HEMODYNAMIC CHANGES INDUCED BY SUB-MAXIMAL EXERCISE PRIOR TO A DIVE AND ITS CONSEQUENCES ON BUBBLE FORMATION.

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What is already known on this topic?

Recent studies in rats have shown that a single bout of high-intensity exercise 20 h before a simulated dive reduced bubble formation and prevented decompression sickness with no effect at any other time. The authors speculated that the main mechanism underlying this protective effect could be related to nitric oxide (NO) production. A human study supported this animal data in which 12 divers reduced venous gas emboli performing a single bout of strenuous exercise 24 h before a simulated dive. However, we have previously shown that a short pre-dive latency can be also protective. In a study of 16 divers we found that a single bout of sub-maximal exercise 2 h before a simulated dive reduced circulating bubbles.

What this study adds?

This report confirmed that a single bout of sub-maximal exercise 2h before a simulated dive significantly reduced the number of bubbles in the right heart of divers. We evaluated the hemodynamic changes and their influence on bubble formation. A moderate hypovolemia induced by a pre-dive exercise can decrease stroke volume and consequently could reduce inert gas uptake and post-dive bubble formation. This protective effect of exercise might be mediated by several mechanisms and not only NO production.
ABSTRACT

Objective: To evaluate the effects of a sub-maximal exercise performed 2 hours before a simulated dive on bubble formation. To observe the hemodynamic changes and their influence on bubble formation.

Material and methods: Sixteen trained divers were compressed in a hyperbaric chamber to 400kPa for 30 min and decompressed at a rate of 100 kPa.min\(^{-1}\) with a 9 min stop at 130 kPa (French Navy MN90 procedure). Each diver performed two dives 3 days apart, one without exercise and one with exercise before the dive. All subjects performed a 40 min constant load submaximal and calibrated exercise which consisted of outdoor running 2h prior to the dive. Circulating bubbles were detected with a precordial Doppler at 30, 60 and 90 min after surfacing. Hemodynamic changes were evaluated with Doppler-echocardiography.

Results: A single bout of strenuous exercise 2h prior to a simulated dive significantly reduced circulating bubbles. Post-exercise hypotension (PEH) is observed after exercise with reductions in diastolic and mean blood pressure (DBP and MBP), total peripheral resistance were unchanged. Stroke volume (SV) was reduced whereas cardiac output (CO) was unchanged. Simulated diving caused similar reduction in CO independently of pre-dive exercise, suggesting that pre-dive exercise only changed DBP and MBP caused by reduced SV.

Conclusion: A single bout of strenuous exercise 2h before a dive significantly reduced the number of bubbles in the right heart of divers and could protect from decompression sickness. Declining stroke volume and moderate dehydration induced by a pre-dive exercise might influence inert gas load and bubble formation.

KEY WORDS

Diving, decompression sickness, bubble, exercise, dehydration.

ABBREVIATIONS

ACSA = aortic cross section area, AoVTI = aortic systolic flow velocity time integral, CO = cardiac output, DBP = diastolic blood pressure, DCS = decompression sickness, HR = heart rate, KISS = Kisman integrated severity score, MBP = mean blood pressure, NO = nitric oxyde, PEH = post-exercise hypotension, PP = pulse pressure, PRU = peripheral resistance units, SBP = systolic blood pressure, SV = stroke volume, VGE = venous gas emboli, VT = ventilatory threshold.
BACKGROUND

