REVIEW ARTICLE

Musculoskeletal alterations in microgravity environment

Cambios musculoesqueléticos en el entorno de microgravedad

Alterações musculoesqueléticas em ambiente de microgravidade

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ABSTRACT

The astronaut is an individual working in a hostile environment of microgravity. This abnormal environment alters human physiology in virtually all organic systems. The musculoskeletal system has clinical repercussions that may extend even after the space mission. Knowing the changes in the musculoskeletal system to act before, during and after spaceflight is essential, as bone hypotrophy can remain years after returning to Earth. Medical intervention aims to reduce the risks of health problems related to the musculoskeletal system. The aim of this study is to conduct a literature review to identify musculoskeletal alterations in the microgravity environment and describe prevention and treatment measures during and after aerospace travel.

Keywords: Astronauts. Microgravity. Musculoskeletal system. Space flight.

RESUMEN

El astronauta es un individuo que trabaja en un ambiente hostil de microgravedad. Ese ambiente anormal altera la fisiología humana en prácticamente todos los sistemas orgánicos. El sistema musculoesquelético tiene repercusiones clínicas que pueden extenderse incluso después de la misión espacial. Conocer los cambios del sistema osteomuscular para actuar antes, durante y después del vuelo espacial es fundamental, porque la hipotrofia ósea puede permanecer años después del regreso a la Tierra. La intervención médica tiene por objeto reducir los riesgos de los problemas de salud relacionados con el sistema musculoesquelético. El objetivo de este estudio es realizar una revisión bibliográfica para identificar los cambios musculoesqueléticos en el entorno de microgravedad y describir las medidas de prevención y tratamiento durante y después de los viajes aeroespaciales.

Palabras clave: *Astronautas. Microgravedad. Sistema musculoesquelético. Vuelo espacial.*

RESUMO

O astronauta é um indivíduo que trabalha em um ambiente hostil de microgravidade. Esse ambiente anormal altera a fisiologia humana em praticamente todos os sistemas orgânicos. O sistema musculoesquelético apresenta repercussões clínicas que podem estender-se mesmo após a missão espacial. Conhecer as alterações do sistema osteomuscular para atuar antes, durante e depois do voo espacial é fundamental, pois a hipotrofia óssea pode permanecer anos após o retorno à Terra. A intervenção médica visa reduzir os riscos de agravos à saúde relacionados ao sistema musculoesquelético. O objetivo deste estudo é realizar uma revisão bibliográfica para identificar as alterações musculoesqueléticas no ambiente de microgravidade e descrever medidas de prevenção e tratamento durante e após viagem aeroespacial.

Palavras-chave: *Astronautas. Microgravidade. Sistema musculoesquelético. Voo espacial.*

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The acronyms and abbreviations contained in this article correspond to the ones used in the original article in Portuguese.

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1 INTRODUCTION

There are two known ways to simulate microgravity environment on Earth. The first is through a huge aircraft, known as “Vomit Comet” that performs a parabola trajectory. The plane, like a roller coaster, rises to approximately 32,000 feet. During the ascent, everything on the plane looks 1.8 times heavier than Earth’s gravity. Upon reaching the top, the occupants float momentarily for about 25-30 seconds until the aircraft becomes parallel to the earth’s surface. After the aircraft descends, the gravity gradually increases to close to 1.8 G, until it reaches the same altitude at which the parabolic arc began – close to 24,000 feet. Each parabolic arc lasts 65 seconds and, within a 2-3-hour training period, the aircraft performs 31 parables per flight, at which point astronauts test their equipment, practice activities such as eating, drinking, and performing motion maneuvers in the microgravity environment. These flights produce nausea and vomiting in some passengers, justifying the nickname given to the plane of “Vomit Comet”.

The second way to simulate microgravity is by building satellites under water. Astronauts dress in space suits to have buoyancy in diving, as if they were floating into space. It can be used to train astronauts on how to work in space. It’s not perfect, because in the water there’s more drag than in space and people still have gravity inside the suits, so they’re working harder than in space.

