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Parul Sharma/ Impact of microgravity on Knee Joint cartilage

Impact of microgravity on Knee Joint cartilage

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ABSTRACT

Human Spaceflight has been shown with deleterious changes in knee joint including Loss of muscle mass & strength, Reduced Functional capacity, Increased Fatigue level , demineralization, Changes in connective tissue, degradation of collagen II network in articular cartilage following proteoglycan degradation and ultimately lead to joint instability. Antigravity muscles are commonly involved such as leg extensors. The mechanism of these changes are not fully understood but can be attributed to muscle usage. Emphasis will be placed on knee extensor and plantar flexor muscles known to be particularly susceptible to deconditioning in space missions .Therefore, Human spaceflight (Pre-Flight, Mid-Flight & Post-flight) Physiotherapy & Conditioning Regimes should be considered for knee joint such as specially integrated resistance training , Treadmill training and Cycle ergometer.

KEYWORDS: Knee Extensors, Flight Rehabilitation, Integrated Resistance Training, Treadmill training, Cycle ergometer

INTRODUCTION:

Gravity or gravitation force is the force of attraction exerted by two masses towards each other. This force of gravity was discovered by Sir Isaac Newton (1642-1727) and described it as a forceproportional to the product of two masses and inversely proportional to the square of the distance between them. He developed an equation for this which stated that $F=G\, m_1 * m\ 2 / r\ 2$ where F is gravitational force acting between two objects, m 1 and m 2 are the mass of the Objects, r is the distance between the centre of their masses, and G is Gravitational constant. He also discovered that force of gravitation is essential to bring an object in motion or to change speed and direction of movement of the object. This gravitational pull is relatively constant in direction and magnitude on Earth. Gravitational attraction acts on all masses of objects on the Earth’s surface. Gravity is an irreversible and constant vector and act as a standardize stimulant to the factors that control growth, movement and behavior of an organism. Gravitational attraction is also being defined as weight of the object, which is the product of the mass of the object and acceleration of gravity.

W = F = m*gwhere W- weight, F- net external force acting on object , m- mass of the object and g-acceleration of gravity. (Barela AMF and Freitas PBD, 2014)

Effect of Gravity on human Physiology

Gravity has a constant downward pull over the all body parts such as shoulder, neck, back, legs, feet and different internal organs. This gravitational loading affects multiple physiological system of the body.

a) Cardiovascular System

The human cardiovascular system plays a vital role in maintaining blood circulation to all parts of body, helps body in maintaining homeostasis and temperature regulation. It also helps the body in fighting with diseases. Gravitational force effects the circulation by pulling it down and leads to swollen legs, varicose veins and decreased circulation to scalp, eyes, ears and skin.

b) Vestibular System

A basic function of the vestibular system is to maintain the body equilibrium in respect to the environment which includes control of the head and trunk position in space, and a control of the head in relation to the trunk. This function required a coordination between the vestibulo-ocular tracts controlling movement of eyes to maintain the gaze, and the vestibulo-colic tracts which innervate the neck muscles to support the head along with the vestibulo-spinal tracts which innervate the motor neurons of proximal and axial muscles of upper and lower extremities to maintain posture and balance. Gravity has an impact on evolution of postural control, homeostatic regulation, and spatial memory in humans.

c) Musculoskeletal System

Musculoskeletal system comprises of muscles and bones and is all related to movement. Gravity plays an important role in development of load bearing structures and maintaining balance. This system is responsive to varying changes in load due to varying gravity. It has been found that muscles and bone becomes weak and there is marked loss in their mass due to zero gravity or microgravity. Humans, animals and even plants have evolved to cope with and rely on gravity. Changes in the biophysical activities of living organisms depends on gravity at different levels of organization in microgravity, partial and hypergravity conditions. (Carpenter RD and Lang T, 2010)

Multiple physiological systems become affected under lack of gravitational loading or microgravity conditions such as balance and support system and moreover fluid flow that are susceptible to destruct or changes during renewed exposure to gravitational forces. Chronic unloading of cartilage has been studied using animal models. After 6 to 8 weeks of immobilization (splinting in flexion to achieve non–weight bearing [NWB]), decreases in proteoglycan content and increases in water content were observed in canines. In a review paper, Vanwanseele and colleagues compiled all studies on immobilization in animal models and reported a trend toward signs of early degenerative changes in articular cartilage after prolonged immobilization.(Demontis GC and Germani MM, 2017)

