Medical Hypotheses 86 (2016) 80–84

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Exercise before and after SCUBA diving and the role of cellular microparticles in decompression stress

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ARTICLE INFO

Article history:
Received 3 June 2015
Accepted 9 December 2015

ABSTRACT

Risk in SCUBA diving is often associated with the presence of gas bubbles in the venous circulation formed during decompression. Although it has been demonstrated time-after-time that, while venous gas emboli (VGE) often accompany decompression sickness (DCS), they are also frequently observed in high quantities in asymptomatic divers following even mild recreational dive profiles. Despite this VGE are commonly utilized as a quantifiable marker of the potential for an individual to develop DCS. Certain interventions such as exercise, antioxidant supplements, vibration, and hydration appear to impact VGE production and the decompression process. However promising these procedures may seem, the data are not yet conclusive enough to warrant changes in decompression procedure, possibly suggesting a component of individual response. We hypothesize that the impact of exercise varies widely in individuals and once tested, recommendations can be made that will reduce individual decompression stress and possibly the incidence of DCS. The understanding of physiological adaptations to diving stress can be applied in different diseases that include endothelial dysfunction and microparticle (MP) production.

Exercise before diving is viewed by some as a protective form of preconditioning because some studies have shown that it reduces VGE quantity. We propose that MP production and clearance might be a part of this mechanism. Exercise after diving appears to impact the risk of adverse events as well. Research suggests that the arterialization of VGE presents a greater risk for DCS than when emboli are eliminated by the pulmonary circuit before they have a chance to crossover. Laboratory studies have demonstrated that exercise increases the incidence of crossover likely through extra-cardiac mechanisms such as intrapulmonary arterial-venous anastomoses (IPAVAs). This effect of exercise has been repeated in the field with divers demonstrating a direct relationship between exercise and increased incidence of arterialization.

Introduction

Open sea SCUBA (self-contained underwater breathing apparatus) diving is an occupational tool as well as a recreational activity. Although diving science has been continuously advancing over the past decades, there remains an effort to increase the safety related to acute and chronic exposures to the undersea hyperbaric environment. With these advances, along with more capable, inexpensive, and user-friendly equipment, the population of divers has grown from elite adventurers to an all-inclusive holiday activity with an estimated 1.2 million divers around the world. While previous empirical development and refinement of diving protocols (decompression tables) has dramatically reduced the incidence of decompression sickness (DCS) [1], cases of "undeserved" DCS are reported in divers who follow safe practices [2]. Additionally, the chronic implications of a lifetime of diving are not yet known. It is important to consider that the original diving procedures were developed and tested on military divers who now represent a small fraction of a diving population. That is, SCUBA divers now include the elderly and those with chronic disease and complications.

The safety of diving and mitigation of decompression stress remains one of the more practical goals of recent SCUBA research. The impact of exercise on diving has been investigated in several studies. Some of these studies utilized simulated dry chamber dives [3], which may not accurately replicate the stress associated with open water diving [4]. While a chamber can recreate the hyperbaric experience of diving there are additional factors such as water immersion, increased effort of breathing, hypothermia, psychological stress and compression from wetsuits that add to the stress of the environment. Currently, exercise is considered by some to be a form of protective preconditioning for SCUBA

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http://dx.doi.org/10.1016/j.mehy.2015.12.006
0306-9877/

diving [5–7]; based on increased animal survival following provocative decompression [8] and decreased VGE in humans after aerobic exercise. Alternative preconditioning interventions besides exercise include administration of antioxidants, whole body vibration, hyper-hydration, heat treatment, and oxygen breathing [7]. Proposed mechanisms of exercise preconditioning include altered hemodynamics [9], increased nitric oxide (NO) synthesis and improved vaso-reactivity [6].

Dujic et al. have previously reviewed the relationships among exercise, NO, and VGE and reported a significant reduction in VGE [6]. Although VGE seem to be part of the mechanisms leading to DCS, their presence alone is not correlated with DCS [10]. Other theories on the pathogenesis of DCS include endothelial dysfunction and damage [11–13], cellular microparticles [14], reactive oxygen species [15,16], and perturbations related to altered coagulation processes and platelet activation [17]. To date, little investigation has been done on the effects that exercise or other preconditioning methods may have on these parameters, or even how these individual theories fit into the grand scheme of DCS pathology.

The dive profiles used in many of these studies (18 msw, 47 min bottom time) would be considered mild, even by recreational standards as most newly certified divers are permitted to go to a depth of 18 msw. One important distinction, in the case of these 18/47 dive profile (depth/bottom time), is that no decompression stop was used. Although this profile constitutes a no decompression dive based on standard dive tables, most dive computers recommend a decompression stop (normally referred to as a "safety stop") in order to minimize DCS risk [18]. Dive stress resulting from no decompression profiles can be compared with a formula ($p\sqrt{t}$) proposed by Hennesy and Hemplemen [19]. It was determined that there is an increase in DCS incidence with values above 25 [20] and the 18/47 profile results in a value of 19.2, which again demonstrates that these are not extreme dive profiles and the results are applicable to amateur and recreational divers as well.

