Short communication

Comparison of venous glucose to finger-prick glucose in patients with diabetes under hyperbaric hyperoxic conditions: a pilot study

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Abstract

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Introduction: Blood glucose is commonly measured in diabetic patients undergoing hyperbaric oxygen treatment (HBOT) from a 'finger-prick' capillary sample. Although this method is an accurate reflection of venous glucose under normal conditions it has not been validated under hyperbaric, hyperoxic conditions.

Methods: Four patients with diabetes mellitus undergoing HBOT had venous blood samples drawn simultaneously with routine capillary samples before, during and immediately after three of four HBOT sessions. The Bland-Altman method of assessing agreement between these two measures was used separately for the three time periods.

Results: The relationship between venous and finger-prick glucose at room air was altered significantly by HBOT. The bias (finger-prick minus venous measurements) was significantly less than zero during the HBOT session but not immediately after completion of the session. Owing to the small sample size, the limits of agreement straddled zero at all time points, although the lower limit was close to zero during treatment (finger measurement appeared to be higher than venous measurement on room air and lower than venous undergoing HBOT).

Conclusion: Finger-prick capillary sampling may not be an accurate reflection of venous glucose during HBOT.

Key words

Diabetes, hyperbaric oxygen, blood sugar level, patient monitoring

Introduction

It has long been accepted as fact in hyperbaric medicine that blood glucose decreases in patients undergoing hyperbaric oxygen treatment (HBOT).[1–3] Several theories have been suggested, but none has gained widespread acceptance.

Our review of the relevant literature determined that many of the reports supporting a drop in blood glucose were only analysed by finger-prick sampling, which measures mixed subcutaneous capillary glucose.[2,3] Further, the accuracy of glucometer assays have previously been validated under HBOT.[4,5] Under normal conditions, these agree well with laboratory measured venous glucose.[6]

We hypothesised that subcutaneous capillary glucose may not be a reliable indicator of venous glucose under HBOT because blood flow in the subcutaneous tissues is reduced via vasoconstriction. This, combined with the hyperoxic state of the blood, will allow oxidative phosphorylation of glucose to continue for longer, and to a lower end point, and this process may be exaggerated in patients with already impaired micro-vascular blood flow.

Aims

Our aim was to determine the relationship between finger-prick capillary and venous glucose measured by glucometer with the patient breathing normobaric air and during HBOT.

Methods

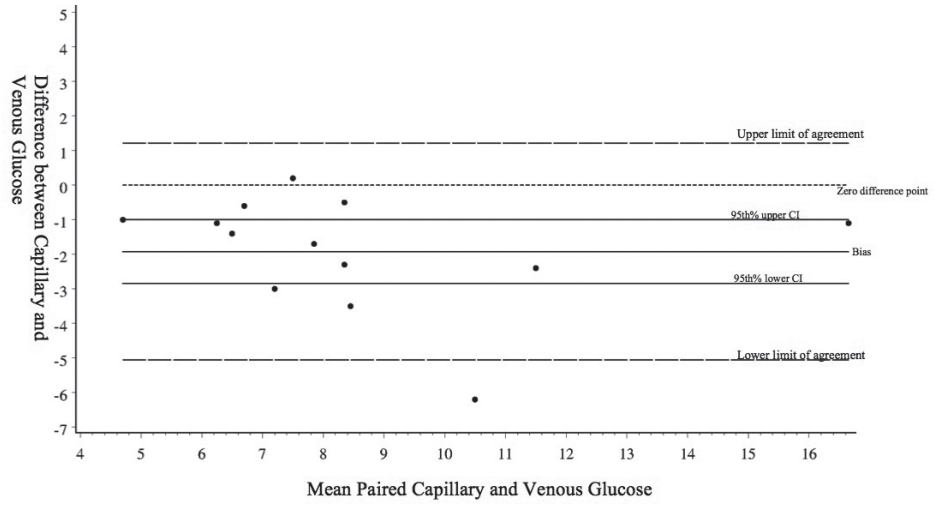
This study was approved by the South Metropolitan Area Health Service Human Research Ethics Committee, and performed in the Fremantle Hospital Hyperbaric Medicine Unit in June and July 2012. Adult patients over the age of 18 years with a diagnosis of diabetes mellitus for more than five years and receiving either insulin or oral hypoglycaemic agents were invited to participate in the study.

Prior to the first hyperbaric treatment session in the series an 18 gauge cannula was placed in an ante-cubital fossa vein. Then, in keeping with our standard practice, finger-prick glucose measurement samples were taken immediately prior to, during and immediately after the treatment session. The samples taken during treatment were obtained after 40 minutes of oxygen, just prior to the first air break. All treatments were at 243 kPa pressure. At the same time as the finger-prick sample, a venous sample was drawn. In collecting the venous sample the first 3 ml of blood was discarded, then 1 ml taken for glucose assay, then the cannula flushed with saline. The cannula remained in place for three days (in accordance with the Western Australia "*Hospital in the home*" service, http://www.health.wa.gov.au/healthyathome/hith/index.cfm), and samples were collected over three consecutive days where possible.

