| | | | |
|---|---|---|---|
| **Fiscal Year:** | FY 2010 | **Task Last Updated:** | FY 01/18/2012 |
| **PI Name:** | Platts, Steven H. Ph.D. | | |
| **Project Title:** | Test of Midodrine as a Countermeasure against Postflight Orthostatic Hypotension: SMO-006 | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | HUMAN RESEARCH | | |
| **Program/Discipline--Element/Subdiscipline:** | HUMAN RESEARCH--Biomedical countermeasures | | |
| **Joint Agency Name:** | | **TechPort:** | No |
| **Human Research Program Elements:** | (1) **HHC**:Human Health Countermeasures | | |
| **Human Research Program Risks:** | None | | |
| **Space Biology Element:** | None | | |
| **Space Biology Cross-Element Discipline:** | None | | |
| **Space Biology Special Category:** | None | | |
| **PI Email:** | steven.platts-1@nasa.gov | **Fax:** | FY 281-244-5090 |
| **PI Organization Type:** | NASA CENTER | **Phone:** | 281-483-8177 |
| **Organization Name:** | NASA Johnson Space Center | | |
| **PI Address 1:** | Cardiovascular Laboratory | | |
| **PI Address 2:** | Biomedical Research and Environmental Sciences Division | | |
| **PI Web Page:** | | | |
| **City:** | Houston | **State:** | TX |
| **Zip Code:** | 77058 | **Congressional District:** | 36 |
| **Comments:** | | | |
| **Project Type:** | FLIGHT | **Solicitation / Funding Source:** | Directed Research |
| **Start Date:** | 10/01/2006 | **End Date:** | 12/01/2009 |
| **No. of Post Docs:** | 0 | **No. of PhD Degrees:** | 0 |
| **No. of PhD Candidates:** | 0 | **No. of Master' Degrees:** | 0 |
| **No. of Master's Candidates:** | 0 | **No. of Bachelor's Degrees:** | 0 |
| **No. of Bachelor's Candidates:** | 0 | **Monitoring Center:** | NASA JSC |
| **Contact Monitor:** | Goodwin, Thomas | **Contact Phone:** | |
| **Contact Email:** | thomas.j.goodwin@nasa.gov | | |
| **Flight Program:** | Shuttle/ISS | | |
| **Flight Assignment:** | ISS 16, 17<br>Note deselected in October 2008, per JSC (4/2009)<br>NOTE: end date changed to 12/1/2009 per HRP Master Task List information dtd 1/12/2012 (Ed., 1/18/2012) | | |
| **Key Personnel Changes/Previous PI:** | NOTE that Steven Platts took over as Principal Investigator from Janice Meck in FY2007. See Meck (Principal Investigator) for reports prior to FY2007. | | |
| **COI Name (Institution):** | | | |
| **Grant/Contract No.:** | | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

| | |
|---|---|
| **Task Description:** | After space flight the capability to remain upright (standing) may be compromised by an inability to maintain adequate cerebral perfusion. This condition, termed orthostatic hypotension, may result in presyncope (lightheadedness) or syncope (loss of consciousness) during reentry or egress from the space vehicle and for several days after landing. Approximately 20% of crewmembers on short-duration missions and 80% of those on long-duration missions experience presyncope during testing on landing day. To date, the potential countermeasures that have been tested (including lower-body negative pressure, fluid loading, Florinef, exercise) have not eliminated postflight orthostatic hypotension. Midodrine is a selective alpha-1 adrenergic agonist that is used clinically to treat orthostatic hypotension. It is almost completely absorbed after oral administration and is hydrolyzed enzymatically to its active metabolite, desglymidodrine, which has a bioavailability of 93%. Midodrine acts by increasing vaso- and venoconstriction, thereby decreasing peripheral venous capacity and blood pooling, but does not pass the blood-brain barrier and therefore has no central stimulant effects. The effect of midodrine as an alpha-adrenergic agonist may be particularly protective of orthostatic tolerance in astronauts who become presyncopal on landing day due to inadequate release of norepinephrine. Midodrine was administered to crewmembers in the manner in which it might be used routinely after space flight. It was administered to five male astronauts 1 hour before landing, near the time of firing the Shuttle main engines to decelerate the Orbiter and begin its descent. The peak therapeutic effect of midodrine occurs approximately 1 hour after ingestion, making it particularly attractive as a landing-day countermeasure, such that its peak effect can be close to the time of the maximum gravitational forces during landing. The purpose of this report is to summarize the preliminary findings from this countermeasure evaluation. The strength of this study is that crewmembers participated in the postflight tilt test of orthostatic tolerance within 60 minutes after wheel stop, and therefore their physical status more closely represented their condition during reentry and immediately upon landing than when testing is conducted in the controlled environment of the baseline data collection facility. Testing in the baseline data collection facility typically occurs about two hours after wheels stop, following the astronauts' walk-around of the vehicle and subsequent transport to the testing facility.<br><br>See also: http://www.nasa.gov/ |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | In addition to benefits for astronauts, millions of people on Earth suffer from orthostatic hypotension and may benefit from information gained from this experiment. |
