Interstellar Interventions to Create Cosmic Calm

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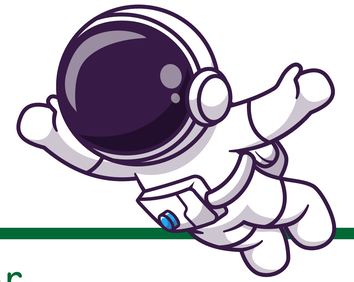

Abstract

Benzodiazepines**, such as lorazepam, are the **standard of care** for **status epilepticus** and are one of the first-line treatments of **acute psychogenic agitation**. However, the commonly-used lorazepam necessitates refrigeration and restocking every 60 days, which can be a challenge in austere environments. Currently, NASA employs intramuscular diazepam injections (that don't need refrigeration) in this role. Concerns exist, though, for the erratic absorption of diazepam via intramuscular route, and its metabolites have an extended half-life. Recent data suggests that **midazolam** is also **stable without refrigeration, quicker acting, more consistently absorbed,** and **superior in the management of agitation and status epilepticus.

Methods 🔬

A broad literature search was performed to identify items of interest to teams planning for missions in austere environments.

Storage Characteristics 📦

McMullan et al. (2014) examined lorazepam, diazepam, and midazolam in EMS services over a period of 120 days, and lorazepam but **not midazolam or diazepam** was associated with significant degradation (avg 31.6°C or 88.9°F).

Routes of Administration 💉💊👃

Meta-analysis: Chhabra et al. (2021) found **intranasal midazolam was as effective** as IV lorazepam and IV or rectal diazepam but **had a shorter time** from hospital arrival to seizure cessation.

Hung et al. (1996) found a **wider variability in blood concentrations** of diazepam after intramuscular injection as compared to midazolam.

Efficacy in Agitation 😠

- Nobay et al. (2004) conducted a head-to-head comparison of 5mg IM midazolam, 2mg lorazepam, or 5mg haloperidol with n=111. **IM midazolam was fastest to sedation** (18.3, 32.2, and 28.3 minutes respectively) **and arousal** (81.9, 217.2, and 126.5 minutes).
- Martel et al. (2005) with n=144 found **midazolam was faster than droperidol and ziprasidone** in achieving adequate sedation (15 versus 30 minutes).
- Klein et al. (2018) compared haloperidol, ziprasidone, olanzapine, and midazolam in the emergency department with n=737. **Midazolam had the highest % of adequately sedated patients** after 15 minutes but also the highest rate of additional rescue medication needed.

Efficacy in Status Epilepticus 🏥

- Glauser et al. (2016) gives guidelines that benzodiazepines are first-line for status epilepticus.
- The RAMPART study (Silbergleit 2013) with n=611 showed **IM midazolam's time savings and effectiveness** in seizure cessation, hospitalization, and ICU admission **compared to IV lorazepam**.
- Meta-analyses: McMullan et al. (2010) with n=774 showed **midazolam superior to diazepam by any route for seizure**, and Zhao et al. (2016) with n=1821 **favored non-IV midazolam and IV lorazepam over diazepam** for pediatric status epilepticus.

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Midazolam Autoinjector

The midazolam autoinjector has recently been approved by the FDA and U.S. Department of Defense for the treatment of status epilepticus and prolonged seizures in adults in Aug 2022 (Rafa Laboratories).

Conclusions ✅

Midazolam as compared to other benzodiazepines:

- **Superior to lorazepam** in austere environments due to: shelf stability, efficacy of seizure control and resolution of acute agitation, time to onset, and variable routes of administration.
- **Superior to diazepam** in austere environments due to: efficacy of seizure control, time to onset, and variable routes of administration. Shelf stability of diazepam appears similar to midazolam and data is lacking as to agitation control with diazepam (Kim et al., 2021).
- Is **more reliably and more quickly absorbed** than diazepam.

Recommendations 💡

For the purposes of deep-space exploration, or other long-distance/long-term expeditions where assistance or rescue is unlikely or impossible, **midazolam is likely the most efficacious and versatile benzodiazepine** to have on board for multiple unexpected contingencies.

