The anaesthetic management of microgravity-exposed individuals

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Abstract

Mankind's imminent occupation of low Earth orbit beyond that of a scientific outpost and daring engineering nature that will land astronauts on Mars, will pose significant challenges to anaesthesia providers. The increased number of space tourists and workers who spend extended periods in zero gravity will present with surgical disease, either in orbit or shortly after return to Earth. A thorough understanding of the physiological changes to which these individuals are susceptible, as well as the effects of anaesthetic agents on this relatively unknown population, is warranted. By actively participating and informing ourselves of the future of space medicine, we will lay the groundwork for an entirely new field of medicine. This article provides a succinct overview of some of these physiological challenges and casts light on some of the anaesthetic and surgical concerns pertaining to space flight. It aims to pique the interest of the reader at a time when privatisation of the space race and space tourism by British and American entrepreneurs is providing new frontiers for anaesthetic science to explore.

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Introduction

Galileo Galilei believed that the Sun, and not the Earth, was at the centre of our universe, following Copernicus's heliocentric theory. Tried before the Spanish Inquisition, and found to be "vehemently suspect of heresy", his vision set in motion the exploration of space.[1] This led to Apollo 11 landing on the moon on 20 July 1969. At first, the "Space Race" was defined by the Cold War. However, international cooperation became the norm when the Russian Space Station MIR was replaced by the International Space Station (ISS). After US President Barack Obama retired the Space Shuttle Program in 2011, the door was opened for the private sector to become involved. Space X's Dragon® capsule became the first private space vehicle to rendezvous with the ISS, and has helped to pave the way for the future corporate development of space travel, an important catalyst to increasing humanity's presence in zero gravity.[2] The private sector is now poised to set up mining, manufacturing, research and hospitality industries in low Earth orbit and beyond. As such, the possibility of individuals requiring surgery in a zero-gravity environment, or shortly thereafter, will increase. Such patients will face increased anaesthetic risk, whether in space, or shortly after their return to Earth.[3]

Humans are designed to live on the surface of the Earth. The contribution of our planet's gravity to cellular homeostasis is easily taken for granted. It is likely that microgravity-exposed persons will encounter unknown risks and have unvalidated responses to known risks, but most importantly, will find themselves isolated.[4] An Earth to Mars round trip could take three years, with an audio transmission delay of between eight and 40 minutes.[4,5] Although radiation, loss of bone mineral density and behavioural adaptation have been identified as the three most important health issues relating to long-duration missions, traumatic injury causes the most concern with regard to probable incidence versus its impact on the mission and health.[4-6] The National Aeronautics and Space Administration (NASA) has predicted that one medical emergency will require evacuation per 68 person-months.[4] As the space tourist population increases, these numbers will rise.

Background

In 1998, the STS-90 Neurolab mission provided the first successful instance of administration to and recovery from general anaesthesia by rat models in space.[7] To date, no off-planet anaesthetic has been performed on humans for emergency management or research purposes.[3, 7]

After the Bion 11 mission in 1997, two Rhesus monkeys underwent anaesthesia for bone and muscle biopsies shortly after their return to Earth. Both monkeys reacted adversely to anaesthesia and one of them died after cardiac arrest. This highlighted the need to better understand the anaesthetic risks associated with zero gravity.[3] With trauma, ISS occupants can be evacuated, treated on board by a medical officer assisted by telemetry, or treated by a rescue medical team sent to the ISS.[4,5]

As astronauts travel beyond low Earth orbit, the moon, and even Mars, such evacuation measures become impractical and onsite management has to be considered. Special attention should be given to physiological and pharmacological changes, airway management, patient and provider restraint, surgical approaches, environmental contamination and the choice of general versus regional techniques.

Physiological changes

Endothelial failure

Zero gravity makes the endothelium vulnerable to oxidative stress due to elevated levels of catecholamines, angiotensin and endothelin.[8] The resultant inflammation is accompanied by reductions in atrial natriuretic peptide (ANP), nitric oxide (NO) and magnesium (Mg^{2+}) levels. In turn, this causes impaired angiogenesis.[9] Cyclic guanosine monophosphate, a second messenger of both NO and ANP, is undetectable after five months in space, and a return to pre-mission levels after three months on Earth.[10] Furthermore, endothelial dysfunction and reduced diurnal blood pressure variation may lead to renovascular hypertension and impaired renal function.[9]

Animal models have shown reduced serum Mg^{2+} levels and Mg^{2+} sensitivity. Mg^{2+} is required for more than 300 enzymatic processes and acts as an antioxidant and calcium antagonist. It is also necessary to metabolise vitamin D, which itself is depleted while in space, and therefore not available to fulfil its cardiovascular protective functions.[8] Mg^{2+} deficiency may also lead to juxtaglomerular hypertrophy, with increased aldosterone secretion and increased renin and angiotensin levels, with the subsequent development of hypertension.[8]