| **Task Progress:** | Eight male crewmembers volunteered to participate in this countermeasure evaluation. Three subjects withdrew from participation after the collection of preflight data. Two of these subjects were waived from participation: one had a prolonged QTc interval on an electrocardiogram during in-flight screening and one experienced significant neurovestibular disturbances on landing day. The third subject voluntarily withdrew from participation after the preflight midodrine tolerance test.<br>Approximately 90-days before flight, the participants will undergo a drug tolerance test for midodrine and will participate in a drug familiarization session. An operational tilt test will be conducted 10-days prior to launch, and the participants will complete a brief questionnaire before they leave the testing room.<br><br>In the course of this study, countermeasure subjects participated in a familiarization session and drug tolerance test, an 80 degree head-up tilt test without medications approximately 10 days before launch (L-10), and the tilt test protocol within 60 minutes of Shuttle landing (R+0). Subjects received verbal and written explanation of all procedures and signed statements of informed consent prior to participation. Preflight Activities<br><br>Approximately 10 days before launch (L-10), crewmembers participated in a tilt test in the JSC Cardiovascular Laboratory. Data were collected for 6 minutes while the subjects were supine, before they were tilted to 80 degrees head-up tilt using an automatic tilt table. The subjects remained in this position for 10 minutes, or until symptoms of orthostatic hypotension and/or presyncope occurred.<br><br>In-Flight Activities<br><br>Crewmembers participated in their scheduled in-flight activities without restriction for the duration of their Shuttle mission. After the decision for deorbit burn was confirmed on the scheduled landing day, crewmembers donned the Advanced Crew Escape Suit (ACES) and ingested 10 mg of midodrine approximately one 1 hour before the scheduled landing time. The midodrine pill and a cue card with medication instructions had been stowed in the subjects' ACES for their convenience. All crewmembers participated in the standard oral fluid-loading protocol (equivalent to isotonic saline at a rate of 15 ml•kg-1 within 2 hours of landing) and inflated their antigravity suits during reentry and landing.<br><br>Postflight Activities<br><br>Postflight testing on landing day (R+0) was conducted on the Shuttle runway at either Kennedy Space Center, FL, or Dryden Flight Research Center, CA, in NASA's Crew Transport Vehicle (CTV), a modified airport "people mover" used to transport the crewmembers from the Space Shuttle to the data collection facility. After Shuttle wheel stop, the CTV approached the Orbiter with the rest of the NASA convoy, and the Shuttle hatch was opened within ~20 min. After a brief medical check by the NASA flight surgeons, the crewmembers exited the Orbiter, with the midodrine test subjects exiting first. The subjects doffed their ACES within 5 min and participated in the same tilt test protocol as during the preflight assessment.<br><br>Summary<br><br>Midodrine appears to prevent orthostatic intolerance in test subjects after bed rest and in astronauts after space flight when testing is conducted in a controlled laboratory setting within 2 to 4 hours after landing. It is unclear at this time whether similar effects can be expected during reentry and immediately after landing, particularly in warmer environments and/or when the crewmembers are still wearing the ACES. Accurate interpretation of the current data requires that similar data be collected in control subjects (without midodrine) on the CTV. However, concerns about drug interactions with commonly used anti-emetics and prolonged QTc intervals observed in astronauts returning from long-duration missions make the routine use of midodrine unlikely and reliance on lower-body compression garments preferable. |

| Bibliography Type: | Description: (Last Updated: 03/01/2018) |
|---|---|
| Abstracts for Journals and Proceedings | Shi S-J, Platts SH, Meck JV. "Promethazine counteracts the positive effects of midodrine on orthostatic intolerance." Presented at Experimental Biology 2006, San Francisco, California, April 1-5, 2006. FASEB J. 2006 Mar;20 (Meeting Abstracts Supplement):A1252. http://www.fasebj.org/cgi/content/meeting_abstract/20/5/A1252?sid=c6503ac3-8082-4ad9-959c-cf84c69d88d6 , Mar-2006 |
| Abstracts for Journals and Proceedings | Platts SH, Shi S-J, Meck JV. "Midodrine exacerbates promethazine-induced akathisia." Presented at Presented at Experimental Biology 2006, San Francisco, California, April 1-5, 2006. FASEB J. 2006 Mar;20 (Meeting Abstract Supplement):A1251-2. http://www.fasebj.org/cgi/content/meeting_abstract/20/5/A1251-d?sid=c6503ac3-8082-4ad9-959c-cf84c69d88d6 , Mar-2006 |
| Abstracts for Journals and Proceedings | Platts SH, Waters WW, Mitchell BM, Meck JV. "Midodrine prevents post-spaceflight orthostatic intolerance when administered 1 hour before tilt test." Presented at Experimental Biology 2004, Washington, DC, April 2004. FASEB J. 2004;18(Meeting Abstract Supplement):A1207. , Apr-2004 |
| Articles in Peer-reviewed Journals | Platts SH, Ziegler MG, Waters WW, Meck JV. "Hemodynamic effects of midodrine after spaceflight in astronauts without orthostatic hypotension." Aviat Space Environ Med. 2006 Apr;77(4):429-33. PMID: 16676655 , Apr-2006 |
| Articles in Peer-reviewed Journals | Platts SH, Shi SJ, Meck JV. "Akathisia with combined use of midodrine and promethazine." JAMA. 2006 May 3;295(17):2000-1. PMID: 16670408 ; http://dx.doi.org/10.1001/jama.295.17.2000-b , May-2006 |