Decompression sickness (DCS) is caused by circulating bubbles of inert gas in blood and tissues resulting from supersaturation during decompression. Since exercise may increase the production of bubbles due to mechanical movement of body structures, intense physical exercise before diving has long been considered as an additional risk factor for DCS [1]. Recently, several studies indicate this notion needs updating. It has been reported that exercise training weeks before dives could reduce the incidence of neurological DCS in pigs [2] and rats [3]. Doppler-detected venous gas emboli (VGE) are widely used as an indicator of decompression stress in man. Although bubbles are frequent after symptom-free dives, the occurrence of many bubbles is clearly linked to a high risk of DCS [4]. It has been demonstrated that aerobically trained runners appeared to be at lower risk for venous bubbling than sedentary subjects [5]. Moreover, recent studies in rats have shown that a single bout of high-intensity exercise 20 h before a simulated dive reduced bubble formation and prevented death with no effect at any other time, i.e. 48, 10, 5 and 0.5 h prior to the dive [6, 7]. A human study supported this animal data in which 12 divers performed a single bout of sub-maximal aerobic exercise 24 h before a simulated dive [8]. It is speculated that the main mechanism of exercise-induced suppression of bubble formation could be related to nitric oxide (NO) production [6, 9]. However, it is not clear why this effect could be seen only within a window approximately 24 h prior to the dive. In fact, we have previously shown in a study of 16 divers that a short pre-dive latency with a sub-maximal exercise performed 2 h before a simulated dive can be also protective [10]. The present work aims to confirm this previous study with a well-calibrated exercise. After reviewing the current hypothesis, this report is the first to suggest that hemodynamic changes and moderate dehydration induced by a pre-dive exercise might influence inert gas load and bubble formation.

MATERIALS AND METHODS

Study population
Sixteen trained military divers, aged 27 – 39 years (33.6 ± 3.7 years, mean ± s.D.) were included. The subjects were all experienced divers with 100-3000 dives. Their body mass index varied between 21 and 27.1 kg.m⁻². None of them had experienced DCS in the past. All experimental procedures were conducted in accordance with Declaration of Helsinki, and were approved by the ethics committee of university of Marseille (CCPPRB Marseille 1). Each level of the study and pertaining potential risks were explained to the participants in detail and they all gave written informed consent before the experiment.

Measurements of maximal oxygen uptake
In order to assess individual exercise aptitude, each subject performed an incremental exhaust treadmill as follows: after 3 min of rest, all subjects carried out a 4 min warm up run session at 8 km·h⁻¹ then, the treadmill speed was increased by 1 km·h⁻¹ every minute until volitional exhaustion. During all exercise tests, subjects breathed through a mouthpiece in order to analyze expired gas using a breath-by-breath rapid response paramagnetic O₂ and infrared CO₂ analyzers (Jaeger Oxycon Pro® gas analyser). Minute ventilation (E, l.min⁻¹), oxygen consumption (O₂ ml·kg⁻¹·min⁻¹), carbon dioxide excretion (CO₂, ml·kg⁻¹·min⁻¹), and respiratory exchange ratio were all calculated. Ventilatory variables used to define the ventilatory threshold (VT) were determined continuously by the moving average of eight respiratory cycles. The first VT (VT1) determination involved the analysis of the behavior of CO₂ as a function of O₂, and corresponded to the breakpoint in the CO₂-O₂ relationship [11]. The
second VT (VT2) corresponded to a significant E-CO₂ relationship increment [12]. The identification of both VT was made by two experienced technicians. The average of the two independent determinations was taken. Heart rates corresponding to VT1 and VT2 (HR1 and HR2) were recorded and used for the following constant load exercise.

Exercise procedure
All subjects performed a 40 min constant load exercise which consisted of an outdoor running beginning 2h before the dive. HR were controlled by using Polar 4000® Sport Tester (Kempele, Finland). Each subject had to keep his HR = HR1 + HR2 / 2 during all the running session. After the exercise, the divers were allowed to drink water liberally.

Simulated dive protocol
The divers were compressed in a hyperbaric chamber (Sainte-Anne hospital, Toulon, France) to 400 kPa at a rate of 150 kPa.min⁻¹ breathing air and remaining at pressure for 30 min. During bottom time, the subjects exercised on a bicycle ergometer under aerobic threshold keeping their HR between 110-120 beats min⁻¹. They were decompressed at a rate of 100 kPa.min⁻¹ with a 9 min stop at 130 kPa (French Navy MN90 procedure).

