Midodrine as a countermeasure for post-spaceflight orthostatic hypotension

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ABSTRACT

One possible mechanism for post-spaceflight orthostatic hypotension, which affects approximately 40% of astronauts after short duration shuttle missions is a presyncope mechanism (release of sympathetic nervous system activity, insufficient orthostatic pressor response), as illustrated by orthostatic hypotension in the lumbal perfused hindlimb model. As part of the post-flight orthostatic intolerance (OIT) countermeasure study, a phase I study determined the effectiveness of midodrine, an α1-adrenergic agonist, as an orthostatic intolerance countermeasure. The first phase of this study was to examine the orthostatic responses of six veteran astronauts after oral midodrine (10 mg) was administered to the subjects within approximately two hours after landing. In addition to the ground control, five crewmembers that were susceptible to post-spaceflight orthostatic hypotension also received a placebo pill. Midodrine was chosen as an investigational countermeasure because: it acts in place of noradrenaline on the blood vessels; it does not stimulate the central nervous system; it does not stimulate the heart directly; its peak effect is at one hour, so it can be taken at Time of Ignition (TIG). Midodrine Tolerance Test

Three months prior to flight, a single 10 mg dose of midodrine was administered orally and the subject was monitored every 15 minutes for brachial artery pressure and heart rate as they went about their normal activities for 4 hours.

Preflight tilt test

Orthostatic responses were determined ten days before flight (L-10). Blood pressure, EKG and stroke volume were acquired during five minutes of supine posture followed by up to ten minutes of 80° head-up tilt. Cardiac output, heart rate and total peripheral resistance were calculated offline.

RESULTS

PHASE I

• A single, 10 mg oral dose of midodrine did not cause any untoward hemodynamic effects on landing day in five male, non-presyncopal subjects, and prevented presyncope in one female subject.

PHASE II

• Four of ten subjects completed to date. One subject withdrew due to unpleasant side effects during tolerance test.

• Two subjects developed presyncopal symptoms on landing day.

• Although two subjects were presyncopal, hemodynamic responses onboard the CTV after midodrine was ingested inflight were similar to those from Phase I.

• Results are confounded by poorly controlled environmental variables on the CTV (temperature, motion, sound, etc).

CONCLUSIONS

• Midodrine had no untoward landing day effects on crewmembers that were not susceptible to post-spaceflight orthostatic hypotension.

• Although two crewmembers developed presyncope symptoms during landing day tilt tests, hemodynamic responses to orthostatic stress appear to be similar whether midodrine was ingested on the ground or in orbit.

• The effectiveness of midodrine as a countermeasure to immediate post-spaceflight orthostatic hypotension has yet to be determined; interpretation is difficult due to low subject number and lack of control subjects on the CTV.