Just say NO to decompression bubbles: is there a real link between nitric oxide and bubble production or reduction in humans?

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Vascular gas emboli (VGE) start forming during the degassing of tissues in the decompression (ascent) phase of the dive when bubble precursors (micronuclei) are triggered to growth. The precise formation mechanism of micronuclei is still debated, with formation sites in facilitating regions with surfactants, hydrophobic surfaces or crevices.[1,2] However, significant inter-subject variability to VGE exists for the same diving exposure and VGE may even be reduced with a single pre-dive intervention.[3,4] The precise link between VGE and endothelial dysfunction observed post dive remains unclear and a nitric oxide (NO) mechanism has been hypothesized.[5]

Subjects in good physical condition are at lesser risk of VGE and DCS observed post dive.[6] More surprisingly, single pre-dive interventions or 'preconditioning' can influence the VGE observed post dive. Studies in rats have shown that a single bout of exercise 20 h pre dive can reduce post-dive VGE and mortality.[4] In humans, the role of exercise has been debated and depending on its timing and intensity may increase or decrease bubbles.[3,7–10]

A NO-mediated change in the surface properties of the vascular endothelium favouring the elimination of gas micronuclei has been suggested to explain this protection against bubble formation.[11] NO synthase activity increases following 45 minutes of exercise and NO administration immediately before a dive reduces VGE.[5] Nevertheless, bubble production is increased by NO blockade in sedentary but not in exercised rats, suggesting other biochemical pathways such as heat-sensitive proteins, antioxidant defenses or blood rheology may be involved.[12]

The first link between NO and DCS protection was shown by chance.[4] In an experiment using explosive decompression of sedentary rats resulting in >80% mortality, some additional rats were needed to complete the experiment but only trained (treadmill-exercised) rats were available instead of sedentary ones. After the decompression, 80% of the trained rats survived. The explanation given for this observation was that the presence of NO in the trained rats resulted in fewer bubbles and less DCS.

However, a French study showed that human volunteers had fewer bubbles post decompression after a treadmill exercise compared to the same exercise (same $\dot{V}O_2$) after a cycle-ergometer stress test. If this was related to NO production, the number of bubbles should be more or less the same. There are some mechanical differences between the two forms of exercise, namely more impacts and vibrations during the treadmill test. It is hypothesized that micronuclei are reduced by a mechanical effect as shown by an experiment with vibration applied before diving, which reduced decompression bubbling.[13]

In conclusion, more investigations are needed to further ascertain the link between NO and post-decompression VGE modulation. Such studies should be directed more on high-intensity training (less NO-related), since aerobic efforts have already been extensively studied in relation to the reduction of decompression stress, this will probably allow more understanding of the subtle mechanisms for DCS protection. The variable effect of oxygen on bubble decay, with transient increase of volume in some cases, also requires further investigation.[14–16]

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