Each diver performed two dives 3 days apart, one without exercise (protocol 1) and one with exercise 2 hours before the dive (protocol 2). The order of the two dives was randomly allocated.

Bubbles analysis
Circulating bubbles detection was performed by an experienced operator using a pulsed Doppler equipped with a 2 MHz probe (Pioneer) on the precordial area. Monitoring was performed every 30 min for 90 min after surfacing (first measurement at 30 min after the dive). During bubble detection, divers were supine for 3 min at rest, then, in order to improve the detection, two successive lower limbs flexions were performed. The Spencer scale was used to evaluate the signal of bubbles [13]. The bubble grades presented are the maximum grades observed at bubble peak, usually observed 60 min after the dive. In order to integrate the bubble kinetics, Kisman Integrated Severity Score (KISS) was calculated according to the following formula: \[ KISS = \frac{100}{4}(t_4-t_1)((d_4^\alpha+d_1^\alpha) + (t_3-t_2)((d_3^\alpha+d_2^\alpha)) + (t_2-t_1)(d_2^\alpha+d_1^\alpha)/2; \] where \( t_i \) = time of observation in minutes after reaching surface, \( d_i \) = doppler score (grades 0 to IV) observed at time \( t_i \) and \( \alpha = 3 \) (the parameter \( \alpha \) takes into account that the bubble grade is not a linear measure of bubble quantity). This calculation allows to distinguish between a diver with a single grade III score during four observations (III, 0, 0, 0) conducted over 2h (KISS = 7) and another diver with four grade III’s during the same periods (KISS = 42.2). KISS was assumed to be a meaningful linearized measure of post-decompression intravascular bubble activity status which may be treated statistically [14].

Body weight measurements
Weight was determined to the nearest 0.01 kg (using model I5S, OHAUS corporation, USA) with the subject wearing only running shorts. Weight measurements have been achieved 10 min before and 1h after each simulated dive (protocol 1 and 2), as well as 10 min before and 10 min after exercise procedures (protocol 2).

Echographic and Doppler study
The ultrasonographic examinations were carried out by an experienced investigator using a Doppler echocardiograph (Mylab 30CV, Esaote SpA, Genova Italy) connected to a 2.5-3.5 MHz transducer array.
Investigations were performed in a quiet room with a stable environmental temperature (25°C) one hour before and after each simulated dive (protocol 1 and 2), and one hour before and after exercise procedures (protocol 2).

We combined 2D echocardiography with pulsed Doppler to estimate cardiac output. HR was recorded by echocardiogram and the rate was averaged over 60 s. Cardiac output (CO) was derived from the aortic blood flow. Aortic cross section diameter was measured by 2D echocardiography from the left parasternal short axis view at the level of the aortic root. Aortic cross section area (ACSA) was calculated as ACSA = 3.14 x (diameter / 2)^2. The aortic systolic flow velocity time integral (AoVTI) was measured by computer assisted determination from the pulsed-wave Doppler profile of the aortic blood flow from the apical four chamber view, allowing the calculation of stroke volume (SV = AoVTI x ACSA) and CO (CO = SV x HR).

Sphygmanometric blood pressure measurements on the right arm were obtained at the end of each echocardiographic examination. Mean arterial blood pressure (MBP) was calculated as: MBP = DBP + 1/3 (SBP - DBP), where SBP and DBP were respectively the systolic and diastolic arterial blood pressure. Pulse pressure was defined as PP = SBP – DBP. Systemic vascular resistance were calculated as mean arterial blood pressure divided by cardiac output and expressed in peripheral resistance units (PRU, mmHg.l⁻¹.min⁻¹).