Another way to simulate the effects of microgravity in the musculoskeletal and cardiovascular systems is the resting in bed with head-down tilt (HDT) of 6 degrees for, at least, 30 days. This tilt of the head down was suggested by Russian researchers in an attempt to compensate for the change of fluids from the lower limbs to the cephalic region that occurs in space. HDT bed rest with normal volunteers is the most common analogue for microgravity simulation and for testing countermeasures for bone loss, muscle and cardiac atrophy, orthostatic intolerance, and reduced muscle strength and exercise ability. (HARGENS, 2016).

NASA does not create a microgravity environment with the sole purpose of helping and training astronauts. Many physical processes and experiments are tested as well.

In the microgravity environment, the weight of the organs of the human body decreases and the musculoskeletal system develops qualitative and quantitative changes. The magnitude of musculoskeletal involvement depends on the duration of space travel (TEIXEIRA, 2005).

The muscles responsible for upright posture during orthostatism are the most affected by microgravity. These muscles, known as antigravitational, atrophy and may even present histological changes, such as the replacement of type I fibers, slow, by type II fibers, of rapid contraction (TEIXEIRA, 2005).

Bone metabolism in space is altered and the astronaut may develop osteopenia or osteoporosis. Bone mass reduction is more prominent in the pelvic region and lower limbs (TEIXEIRA, 2005).

It is necessary that astronauts have a diet rich in calcium, vitamin D and protein, do aerobic exercises of impact and anaerobic to mitigate the reduction of bone stock, while seeking to maintain muscle trophism.

Knowing the changes in the musculoskeletal system related to spaceflight is essential. Medical intervention aims to reduce the risks of health problems related to the musculoskeletal system, in addition to avoiding compromising the safety and objectives of aerospace missions.

The aim of this study is to conduct a literature review to identify musculoskeletal alterations related to the microgravity environment, in addition to describing prevention and treatment measures during the aerospace trip and after their return.

2 METHOD

A search was conducted in LILACS and PUBMED databases with the following descriptors in 2012: astronauts, muscle atrophy, aerospace medicine, microgravity, osteoporosis, microgravity simulation, and spaceflight. Of a total of 12,619 articles, only 15 were selected, as they were related to musculoskeletal alterations in humans in the microgravity environment.

A new research was carried out in the PUBMED database in the period from 06/08/2018 to 08/08/2018, with the same descriptors, considering studies in humans, in the last five years, in the Spanish, English and Portuguese languages, and 17 more scientific articles were selected for meeting the selection criteria strictly related to muscle and bone changes in a microgravity environment.

The two moments of the survey correspond to the year of realization of the monograph of the Aerospace Medicine Course in IMAE (UNIFA), in 2012, and the year of the second collection of data for bibliographic update, in 2018.

3 DISCUSSION

Muscles lose mass, strength, and tendon stiffness during spaceflight. The most affected are the postural muscles that keep the human body in orthostatism in a gravitational environment. From seven days of space flight, muscle and tendinous structural changes are detected (RILEY, 1990). After two weeks in the microgravity environment, muscle mass decreases by up to 20% (CLEMENT, 2003). On longer missions - three to six months - a loss of 30% of muscle mass volume may occur (SHACKELFORD, 2008).

The fundamental cause of this muscle atrophy is the absence of gravitational load on bones and muscles during spaceflight. Muscles without any loads present biochemical and structural changes with reduction of the length of the sarcomeres and reduction of their optimal working position. Additional factors such as malnutrition and physical and psychological stresses during aerospace travel may contribute to increased muscle loss(BUCKEY, 2006b). Muscle atrophy occurs by reducing the size of the muscle fiber and not by its quantity. There are two types of muscle fibers: type I, antigravitational, postural or slow contraction, which have resistance to muscle fatigue, have a large number of mitochondria and myoglobins, besides being richly vascularized (BUCKEY, 2006b). Type I muscle fibers are very sensitive to inactivity, immobilization and the absence of gravity. Type II, or rapid contraction muscle fibers, have ease of fatigue and have a lower number of mitochondria and myoglobins (BUCKEY, 2006b). These seem to suffer greater losses than type I fibers. Muscle biopsies after landing also indicate a phenotypic change of type I fibers to type II fibers, providing faster contraction, but with greater fatigue (BUCKEY, 2006b; CLEMEND, 2003).

