Registrar in the Department of Intensive Care at the Flinders Medical Centre, Adelaide, South Australia.

Dr Whyte's address is 25 Woodhouse Crescent, Wattle Park, South Australia 5066. E-mail <docwhyte@hotmail.com>.

EFFECTS OF HYPERBARIC OXYGEN TREATMENT ON BLOOD SUGAR LEVELS AND INSULIN LEVELS IN DIABETICS

Lalith Ekanayake and David J Doolette

Key Words

Diabetes, hyperbaric oxygen, hyperbaric research.

Summary

Hyperbaric oxygen (HBO_2) is commonly used to treat non-healing wounds in diabetic patients. Although anecdotal evidence from hyperbaric centres suggests that diabetics are vulnerable to hypoglycaemia when they are treated with hyperbaric oxygen, there has been little definitive human or animal research showing the effects of hyperbaric oxygen on blood sugar and insulin levels. Blood sugar levels and insulin levels in five diabetic and five non-diabetic subjects were measured both while breathing normobaric air and hyperbaric oxygen . Mean blood sugar levels decreased significantly by 3.5 ± 0.7 mmol/l during hyperbaric oxygen breathing in the five diabetics. Insulin dosage was not changed in either condition.

Introduction

Apart from treatment for diving related illness, hyperbaric oxygen (HBO_2) treatment has therapeutic value in many illnesses including non-healing wounds in diabetics. The use of hyperbaric oxygen treatment for diabetes (but not wounds) has its origins in the 1920s with the American physician Dr Orval J Cunningham, who used hyperbaric oxygen for the treatment of various illnesses (syphilis, pernicious anaemia, and cancer) including diabetes mellitus.[1] Anecdotal evidence from hyperbaric centres shows that diabetics are prone to develop hypoglycaemia when they are exposed to HBO_2.

Blood sugar levels (BSL) decreased in some[2] or all[3] insulin dependent diabetics after HBO_2 treatment. Insulin requirements are reduced during HBO_2.[4] Some additional evidence from underwater diving indicates that the long and short-term insulin requirements of diabetics decreased over a period of 7 days of diving.[5]

Although there is disagreement in the diving medical fraternity, a majority of experts believe that diabetes, mainly insulin dependent diabetes mellitus (IDDM), is a contraindication to recreational and commercial diving because hypoglycaemic signs and symptoms may be confused with other diving maladies, hypoglycaemia can cause unconscious underwater and there may be increased likelihood of decompression illness (DCI) in diabetics.[6-9]

The mechanisms of hypoglycaemia during HBO_2 treatment are unknown, but it has been postulated[10,11] that HBO_2 might:

1 increase tissue oxygen and increase aerobic metabolic energy generation (oxidative phosphorylation), driving up glucose consumption;
2 increase aerobic metabolism in the pancreatic Islets of Langerhans which may stimulate insulin secretion;
3 inhibit the actions of anti-insulin hormones (somatotropin and glucagon); or
4 increase tissue sensitivity to insulin.

BSL have not been previously reported for non-diabetics during HBO_2 treatment. However, if hypoglycaemia occurs during HBO_2 in diabetics but not in non-diabetics, this may result from failure, in diabetics, of the normal protective mechanism. For instance in non-diabetics during exercise, BSL is maintained by decrease in insulin and rise in glucagon and catecholamine levels. These mechanisms fail in some diabetics, mainly in IDDM patients, resulting in hypoglycaemia.[12]

This study investigates BSL and insulin in diabetics and non-diabetics during HBO_2 and normobaric air breathing. The specific hypotheses tested are;
1 HBO_2 increases insulin in diabetics but not in non-diabetics and
2 BSL decrease is a result of increase in insulin.

Method

This study was approved by the Research Ethics Committee of the Royal Adelaide Hospital and was conducted in accord with the National Statement on Ethical Conduct in Research Involving Humans.

