An observation of venous gas emboli in divers and susceptibility to decompression sickness

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Abstract

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Introduction: Decompression sickness (DCS) results from the formation of bubbles within the tissues and blood in response to a reduction in environmental pressure. Venous gas emboli (VGE) are common after diving and are usually only present in small numbers. Greater VGE numbers are an indication of decompression stress, and can be reliably detected using ultrasound imaging.

Aim: To examine the relationship between production of VGE following a routine dive and the risk of DCS.

Methods: A matched population of divers with and without a history of DCS were monitored for the production of VGE at 15-minute intervals using ultrasound, following a 405 kPa air dive in a hyperbaric chamber using the DCIEM air decompression table. VGE production was graded using a validated grading system and the data analysed to compare maximum VGE grade and duration of VGE formation.

Results: Eleven divers with a history of DCS were compared with 13 divers with no history of DCS. Divers with a history of DCS demonstrated both a higher maximum grade ($P = 0.04$) and longer duration ($P = 0.002$) of VGE production compared to divers without a history of DCS.

Conclusion: Higher maximum VGE grades and longer durations of VGE following decompression were associated with a history of DCS and, in particular, musculoskeletal DCS. Although the exact mechanism of DCS remains poorly understood, our data suggest some individuals are inherently more prone to develop VGE, increasing the probability of DCS. Modification of diving practices in those with high VGE grades could potentially decrease DCS risk in these individuals.

Key words

Decompression sickness, Doppler, venous gas emboli, scuba diving

Introduction

Decompression sickness (DCS) arises from the formation of bubbles within the tissues and blood in response to a reduction in environmental pressure. These bubbles can be measured in the form of venous gas emboli (VGE) by ultrasound imaging. The number of VGE can be used to indicate a diver's exposure to decompression stress.[1,2] Standardised grading systems of these VGE have been established to predict this risk.[3–5]

It appears that some divers are more prone to developing DCS than others. Although the grade of bubble production and subsequent risk of developing DCS has been studied widely, it is not known whether divers with a history of DCS produce higher levels of VGE after routine diving. The aim of this study was to establish whether there is an association between the production of VGE in an individual diver and the risk of developing DCS.

Methods

We performed an observational cohort study comparing a population of divers with a history of DCS to a control group of divers with no history of DCS. The study was approved by the South Metropolitan Health Service Human Research Ethics Committee (HREC), Western Australia (approval no: 13/27), and The University of Notre Dame Australia HREC, Western Australia (approval no: 13057F). Informed, written consent was obtained for all subjects.

STUDY POPULATION

Divers with a history of DCS were recruited from the Fremantle Hyperbaric Unit database of divers treated between 2009 and 2013. The control group was a sample of volunteer contacts recruited from local diving clubs, and divers known to the researchers.

Inclusion criteria for DCS subjects included a history of mild to moderate DCS that had been medically diagnosed and treated at the Fremantle Hospital Hyperbaric Unit. All the divers had been medically cleared to dive again. Subjects in the control group were experienced recreational divers with a minimum of 50 logged dives who had not previously been medically diagnosed with DCS. Similarly the DCS subjects were all experienced recreational divers with over 50 logged dives. The age range for inclusion in the study was 18 to 60 years of age.

Divers with DCS who were excluded from the study were those who had been recommended to cease diving permanently because of severe DCS, those with a history of neurological symptoms and signs consistent with a diagnosis of cerebral artery gas embolism (CAGE) and those with a known history of DCS features that were suggestive of a

patent foramen ovale (PFO). Control divers who had no history of DCS were excluded if a PFO or other atrial septal defect was identified during echocardiography.

DIVING PROTOCOL

The simulated diving protocol involved a no-decompression bounce dive to 405 kPa with a 15-minute bottom time in a multiplace chamber. The dive profile followed the Defence and Civil Institute of Environmental Medicine (DCIEM) air table and was used due to its recognised safety profile. Groups of up to six divers were studied over four consecutive weekends out of the diving season in July 2013. None of the divers in the study had dived during the week prior to the study.

VGE MONITORING

Observations began immediately following the dive at time zero and then every 15 minutes until a minimum of at least 75 minutes had elapsed if no VGE had been detected, or for a minimum of two clear scans (30 minutes) post cessation of any detected VGE. Subjects were imaged supine in the left lateral position with a phase-array cardiac ultrasound probe (1–4 MHz) attached to a Zonare Z1 ultrasound machine. A right ventricular foreshortened apical view of the heart was performed to assess for VGE production and the left side of the heart assessed for the presence of VGE that may have 'arterialised'. The scans were performed by a hyperbaric physician with a formal qualification in ultrasound. VGE were graded using the Eftedal and Brubakk two-dimensional echocardiographic imaging scale.[3] The grading system is described as follows:
Grade 0 – No observed bubbles
Grade 1 – Occasional bubbles
Grade 2 – At least one bubble every four cardiac cycles
Grade 3 – At least one bubble every cardiac cycle
Grade 4 – At least one bubble per cm^2 in every image
Grade 5 – White-out, single bubbles cannot be discriminated

Subjects were imaged for up to 60 seconds at a time and the images were recorded as 10-second prospective loops and saved on to a database for review. No dynamic manoeuvres were performed prior to or during the imaging. The divers were carefully monitored and reviewed for symptoms of DCS by a hyperbaric physician.

