UNIVERSITY OF MINNESOTA ROCHESTER

Journey of Midazolam

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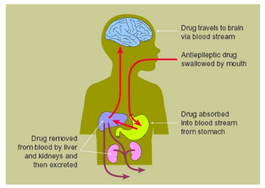
Introduction

- Midazolam is a very versatile drug. It is used in end of life sedation, pediatric dentistry, seizures, and anxiety
- But, more specifically midazolam is a sedative, that is why it can be used to treat all of these different things.
- it also comes in different forms: nasal, injection, and pill form
- Midazolam is most effective in children
- Midazolam is a benzodiazepine, which affects the nervous system
- Midazolam targets the nervous system, more specifically it targets the GABA neurotransmitter. In targeting the GABA neurotransmitter, midazolam slows the brain down and stops anxiety and seizures



Pre-Clinicals

- Rats were used in testing the safety of midazolam because:
  - genetically similar to humans
  - small
  - easy to handle
  - fast reproduction rate
- When low doses of the drug were used in rats, Pain (1989) found that midazolam has no adverse effects on the locomotion of the rats
- Midazolam also passed a series of tests that proved it was working for its intended purpose
  - reducing fear
  - alleviating anxiety

Discussion/Conclusion

- Midazolam has shown itself to be a safe and effective alternative to related medications
- Has been used in the treatment of pre-operational stress and status epilepticus
- Less adverse effects than other benzodiazepines
- Can be used in patients of all ages
- Multiple routes of administration
- Meets safety requirements
- Effective in seizure reduction and decreased anxiety

References

Reference link

Clinicals

- Phase I
  - Examines efficacy and safety of midazolam
  - Phase I trial done by Shin-Ichiro Hamano and others
    - Intravenously administered
    - 34 status epilepticus pediatric patients
    - Open-label, multicenter
    - Initial bolus of 0.15 mg/kg was given, with additional doses of 0.1-0.3 mg/kg up to a cumulative dose of 0.6 mg/kg (Hamano et. al, 2019)
    - Non-participant observation
  - Results
    - Seizure termination rate with bolus midazolam was 88% (Hamano et. al, 2019)
    - Unfavorable reactions were recorded in three of the patients

Clinicals

- Phase II
  - Determining if the drug is ultimately useful and effective compared to its predecessor treatment plan
  - Finding a safe and effective administration method is a crucial step to continue approval for the drug
  - Quantitative data has shown improvement of the effectiveness in children and adults who struggle with pre-existing conditions
  - Parenteral administration in children has shown an increase in discomfort and anxiety, and can be traumatic
  - Dr. Peterson (1990) conducted a study to develop a safe method for oral administration of midazolam in children. The oral agent of midazolam has a bad taste that is very difficult to mask. During trials, many children refused to take or expectorated the drug
  - In 1990, a study by the Society for Anesthesia and Resuscitation of Belgium tested midazolam for pediatric premedication in 128 children. This study showed that rectal administration in children often led to a sense of embarrassment, discomfort, and side-effects such as: intraoperative defecation, rectal pain, and itching
  - A study conducted by Wilton NCT (1998) showed nasal administration of midazolam to be effective. This study showed that children were passive and mildly sedated with little to no side effects, which is beneficial for surgeries that do not require full sedation
  - Conducting studies and finding safe and reliable administration methods of midazolam has been positive in both pediatric treatment and any patient who has a medical prognosis or disability that prevents them from receiving proper administration parenterally, orally, or rectally