Subjects

Five diabetics (3 males and 2 females) gave their informed consent to participate in this study. Four of them received HBO_2 for diabetic foot ulcers and the other for osteoradionecrosis. Mean age of the diabetics was 60 years (range 46–86 years). There were 4 IDDM and 1 Non-insulin Dependent Diabetes Mellitus (NIDDM). The mean diabetic duration was 22 years (range 7-40 years).

Diabetic group inclusion criteria were:

1 diabetes of more than 6 years duration but no hypoglycaemic events for the last 12 months;
2 no contraindication for venipuncture, lignocaine, or heparin;
3 no advanced diabetic complications such as autonomic neuropathy or nephropathy; and no concomitant liver diseases. Autonomic neuropathy was an exclusion criterion because it may mask the signs and symptoms of hypoglycaemia; therefore, patients with orthostatic intolerance (faintness or blood pressure drop on standing) and gastroparesis (nocturnal diarrhoea/ vomiting) were excluded.

Only well-controlled diabetics were selected because they were required to be assessed under hyperbaric oxygen breathing and normobaric air breathing conditions on separate days whilst diet, insulin or oral hypoglycaemics dosage and exercise remained unchanged.

There were 4 males and 1 female in the non-diabetic group and mean age was 65 years (range 53-75 years). Three of them received HBO_2 for sudden onset hearing loss, one for a poorly healing ulcer and one for osteoradionecrosis. The same contraindications as for the diabetics applied to this group. All the patients selected for this study were "medically fit" for HBO_2 treatment and underwent a full course of HBO_2 treatments.

Study design

This study consisted of four arms. Diabetics during normobaric air breathing (control) and during hyperbaric oxygen breathing (HBO_2) conditions, and non-diabetics under same control and HBO_2 conditions. The study occurred on two days. The HBO_2 day was the 3rd, 4th or 5th day of HBO_2 to minimise the other hormonal effects on BSL and insulin levels that might have occurred when subjects were stressed or anxious during first days of HBO.

On the both the control and HBO_2 day all subjects had an 18 gauge intravenous cannula (Insyte®, Becton Dickinson Vascular Access, Sandy, Utah) placed in the antecubital fossa or a forearm vein. The skin was locally anaesthetised with 1% lignocaine (Delta West, Perth, Western Australia) before insertion of cannula. This was connected to a short extension tube (Connecta®, BOC Ohmeda AB, Helsingborg, Sweden) attached to a 3-way tap and pre-filled with 10% heparinised saline (Astra, North Ryde, New South Wales). Five ml of blood was withdrawn to eliminate cannula dead space and then 1 ml blood samples were taken and the cannula flushed with 5 ml of heparinised saline. Samples were taken at 0, 15, 30, 45, 60, 75, 90 and 120 minutes.

The control day of the study took place on the day before the first HBO_2 treatment. It was performed in the Hyperbaric Medicine Unit treatment room. Although study order was not randomised, having the control before HBO_2 was thought to exclude any possible long-term effects of HBO_2 treatment on BSL and insulin.

The HBO_2 treatment protocol was compression to 10 msw (202 kPa or 2 bar) where 100% oxygen was delivered for 90 minutes (with a 5 minutes air break at 45 minutes) and followed by 30 minutes decompression while breathing oxygen. This was the standard daily treatment regimen for the patients' conditions and occurred in the multiplace hyperbaric chamber in the Hyperbaric Medicine Unit, Royal Adelaide Hospital.

On both days each diabetic subject received the same amount of insulin or oral hypoglycaemic and his or her exercise regimen and diet were unchanged. No food or drink was allowed during the two-hour study period. All the subjects were monitored for hypoglycaemia and oxygen toxicity during the treatment but no complications were encountered.

All blood samples were analysed for BSL (Hexokinase Method) and insulin (Abbott Insulin Kit Microparticle Enzyme Immuno Assay) at the Institute of Medical and Veterinary Sciences, Adelaide, South Australia.

Statistical analysis

In statistical analysis, BSL and Insulin data were treated identically. BSL were compared using 3-way analysis of variance (ANOVA) with one between groups factor and two within groups (repeated measures) factors. The between groups factor (diabetes) had two levels (diabetic and non-diabetic). The first within groups factor (oxygen) had two levels (control and HBO_2) and the other within groups factor (time) had 8 levels (0, 15, 30, 45, 60, 75, 90, and 120 minutes).