The decrease in muscle volume is accompanied by lower muscle strength, although not proportional to this reduction. Muscles with a higher muscle atrophy index are: quadriceps, hip adductors, sural triceps (mainly soleus muscle) and lumbar paravertebral muscles, with special emphasis on the multifidus muscles (KAWASHIMA et al., 2004). Changes in lordosis and range of motion (ROM) associated with muscle multifidus atrophy occurs in most astronauts. However, only those with severe terminal plaque irregularities had post-flight lumbar symptoms: chronic low back pain or herniated disc. Pre-flight vertebral plate insufficiency may increase astronauts' risk of injury by returning to gravitational load (BAILEY, 2017).

Bed rest, an analogue of spaceflight in soil, induces a robust atrophy of skeletal muscles, being exacerbated with increasing age. It is already evident after 14 days of bed rest (ARENTSON-LANTZ, 2016).

The reduction of tendon stiffness is due to changes in the alignment and length of collagen fibers due to the absence of gravity.

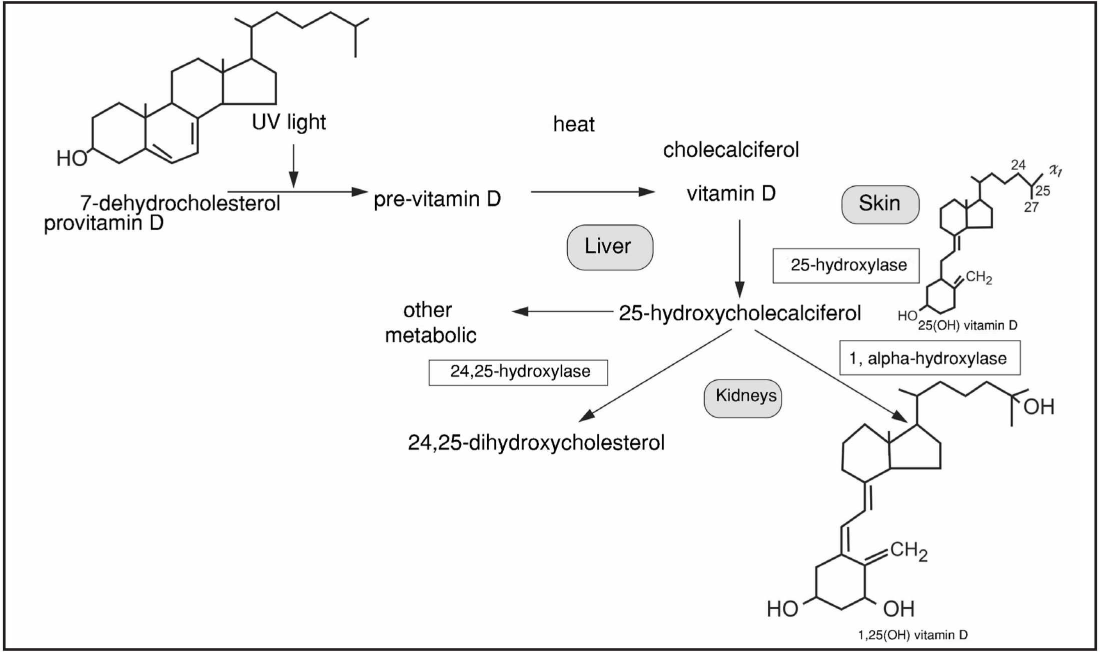
The return to Earth can trigger in astronauts low back pain, pain in the calves and thighs and, in some cases, plantar fasciitis (CLEMEND, 2003; SHACKELFORD, 2008). Upon returning from the space station, the astronaut must undergo a rehabilitation and muscle conditioning program to regain muscle mass and strength, which usually occurs between one and two months. (SHACKELFORD, 2008).

Muscle imbalance caused by flexor hypertrophy and extensor and loin-pelvic muscle atrophy increases the risk of post-space mission injury. A method currently used in manned space flights in Europe to assist in post-mission recovery focuses on teaching voluntary contraction of specific loin-pelvic muscles and positioning the spine, progressing to functional training with load. An alternative approach would be to use a Functional Readaptation Exercise Device to adequately recruit the musculature (EVETTS, 2014).

