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Anesthesia and critical-care delivery in weightlessness: A challenge for research in parabolic flight analogue space surgery studies

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ABSTRACT

Background: Multiple nations are actively pursuing manned exploration of space beyond low-earth orbit. The responsibility to improve surgical care for spaceflight is substantial. Although the use of parabolic flight as a terrestrial analogue to study surgery in weightlessness (0 g) is well described, minimal data is available to guide the appropriate delivery of anesthesia. After studying anesthetized pigs in a 0 g parabolic flight environment, our group developed a comprehensive protocol describing prolonged anesthesia in a parabolic flight analogue space surgery study (PFASSS). Novel challenges included a physically remote vivarium, prolonged ($>$10 h) anesthetic requirements, and the provision of veterinary operating room/intensive care unit (ICU) equivalency on-board an aircraft with physical dimensions of $<1.5\,m^2$ (Falcon 20). Identification of an effective anesthetic regime is particularly important because inhalant anesthesia cannot be used in-flight.
Methods: After ethical approval, multiple ground laboratory sessions were conducted with combinations of anesthetic, pre-medication, and induction protocols on Yorkshire-cross specific pathogen-free (SPF) pigs. Several constant rate infusion (CRI) intravenous anesthetic combinations were tested. In each regimen, opioids were administered to ensure analgesia. Ventilation was supported mechanically with blended gradients of oxygen. The best performing terrestrial 1 g regime was flight tested in parabolic flight for its effectiveness in sustaining optimal and prolonged anesthesia, analgesia, and maintaining hemodynamic stability. Each flight day, a fully anesthetized, ventilated, and surgically instrumented pig was transported to the Flight Research Laboratory (FRL) in a temperature-controlled animal ambulance. A modular on-board surgical/ICU suite with appropriate anesthesia/ICU and surgical support capabilities was employed.
Results: The mean duration of anesthesia (per flight day) was 10.28 h over four consecutive days. A barbiturate and ketamine-based CRI anesthetic regimen supplemented with narcotic analgesia by bolus administration offered the greatest prolonged hemodynamic stability through an IV route (within multiple transport vehicles and differing gravitational environments). Standardization and pre-packaging of anesthesia, emergency pharmaceuticals, and consumables were found to facilitate the interchange of the veterinary anesthesia team members between flights. This operational process was extremely challenging.
Conclusions: With careful organization of caregivers, equipment and protocols, providing anesthesia and life support in weightlessness is theoretically possible. Unfortunately, human resource costs are extensive and likely overwhelming. Comprehensive algorithms for extended spaceflight must recognize these costs prior to making assumptions or attempting to provide critical care in space.

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1. Introduction

The potential to regularly extend human spaceflight beyond low-earth orbit is current. Over the coming years, both the White House and National Aeronautics and Space Administration (NASA) expect to return to the Moon with an anticipation of lunar inhabitance, and move towards a human exploration of Mars (Hamilton et al., 2008). Other nations, as well as private industry, are also developing the space-faring technology and hardware (Stewart et al., 2007; Norfleet, 2000). Exploration has always had a human cost though, and space exploration is no exception. In 1994, Billica et al. (1994) ranked traumatic injury at the highest level of concern regarding the probable incidence versus impact on mission and health (Kirkpatrick et al., 2009a). When the extended duration of these missions is coupled with the high risk of the occurrence of a traumatic event, it is possible that invasive surgical and interventional procedures may be required (Norfleet, 2000). Furthermore, life-threatening emergency surgical conditions may arise without prior warning in the healthiest and fittest of young crewmembers (Campbell, 2002; Kirkpatrick et al., 2005a). Because of our difficulty in providing an optimal anesthetic in space, the humane provision of surgical care necessitates a realistic review of peri-operative and anesthetic capabilities during spaceflight (Billica et al., 1994; Emergency and continuing care, 2001; Silverman and McArtney, 2008). In addition to the inherent hostility of this environment, crew medical officers (CMO) and flight surgeons must also consider mission objectives when assessing a flight crew's response to a sick crewmember. Unlike the past strategy of a "scoop and run" concept that required only stabilization and rapid evacuation, the current reality of a "stand and fight" scenario is much more involved (Bacal et al., 2004). This will undoubtedly describe the situation on remote outposts such as the Moon or Mars. As a result, this shift in philosophy has forced a reassessment of our ability to provide appropriate medical care during spaceflight and habitation.