MICROGRAVITY

Micro- means "very small," so microgravity refers to the condition where gravity seems to be very small. More often it is said to be the condition in which people or objects feel weightlessness. Weightlessness or Zero gravity is the term used for absence of gravity whereas microgravity is the condition of very low gravity, especially approaching weightlessness. The effects of microgravity can be seen when astronauts and objects float in space. So microgravity is also said to be a measure of the degree to which an object in the space is subjected to acceleration. Its measure is equivalent to one millionth (10^{-6}) of the force of gravity at Earth's surface**.** (Dreiner M and Willwacher S, 2017)

EFFECT OF MICROGRAVITY ON HUMAN PHYSIOLOGY

According to various studies, it has been found that there are physiological and biochemical changes occurring in human beings due to long exposure to microgravity, out of which most significant ones are: 1) loss of bone density due to negative calcium balance, 2) Fluid shift and decreased plasma volume, 3) cardiovascular deconditioning leading to orthostatic intolerance, and 4) atrophy of antigravity muscles. (Fitzgerald J, 2017)

These changes are reversible if exposure to microgravity is acute (<2 weeks) but astronauts may have to remain in space for 300 days to 3 years for one mission. The effects of microgravity varies from acute to chronic depending on the duration of exposure. Acute changes occurs immediately after exposure to microgravity and it includes, decrease in hydrostatic pressure, increased intracranial pressure, difficulty in heat dissipation and motion sickness. Adaptive responses occurs after short-duration space resulting in a decreased plasma volume and red cell production as well as changes in cardiac output and peripheral vascular resistance**.** Chronic changes occurs only after longer duration exposure, when the human body tries to adapt to the needs of the new environment for long-term to establish a new homeostasis. These changes include loss of lean body mass, loss of bone in weight bearing areas, formation of renal calculi etc. These changes are discussed in detail below.

A. Bone Loss

Under zero gravity conditions, there will be no constant force acting on the bone, which affects the bone strength. It has been found that bone mineral density reduces at a rate of 1-2% per month. It might reach upto 40% decrease in bone mass during a space flight lasting two years. Bone loss is more common in the weight bearing areas such as spine, pelvis, femoral neck, trochanter, calcaneus and leg. These changes are detected only after one month but cumulative bone loss increases with duration of space flight. These changes are relatively irreversible and therefore increase the risk of fracture and osteoporosis on Earth's surface. Microgravity also affects fracture healing and increased incidence of renal stone formation, which are related with bone demineralization. (Ganse B and Jochen Zange J, 2015)

Studies were conducted on astronauts and cosmonauts to analysed different factors responsible for bone loss. It was found that the specific biomarkers such as C-terminal or N-terminal telopeptides of type I collagen (CTX-I and NTX-I, respectively) were circulating and excreted in urine and blood samples. Presence of these biomarkers is responsible for compresensive alterations in bone reabsorption and formation. Along with this, there was increased concentration of pyridinium crosslinks in urine which specify increased bone reabsorption activity. In contrast to it, bone formation biomarkers such as propeptide of type I N- terminal procollagen (P1NP), propertied of type I C- terminal procollagen (P1CP), alkaline phosphatase and osteocalcin were reduced after first week of spaceflight compared to their pre-flight values. This concludes that increased bone reabsorption markers leads to alteration in bone metabolism but etiology remains unclear. Osteocytes marker were also investigated and it was found that sclerostin (an inhibitor of osteoblast-mediated bone formation) levels were increased. Periostin which is a matricellular protein found in cortical bone and periosteum and a mediator of cortical bone in response to mechanical forces, remained constant in pre-flight and post-flight readings. Studies were conducted to assess mineral metabolism and it was noted that concentration of calcium has considerably increased in urine and faeces of astronauts. In a study, 0.2% of their estimated total body calcium and 0.7% of phosphorus concentration in body was reduced in a 12.6 day lunar flight. Along with calcium and phosphorus, decrease in vitamin D and its precursor 25(OH)-Vitamin D level and decreased concentration of parathyroid hormone was also noted. All these above results states that there is increased osteoclastic activity which leads to altered bone metabolism. But studies related to osteoarticular alterations occurred during spaceflight are limited. (Gaffney CJ and Fomina E, 2017)

