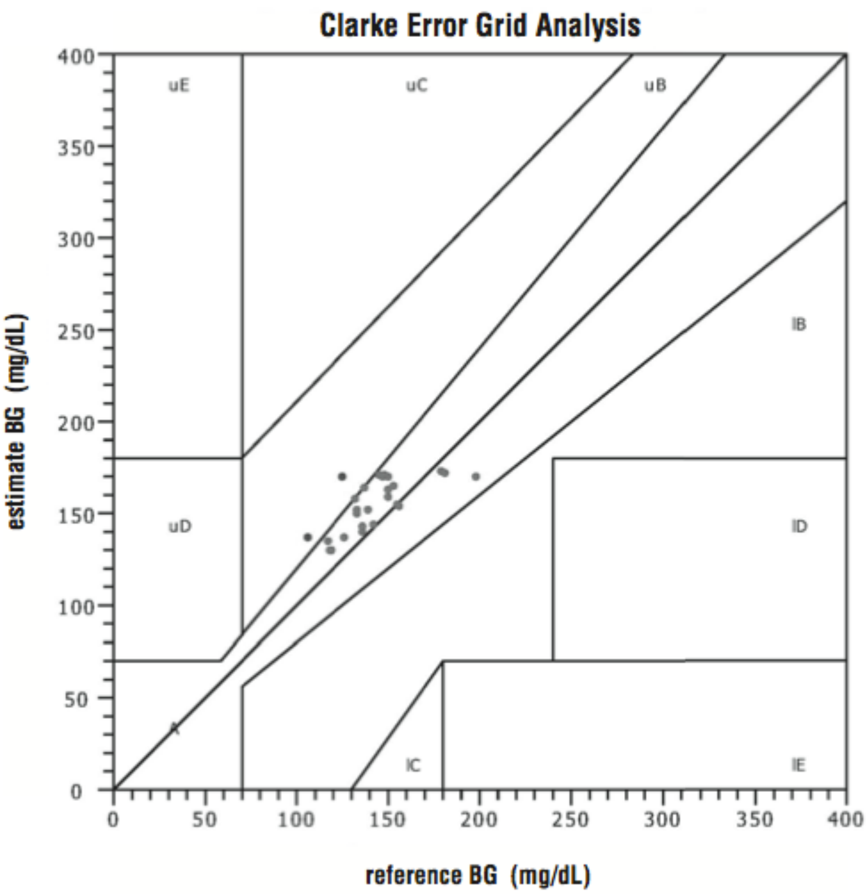

Figure 3: The Clarke Error Grid Analysis showed 92.3% of the values in Zone A and 7.7 % in Zone B.

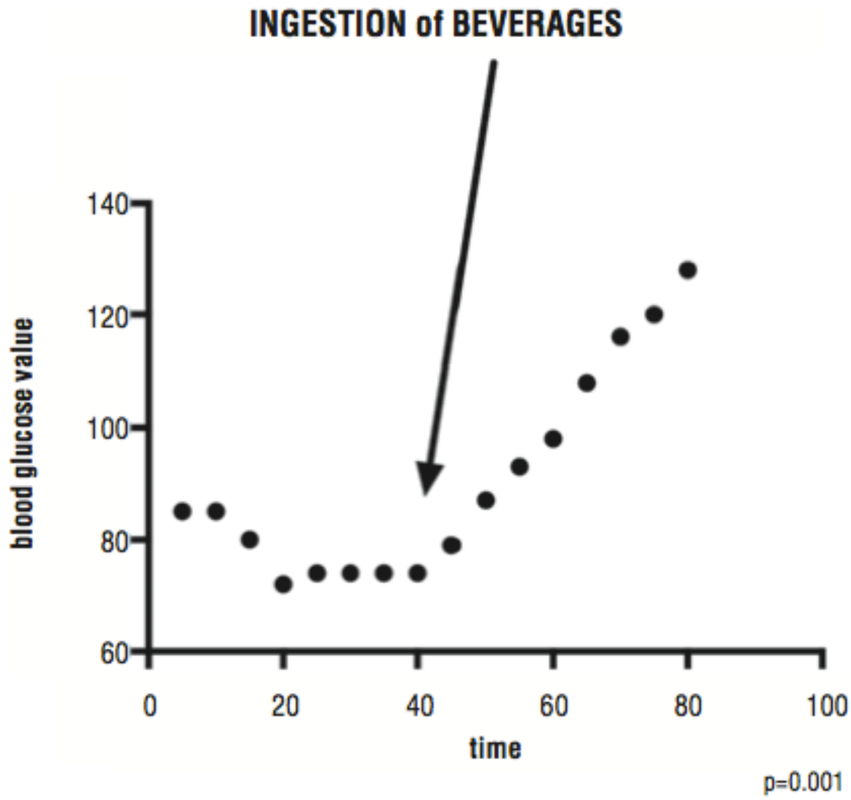

Figure 4: We found a statistically significant increase of BG when the divers consumed glucose gel while diving.The arrow shows the exact time when divers drank Glucogel 25g. This aspect can be very important to improve the safety of diabetic divers.

Table 1: Behavior of blood glucose value in the two divers while diving; a gradually decreasing BG value

RISK FACTOR diving condition	NB	RD	NON-DIABETIC	P-VALUE	SIGNIFICANCE
depth/meters	32.03 +/- 5.7	29.2+/- 5.9	30.80+/- 5.6	NB vs. non-diabetic diabetic vs. non-diabetic	NS NS
diving time/ minutes	49.8 +/- 7.2	54.3 +/- 8.4	51.8 +/- 7.5	ND vs. non-diabetic diabetic vs. non-diabetic	NS NS
GF	0.77 +/- 0.1	0.74 +/- 0.1	0.73 +/-0.1	ND vs. non-diabetic diabetic vs. non-diabetic	NS NS
EF	29.6 +/- 4.3	28.07 +/- 4.5	29.03 +/- 4.5	ND vs. non-diabetic diabetic vs. non-diabetic	NS NS

NB = female subject; RD = male subject; NS = not significant
GF = inert gas supersaturation gradient factor; EF = Hennessy and Hempleman exposure factor

	PRE-DIVING	DURING DIVING	POST-DIVING	P=VALUE		EB BUBBLE GRADES
RD	184 mg/dL (75-271)	140 mg/dL (70-264)	163 mg/dL (57-273)	pre vs. during pre vs. post during vs. post	*** * Ns	3 (0-4)
NB	171 mg/dL (69-324)	152.5 mg/dL (70-329)	123.5 mg/dL (41-263)	pre vs. during pre vs. post during vs. post	Ns *** ***	1 (0-2)