Altitude-Induced Changes to the Blood Brain Barrier’s Permeability Adversely Impact Patient Safety in Aeromedical Evacuation

Megan Kirk, Nadja Grobe, PhD, Richard R. Chapleau, PhD

1Henry M Jackson Foundation; 2Molecular Bioeffects Branch, Bioeffects Division, Airman Systems Directorate; 3Applied Technology & Genomics Division, Aeromedical Research Department, U.S. Air Force School of Aerospace Medicine, 711th Human Performance Wing, Air Force Research Laboratory, Wright-Patterson AFB, OH

INTRODUCTION: The cumulative effects of flight during aeromedical transport are of great interest to all nations engaged in contingency operations, and especially to the U.S. Air Force, the sole provider of U.S. aeromedical evacuations (AE). Key factors affecting clinical outcome include the optimal choice of pain management strategies, the relative efficacy of medications en route and, most importantly, the safety of such medications; AE may have an adverse impact on these factors. Here, we investigated the potential for neuroactive and non-neuroactive drugs to enter the brain at common AE cabin altitudes.

METHODS: The human blood brain barrier was simulated using porcine brain extracts in the parallel artificial membrane permeability assay (PAMPA) arrangement. Multi-well PAMPA plates were exposed to a simulated cabin altitude of 8,000 ft mean sea level (MSL) in a hypobaric chamber with an identical plate held constant at 800 ft MSL (Wright-Patterson AFB, OH). Drugs were added to a single side of the membrane prior to exposure, and drug concentrations post-exposure were analyzed using liquid chromatography mass spectrometry. Flight profiles represented 2-h and 12-h AE missions.

RESULTS: The average drug concentration ratio between altitude and ground on the brain side for the 2 h flight was 0.61±0.49 versus an average ratio of 1.25±0.37 after the 12 h flight (n=17 drugs, p=0.00062). After the 2 h flight, only 3 drugs had altitude-to-ground ratios above 0.8; whereas, after the 12 h flight only 1 drug was below 0.8 and 13/17 (76%) were above 1.

DISCUSSION: The altitude-induced permeability increase for numerous drugs that are not normally neuroactive poses a clear safety risk. Furthermore, a potentially even greater threat to patient safety is posed by pharmaceuticals that are normally active in the brain, but are dosed at low levels to account for their activity. When present at higher levels, these drugs can potentially slow, or even damage, brain function. The pilot study here demonstrates that a systematic investigation of additional cabin altitudes and more drugs will better define drug effects at altitude, potentially improving patient outcomes during and after transport. Such outcomes can be realized through development of a clinician-friendly “app” for use in routine and emergency transports.

ACKNOWLEDGMENTS

The authors greatly appreciate the efforts of Ms. Shana Huntsberger in helping prepare samples and diluting drugs. This work was funded by the Defense Health Program and the United States Air Force Surgeon General’s office through an intramural award to RRC. The authors would like to thank the contracting and research support divisions of AFRL. The views expressed are those of the authors and do not necessarily reflect the official policy or position of the Air Force, the Department of Defense, or the U.S. Government.