Although mass of an individual is constant on Earth's surface and in space, mechanical loading and ground reaction forces are highly reduced in spaceflight. So they are the primary factor responsible for changes in strain energy within bone tissue. To overcome the decreased ground reaction force and altered bone mass, artificially produced gravity of 1G and on board exercise regimens are induces to recover bone mass loss. (Grimm D and Egli M., 2018)

EFFECT ON CARTILAGE

Articular cartilage is highly specialized avascular, alymphatic, aneural and lubricious tissue and is composed largely of water, collagen and proteoglycans. The effect of microgravity on articular cartilage are unknown. It has been found that unloading and immobilization in humans causes thinning and softening of cartilage. Evidence also suggest changes in the levels of serum COMP due to micro- and hypergravity. Exposure to microgravity also causes changes in molecular biomarkers of cartilage metabolism within 5 to 6 months. According to a study, the levels of serum COMP were increased on 7th and 30th days after return to gravity in astronauts. These changes suggests that the extracellular matrix of cartilage is sensitive to exposure to microgravity and acute hypergravity. (Herranz R and Anken R, 2013). Unloading of joints results in loss of glycoaminoglycans from cartilage which is an early sign for degeneration of cartilage and decrease in it thickness. Similar results were obtained in a study which was done on rat population. In this study rats were suspended from tail for 4 weeks and it was found that cartilage thickness of patella and medial femoral condyle was decreased. Another study which was performed on human subjects and they were in HDBR (Head down tilt bed rest) for 14 days also concluded that thickness of articular cartilage is sensitive to unloading. They found a substantial decrease in thickness of tibial knee joint cartilage but not in the thickness of femoral knee joint cartilage. (Julie H and Gunda L., 2017).

From above studies it was found that moderate joint loading is essential to maintain cartilage health. In unloading experimental studies conducted on humans, was found that reduced biomechanical forces over a longer period of time can lead to proteoglycan loss in articular cartilage and to an average loss of cartilage thickness of about 8%. Some studies suggested that reduced loading on joints leads to degeneration in knee ligaments and menisci which increases the chances of subluxation or dislocation. [11]

Poor regenerative capacity of cartilage and cartilage degeneration due to microgravity conditions influence space mission activities as well as mobility of flight crew members which accelerate short and long term destructive changes in the joints. Several studies shown that loading or gravitational force of articular cartilage is necessary for stimulation of chondrocytes and normal joint function.(Kohn PMF and Koch C, 2018)

MUSCLE LOSS

Muscle atrophy and reduced muscle mass are seen primarily in postural or antigravity muscles. On comparison to muscle strength, maximum voluntary contraction ability of muscles was more reduced. In a study, different postural muscles were assessed and it was found that muscle volume in calf muscle reduced to 6-20%, gastrocnemius up to 19% and approx. 10% decline in quadriceps muscle after 112-196 days leading to muscle atrophy. The muscle strength can reduce to 15%-48% depending on the duration of stay in microgravity. (Lützenberg R and Solano K, 2018)

As the muscle loses strength, the fibres within muscle also changes. One of the study revealed that 15% of the slow twitch fibres get converted to fast twitch fibres within 14 days of spaceflight. Loss of muscle mass, reduction in fascicle length and change in pennation angle was also observed. Few studies have been done using electromyography (EMG) to investigate neuromuscular activity of plantar flexor muscle and showed a 35-40% reduction in their activity after 90-180 days in space.

Due to these physiological variations in body system, locomotion, posture and spatial disorientation were greatly affected. With longer duration of spaceflight, physiological changes become irreversible leading to greater amount of muscle loss which in turn could develop permanent damage or deformities. In such poor condition of muscle and connective tissue, increased demand of activity can lead to risk of fatigue and injuries.

Preferential type I muscle fibre atrophy is associated with microgravity and disuse. Data from this study show that strength was lost in the quadriceps/hamstrings but not the calf muscles. The calf contains a high proportion of type I fibres and the vastus lateralis (quadriceps) and biceps femoris (hamstrings) contain a higher proportion of type II fibres. Spaceflight is associated with a preferential loss of type I muscle fibres and muscle atrophy , which is associated with reduced strength (maximum voluntary contractions (MVC). In the calf, there are up to double the quantity of type I muscle fibres (soleus ~ 70–80%; gastrocnemius ~ 50–57%) known to be preferentially lost in spaceflight than in the thigh (vastus lateralis ~ 32–42%; biceps femoris ~ 47%). (Park SY and Ahn SH, 2019)

B. CARDIOVASCULAR DECONDITIONING

Cardiovascular deconditioning is defined as shifting of fluid throughout the human body. Under the impact of microgravity, motion of fluid increases more to head and chest area which leads to increased heart rate, light headedness, fainting and puffiness in the face. Decrease in red blood cells and reduced plasma volume as well as changes in cardiac output and peripheral vascular resistance are few of the adaptive changes that has been noticed in the astronauts. After a short span in space decreased tissue oxygenation could occur and as the astronaut returns to Earth's gravity pull orthostatic intolerance and syncope increases along with fatigue and dyspnea.