Statistical analysis
Statistical tests were run on Sigma Stat software. Each subject has served as his own control. Data distribution was studied using a Kolmogorov-Smirnov test. For values obtained at 2 time points, a t test for paired data was used when the data were normally distributed. If not, the Wilcoxon’s paired signed-ranks test was used. For values obtained at 3 or 4 time points, one way repeated measures ANOVA was used when the data were normally distributed with Holm-Sidak method for all pairwise multiple comparison procedures. If the distribution was not normal, comparisons were performed with a Friedmann’s test and the post-hoc dichotomous comparisons with a Dunn’s test. Differences between groups were considered significant at p < 0.05.

RESULTS

Maximal oxygen uptake and ventilatory thresholds
The mean VO2max was 51.7 ± 8.3 ml.kg⁻¹.min⁻¹ (mean ± SD) with a mean HRmax at 190 ± 8 beats min⁻¹ (mean ± SD). Mean HR1 was 164 ± 14 beats min⁻¹ and mean HR2 177 ± 14 beats min⁻¹ (mean ± SD).

Circulating bubbles detection (Table 1)
None of the divers suffered from DCS after the dives.
The overall distribution of bubbles was not modified, the maximum bubble count (bubble peak) was always observed 60 minutes after surfacing following the respective protocol (with or without exercise).
40 min-endurance running 2 h before the dive significantly reduced maximum bubble grades (p = 0.023), and KISS (p = 0.049). Two divers (n°11 & 16) showed an increase in venous bubble grade after performing the exercise.

TABLE 1
Bubble grade following hyperbaric exposure to 400kPa for 30 min with (protocol 2) or without (protocol 1) exercise 2h before the dive. * = p<0.05
Body weight measurements
For protocol 1, we observed a significant reduction of weight after diving (mean: -0.28 kg, p<0.001). For protocol 2, we noted a significant decrease of weight after exercise (mean: -0.67 kg, p = 0.009); this reduction was partially corrected by post exercise hydration (mean: +0.31 kg, p = 0.017) but the final weight (after diving) remained significantly lower to weight before exercise (mean: -0.41 kg, p = 0.01).

Hemodynamic measurements (Table 2)

Protocol 1
HR, SBP, PP and systemic vascular resistance remained unchanged after the dive. MBP, DBP, SV and CO decreased significantly.

Protocol 2
HR increased significantly after exercise but returned to the baseline after the dive. SV was significantly decreased after exercise and after the dive. In total, CO remained unchanged after exercise but was significantly decreased after the dive. SBP and PP were not significantly modified. MBP and DBP decreased significantly after the exercise and after the dive. Systemic vascular resistance remained unchanged after the exercise but increased after the dive.

Comparison between protocol 1 & 2
Similar decreases in SV, CO and arterial pressures were observed following the two hyperbaric exposures, with no significant difference between the 2 conditions.

TABLE 2

| Diver | Protocol 1 | | | | | | Protocol 2 | | | | | |
|-------|------------|----------|----------|----------|----------|----------|------------|----------|----------|----------|----------|
| | Sedentary | | | | | | Exercise | | | | | |
| | Bubble grade | | | | | | Bubble grade | | | | | |
| | 30 min | 60 min | 90 min | KISS | 30 min | 60 min | 90 min | KISS | 30 min | 60 min | 90 min | KISS |
| 1 | 1 | 3 | 3 | 31.98 | 0 | 0 | 1 | 0.39 |
| 2 | 2 | 3 | 2 | 27.3 | 2 | 1 | 1 | 4.29 |
| 3 | 1 | 1 | 1 | 1.56 | 1 | 0 | 0 | 0.39 |
| 4 | 3 | 3 | 1 | 31.98 | 1 | 1 | 1 | 1.56 |
| 5 | 1 | 0 | 1 | 0.78 | 1 | 0 | 0 | 0.39 |
| 6 | 3 | 3 | 3 | 42.12 | 3 | 3 | 3 | 42.12 |
| 7 | 2 | 1 | 1 | 4.29 | 1 | 0 | 0 | 0.39 |
| 8 | 1 | 0 | 0 | 0.39 | 1 | 0 | 0 | 0.39 |
| 9 | 3 | 3 | 3 | 42.12 | 0 | 0 | 0 | 0 |
| 10 | 0 | 2 | 1 | 6.63 | 0 | 1 | 0 | 0.78 |
| 11 | 1 | 2 | 1 | 7.02 | 2 | 3 | 3 | 34.71 |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.39 |
| median | 1 | 1 | 1 | 0.5 | 0* | 0 | 0 |
| mean | | | | 12.26 | | | 5.36* |
Hyperbaric exposure without exercise before the dive (protocol 1) and hyperbaric exposure with exercise 2h before the dive (protocol 2)