Impaired angiogenesis and endothelial dysfunction cause an endothelial leak with plasma loss associated with reduced erythropoietin (EPO) levels.[8] EPO, which in itself is also cardioprotective, plays a role in angiogenesis and the correction of anaemia. EPO deficiency may be treated with plasma volume expanders and EPO gene therapy.[8] However, chronic exposure to EPO gene therapy may cause hypertension and thrombosis.[8] On the other hand, NO and ANP gene therapy, which are used to correct deficiencies in space flight, may lead to hypotension and shock if not tightly controlled.[8]

Autonomic dysfunction

Autonomic neural functions have been studied in various space shuttle and parabolic flights and compared to head-down bed rest and lower body positive pressure.[11] Orthostatic hypotension is a major problem after a long-duration space flight due to cardiovascular deconditioning.

Several mechanisms have been hypothesised for the cause of orthostatic hypotension, including:

- A headward fluid shift, causing reduced circulatory plasma volume.
- Changes in the vascular adrenoreceptors, instigating reduced vascular responsiveness to sympathetic stimulation.
- Cardiac muscle dysfunction.
- Attenuated baroreceptor responsiveness.[11]

These effects can be collectively described as a "syndrome of inadequate sympathetic responses after microgravity exposure".[3]

An inverse relationship exists between plasma noradrenalin levels and adrenoceptor sensitivity. Microgravity may also cause increased end-organ sensitivity to neuroendocrine stimuli.[3] An α-receptor predominance in the lower limbs exists in normal individuals, but there is no difference in β-receptor responses between the upper and lower limbs. Microgravity-exposed individuals have a selective increase in β_1- and β_2-adrenoceptor responses. Some studies have showed no change in β-receptor vascular responses, while others have showed decreased β-receptor responsiveness.[12] Therefore, vasopressors and β-blocking agents may exhibit exaggerated and differential effects on β_1 and β_2 receptors. The peripheral sympathetic response to hypovolaemia in trauma will also be attenuated. Thus, a higher dosage of β agonists will be required. Vagally mediated baroreceptor reflexes are altered during short- and long-duration space flight, which causes significant variation during return to the 1-G environment. This reduction persists for one week after return to Earth gravity.[3] Astronauts receiving neuraxial anaesthesia would be at theoretical risk of cardiovascular collapse due to autonomic dysfunction. These changes should be taken into account when planning an anaesthetic.

Cardiac dysfunction

Decreased physiological loading in zero gravity leads to cardiac muscle atrophy.[13] This deconditioning may lead to decreased end-diastolic volume and left ventricular mass. Three Skylab 4 astronauts showed an 8% decrease in left ventricular mass during an 84-day mission, as seen with M-mode echocardiography.[13] Although the observed cardiac atrophy has not been shown to impair systolic function, invasive studies of cardiac performance before and after two weeks of head-down bed rest have revealed a leftward shift in the diastolic pressure-volume curve that leads to a smaller end-diastolic volume for any given filling pressure. In turn, this causes a reduced stroke volume and aggravates orthostatic intolerance.[13] Dysrhythmias have been reported in astronauts during extravehicular activity, as well as during take-off and re-entry. Premature atrial contractions, supraventricular dysrhythmias and premature ventricular contractions may also extend into the post-flight period.[3] Coronary artery disease has been found in astronauts post-flight, even though no evidence of coronary heart disease was detected during pre-flight screening.[14]

Haemodynamic changes

The most important haemodynamic alterations that concern anaesthesia are elevated venous compliance, decreased blood and plasma volume, decreased stroke volume and central venous pressure (CVP) changes, as well as in-flight bradycardia and post-flight tachycardia.[3] An elevated heart rate (HR) of more than 160 beats per minute, as well as a decrease in systolic blood pressure of more than 25 mmHg, may persist for up to one week post-space flight.[3] Central hypervolaemia that is experienced in space stimulates the carotid arch baroreceptors, activating a neurohormonal reflex, that, in turn, causes diuresis and hypovolaemia.

