Lorazepam Injectable Shortage (not oral, only injectable) 2020.04.09 S Powsner MD

Situation: Lorazepam for injection is in short supply. It's being used for intubated patient care, much increased by COVID-19 Pandemic.

Background: Lorazepam is routinely used to keep patients comfortable & relaxed when intubated and mechanically ventilated. COVID-19 is causing much more Lorazepam than usual to be used at YNHH and around the country, leading to a shortage of injectable agent. The shortage creates a problem for treatment of very agitated psychiatric patients, and for treatment of alcohol withdrawal, and other conditions.

Assessment: Lorazepam is hard to replace as a general-purpose agent that reduces anxiety / agitation from many causes, and yet has little effect on the cardiopulmonary system. It is available for oral, intramuscular, and intravenous administration. Lorazepam is also easily metabolized (by glucuronidation). It has a relatively rapid onset of action, and an intermediate half-life.

Diazepam is currently available in adequate supply and can be administered both orally and parenterally. However, its intramuscular absorption is not as fast as its oral absorption, and its serum peak is not as great because it takes longer overall to be absorbed. Indeed, it may appear to be significantly less sedating based on one study. However, like Lorazepam, it is a general-purpose agent and has little cardiopulmonary effect.

Recommendation:

1) Oral Lorazepam 1-2mg will work as fast as intramuscular Lorazepam. Try to get the patient to accept it. Oral Diazepam 10mg is almost as fast, if the patient happens to prefer it.

2) Use Diazepam 10mg IM in place of Lorazepam 1mg IM for acute agitation. Unfortunately, it cannot be mixed with haloperidol, and at a concentration of 5mg/1ml, it would not fit into one IM injection with anything else. So, Haloperidol + Diazepam by injection will imply two injections. Overall, Diazepam is likely to sedate the patient longer.

3) Diphenhydramine 25-50mg IM could be used and may be preferable in patients below age of 18.

4) Consider using Haloperidol alone or with Diphenhydramine or with oral Benztropine later if necessary. It is not necessary to give 5mg all the time; lower doses can be used if agitation is not so severe.

5) Chlorpromazine 50mg-100mg IM could be used, but only 50mg fits in a single injection. NB: Chlorpromazine is a potent alpha-adrenergic blocker as well as being quite sedating. It is not recommended for the elderly or anyone on beta-blockers (they may not be able to maintain their blood pressure). It is not recommended in patients using cocaine and other stimulants-- we have had it lead to extreme sedation for extended periods.

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Bibliography:

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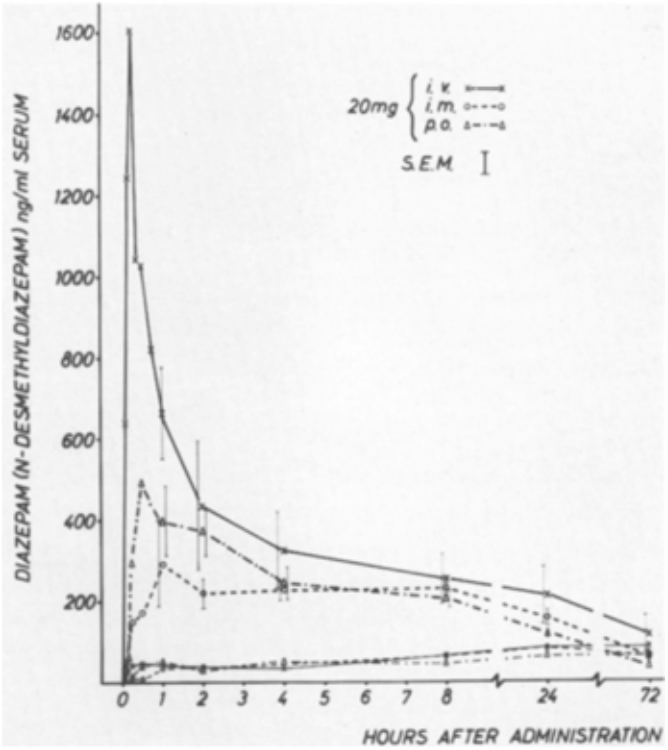
(from Hillestad et al p.480)

Fig. 1. Serum concentrations of diazepam and N-desmethyldiazepam following 20 mg diazepam administered intravenously, intramuscularly, and orally. Mean values in 6 normal subjects. Thick line: diazepam; thin line: N -desmethyldiazepam.



IM < PO < IV from peak until 4h later

(lower curve is metabolite)