* = p<0.05 and ** = p<0.01 from baseline
§ = p<0.05 and §§ = p<0.01: from postdive

<table>
<thead>
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<th></th>
<th>Baseline</th>
<th>Protocol 2</th>
<th>Protocol 1</th>
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<td></td>
<td>Protocol 2</td>
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<tr>
<td></td>
<td>Exercise</td>
<td></td>
<td></td>
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<tr>
<td>Heart Rate (beats/min)</td>
<td>62 +/- 2</td>
<td>69 +/- 3 ** §§</td>
<td>61 +/- 3</td>
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<tr>
<td>Stroke Volume (ml)</td>
<td>89 +/- 4</td>
<td>82 +/- 4 **</td>
<td>81 +/- 3**</td>
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<td>Cardiac output (l/min)</td>
<td>5.5 +/- 0.3</td>
<td>5.6 +/- 0.4</td>
<td>4.9 +/- 0.3*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>120 +/- 1</td>
<td>114 +/- 2</td>
<td>117 +/- 3</td>
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<td>DBP (mmHg)</td>
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<td>63 +/- 1**</td>
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<tr>
<td>MBP (mmHg)</td>
<td>85 +/- 1</td>
<td>80 +/- 1**</td>
<td>81 +/- 1**</td>
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<tr>
<td>PP (mmHg)</td>
<td>53 +/- 1</td>
<td>51 +/- 3</td>
<td>53 +/- 3</td>
</tr>
<tr>
<td>PRU (mmHg.l^-1.min)</td>
<td>13 +/- 0.6</td>
<td>12 +/- 0.7§</td>
<td>13.5 +/- 0.5</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In our study, diastolic and mean blood pressure decrease significantly one hour after exercise before the beginning of the dive. After a single bout of dynamic exercise, there are profound changes in the mechanisms that regulate and determine arterial pressure, resulting in a postexercise hypotension that lasts nearly 2 h in healthy individuals. Postexercise hypotension (PEH) is consistently elicited after 30- to 60-min bouts of sub-maximal exercise [15]. In sedentary individuals, PEH after a single bout of aerobic exercise is due to a peripheral vasodilation with a drop in peripheral vascular resistance [16]. The mechanisms responsible for post-exercise vasodilation have not been established definitely. Those that were proposed include inhibition of central sympathetic outflow, antagonism of vasoconstrictor neurotransmitter actions, and generation, by exercise, of vasodilator substances such as NO, prostaglandins, histamine, natriuretic peptides, ATP, and adenosine [17]. The NO role needs to be analysed more thoroughly. Experimental studies suggest that bubbles originate as persistent bodies of undissolved gas called pre-existing gas nuclei [18, 19]. The main site for these gas nuclei could be on the walls of the blood vessels, such as the contact between adjoining endothelial cells. Since NO is vasodilator and has anti-atherogenic properties, it is speculated that NO could increase the elimination of gaseous nuclei from which bubbles form.
However, it has been shown that bubble production is increased by NO blockade in sedentary but not in exercised rats [9]. In studies involving healthy young subjects, post-exercise vasodilation was not reversed by NO synthase, excluding a major role for exercise-induced NO production [15]. In fact it has been found that in endurance trained women, PEH was the result of peripheral vasodilation as was previously shown in sedentary individuals, whereas in endurance trained men it was caused by reduced cardiac output (due to fall in stroke volume) and unchanged total peripheral resistance [16]. In our study, divers were all endurance trained men with a mean VO$_2$max around 52 ml.kg$^{-1}$.min$^{-1}$ and systemic vascular resistance remained unchanged after the exercise from baseline. This indicates that the exercise effect might be mediated by others factors than NO and peripheral vasodilation.