STATISTICAL ANALYSIS

Descriptive data are described as means ± standard deviations (SD). Test of normality was carried out using the Shapiro-Wilk test, showing normally distributed data; normal distribution was not significantly skewed. Normality was confirmed using Q-Q plots for both age and BMI. Between-group comparisons for continuous data were assessed with Student's *t*-tests. Non-parametric data were assessed using the χ^2 comparison for independence. Effect size was calculated using the phi coefficient. The Mann-Whitney U test was used to compare bubble formation and duration for those with and without DCS. Statistical significance was set at $P < 0.05$. Analysis was performed using SPSS version 20.

Results

Twenty-six subjects were recruited into the study with 24 included in the final data analysis. One subject was excluded for a previous episode of cutaneous DCS that had not been formally assessed for the presence of a PFO, whilst a second participant, a very thin female, from the non-DCS group was excluded due to difficulty attaining high-quality ultrasound images. The 24 subjects consisted of 18 males and six females (Table 1). From the 11 subjects in the DCS group, six had a history of musculoskeletal DCS, three lymphatic, one mild spinal and one constitutional DCS. The three patients with lymphatic DCS had undergone formal PFO testing with transthoracic bubble contrast echocardiography and no PFOs were detected.

No subjects developed symptoms or signs of DCS during the study. VGE were only observed in the right heart with no subject having an obvious PFO or other atrial septal defect.

Neither age ($P = 0.94$) nor body mass index ($P = 0.62$) were associated with a history of DCS in this study. Overall, the DCS group was more likely to produce bubbles at any grade compared with the non-DCS group: (χ^2 [1, $n = 24$] = 4.847, $P = 0.04$, phi = 0.44). Non-parametric assessment of bubble producers against DCS showed that there was a significant difference in maximum grade across DCS types (Mann-Whitney U test: Z-value -2.2, $P = 0.03$). The median bubble grade for those without a history of DCS was 0 (no bubbles produced), and 1 for those with DCS.

Because of single subjects in the groups representing mild spinal and constitutional forms of DCS post hoc, Bonferroni analysis was not possible on the group as a whole. With the removal of the two groups mentioned above, those who formed bubbles remained more likely to have had DCS than those who did not: (χ^2 [2, $n = 22$] = 9.1, $P = 0.01$, phi = 0.56). There remained a significantly higher bubble grade across the DCS types (Mann-Whitney U test: Z-value -1.8, $P = 0.04$).

Table 1
Demographic profile of divers involved in the study; means (SD) shown for age and BMI – body mass index; there were no differences between the groups

	Male	**Female**	**Age** (years)	**BMI** ($kg \cdot m^{-2}$)
No DCS	11	2	42 (9)	27 (4)
History of DCS	7	4	41 (9)	26 (5)
Combined group	18	6	42 (8)	27 (4)

Table 2
Group comparison of DCS type and VGE grade; * 15 minute intervals

	Bubble grade		Time points (*n*) with bubbles *		Subjects (*n*) with bubble grade ≥
	median	maximum	median	maximum	
1					
No DCS (*n* = 13)	0	2	0	1	5
Musculoskeletal DCS (*n* = 6)	1	3	4	6	6

The same assessment was performed for DCS type against VGE duration, demonstrating a significant increase in duration of VGE production among those with prior DCS: (χ^2 [1, n = 24] = 9.151, P = 0.002, phi = 0.66). As above, constitutional and mild spinal groups were removed from analysis due to single participants and the assessment performed again with duration of VGE production compared to no DCS, lymphatic DCS and musculoskeletal DCS. This again demonstrated a significant difference in distribution of duration of VGE production across the groups: (χ^2 [1, n = 22] = 7.84, P = 0.005, phi = 0.66]. Table 2 shows differing DCS types with respect to the median and maximum bubble grades and detectable bubble durations.

Discussion

Previous research has suggested no direct correlation between the increased presence of VGE and the risk of DCS development; however, the absence of VGE has been strongly associated with decompression safety.[2,6–8] This seems to suggest that there is a complex relationship between the presence of bubbles and their pathological effects. Our research suggests that divers with a history of DCS, on average, produce VGE over a longer period and at a higher grade than divers never having experienced DCS. This indicates that an individual diver's characteristics influence bubble formation following decompression even in the absence of DCS.

