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A REVIEW EVALUATING THE EFFICACY OF NON-PHARMACOLOGICAL
COUNTERMEASURES FOR SPACEFLIGHT-ASSOCIATED NEURO-OCULAR SYNDROME**Abstract**

Background: Spaceflight-associated neuro-ocular syndrome (SANS) denotes structural and functional neuro-ocular changes due to prolonged microgravity exposure in long-duration spaceflight (LDSF). The precise pathophysiology driving SANS is not fully understood, but a prevailing hypothesis is that microgravity-induced cephalad shift raises intracranial pressure (ICP) and leads to intra-ocular fluid accumulation. Given the significant occupational hazard posed by SANS, several countermeasures have been developed, including Lower Body Negative Pressure (LBNP) chambers and suits, Artificial gravity (AG), Venokonstrictive Thigh Cuffs (VTC) and Goggles. However, at present there is limited evidence comparing the efficacy and safety of these countermeasures. This review aims to address this literature gap by comparing the efficacy and adverse effects of non-pharmacological countermeasures for long-duration spaceflight.

Methods: A literature search was conducted to identify key studies on the non-pharmacological countermeasures. Efficacy was assessed using defined outcomes: ICP, intraocular pressure, internal jugular venous pressure, internal jugular venous cross-sectional area, optic nerve sheath diameter and maximum percentage of body weight. To facilitate comparison, results from studies using the same outcomes for each countermeasure were averaged.

Results: 13 key studies were included in the review. LBNP emerged as the most effective in reducing ICP and optic nerve sheath diameter. Conversely, VTC exhibited a greater reduction in IOP than LBNP (9.8 +/- 13mmHg vs 1.7 +/- 0.64mmHg). The LBNP suits had a greater maximum percentage of body weight than the chamber (125 vs 91%), suggesting greater efficacy. Due to the limited available literature, the efficacy of AG and goggles remained inconclusive. All countermeasures were associated with adverse effects, including LBNP-induced syncope, ocular migraines with goggles and venous pathology with VTC. However, at lower dosages of LBNP (-20mmHg), no adverse symptoms were reported.

Conclusion: Lower-dose LBNP emerges as the most promising non-pharmacological countermeasure, balancing efficacy and minimal adverse effects. This review underscores the need for further evaluation of non-pharmacological countermeasures, encompassing the assessment of multimodal treatments including pharmacological adjuncts. Such continued research is essential to maintain and enhance the safety of spaceflight personnel.