While there has been a modest amount of attention paid to the challenges of providing surgical care and support in space, study of anesthetic issues has been minimal (Norfleet, 2000; Silverman and McArtney, 2008). These concepts are critical as there is uncertainty regarding many aspects of both anesthesia delivery and maintenance, as well as the altered molecular pharmacokinetics (Santy and Bungo, 1991a), pharmacodynamics (Levy, 1991a), and bioavailability (Tietze and Putcha, 1994a) of drugs in microgravity. Even if the issue of a lack of gravitational separation between liquids and vapors could be addressed, gas scavenging equipment would still be required given the fragile atmosphere. During the recently initiated Canadian parabolic flight analogue space surgery study (PFASSS) (Kirkpatrick et al., 2009b), a concurrent evaluation of the appropriate anesthesia delivery techniques for the parabolic flight environment was completed. The primary goal of this study was to evaluate the process of providing anesthesia and critical care during all phases of a PFASSS, building towards the actual parabolic flight. We hoped that by examining the anesthetic tools required to facilitate surgical research in an operational flight environment, theoretical extrapolation to actual long-duration human spaceflight might be possible. This was done using hierarchal and translational testing from laboratory to flight.

2. Methods

The study was approved by the Canadian Space Agency (CSA), the Institutional Animal Care Committees of the Universities of Calgary (UofC), and the University of Ottawa (UofO), as well as National Research Council of Canada's Central and Institute for Biodiagnostics Animal Care Committees. Purpose-bred SPF Yorkshire-cross pigs composed the experimental subjects. The translational program regarding operational delivery of anesthesia was divided into 3 phases. Phases I and II were experimental readiness segments. More specifically, Phase I was conducted entirely within the animal care laboratories (UofO) vivarium, while Phase II comprised all terrestrial care (1) during transporting the animal from the UofO vivarium to the NRC–FRL, (2) at the NRC–FRL itself and (3) on-board the aircraft prior to flight. Phase III incorporated all in-flight experimental work (four consecutive flight days (one pig/day)). The purpose of Phase I was to develop and rehearse the anesthetic protocols pre-flight that could adequately be utilized in the analogue environment during Phases II and III. Phase II advanced this hierarchy to study the chosen regimen both in 1 g transport and on-board the research aircraft prior to flight. By flying a parabolic or ballistic profile, the Falcon 20 research aircraft (http://en.wikipedia.org/wiki/Dassault_Falcon_20; Campbell et al., 2001) generates up to 25 s of effective weightlessness (0 g). This constitutes the most realistic space research analogue environment available on the earth's surface. The 0 g periods are preceded, and followed, by intervals of hypergravity (2 g). Finally, Phase III consisted of studying and refining the regimen in a true PFASSS.

During Phase I (days 37 and 30 pre-flight), the experimental team developed the animal transport and in-flight anesthetic regimen, as well as the surgical instrumentation methodology. The anesthetic regimen accounted for both the surgical requirements of the study, as well as species-specific drug pharmacology. Detailed medication information is provided (Tables 1 and 2).

2.1. *Phase I—1 g terrestrial vivarial surgical laboratory research environment*

The anesthetic drug regimen of each pig is described in Table 2. The animals were first sedated via IM injection (tiletamine/zolazepam/xylazine) in their pens, and then transferred onto a surgical table for an inhalational induction with isoflurane. Due to the species-specific risk of laryngospasm, lidocaine spray was applied directly to the vocal cords prior to intubation. Once the tube was secured, monitors were applied. This included 2 peripheral intravenous lines in the marginal ear veins and 1 line in each external jugular vein. Blood pressure was measured via cannulation of both the carotid arteries. Heart rate, EKG, blood pressure, rectal core temperature, pulse oximetry, and end-tidal carbon dioxide were measured at all times using a portable physiologic monitor (SurgiVet, Smith Medical PM Inc., WI). There was no central venous monitoring, however the bladder was catheterized. Arterial blood gases were measured in intervals during the anesthetic. Normothermia was maintained.

Anesthesia was maintained for this pre-flight groundwork with isoflurane during line placement, urethral catheterization and placement of the surgical ports. Depth of anesthesia was judged based on clinical assessment of physiologic variables (coronet–hoof pinch; anal sphincter pinch; corneal positioning; muscle relaxation of tongue and lower jaw; heart rate; blood pressure). Buprenorphine intravenous was utilized for supplemental analgesia intermittently. Normothermia was maintained.

2.2. *Phase II—1 g environment*

On flight days minus 14 and minus 1, the Phase I protocol was expanded to further refine the anesthetic regimen. It facilitated the transfer of a fully anesthetized and ventilated animal with complete physiological monitoring/support from the vivarium to