Finally, research into the physiology of SCUBA diving may have applicability to broader areas of biology and medicine. MPs are no longer thought to be inert cellular waste, but contribute to the pathogenesis of many conditions [21–23] and they likely also play a normal or homeostatic role in physiological processes. SCUBA diving elevates these MPs along with radical oxygen species (ROS, both of which have been found to play a significant role in the pathogenesis number of severe diseases) levels for at least 24 h following decompression [24], whereas exercise-induced increases lasts only 2–3 h (ref), suggesting that SCUBA diving represent a unique combination of multimodal stressors. Right-to-left shunt is always of interest in stroke research [25] and results from some of these exercise and IPAVA studies may be of interest outside the diving community as well. Furthermore, SCUBA diving is a useful mechanism for study of endothelial dysfunction lasting up to 48 h in some subjects [26,27].

The hypothesis

Current decompression protocol is a "one-size-fits-all" procedure. A growing body of research suggests that variations in both procedure (such as exercise before or after diving) and individual physiology (PFO, IPAVAs) may influence the decompression process. This leads to the following hypotheses: (1) Individuals with "undeserved" DCS may be sensitive to one or more of the factors listed above and, (2) If these sensitivities are known by the individual, utilizing a more conservative protocol would decrease the incidence of injury. Additionally, the authors propose that MPs and IPAVAs are a part of the mechanism behind the influence of physical activity on diving and decompression.

Evaluation of the hypotheses

Exercise before SCUBA diving

Exercise protocols tested before diving have varied in intensity from 60% age-predicted maximal heart rate (HR_{max}) [28] to intervals at 90% HR_{max} [5], with running as the mode of exercise. Studies examined the impact of exercise undertaken within 2 [9,28,29] or 24 h [5] prior to diving. In these studies exercise reduced the quantity of VGE to varying degrees. Although many of these studies were conducted in the open sea, whether or not a reduction in VGE alone is enough to mitigate decompression stress is yet to be determined. There has been little discussion of mechanisms other than VGE reduction such as preservation of endothelial function or a reduction in platelet aggregation and MP expression.

Microparticles were once thought to be useful simply as biomarkers of physiological/pathophysiological stress, whereas newer research has linked them to pathogenesis of many chronic conditions including certain cancers [30] and cardiac disease [21]. Hence, there is increasing interest in activities, such as exercise and diving, that result in an elevation of circulating MPs. They increase with traumatic and inflammatory disorders, and may serve as intercellular messengers because they can directly stimulate the release of cytokines or other signaling proteins, mRNA, and micro-RNA [31]. It is widely accepted that MPs form when the normal asymmetric distribution of lipids between the inner and outer leaflets of the plasma membrane is lost. MPs commonly exhibit elevation of phosphotidylserine on the outer membrane leaflet which leads to binding of the plasma protein, annexin V. Annexin V-positive platelet derived MPs exhibit pro-coagulant properties in addition to leukocyte activation and aggregation [32]. Research in the murine model has been interesting enough to warrant further investigations in human subjects.

Due to the highlighted relationship between MPs, inflammation, and vascular damage Thom et al. hypothesized that MPs generated during decompression play a role in the pathogenesis of DCS, and, that abatement of such MPs would disrupt the process that leads to injury [14]. This was demonstrated in mice where several abatement strategies resulted in significantly lower tissue damage in the brain, omentum and several muscle beds [33]. Animal studies have the advantage of potentially producing more concrete evidence since protection from DCS can be observed as changes in survival rate and they can be sacrificed to achieve a deeper level of tissue analysis. The disadvantage to such studies is, despite the similarities in all mammals, there are limits to the translation between human and animal models.

Yang et al. hypothesized that some MPs contain an gas phase, which may serve as a nucleation site for nitrogen bubbles as gas is released from the saturated tissues during decompression, resulting in VGE [34]. Furthermore, as decompression continues, these MPs grow in size proportional to the decrease in ambient pressure. These larger particles maintain a hard shell composed of the original MP fragments and have the potential to cause greater harm (Fig. 1). An increase in these enlarged MPs (LMPs, 1.0–3.0 μm in diameter) was found in mice immediately on decompression and they continued to increase for 24 h. Experimental support for the presence of a gas core came from studies using hydrostatic pressure, which diminished the number of LMPs. with no change in the normal sized MPs. Moreover, neutrophil activation and tissue injury associated with decompression stress could be recapitulated by injecting naïve mice with enlarged MPs from decompressed mice, but this did not occur if the MPs were first subjected to hydrostatic pressure to diminish their size [34].

Follow up diving studies in human subjects demonstrated an increase in MPs and several inflammatory parameters [35,36]. In