Letter to the Editor re: Multinational Studies Are Required to Determine the Efficacy of Oxygen Prebreathing

Dear Editor:

With great interest we read the paper by Cheok et al. concerning decompression sickness (DCS) after hypobaric hypoxic exposure.[1] The usefulness of prebreathing 100% oxygen before hypobaric hypoxic exposure is an ongoing discussion that has been going on for several decades and any paper that addresses this issue contributes to the field. Especially since DCS can have a profound effect on the health and career of aviators and aircrew, prevention of DCS in training scenarios is paramount. While the results of the aforementioned study are well worth publication, we believe the data should be interpreted carefully due to limitations.

When testing the data (group 1 without prebreathing: N = 1530 with 2 cases of DCS; and group 2 with prebreathing: N = 1729 with 2 cases of DCS) two-sided using a Fisher's Exact test, the P-value is 1.0. As this is far from the dogma of $P < 0.05$, one could conclude there is no statistical significance. However, this cannot be derived from these data, as this study is underpowered to reject the null hypothesis and conclude that (30 min of) prebreathing does not lead to a decrease in DCS incidence after hypobaric hypoxia.

The incidence of DCS after a short hypobaric hypoxic exposure training is very low, with incidence rates usually in the range of 0.25%.[2] When designing a study to detect changes in such low incidences, very large sample sizes are required. The sample size increases even further when the effect of the intervention is small.[3]

For example, let us assume that prebreathing 100% oxygen 30 min prior to hypobaric hypoxic training decreases the risk of DCS by 100% (which probably is a generous overestimation) and that the base incidence of DCS is 0.25%; a study would require a sample size of 6268 subjects (3134 in both study arms) to reject the null hypothesis with an alpha of 0.05 and beta of 0.2 (80% power). Alternatively, when calculating the required sample size using the incidence of Cheok et al.[1] (0.0013%), while assuming the prebreathing to give a reduction of DCS of 20%, this gives a sample size of 40,116,032 subjects. While this example may be exaggerated, it illustrates the need for large sample sizes to correctly answer the research question.

Studies of this size are unachievable for a single center; thus, international collaborations are required to pool sufficient data. As variation in training profiles used introduces heterogenicity and individual risk factors might affect the incidence of DCS, it is important to establish a framework for which data should be recorded and which training profiles are eligible for inclusion.

We concur with the authors of the paper that hypobaric hypoxic training is generally safe with a (very) low incidence rate of DCS. However, at least until a sufficiently powered study has been able to reject the null hypothesis, we feel the need to emphasize prebreathing prior to hypobaric hypoxic training as it has no known negative side effects and might reduce the chance of DCS, which could have significant impact on the career of aviators and aircrew.

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In Response:

We would like to thank Dr. Thijs T. Wingelaar and Dr. Yara Q. Wingelaar-Jagt for their interest in our paper and for taking the time to express their concerns, which we agree with.

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In their letter to the Editor, they brought up the valid point that the study was not large enough to reject the null hypothesis with statistical significance. This limitation was similarly highlighted in our paper and was expected given the sample size a single-center study could produce. In our paper, we stated that one of the possible reasons why pre-breathing did not result in a lower reported incidence of decompression illness (DCI) was because its incidence was already low at 0.1% without pre-breathing, and that a larger study would be necessary to reveal significant differences, if any. While we ran Fisher's exact test on the study results, no significant associations were found ($P > 0.05$) due to the low incidence of DCI in both groups (with and without pre-breathing). As such, we acknowledge that there was insufficient data to reject the null hypothesis as well.

Recognizing this important limitation of our study and the significant impact of DCI on the career of aviators and aircrew, the Republic of Singapore Air Force has maintained the precautionary procedure of ensuring 30 minutes of pre-breathing during our hypobaric hypoxic training. As stated by Drs. Wingelaar and Wingelaar-Jagt, pre-breathing has no known adverse effects on the health of our aircrew. With the potential to further mitigate the risk of DCS due to hypobaric hypoxia training, the benefit of maintaining pre-breathing currently outweighs the risk of removing it until further data proves otherwise.

We hope that our paper helped to provide some insight on the DCI incidence rates with and without pre-breathing in short duration hypobaric hypoxic training, but at the same time recognize the limitations of it being a single-center study. We certainly look forward to opportunities for collaboration in international multicenter studies, as this would help to further expand the knowledge in this field of study, as well as help fine-tune training pedagogies centered on hypobaric hypoxic training.

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