One measure that addresses both the preservation of musculoskeletal and cardiovascular muscles is high intensity and short duration rowing exercise followed by supplementary resistance strength exercises. Rowing training effectively preserved skeletal muscle function and structure, partially avoiding atrophy in the main antigravitational muscles (KRAINSKI, 2013).

Microgravity decreases bone mineral density. Bone formation depends on the degree of load on the bone. Thus, the decrease of the load on the bone hinders and even inhibits its formation (BUCKEY, 2006a; CANN, 1997; SHACKELFORD, 2008). Other factors contribute to bone loss, such as low sunlight, which decreases vitamin D formation, and the environment with high CO_2 concentration, which leads to respiratory acidosis (BUCKLEY, 2006a).

Figure 1 - Synthesis of 1.25 (OH) Vitamin D.



Source: PREMAOR; FURLANETTO, 2006. 7-dehydrocholesterol, through the action of ultraviolet light and heat, is isomerized in cholecalciferol in the skin. It is then transported to the liver, where it undergoes the action of 25-hydroxylase, turning into 25-hydroxyvitamin D. When this molecule reaches the kidney, it can either become the active or inactive form of this hormone, through the action of 1, alpha, hydroxylase or 24.25 hydroxylase, respectively.

The microgravity environment deregulates calcium homeostasis because of the poor diet of this ion, the absence of sunlight, the high concentration of CO_2 and the absence of load on the bone. The decrease in serum calcium increases the secretion of parathyroid hormone (PTH), causing an increase in the production of 1.25-dihydroxyvitamin D, increased intestinal absorption of calcium and phosphate, stimulates renal resorption of calcium, inhibits renal phosphate resorption, and increases bone resorption (Figure 2).

Bone demineralization begins as soon as you reach space and can continue throughout the mission. In the first days, an increase of 60 to 70% of urinary and fecal calcium is observed (BUCKEY, 2006a; CLEMENT, 2003).

Bone density loss during bed rest is 1 to 2% per month in load bones such as lumbar vertebrae, pelvis, femoral neck, trochanteric region, tibia and calcaneus (BUCKEY, 2006a; CANCEDDA, 2001; CLEMENT, 2004; LANG et al, 2006a; LEBLANC et al, 2002). In these regions, the loss of bone mineral density after 6 months in the space station is 8 to 12% (SHACKELFORD, 2008).

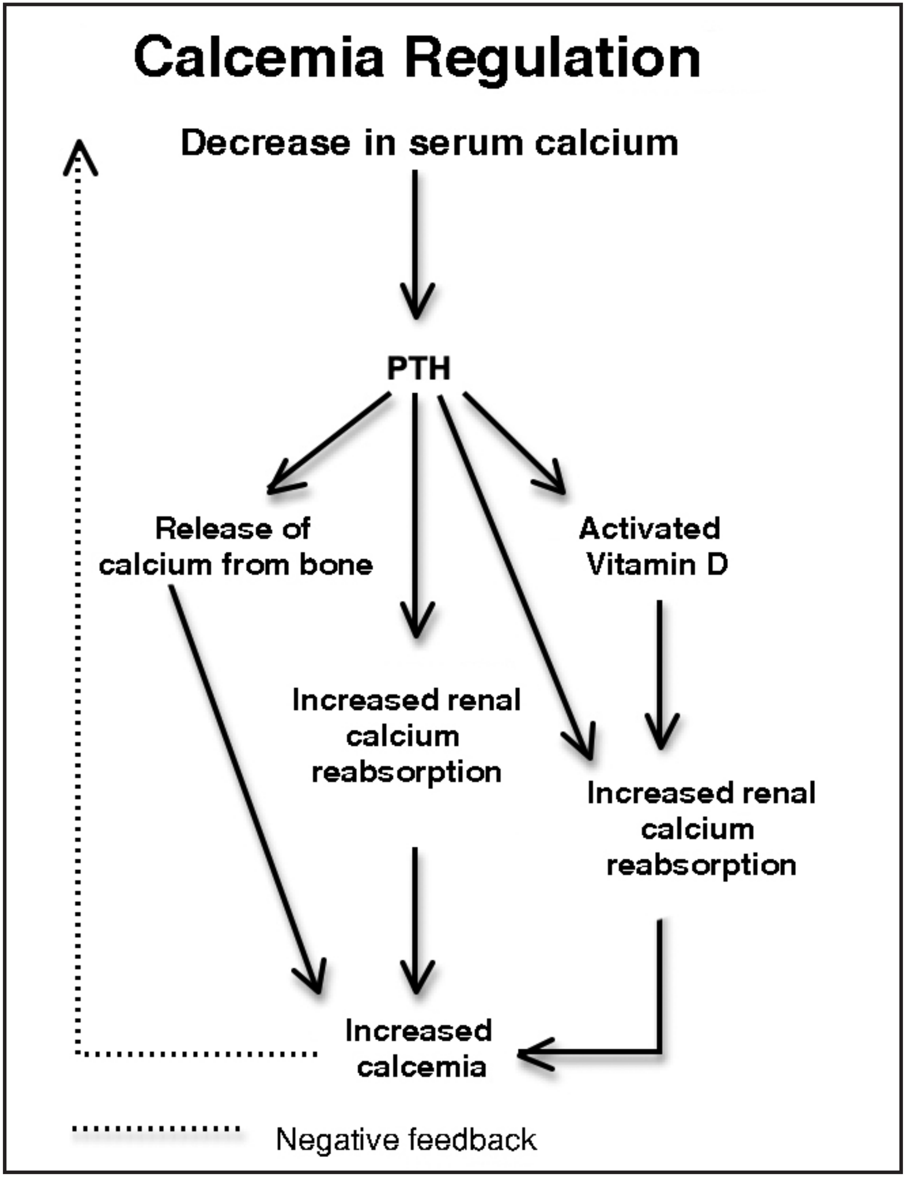
The highest mean absolute bone loss per disuse occurs in the cortical compartment, apparently only during the first 60 days. After this period, trabecular loss may become more prominent (CERVINKA, 2014).