No single mechanism has been elicited for the formation of DCS, with a multitude of processes likely to contribute. Such processes include gas bubbles causing direct mechanical effects, gas emboli resulting in downstream ischaemia and interactions with the endothelium of blood vessels resulting in the release of inflammatory mediators.[9–12] Given the complex relationship between the grade of VGE formation and the development of DCS, the duration of bubble formation may become increasingly important. A prolonged action of VGE formation could potentially increase the risk of DCS via two mechanisms. Firstly a sustained action of bubbles could increase the degree of endothelial interaction, and the release of inflammatory mediators. Secondly given that DCS may develop in the absence of high bubble grades, longer durations of VGE formation could increase the risk of DCS occurring simply by increasing time-exposure to the abnormal intravascular milieu.

Divers with a history of DCS, specifically those with musculoskeletal manifestations, appear more prone to producing longer durations of VGE and higher grades in comparison to those divers having never experienced DCS but also possibly in those having experienced other DCS types. However, the limited numbers in our study mean no firm conclusions can be drawn in this regard. Lymphatic DCS remains poorly understood and has traditionally been grouped with other cutaneous forms of the disease. Cutaneous DCS is associated with a PFO;[13] however, the three divers with lymphatic DCS had been formally screened for inter-atrial shunting. It is hypothesised that lymphatic DCS could be caused by local tissue compression whilst diving from the pressure effect of, for example, a buoyancy control device and, therefore, may only need small bubble loads to cause symptoms that may not be related to the degree of intravascular bubble formation.[14] Further, this independent mechanism, if unrelated to intravascular VGE formation, may not be associated with as high a risk as musculoskeletal and neurological DCS.

The variability between divers identified in this study is suggestive of certain physiological catalysts that facilitate bubble production, found in differing degrees between subjects. One explanation may be the varying presence of hydrophobic surfaces within the body. It has long been suggested that large bubbles require a pre-existing gas nucleus to form around, with studies aimed at decreasing these gas nuclei being successful in reducing the observed rate of DCS in rats.[15,16] Caveolae have been proposed as possible sites for the formation and stabilisation of bubble nuclei within the endothelium.[17] These 50–100 nm cup-shaped depressions found in plasma membranes are composed of specialised lipid domains and thought to be involved in numerous processes including cell signalling, endocytosis and cell metabolism.[18] Since hydroxymethyl coenzyme A reductase inhibitors (statins) have been demonstrated to decrease levels of caveolae, one intriguing possibility would be the effect of statins on bubble formation.[19]

Following experimental studies it has been proposed that nanobubbles may spontaneously form on flat hydrophobic surfaces from dissolved gases in solution under hyperbaric conditions.[20] This, in combination with the structure of caveolae and their propensity for distribution within endothelial and muscle tissues, could possibly be a factor in bubble formation.[21] Their regulation in response to the

expression of proteins and the role that cholesterol plays in their existence could account for varying degrees of bubble formation demonstrated between participants.[22]

Fremantle Hyperbaric Unit treats on average 35 to 40 patients with decompression illness (DCI) a year from across Western Australia. We hope to increase our study population in future studies. A number of additional factors also clearly play a role in the development of DCS. Previous studies have associated increasing age, gender and weight with an increased production of VGE.[23] We found no such statistical correlations but do note the mean age of our DCS group is higher. The presence of a PFO has been linked to an increased risk of developing DCI, so we attempted to exclude any patients with known PFOs or diagnostic features of PFOs, such as a history of migraines, characteristic skin rashes or neurological symptoms.[24,25]

The low levels of VGE production seen in this study are consistent with previously published data on short bounce dives and low levels of bubbling in keeping with the DCIEM tables.[26] The DCIEM tables were developed with the exclusion of diver profiles that produce a greater then 50% incidence of grade 2 bubbling.[27] The schedule used in the study was chosen for its safety profile. It will be interesting to see if we can replicate the results in future studies over a range of diving tables and with more provocative dive profiles producing higher levels of VGE. Dynamic manoeuvres, often in the form of knee bends, can be performed during monitoring for VGE to 'squeeze' bubbles into the venous circulation. This provides showers of bubbles that can be easily detected; however, these dynamic manoeuvres are hard to standardise and were not used in this study.

Conclusions

This study has demonstrated that a higher maximum VGE grade and longer durations of VGE production following decompression from a pressure of 405 kPa were associated with a history of DCS, and in particular musculoskeletal DCS. Although the exact mechanism of DCS remains poorly understood, our data suggest that some individuals are inherently more prone to develop VGE, increasing their likelihood of DCS. We would suggest that patients who have been treated for DCS be advised to modify their diving practices as they appear to be at an increased risk. Further studies are needed to identify the exact mechanisms of VGE production, so that targeted therapies can be applied to individuals at risk of DCS.

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