On Earth, a cephalad fluid shift favours increased CVP. However, in space, the CVP is decreased from the normal 7-10 mmHg on Earth to 0-2 mmHg, despite the fact that left ventricular end-diastolic volume increases. This paradox may be explained by a larger reduction in pericardial pressure than CVP, because of a decrease in restraining forces on the chest wall.[13]

Microgravity causes a reduction in both the red cell mass and blood volume (between 10% and 23% of the latter).[5] This approximates a class I Advanced Trauma Life Support haemorrhage, which shifts the operating point on the Frank-Starling curve to a steeper portion, causing a greater decrease in stroke volume for a smaller decrease in left ventricular filling pressure.[3] The fluid loading of astronauts prior to the return flight has not been shown to restore either the plasma volume deficit or attenuate orthostatic impairment. The administration of subcutaneous erythropoietin also appears to be ineffective in treating diminished red cell mass.[4]

Respiratory function

Because of the cephalad fluid shift, astronauts may experience facial oedema and nasal congestion.[15] Reduced tidal volume with tachypnoeic breathing has also been observed, with decreased dead space ventilation and improved carbon dioxide diffusion capacity.[4] Overall, no significant problems have been identified in terms of pulmonary function in zero gravity.

Neuromuscular adaptations

Skeletal muscle atrophy occurs after 1-2 weeks in zero gravity. Therefore, the use of succinylcholine could be contraindicated because of the risk of hyperkalaemia and ventricular fibrillation.[3] The microgravity environment may also cause an upregulation in acetylcholine receptors, which has been shown to result in resistance to nondepolarising muscle relaxants. Sufficient dose adjustments will have to be made in order to provide adequate muscle relaxation throughout surgery and allow enough time for the induction of anaesthesia.[3]

Other anaesthetic considerations

Many astronauts develop "space motion sickness", which causes a marked reduction in gastric motility. The increased incidence of ileus may put them at risk of aspiration, both in-flight and post-flight.[16]

A shift from performing airway procedures that are considered to be most effective on Earth, to those with the highest likelihood of success, has led to advisory committees recommending the avoidance of endotracheal intubation in zero gravity at all costs.[4] This is because of the potential catastrophic consequence of a difficult airway or failed intubation in an already challenging environment. The use of neuromuscular blocking agents is also discouraged because of the sheer difficulty of ventilating a paralysed patient in space.[4]

In one study, laryngoscope-guided tracheal intubation was performed by inexperienced providers during 23 seconds of microgravity in parabolic flight to compare successful intubation in a free-floating condition. A mannequin was employed, with the head first gripped between the operator's knees, and then placed in the restrained position with the torso strapped down. There were no differences in ventilation success or time to successful intubation.[17]

Pharmacological changes

Owing to endothelial dysfunction and impaired hepatic and renal perfusion, many drugs that require hepatic metabolism and renal excretion will have prolonged half-lives and altered bioavailability.[8] In a case series, 21 crew members were given 25-50 mg promethazine intramuscularly. The sedation rate in space was only 5%, compared to 60-73% on Earth.[4] Some of these effects could be explained by altered receptor interactions because of induced hypovolaemia. Protein binding is presumably altered because of muscle and tissue atrophy, as well as drug distribution being affected by the redistribution of fluids. The effects of these changes on receptor interaction, protein binding and drug distribution on anaesthetic agents are not yet known. Furthermore, known drug models for the administration of total intravenous anaesthesia have not yet been validated for use in zero gravity.

Surgical considerations

Emergent trauma in space may vary from penetrating injuries (due to interactions with micrometeorites, with the resultant failure of the spacesuit and a flash fire), to crush injuries from collision with floating objects. Tension pneumothoraces may be exacerbated by the hypobaric stress of extravehicular activities, but have also been successfully decompressed during parabolic flight experiments.[5]

External compressible bleeding can easily be managed with pressure, and tissue sealant bandages with fibrin glue. However, intracavitary haemorrhage is the leading cause of potentially preventable injury-related death worldwide.[5] Research performed on the 1998 Neurolab mission suggests a standard surgical approach is possible in space. However, the restraint of operators, subject and equipment has to be possible.[5,7] Laparoscopy in zero gravity has been achieved with a large rounded abdominal cavity and good visualisation, although the tendency of viscera to float around obscured the surgical field when gasless laparoscopy with abdominal wall lift devices was performed.[5] Animal surgery undertaken during parabolic flight has revealed increased venous bleeding. The normal gravitational force on Earth helps to collapse veins. External pressure will have to be applied to achieve the same effect in zero gravity.[4]

Telementored non-surgeons may be able to perform minimally invasive surgery using mini-laparoscopy sets. The physiological stress associated with raised intra-abdominal pressure on astronauts who are already at a physiological disadvantage needs further investigation. Damage control surgery is being explored as the minimum desirable surgical capability in space flight.[5] Non-surgeons have successfully completed laparotom. The ability to place surgical packing around intracavitary bleeding could be life-saving.

Regarding orthopaedic pathology, impaired callus formation and angiogenesis will occur in long-bone fractures. Although nonsurgical splinting might be adequate in true zero gravity, the risk of fat emboli cannot be excluded.[5] A chronic musculoskeletal injury of the upper limbs has also been reported as a consequence of hardened torso spacesuits.