Bone densitometry and computed tomography are useful tests to monitor bone loss and also to test the effectiveness of resistance exercises and the effectiveness of bisphosphonate therapy in astronauts who have returned from space travel (WILLIAMS et al, 2009). Bone mineral density (MOD) measurement by dual-energy X-ray absorptiometry (DXA) is used at NASA Johnson Space Center. The crew's DMO DXA scans showed sharp declines in DMO for the hip and spine after typical six-month space missions (SIBONGA, 2015).

The laboratory findings of astronaut returning to Earth are characterized by increased bone resorption markers, unchanged bone formation markers, decreased vitamin D synthesis, decreased intestinal calcium absorption, and increased serum calcium (LEBLANC et al. 2000). Tables 1, 2 and 3 characterize the criteria for vitamin D deficiency, the risk factors for hypovitaminosis D, and the reference values of serum calcium in adults, respectively.

The Department of Bone and Mineral Metabolism of the Brazilian Society of Endocrinology and Metabology (SBEM) had been discussing the normality values of 25-OH-vitamin D for some time. The normal value proposed pela Endocrine Society and SBEM, previously above 30 ng/mL, was changed in 2017, and higher than 20 ng/mL is desirable for healthy general population, and between 30 and 60 ng/mL is recommended for risk groups.

Figure 2 - Calcium Homeostasis.



Source: The author. Calcium and phosphorus metabolism. The PTH activates vitamin D, increases the intestinal absorption of calcium, inhibits the renal elimination of calcium, increases the renal elimination of phosphate and increase the bone resorption. When the serum calcium is increasing, it inhibits the release of the PTH: negative feedback.

Table 1 - New diagnostic criteria proposed by SBEM in 2017 for vitamin D deficiency.

Dosage of 25-hydroxivitamin D (ng/mL)	
10 to 20 ng/mL	considered low: at risk of increasing bone remodeling and, thereby, loss of mass bone, in addition to the risk of osteoporosis and fractures
> 20 ng/mL	desirable for healthy general population
30 to 60 ng/mL	recommended for risk groups such as the elderly, pregnant women, patients with osteomalacia, rickets, osteoporosis, secondary hyperparathyroidism, inflammatory diseases, autoimmune diseases and chronic renal and pre-bariatric diseases

Source: Department of Bone and Mineral Metabolism of SBEM.

Tabela 2 - Risk factors for hypovitaminosis D.