We rejected the null hypothesis if there was a significant F test (α=0.05) for the main effects of oxygen or time or any interaction of the main factors with time. Specific differences were identified by post-hoc analysis using Tukey honest significant difference.

Statistical calculations were performed using the general linear model module of Statistica for Windows V5.5 (Statsoft Inc., Tusla OK., USA)

Results

The 3-way ANOVA returned significant F tests for the main effects of diabetics and time and the interaction of diabetics and time. Post-hoc analysis showed there were no significant difference in BSL in the non-diabetics (see Figure 1). For diabetics there was no significant difference

between mean BSL before HBO_2 and the normobaric control measurements at time 0. As can be seen in Figure 2, BSL declined over the two-hour measurement period under both normobaric (control) and HBO_2 conditions in diabetics, but more rapidly in the latter. Post-hoc analysis showed that this decline was significant for HBO_2 but not for normobaric air breathing. For instance, mean BSLs at all times beyond 45 minutes were significantly lower than mean BSL at time 0 during HBO_2. The mean decline in BSL in the 5 diabetics over the 2 hours was 3.5 ± 0.7 mmol/l. However, there was no significant difference between any time points in the normobaric group.

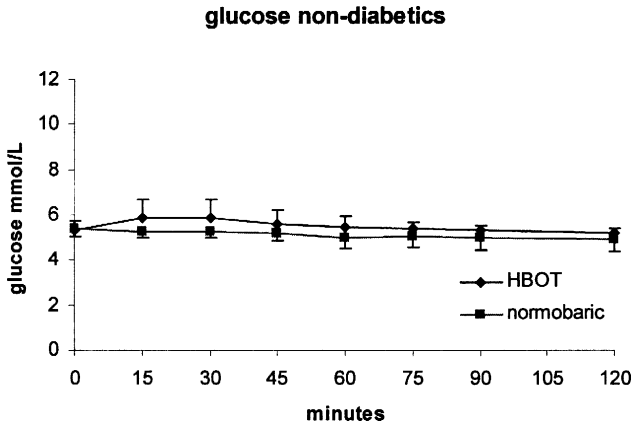

Figure 1. Mean BSL in non-diabetics, mmol/l plasma on the y-axis against duration in minutes of HBO_2 or air breathing on the x-axis. Error bars are one standard error of the mean.

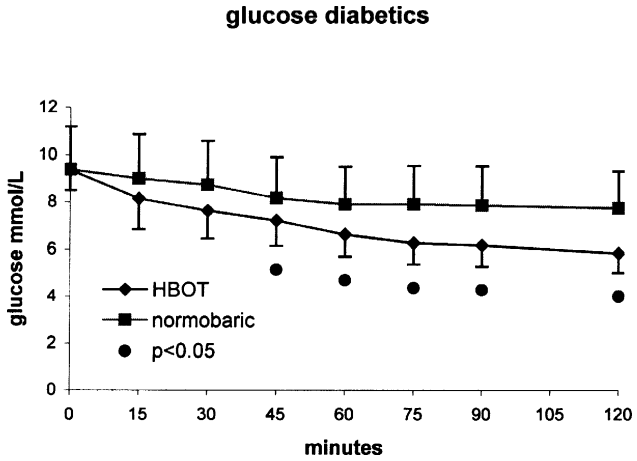

Figure 2. Mean BSL in diabetics, mmol/l plasma on the y-axis against duration in minutes of HBO_2 or air breathing on the x-axis. Error bars are one standard error of the mean. Circles indicate significant difference (2-tailed $p<0.05$) from time 0 for the HBO_2 group.

Insulin

Significant F tests were found for the main effect time and interaction of diabetes x HBO_2. However no consistent pattern emerged from post-hoc analysis as can be seen in Figure 3 and 4 indicating no change in insulin in any group.