MANAGEMENT OF CARTILAGE DEGENERATION ON SPACEFLIGHT:

Whole Body Vibration : Whole-body vibration (WBV) has been used to treat musculoskeletal diseases like osteoarthritis (OA), but the direct effect of vibration on joint cartilage is not clear. A recent study showed that WBV induced cartilage degeneration in mice. Higher frequencies of WBV (30 Hz and 40 Hz) in a rabbit model had a negative influence on cartilage volume and cartilage resorption, whereas lower frequencies (10 Hz and 20 Hz) decreased cartilage resorption, accelerated cartilage formation, and delayed cartilage degradation especially at the 20 Hz regimen. (Souza RB and Baum T, 2012)

Resistance exercise coupled with vibration (WBV) has prevented muscle atrophy during 56-day bed rest and may provide a simple intervention suitable for exploration class missions and these interventions can prevent isolation-induced lower-limb loss of strength. WBV enhances motor unit recruitment promoting an efficient, specific warm-up effect that allows the muscle to produce more force and power and aids flexibility.

Cycle ergometry with a Vibration Isolation and Stabilisation System (CEVIS): It using loads of 25–350 W and treadmill running with a vibration isolation system (TVIS) (a treadmill with a harness to secure the user and mimic gravitational loading) are routinely employed but cannot prevent loss of calf and thigh muscle volume during 6-month ISS missions. Resistance exercise may also alter the hormonal milieu with exercise to prevent muscle catabolism and promote the maintenance of muscle protein synthesis.

Advanced resistive exercise device (ARED) : It appears promising. For e.g: Squat, bench press, dead lift, lateral pull, back extension, and rowing, in addition to calf raises and leg presses.

Endurance exercises—treadmill running and cycle ergometry : Endurance exercise interventions to prevent loss of strength comprised of active (motorized) treadmill running, passive mode (non-motorized) treadmill running, and cycling .According to one study including active and passive mode treadmill running were completed on a Cybex International 750T treadmill (Medway, MA, USA) and a non-commercial treadmill (BD-1) used in the Russian module of the International Space Station followed the training protocol**.** Training on the cycle ergometer was completed on a Kettler Velergometer (Ense, Germany). Subjects were instructed to maintain a cadence of 60–70 rpm whilst cycling. All endurance mode of exercises were completed as 3 days training followed by 1 day of rest (training therefore 5–6 days/week throughout the 70-day block).

Resistance exercise—Expanders, WBV, and MDS : Resistance exercise interventions to prevent loss of strength comprised of expanders, WBV, and MDS. According to one study, before completing expander training (elastomer-based resistance exercise), the subjects completed a non-prescriptive 10-min warm-up comprising of low-velocity closed-chain movements (e.g. squats) and passive stretching (e.g. quadriceps, hamstrings, and calf stretches). Subjects completed three different exercise protocols using expanders weekly, throughout the 70-day training block (total training of 3–4 days/week). Protocol 1 comprised of 2 × 15–20 reps of elbow flexion, calf raises, abdominal crunches, and standing trunk extensions; protocol 2 comprised of 2 × 15–20 reps of press ups, squats, rowing, and pull downs; protocol 3 (recovery) comprised of three to five hamstring stretches in two positions. Training sessions were completed every other day during the 70-day training block (3–4 days/week). Exercise using WBV was completed on a Galileo oscillating platform (Novotec Medical-Stratec Medizintechnik, Germany) at amplitudes of 2–6 mm depending upon foot position, and at a fixed range of frequencies from 16 to 25 Hz. (Wolfe JW and Rummel JD, 1992)

SUMMARY AND CONCLUSION: Human spaceflight (Pre-Flight, Mid-Flight & Post-flight) Physiotherapy & Conditioning Regimes should be considered for knee joint such as specially integrated resistance training , Treadmill training and Cycle ergometer.

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