URINE CONCENTRATION OF CARTILAGE DEGRADATION MARKER CTX-II IS SENSITIVE TO MICROGRAVITY

Anna-Maria Liphardt[1], Nadja Djalal[1], Scott M. Smith[2], Anne Mündermann[3], Frank Zaucke[4], Georg Schett[1], Anja Niehoff[5, 6]

[1]Friedrich-Alexander-University Erlangen-Nürnberg (FAU) & University Hospital Erlangen, Erlangen (Germany), Email: anna-maria.liphardt@uk-erlangen.de [2]Human Health and Performance Directorate, NASA, Lyndon B Johnson Space Center, Houston, Texas (USA),[3]University Hospital Basel, Basel (Switzerland), [4]University Hospital Frankfurt, Goethe University, Frankfurt am Main (Germany), [5]German Sport University Cologne, [6]University of Cologne, Cologne (Germany)

INTRODUCTION

Mechanical and gravitation load are both important regulators of articular cartilage metabolism. Immobilization and the absence of gravity likely change tissue characteristics that can result in atrophy and softening of cartilage. Type II collagen is the most abundant cartilage matrix protein. Assessing urinary excretion of crosslinked C-telopeptide (uCTX-II) provides an index of total type II collagen degradation. We hypothesized that reduced mechanical and gravitational loading during a 4 – 6 months International Space Station (ISS) mission will result in increased uCTX-II levels.

METHODS

Twelve United States orbital segment (USOS) crew members with a mission length of four to six months on the ISS participated in this study. 2nd void urine samples were collected on two consecutive days for each time point (pre-flight (launch -60 days), post-flight (Return (R)+1day, R+1week (R+6, R+7), R+1month (R+30, R+31), R+1year (R+365, R+366)). 24-h urines were collected in-flight (FD15, FD30, FD60, FD120, FD180). uCTX-II concentration was determined using a commercially available enzyme-linked immunosorbent assay (ELISA) (Urine CartiLaps® (CTXII) EIA, Immunodiagnostic Systems Limited). Urine concentrations were normalized to creatinine (Cr) excretion. Repeated measures ANOVA was performed using IBM SPSS (Version 24.0), p-values ≤ 0.05 were considered significant.

RESULTS

Absolute pre-flight uCTX-II concentration for 2nd void morning urine was 210.4 (±116.0) ng/mmol Cr. 2nd void uCTX-II concentration was elevated one day after landing compared to pre-flight values (R+1day: 309.1±103.5 ng/mmol Cr; change vs. pre-flight: 174.96 ±68.59%, p = 0.008) and values did not recover to baseline values within the first month of return (R+1week: 361.7 ±154.7 ng/mmol Cr; %change vs. pre-flight 198.9 ±77.6%, p = 0.176, R+1 month: 330.5 ±123.4, %change vs. pre-flight: 186.43 ±90.39%). While the mean concentration seemed to recover one year after landing (R+1year: 215.1 ±120.1 ng/mmol Cr, change vs. pre-flight: 99.6 ±38.9%) individual values of four crew members did not reach baseline values. In-flight 24h uCTX-II concentrations were higher after the first month of flight compared to preflight values (ISS Month 1: 256.4 ±129.8 ng/mmol Cr; change vs. pre-flight: 140.67 ±67.4%). uCTX-II concentration increased further until month 6 of the flight, reaching a maximum on FD120 (ISS Month 2: 356.3 ±212.5 ng/mmol Cr; change vs. ISS Month 1: 135.6 ±36.1%; ISS Month 4: 392.2 ±146.3 ng/mmol Cr; change vs. ISS Month 1: 162.6 ±51.1%; ISS Month 4: 392.2 ±146.3 ng/mmol Cr; change vs. ISS Month 1: 162.6 ±51.1%; ISS Month 6: 392,8 ±148.6 ng/mmol Cr; change vs. ISS Month 1: 164.3 ±46.0%).

CONCLUSIONS

uCTX-II concentration increased during a 4 – 6 months space mission to the ISS indicating enhanced cartilage degradation. While a more pronounced increase in uCTX-II was observe in the first 4 months of flight, mean levels seem to plateau towards 6 months into flight. Post-flight uCTX-II is increased compared to pre-flight values and remains elevated for the first month after landing. In 7 of 12 crew members uCTX-II recovers to pre-flight values one year after landing.

FUNDING

Federal Ministry for Economic Affairs and Energy, Germany, Project #: DLR 50WB0913, DLR 50WB1217, DLR 50WB1719, DLR 50WB1520, DLR 50WB2021, DLR 50WB2022