Low UVB light exposure	Decreased synthesis of vitamin D by the skin	Diseases that alter vitamin D metabolism
Excessive use of clothing		
		Cystic fibrosis
Low-heat countries (high latitude)	Yellow race	Immobilization for bone fracture treatment
Little penetration of UVB light during winter in the atmosphere	Aging	Heart failure
Using solar blockers		Kidney Diseases
Confinement in places where there is no UVB light exposure		Hematological diseases
		Diseases of the gastrointestinal tract

Source: PREMAOR; FURLANETTO, 2006.

Table 3 - Serum calcium reference values in adults (PREMAOR; FURLANETTO, 2006).

Total calcium	8.8 to 11.0 mg/dL
Ionic calcium	4.60 to 5.40 mg/dL

Source: PREMAOR; FURLANETTO, 2006.

Table 4 shows biochemical markers of bone metabolism.

Table 4 - Biochemical markers of bone metabolism.

Formation	Reabsorption
	Hydroxyproline (urine)
	Collagen cross-links (urine and serum)
	Total pyridinolines
Alkaline bone and/or total phosphatase	Pyridinoline and/or free
Osteocalcin (serum)	N-telopeptídeo (NTX)
Type 1 collagen propeptides (serum)	C-telopeptídeo (CTX)
	Acid phosphatase tartrate-resistant (serum)

Source: PREMAOR; FURLANETTO, 2006.

Accelerated bone loss in a microgravity environment causes lead to be released from the bones where they were stored. This would increase the risk of saturnism, which causes concern about the acceptable concentration of lead in the drinking water of space vehicles. However, according to Garcia (2013), most astronauts on long space missions will not be affected by the release of lead from the bones in the blood. A small percentage of astronauts with high lead concentration in their bones could have increased plumbemia, depending on the individual rate of bone loss (GARCIA, 2013).

Due to bone fragility, astronauts who have just returned from a space trip should stay away from impact activities and flights on high-performance aircraft (CLEMENT, 2003; LANG et al. 2006).

However, this bone loss may persist for longer. The time for recovery of bone stock is longer than the time of permanence in space. Bone density recovery may take up to three years after completion of space travel and may not return to pre-trip levels (CLEMENT, 2003). Bone stock re-composition may form a trabeculate and bone mineralization different from bone architecture before flight (LANG et al. 2006).

> In the tibia, in addition to the decrease in bone mineral density in the cortical and trabecular compartments, a 4% decrease in cortical thickness and a 15% increase in cortical porosity were observed at landing. Cortical size and density subsequently recovered and the serum changes of the periostin [marker of osteocyte activity or periosteal metabolism, along with sclerostin] was associated with cortical recovery for one year after landing. However, cortical porosity of the tibia or trabecular bone did not recover, resulting in impaired strength. The radius, preserved on landing, unexpectedly developed post-flight fragility, starting 3 months after landing, particularly in its cortical structure. The remodeling markers, decoupled in favor of bone resorption at landing, returned to the previous values in 6 months, then declined to values below the preflight values. Our findings highlight the need for specific protective measures, not only during, but also after space flights, because of ongoing uncertainties about the skeleton's recovery long after landing(VICO, 2017, p. 2).

It is believed that high-energy linear transfer radiation (LET: Linear Energy Transfer) in space exacerbates the loss of bone density induced by microgravity via CHK1 (Checkpoint Kinase 1)/ MEPE (Matrix Extracellular Phosphoglucoprotein) activated by the radiation that exacerbates the effects of microgravity on bone mineral in astronauts (ZHANG, 2015).

There is concern about this bone fragility due to the possibility of early osteoporosis and fracture in astronauts (CLEMENT, 2003). Fracture can occur during strenuous space activities – walking – or especially after returning to Earth (SHACKELFORD, 2006).

The lack of mechanical signs due to disuse can inhibit osteogenesis and induce adipogenesis of mesenchymal stem cells. Thus, osteoporosis can also be caused by the reduced number of osteoblasts. The adequate mechanical stimulation for osteogenesis, particularly under microgravity conditions, can restore normal osteogenic differentiation using low intensity pulsatile ultrasound (LIPUS: Low Intensity Pulsed Ultrasound) by short-term daily stimulation (UDDIN, 2013).