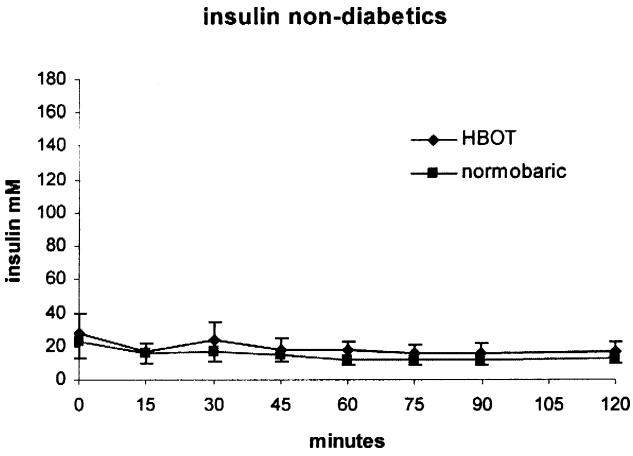

Figure 3. Mean insulin levels in non-diabetics, mU/l serum on the y-axis against duration in minutes HBO_2 or air breathing on the x-axis. Error bars are one standard error of the mean.

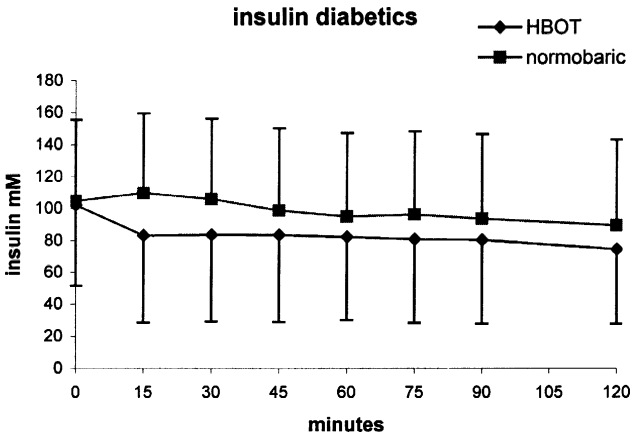

Figure 4. Mean insulin levels in diabetics, mU/l on the y-axis against duration in minutes of HBO_2 or air breathing on the x-axis. Error bars are one standard error of the mean.

One patient had hyperinsulinaemia and this accounts for the large error bars in Figure 4. However excluding this patient resulted in similar statistical conclusions.

Discussion

The decline in BSL in diabetics but not non-diabetics in the present study supports the anecdotal reports of hypoglycaemia in diabetics when they receive HBO_2 treatment.

This study confirms the previous brief reports of decrease BSL. These reported that whole blood glucose

concentration decreased by an average of 2.8 mmol/l in 25 IDDM patients[3] and BSL dropped below 100 mg/dl in 26.4% patients after HBO_2 treatment,[2] decreases similar to the present study. However, in a study of diabetic underwater divers, although no hypoglycaemic episodes were encountered due to high BSL maintenance before the dive, insulin requirement dropped significantly with repeated dives.[5]

The high partial pressure of oxygen encountered in diving apparently does not lower serum glucose levels significantly in diabetic divers.[13] However there is a considerable difference in partial pressure of oxygen encountered by underwater divers and HBO_2 patients. In the present study subjects breathed almost 202 kPa (2 bar) oxygen partial pressure in contrast to 74 kPa partial pressure oxygen in the compressed air divers. Also, HBO_2 patients in the present study were at 202 kPa (2 bar) ambient pressure while the compressed gas divers were at 375 kPa (3.7 bar or 27 m) ambient pressure. This comparison confirms that it is the partial pressure of oxygen and not the ambient pressure that is responsible for hypoglycaemia in diabetics.

