



Medical Direction and Practices Board

WHITE PAPER

Seizure Management

Status epilepticus represents one of the true emergency conditions in which early intervention by EMS can significantly reduce morbidity and mortality. The faster status epilepticus is halted, the less refractory seizures become and the fewer complications result. The updates to the 2013 Maine EMS protocols for the treatment of seizures are based on compelling, new evidence presented in February, 2012 in the New England Journal of Medicine in a study titled Intramuscular Versus Intravenous Therapy for Prehospital Status Epilepticus, Silbergleit et al.

The above study, referred to by the authors as the RAMPART (Rapid Anticonvulsant Medication Prior to Arrival Trial) was a randomized, double-blinded, phase three, non-inferiority clinical trial. It compared the efficacy of intramuscular midazolam (Versed) to standard dosing of intravenous lorazepam (Ativan). Patients weighing more than 40kg received either 10mg of intramuscular midazolam and 4mg of intravenous placebo or 10mg intramuscular placebo and 4mg intravenous lorazepam. Patients weighing 13-40kg received 5mg of intramuscular midazolam and 2mg intravenous placebo or 5mg intramuscular placebo and 2mg intravenous lorazepam. Lorazepam has long been the preferred agent in the Emergency Department for seizure treatment but has not been used much in EMS due to the need for refrigeration. Due to potential difficulties in establishing IV access in a seizing patient, the authors chose the intramuscular route for midazolam which, they observed, had already been used in many EMS systems. Patients included children with an estimated weight of 13kg or more and adults. Patients were blindly randomized into intramuscular midazolam or intravenous lorazepam. Each patient received both an intramuscular dose and an intravenous dose of medication, one of which was a randomized placebo medication. The primary outcome for the study was seizure termination prior to arrival at the Emergency Department. Secondary outcomes were rapidity of seizure termination once the study medication box was opened, frequency and length of hospitalizations, the need for acute endotracheal intubation and acute seizure recurrence. Seizure recurrence was defined as seizures recurring in the first 12 hours in the hospital after termination of seizures by EMS.

The results of the RAMPART study were compelling. Nearly 900 patients were assigned randomly to treatment groups and included equal numbers of males and females as well as children and geriatric patients. Seizure activity was noted to be absent on arrival to the ED in 73.4% of the intramuscular midazolam patients and 63.4% of the intravenous lorazepam patients. Not surprisingly, failure to gain intravenous access was cited as the major problem in giving intravenous lorazepam.

The authors of the RAMPART study concluded that intramuscular midazolam was at least as effective as intravenous lorazepam for status seizures. Removing the challenge of intravenous access made the intramuscular route quicker and ultimately more effective than the current standard of care with intravenous lorazepam.

The Medical Direction and Practice Board has reviewed and discussed the RAMPART study and have elected to adapt our protocols based on what we feel is excellent clinical evidence. The new protocols will be as follows:

For adult seizures lasting longer than 5 minutes or 5 minutes of intermittent seizures with no return of consciousness:

Midazolam 10mg IM or, if intravenous access is available, 5mg IV. Repeat doses are to be 5mg IV/IM/IO every 5 minutes up to 3 doses. If seizures persist, contact On Line Medical Control.

For obviously pregnant patients or up to 2 weeks post partum:

Magnesium sulfate 4gm IV/IO over 10 minutes or 8gm intramuscularly injected, 4mg into each buttock.

For pediatric Seizures lasting longer than 5 minutes or 5 minutes of intermittent seizures with no return of consciousness:

Midazolam 0.3mg/kg intramuscular injection up to a maximum of 10mg or 0.15mg/kg IV up to a maximum of 5mg .

Rectal midazolam can also be given at 0.3mg/kg up to 10mg maximum.

If the agency carries an intranasal atomizer, 0.2mg/kg up to a maximum of 6mg with half of the dose administered into each nostril over 15 seconds.

Notice that these initial doses are significantly higher than what was previously recommended in the 2011 Maine EMS protocols and are higher than many of our Emergency Department colleagues are used to. These doses are, however, are in line with those used in the RAMPART study and were shown to be safe and effective. The MDPB feels strongly that by treating status seizures earlier with higher doses of midazolam, patients will benefit by having earlier termination of seizures, fewer recurrent seizures, shorter hospitalizations, fewer ICU admissions and reduced need for intubation. The EMS provider in Maine should feel confident in adopting this protocol knowing that this practice is state of the art care for patients based on the most timely, peer reviewed clinical evidence available today.

References:

1. Silberglert R, et al. Intramuscular versus Intravenous Therapy for Prehospital Status Epilepticus. N Engl J Med 2012;366: 591-600.