Clinical Pharmacy Response to Evidence Report: Risk of Therapeutic Failure Due to Ineffectiveness of Medication

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September 30, 2013
General Review

• How well the report:
  – Explains the current state of knowledge about the risk;
  – Summarizes the critical areas of debate about the risk;
  – Identifies the main gaps in knowledge or fundamental research about the risk; and
  – Addresses possible interactions between the risk of unpredicted medication effects and other risks identified in NASA’s evidence reports.
General Review

- Current report public August 2011
  - Update to report in review cycle; publish date unknown
  - Captures essence of the risk
    - Assumptions are terrestrial practice = microgravity practice
  - Report lists seven systems that could be impacted by the risk
  - Other evidence report reviews that involve medication are compounded by the unknown aspects of this risk
    - Bone, DCS, renal stone, reduced muscle mass (IM injection)
General Review

• Two major concerns highlighted
  – Pharmacokinetics/Pharmacodynamics (PK/PD)
    • The absence of evidence doesn’t mean there is no risk
      – Extremely limited concrete information available
    • The use of medications without data to support their actual activities is a risk to the crewmember and the mission
      – Microgravity ‘patients’ are a specialized population due to the systemic changes that are known to occur
        » additional changes/issues should be expected
General Review

• Two major concerns highlighted
  – Stability of Medications
    • Answers to the questions regarding the stability of the medications are not complete
      – Do shelf-life rules apply?
      – Need solid data to support extension for future missions
      – Information would help drive contents of medical kits
Clinical Pharmacy Perspective

• Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?
• Question: Are there any issues you have raised which have NOT been addressed effectively?
  – Evidence report and the information therein are relevant to operations and in my opinion have not been addressed effectively
  – Stability of Medications
    • Medication expiration date consistently questioned
      – Resupply upmass, time, trash
      – Reality of pharmacy operations
        » Pharmacy regulations come into play
        » Market changes
      – Medical kit design and selection of medication
Clinical Pharmacy Perspective

• Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?

• Question: Are there any issues you have raised which have NOT been addressed effectively?
  – Confounding elements – is the drug ‘bad’ or is there a PK/PD issue?
    • ‘Bad’ could mean expired, altered or both to the point of ineffectiveness
  – Clinical and operational issues blend
    • Changes to body systems
    • Medications used to treat symptoms
    • Medications used to handle occupational hazards
    • Polypharmacy at play
    • Environmental/engineering constraints
Clinical Pharmacy Perspective

• Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?

• Question: Are there any issues you have raised which have NOT been addressed effectively?
  – Documentation of medication usage information
    • Processes evolving to get better information
    • Expect gaps due to crewmember’s desire
Clinical Pharmacy Perspective

• We don’t know the extent to which spaceflight alters pharmacodynamics
  – Actively discussed ‘to do’ or ‘not to do’ research
    • Anecdotally there is no clinically significantly alteration
      – What about the asymptomatic clinically significant alteration?
  – Clinical Pharmacy: ‘to do’ review and research
    • The issue needs to be studied
      – New clinical issues have developed during the ISS missions
      – Is medication use a factor in new clinical issues? If so, what is the cause?
    • Exploration missions
      – Reasonable to expect additional concerns/issues
Clinical Pharmacy Perspective

- Insights regarding drug stability (pre, during and post-flight)
  - Pre-flight is the terrestrial model
    - Pharmacy Ops works hard to keep tabs on appropriate storage until spaceflight
      - Temperature data captured during shipment
  - During flight
    - Current medical kits are stored in their manufacturer’s packaging wherever possible
    - Repackaging is kept to a minimum
    - Research report pending on 6 medications returned from spaceflight
  - Post-flight
    - Medications not returned routinely
Clinical Pharmacy Perspective

• Insights regarding drug stability (pre, during and post-flight)
  – Forward work
    • Integrated team looking at long-term and exploration flight concerns
    • Work being conducted through ExMC
Clinical Pharmacy Perspective

• Have any mitigation strategies regarding drug stability of particular dosage forms been altered as a consequence of the work Dr. Putcha's lab has been involved in (and published in the last 10 years?) Please provide specifics.
  – Mitigation strategies to date have been to select medications that have not been shown to be altered
  – Change in how most medications are packed (now using manufacturer’s packaging wherever possible)
  – Ongoing research by the Pharmacology Lab
Clinical Pharmacy Perspective

- Are you aware of any specific drug misadventures which occurred as a consequence of likely altered PK/PD of a medication during spaceflight? Please provide specifics.
  - I am not aware of any specific drug misadventures that have occurred as a consequence of likely altered PK/PD.
- A systematic review has not been done to date.
- Processes are under development to use an integrated approach to medication use evaluation with a multi-disciplinary team.
Clinical Pharmacy Perspective

• In your professional opinion, what should the research priorities be with regards to PK/PD and spaceflight?
  – Start with a baseline
    • Based on the clinical medication use evaluation, direction for PK/PD research is an expected outcome
  – In-flight research is necessary
    • One year mission
  – Needs to happen while on station and continue through to the next generation of missions
Clinical Pharmacy Perspective

• Evidence Report Review Summary
  – Current report captures the knowledge gap that exists with respect to the risk of therapeutic failure due to ineffectiveness of medication
  – Active research requests being made – hopefully translates to funding
  – The use of medications will continue to occur as we transition into exploration missions
  – Need to understand the impacts of the environment on medications and the interactions between pharmacologic therapy and the microgravity population to better inform clinical care