The thyroid controls the cardiovascular, musculoskeletal, nervous and immune systems and affects cognitive behavior and functions. It is known that microgravity can induce functional alterations in the thyroid gland (ALBI, 2017) with consequent impairment of the aforementioned systems.

As the recovery of bone mass lost after spaceflight is long, it is important to act in the prevention of bone loss before and during the flight. Thus, there are measures to avoid the musculoskeletal catabolism of astronauts in the microgravity environment. Such measures consist of:

- proper selection of astronauts, excluding those with low bone mass or treating them before the flight (BUCKEY et al. 2006).
- balanced diet, with low salt concentration (excess may contribute or facilitate bone loss), but with high calcium concentration and high protein (BUCKEY et al. 2006).
- high intensity resistance exercise program with low repetitions and in short time (BUCKEY et al. 2006). However, a mechanical load of low magnitude and high frequency, experienced in activity for postural control, has also been shown to be anabolic to bone and can mitigate the bone loss experienced by astronauts (NAGARAJA, 2014). There is also a Hybrid Training System (HTS) to maintain muscle trophism and prevent atrophy of an astronaut's musculoskeletal system (SHIBA, 2015).

Figure 3 - *Hybrid Training System (HTS).*

Source: NASA.

- aerobic training for cardiorespiratory conditioning before and during space travel (QUIRINO et al. 2012). There are some obstacles to overcome so that the astronaut can step on the treadmill. First of all, they must hold on, not to float. For the astronaut to run in space, it is necessary to attach him to the treadmill so that an armor (strap) passes over the shoulders and around the pelvis, fixing the straps on them. Two side harnesses connect the armor to the mat and this connection can be adjusted according to the load the astronaut desires. More loading means that harnesses bring the person more toward the treadmill: it's like trying to run with a heavier backpack. The astronauts need to adjust the correct speed and load so the race is not uncomfortable. The track has a vibration isolation system so that the runner does not transmit load to the structure of the space station.

- physical exercises such as: hip abduction and adduction, trunk extension exercises, squatting and plantar ankle flexion by means of a machine known as the Advanced Resistive Exercise Device (ARED), where adjustable resistance piston-driven vacuum cylinders are used to provide load to astronauts and maintain strength and muscle mass for long periods in space.
- use of supplements and medications such as calcium, vitamin D and bisphosphonates (BUCKEY et al, 2006).
- urinary and serum calcium monitoring, in addition to markers of resorption and bone formation (BUCKEY et al. 2006). Bone resorption caused by space missions increases serum and urinary calcium and the risk of nephrolithiasis. The easiest way to prevent the risk of kidney stones is to increase the water consumption (SMITH, 2015).
- intermittent exposure of the crew to an environment with gravity during spaceflight: centrifugation is a plausible way to generate artificial gravity. In space, you can create "artificial gravity" by rotating the space station. A rotating system is created that produces the same effect of gravity, because it produces a force (centrifugal force), which acts to pull the inhabitants outwards. This process can be used to simulate gravity. By adjusting certain parameters of a space station, such as radius and rotation rate, you can create a force on the outer walls that would equal the force of gravity. Thus, the outer walls of the space station would be the floor on the space station. The centrifugal "force" pushes objects out, but the force of the space station provides an opposite "centripetal force" that pushes inwards. This would be similar to walking on the surface of a planet (if the space station is spinning at the correct speed). However, the great forces of Coriolis would also be present, and the objects would fall into curves instead of straight lines (ANDERSON, 2015).

Figure 4 - *Advanced Resistive Exercise Device (ARED).*

Source: NASA.

4 CONCLUSION

The exposure to the space microgravity environment deconditions the astronaut, causing atrophy of the musculoskeletal system with decreased volume and muscle strength and loss of bone mass. These physiological adaptations occur soon after their arrival in the microgravity environment. These changes have deleterious potential to the astronaut's musculoskeletal system, with increased risk of fracture upon returning to Earth, as well as the potential to impair the effectiveness of the mission in space. Therapeutic intervention before, during and after the aerospace trip, through a balanced diet and with a defined physical exercise program, should be implemented in order to avoid the astronaut's musculoskeletal deterioration.

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