The samples were all analysed on the same Medisense Optium® glucometer, using Abbott® glucose test strips.

Figure 1

Comparison of measurements taken during the HBOT session. The dots show the actual data points, the three solid lines are the bias (central line), and its upper and lower 95% confidence limits, the two dashed lines are the upper and lower limits of agreement, and the dotted line marks the zero-difference point. Axis labelled *"Difference"* refers to finger-prick minus venous glucose values; axis labelled *"Mean"* refers to the mean of the paired finger-prick and venous glucose values.



This glucometer uses the glucose dehydrogenase reaction as the basis of its assay, which has previously been suggested to be most accurate under hyperbaric conditions.[5] The decision not to send a venous sample to the laboratory was to eliminate any bias introduced by using a different assay.

Data analysis

The Bland-Altman method was used to assess any consistent bias between the two measures.[7] Bland-Altman plots show the calculated bias, its upper and lower 95% confidence limits, and the upper and lower limits of agreement (LOA) between the two methods displayed graphically. The analysis was applied separately to the pre-, during- and post-treatment data. Statistical analyses were carried out with the SAS version 9.2 software (SAS Institute, Cary, NC, USA; 2008).

Results

Four patients were studied. Two subjects were sampled on three separate days and the other two over four consecutive treatment days. For both the pre- and post-HBOT figures, the biases on the Bland-Altman plots are close to zero, indicating very close agreement. The venous measures were slightly lower than mixed capillary (i.e., the value for the difference is slightly positive), and the LOA straddle zero. During HBOT, the bias is negative and statistically significantly different from zero ($P = 0.0006$), indicating that the finger estimate of glucose is significantly lower than the venous measurement under hyperbaric conditions, and the LOA are wider apart (Figure 1). The LOA still straddle zero, but this is largely because of the small sample size, and the large variability in measurements. Table 1 shows the summary of the bias at each time point, its 95% confidence interval and the limits of agreement.

Discussion

Oxidative phosphorylation of glucose occurs only in the capillaries, so from first principles, arterial glucose should be higher than venous and mixed capillary should be between the two as it samples blood from the arteriolar and venular sides of the capillaries. This is supported by experimental work, with a difference in the region of 0.5–1.0 mmol L^{-1} between venous and mixed capillary measurements.[6] It has been assumed implicitly, although never validated, that this

Table 1

Characteristics of the difference between venous and finger-prick glucose; the bias is calculated as the mean of the difference (finger-prick minus venous), along with its standard deviation and 95% confidence interval. The *P*-value tests whether the bias is significantly different from zero; note that bias is significantly less than zero during treatment, while it is marginally positive pre-treatment and not significantly different from zero post-treatment.

Timing	*n*	Bias: mean (SD)	95% confidence interval for bias	*P*-value	Limits of agreement (Bland-Altman)
Pre-HBOT	13	0.56 (0.90)	0.02 to 1.11	0.0445	-1.21 to 2.33
During HBOT	14	-1.92 (1.60)	-2.85 to -1.00	0.0006	-5.06 to 1.21
Post HBOT	14	0.26 (0.75)	-0.18 to 0.69	0.2208	-1.21 to 1.72

agreement holds under hyperbaric oxygenation conditions, as the finger-prick method for blood glucose measurement has been accepted as an accurate surrogate measure of venous glucose.

These results suggest finger-prick mixed capillary blood glucose measurement may not be an accurate reflection of venous glucose measured during HBOT. During treatment sessions, the values obtained for finger-prick glucose samples read lower than for venous samples. It also appears the difference between the two values is less predictable under conditions of hyperbaric oxygenation than at room air and pressure (the larger standard deviation leads to LOA that are wider apart).

Although the cohort of patients was small, the line of best fit from the Bland-Altman plot prior to and post the HBOT session shows mixed capillary to be around 0.5 mmol L^{-1} higher than venous, which is consistent with other larger studies. It then shows a very different relationship under HBOT where mixed capillary glucose appears to be significantly lower than venous glucose.

No symptomatic hypoglycaemic episodes were observed during the course of the study. In clinical practice, a low reading is accepted as representing true hypoglycaemia leading to the administration of glucose or glucagon. If, however, these measurements are not in close agreement, we may be raising the blood glucose, or tolerating high blood glucose levels unnecessarily, which may have a negative effect on wound healing. If the common in-chamber practice of assessing blood glucose with the finger-prick method is proven to exhibit bias, then a correction may need to be applied to the measurement (if possible), or some alternative method of blood glucose measurement may need to be used.

We suggest that any further work into the effects of HBOT on blood glucose will require measurement of central or venous glucose in addition to capillary sampling. A more definitive study is already planned to include non-diabetic volunteers to ascertain whether they behave in a similar fashion to diabetic patients. We would suggest that in-chamber finger-prick capillary blood glucose measurement is used with caution, as it does not appear to be an accurate or validated tool for blood glucose measurement during HBOT.

Conclusion

The relationship between subcutaneous mixed capillary glucose ('finger-prick') and venous glucose may be altered during HBOT. This alteration may be to such an extent that finger-prick glucose is not an accurate representation of venous glucose under hyperbaric conditions.

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