Altered cell-mediated immunity can lead to more aggressive bacterial growth in the weightless environment of space. Bacteria have been reported, with thicker cell walls requiring higher minimal inhibitory concentrations of antibiotics.[4,5]

Histologic and tensiometric data from rat abdominal incisions have shown impaired wound healing. Increased inflammatory reponses, fibroplasia, abnormal collagen deposition and a reduced stress loading capacity of wounds have also been noted.[5]

Because of the lethal consequences of unoperated appendicitis and cholelithiasis, consideration must be given to prophylactic cholecystectomy and appendicectomy before off-planet missions.[4]

Telemedicine

The first intercontinental telesurgery procedures were performed in the 1990s. Since surgeons mostly navigate using camera imaging, telesurgery in space is a natural solution when performing minimally invasive surgery and laparoscopy. Commercialised surgical robots, like the da Vinci Si from Intuitive Surgical Inc, have already performed more than 500 000 procedures worldwide. In September 2007, NASA successfully carried out zero-gravity robotic surgery experiments during parabolic flight. Network latency and communication lag times remain as inherent and unavoidable limiting factors. Low Earth orbit causes trip signal delays of 540-700 ms, while on Mars, this can be anything between 6.5 and 44 minutes.[18]

Preoperative computed tomography scans and smart systems that can create a surgical plan based on anatomical variations may negate the necessity for real-time intervention. In the future, indwelling nano-robots could enter the abdominal cavity through a small incision. Various ingestible, self-assembling robots controlled by external magnets are already being investigated by engineers at the University of Nebraska.[18] Computer-assisted design and manufacturing and the use of three-dimensional printers could also provide on-board prostheses and equipment as needed, without the need to sacrifice precious payload capacity.

Technical challenges

Special consideration must be given to the zero gravity-induced separation of fluids and gases. Vials of drugs and bags of fluids will tend to separate into droplets, forming foam. Degassed solutions with constant pressure infusions will have to be employed. Anaesthetic vaporisers will malfunction, and consideration will have to be given to total intravenous anaesthesia or regional techniques.[19] The closed environment of a spacecraft will put astronauts at risk of the unintentional inhalation of drugs and fire hazards in case of an oxygen leak. The minimal flow system developed for Xenon anaesthesia may find a useful place in the theatre on board a spacecraft. Severe injuries may rapidly deplete the on-board stock of intravenous fluids. The ability to generate medically suitable fluids from processed water is being investigated.[5]

The evacuation of a critically injured astronaut with subsequent exposure to the rigors of re-entry and landing may necessitate the provision of definitive surgery on the lunar surface or a low Earth orbit facility. Investigative resources, such as radiological support, will have to be considered. Currently, the ISS only has ultrasound capability.[4]

Suspended animation

The ultimate paradigm for trauma management in space would be the ability to store and forward major pathology back to Earth for definitive treatment.[5] Major advances in our understanding of suspended animation are making this therapeutic intervention for trauma care in space a possibility, and also on Earth. Suspended animation is the therapeutic induction of a state of tolerance to temporary complete ischaemia that results in decreased energy consumption and production. The rapid removal of oxygen and the induction of ultra-profound hypothermia arrests all metabolic processes and prevents further cell damage. The addition of hydrogen sulphide, a reversible inhibitor of oxidative phosphorylation, augments the reduction in metabolism.[5] Researchers at the Boston Massachusetts General Hospital have successfully induced suspended animation in pigs with a successful revival rate of 80%.[20] The extra time bought with such an intervention may allow for a virtual-reality rehearsal of a procedure prior to on-board repair in a bloodless field.

Conclusion

The provision of anaesthetic care to patients in zero gravity, and those who have recently returned from space, will necessitate a thorough working knowledge of the associated risks and physiological changes. The zero gravity-exposed patient will require a systemic work-up to identify organ dysfunction and fluid and electrolyte abnormalities. The decision to provide general versus regional anaesthesia will have to be weighed against the risks of a syndrome of inadequate sympathetic responses from microgravity exposure that could lead to cardiovascular collapse. The pharmacological changes and physics of zero gravity must also be understood in order to provide a safe and adequate anaesthetic.

As the world prepares to send the first paying customers into low Earth orbit in 2013, and an exploration class mission to Mars in 2030, the anaesthetic community would do well to familiarise itself with the challenges of zero gravity. Presently, the luxury of an all-robotic chamber able to perform anaesthesia and surgery at the touch of a button remains safely in the realms of speculative fiction, together with cold fusion and faster-than-light travel. However, we should watch this space. Readers scoffed at Jules Verne, when in 1865, he first proposed a voyage to the moon in his seminal novel, *De la terre à la lune.*

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