In the present study the decline in BSL was initially progressive during treatment but reached a plateau towards the end of treatment. This suggests that diabetics may be more vulnerable to hypoglycaemia in the second half of longer HBO_2 treatment protocols. An additional capillary BSL measurement in the middle of treatment might allow intervention to prevent hypoglycaemia in diabetics. However, one must be cautious about the accuracy of in-chamber glucometer testing.[14,15]

The average BSL drop in the five diabetics was 3.5 $\pm$ 0.7 mmol/l over 2 hours in this study indicating that patients with BSL 6 mmol/l or less before treatment would be at the greatest risk of hypoglycaemia during HBO_2 treatment since hypoglycaemic symptoms usually begin at a BSL of less than 2.5 mmol/l. Whether pre-HBO_2 glucose supplementation in such patients might reduce the risk of hypoglycaemia is an area for further study.

There was a non-statistically significant drop in serum insulin levels in diabetics during HBO_2 which may have been secondary to the hypoglycaemia. The fact that insulin levels did not rise excludes of some of the postulated mechanisms for HBO_2 induced hypoglycaemia. First, in Figure 4, the lack of increase in insulin levels in diabetics during HBO_2 indicates there was probably not a stimulation of insulin secretion. Secondly, since insulin levels did not change with HBO_2 in non-diabetics, insulin is not a mechanism of protection against hypoglycaemia in this group as it is in exercise; hypoglycaemia in diabetics cannot be a failure of this mechanism.

However, this study provides no evidence for the other postulated mechanisms of hypoglycaemia during HBO_2: increase aerobic metabolism or inhibition of anti-insulin hormones (somatotropin and glucagon).

It could be argued that BSL would be influenced by stress related to the HBO_2. However, it would be expected that stress hormones (catecholamines, cortisol, growth hormones etc.) would elevate BSL. In the present study, there was no rise in BSL. This suggests that there were no stress-related hormonal effects in either group under HBO_2 or normobaric conditions. However, direct measurement of stress hormones should be the subject of another study.

Conclusions

HBO_2 reduces BSL in diabetics by a mechanism other than insulin. Control of BSL is extremely important during HBO_2 treatment since signs and symptoms of hypoglycaemia mimic oxygen toxicity and can lead to convulsions or even unconsciousness in the chamber. Furthermore, patients with diabetic autonomic neuropathy with inadequate somatotropin response to hypoglycaemia may not manifest the warning autonomic symptoms, which normally precede those of central nervous system dysfunction (sweating, shaking, palpitation, paraesthesia, numbness etc).

Pre-HBO_2 glucose supplementation in any diabetic with pre-HBO_2 BSL of 6 mmol/l or lower and capillary BSL testing at the middle of HBO_2 treatment in diabetics may reduce the in-chamber risk of hypoglycaemia in diabetics.

References

1 Bureau of Investigation. The Cunningham "Tank Treatment". *J A M A* 1928;1494-1496

3 Springer R. The importance of glucometer testing of diabetic patients pre and post-dive. [Abstract] *Undersea Biomed Res* 1991; 18 (Suppl): 20

2 O'Malley E, Otto G, Berkowicz L, Suttle K, Kulikovsky M, Cetina S and Fife C. Blood glucose screening in diabetics undergoing hyperbaric oxygen therapy. [Abstract] *Undersea Hyper Med* 1998: 25 (Suppl): 49

4 Longoni C, Camporesi EM, Buizza M et al. Reduction in insulin requirements during HBO therapy. [Abstract] *Undersea Biomed Res* 1988; 15 (Suppl): 16-17

5 Lerch M, Lutrop C and Thurm U. Diabetes and diving: Can the risk of hypoglycaemia be banned? *SPUMS J* 1996: 26 (2): 62-66