In our study SV was significantly decreased after exercise. It is well established that a moderately intense exercise provokes dehydration resulting from sweat response. Declining SV is the primary problem encountered with dehydration; it appears largely related to increases in HR and reductions in blood volume [20]. Therefore, since exercise-induced hypovolemia is present at the beginning of the dive, inert gas load must be less important in tissues during the dive. The variables that determine the rate of inert gas uptake by any tissues in the body may be expressed as a simplified mass balance equation: $S_b(dP_t/dt) = Q.S_b.(P_a-P_v)$, where $S_b$ and $S_t$ are the solubilities of the gas in blood and tissue, $Q$ is the blood flow, $P_t$ is mean tissue gas tension, and $P_a$ and $P_v$ are the gas tensions in arterial and venous blood. The uptake or release of gas by a particular tissue depends on both the rate of blood flow to the tissue and the rate of gas diffusion into the tissue from blood. It may be seen that if the blood flow $Q$ is lower, the rate of inert gas uptake would be slower and consequently bubble formation would be reduced [21]. In our study, exercise-induced hypovolemia is present at the beginning of the dive with a significant reduction of body weight (~ 0.67 kg mean) and SV. During all the simulated dives (protocols 1&2), subjects exercised on a bicycle ergometer keeping constant their HR. If SV is reduced during protocol 2 but not in protocol 1, consequently CO is lower in protocol 2 than in protocol 1, associated with a lower inert gas load and a lower bubble formation after decompression (see figure).

Hydration status is considered as a physiological factor that may influence DCS development, but this notion is suggestive and only few animal data have been conducted to support this evidence. To date there are no data concerning predive dehydration as DCS risk factor in man. On experimental basis, it is plausible that dehydration and hemoconcentration takes part in microcirculatory perfusion alteration when bubble formation occurs. Broome et al [22] showed that acute predive intravascular volume loading in pigs did not reduce the risk of DCS. However Fahlman & Dromsky [23] showed that normally hydrated pigs had a lower risk of DCS than those subjected to fluid intake restriction and diuretic administration. Consequently, in our study we let the divers drink water ad lib for ethical reason. One can debate the influence of the oral rehydration before the dive. Hjelde et al [24] showed that bubble formation after decompression was inversely proportional to serum surface tension, and it seems plausible that plasma surface tension might be elevated in the well-hydrated diver. In fact, this hydration doesn't correct completely body weight variations, and it is well established that rapid oral fluid replacement following dehydration does not effectively restore plasma volume or serum osmolality to the predehydration level within few hours [25].
CONCLUSION

This report confirms that a single bout of strenuous exercise 2h before a simulated dive significantly reduces the number of bubbles in the right heart of divers. Variations in hemodynamic state with moderate hypovolemia induced by a pre-dive exercise might influence inert gas load and bubble formation. In order to confirm this hypothesis, it would be of interest to conduct further studies with plasma volume measurements in trained and untrained divers. Moreover, since immersion is also susceptible to modify the hemodynamic status [26], it would be interesting to achieve this survey within a field environment.

There is no financial or other relationship that might be perceived as leading to a conflict of interest (i.e., affecting author objectivity).

CAPTION FOR FIGURE

Hemodynamic changes induced by sub-maximal exercise 2h prior to a dive. Declining stroke volume and moderate dehydration induced by a pre-dive exercise might influence inert gas load during the dive and bubble formation after the dive.

REFERENCES


Hemodynamic changes induced by sub-maximal exercise prior to a dive and its consequences on bubble formation

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