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EXPLORING THE FEASIBILITY OF DRIED BLOOD SPOT (DBS) SAMPLING FOR CAFFEINE EXPOSURE ANALYSIS IN MICROGRAVITY DURING PARABOLIC FLIGHTS

Abstract

Introduction: Currently, therapeutic drug monitoring for astronauts faces limitations in conventional blood sampling and sample management onboard the international space station. Here, we explored the feasibility of dried blood spot (DBS) collection method during parabolic flights to overcome these constraints.

Method: Twenty volunteers participated in a pharmacokinetic study on caffeine and its metabolite, paraxanthine (as proof of concept), conducted during parabolic flights (Novespace, France). After >18h caffeine washout, coffee (115 mg) or tea (30 mg), or 3 dark chocolate squares (11 mg) were administered. Four blood samples were self-collected by DBS from finger pricks: baseline on the ground, during weightlessness, and twice post-return on the ground. All DBS were self-performed after attending a 30-minute training session. Five volunteers repeated the study on the ground. Caffeine and paraxanthine were analyzed by liquid chromatography-tandem mass spectrometry after 6 months storage at room temperature mimicking space conditions. Areas under the curves for caffeine and paraxanthine (AUC_CAF and AUC_PAX, respectively) were calculated. Genotyping for Cytochrome P4501A2 (CYP1A2) was performed by Taq-Man real-time PCR from salivary sample (ORAGEN®). Subjects were categorized into ultra-rapid (UM), intermediate (IM), or poor metabolizer (PM). A metabolic ratio for CYP1A2 was determined by the AUC_PAX/AUC_CAF ratio.

Results: Nineteen (12 males and 7 women) completed pharmacokinetic profiles, with repeated pharmacokinetic study for 6 subjects. Among women, 4 were on estrogen contraceptives, a known inhibitor of CYP1A2, and were thus considered as CYP1A2 PM. CYP1A2 genotyping resulted in n=9 UM, n=10

IM, and n=1 PM (further excluded because of motion sickness). The mean caffeine AUC for coffee, tea, chocolate were 9419 ng.h/mL (n=10), 6917 ng.h/mL (n=7), 3039 ng.h/mL (n=12) respectively, and the mean paraxanthine AUC were 10566 ng.h/mL (n=10), 4011 ng.h/mL (n=7), 3638 ng.h/mL (n=12) respectively. The baseline for chronic consumers (moderate to high) was above the limit of quantification. We observed expected differences in kinetic profiles, consistent with consumption habits, the ingested dose and the genotypic/phenotypic information. The metabolic ratio in estrogen-treated women was 0.530.17 compared with 1.190.36 in others. The metabolic ratio did not significantly differ between parabolic flights conditions and ground conditions ($p>0.05$, paired t-test).

Conclusion: DBS collection was safe, stable and feasible in weightlessness. Parabolic flights were not associated with physiological variations in caffeine pharmacokinetic, however expected differences related to subjects characteristics could be found.This method offers valuable insights into human metabolism adaptation during long-term spaceflight, addressing space pharmacology challenges.