6 Davies D. SPUMS statement on diabetes. *SPUMS J* 1992; 22: 31-32

7 Dear G de L. Diabetes and Diving. *Alert Diver* 1997; (Jan/Feb): 34-36

8 Dear G de L, Dovenbarger JA, Corson KS, Stolp BW and Moon RE. Diabetes among recreational divers

[Abstract] *Undersea Hyperb Med* 1994; 21 (Suppl): 94
9 Uguccioni DM and Dovenbarger J. The diabetes question. *Alert Diver* 1996; (Jan/Feb): 21-23
10 Capelli-Schellpfeffer M, Philipson LH, Bier M, Howe L and Boddie A. HBO and hypoglycaemia in diabetic surgical patients with chronic wounds. [Abstract]. *Undersea Hyperb Med* 1996; 23 (Suppl): 81
11 Jain KK. *Textbook of Hyperbaric Medicine*. *2nd Edition.* Toronto: Hogrefe & Huber, 1996; 333
12 Roger HU and Daniel WF. *Williams Textbook of Endocrinology*. 8th Edition. Philadelphia: Saunders, 1992; 1310
13 Edge CJ, Grieve AP, Gibbons N, O'Sullivan F and Bryson P. Control of blood glucose in a group of diabetic scuba divers. *Undersea Hyperb Med* 1997; 24 (3): 201-207
14 Price ME Jr, Hammett-Stabler C, Kemper GB, Davis MG and Piepmeir EH Jr. Evaluation of glucose monitoring devices in the hyperbaric chamber. *Mil Med* 1995; 160: 143-146
15 Moon RE, Dear G de L, Stolp BW, Doar PO and Vote DA. Measurement of plasma glucose under hyperbaric oxygen conditions. [Abstract] *Undersea Biomed Res* 1999; 14 (Suppl): 53

Surgeon Captain Lalith Ekanayake, MBBS, MD, is Consultant Physician and Gastroenterologist at the Naval Hospital, Colombo 01, Sri Lanka. This paper was produced while he was Diving and Hyperbaric Medicine Fellow at the Hyperbaric Medicine Unit, Royal Adelaide Hospital, North Terrace, Adelaide, South Australia 5000.

David J Doolette, PhD, is a Research Fellow in the Department of Anaesthesia and Intensive Care, University of Adelaide, South Australia 5005. He is also the Education Officer of the South Pacific Underwater Medicine Society.

EFFECTS OF RECREATIONAL DIVING ON ATTENTION: A Preliminary Study

Karen L Schiltz, Cathy M Ary and J Thomas Millington

Key Words
Recreational diving, research, risk, safety.

Abstract

The neuropsychological functions of healthy recreational divers with varied cumulative diving experience and across repetitive dives have not been investigated. This preliminary study was conducted:
1 to determine attentional and concentrational levels in a group of healthy recreational divers,
2 to investigate the effects of years of diving experience on attentional and concentrational skills, and
3 to test the effects of repetitive recreational dives on attentional and concentrational levels.

The subjects consisted of 22 individuals aged between 16 to 71. The mean years of diving experience was eight years. A battery of Digit Span Forward, Digit Span Backward, and the Stroop Test was administered before and after the first and second dive on sport dive boats. Our results revealed that attentional and concentrational skills of healthy recreational divers generally fell within normal limits, were unrelated to years of cumulative diving experience, and were not compromised across repetitive recreational dives.

Introduction

Previous studies have not investigated attentional and concentrational skills in healthy recreational divers. In addition, there have been no studies examining effects of years of cumulative diving experience and repetitive dives on neuropsychological functioning levels.

Most diving studies have focused on divers who have suffered from decompression sickness (DCS). Results of these studies have been contradictory. Specifically, selective neuropsychological deficits have been identified in professional divers with focal neurological manifestations of DCS.[1-3] On the other hand, Andrews et al.[4] found no evidence of cognitive impairment in abalone divers who showed evidence of DCS. While measures assessing attentional and concentrational skills were not directly administered, these functions are important to examine since they underlie all cognitive skills. Intact attentional and concentrational skills are necessary for safe self-monitoring of diving protocols. Andrews et al. suggested that professional and recreational divers who follow the appropriate safety protocols should not be at risk for progressive brain damage resulting from diving.

Neuropsychological functioning has not been thoroughly investigated in recreational divers. For example, Levin et al.[5] reported on two divers who were administered limited neuropsychological tests and neuroradiological examinations within the first month of sustaining DCS. These patients had negative medical and psychiatric histories before their episodes of DCS. Magnetic resonance imaging (MRI) results revealed paraventricular and subcortical white matter lesions in both patients. The neuropsychological screening indicated compromises across measures sensitive to information processing skills, visual-motor skills and selective verbal