Disaster Medicine and Public Health Preparedness

www.cambridge.org/dmp

Responder Tools

Cite this article: Wassner C, Creary K, Miele J, Flynn C, Wittman I. Use of a nerve agent antidote-dosing tool for mass casualty incident emergency preparedness. *Disaster Med Public Health Prep*. **17**(e337), 1–4. doi: https://doi.org/10.1017/dmp.2023.5.

Keywords:
mass casualty incident; nerve agents; disaster planning; emergency preparedness; antidotes

Corresponding author:
Chanie Wassner,
Email: cwassner1@gmail.com.

Use of a Nerve Agent Antidote-Dosing Tool for Mass Casualty Incident Emergency Preparedness

Chanie Wassner PharmD, BCCCP, BCIDP[1], Kashif Creary MPA, PA-C[2], Johanna Miele MPH[2], Caitlin Flynn CHSP, CHPCP[2] and Ian Wittman MD[2]

[1]NYU Langone Hospital – Brooklyn, Department of Pharmacy, Brooklyn, New York, USA and [2]NYU Langone Hospital – Brooklyn, Department of Emergency Medicine, Brooklyn, New York, USA

Abstract

Objective: Nerve agent attacks pose a serious threat worldwide and ensuring optimal readiness is essential to management. We review a mass casualty incident (MCI) drill in a busy urban New York City Emergency Department incorporating an antidote-dosing tool.

Methods: Emergency Management and Preparedness planned an MCI drill involving a nerve agent exposure and engaged the pharmacy department to participate on a more comprehensive level. The clinical pharmacist prepared a treatment tool with antidote dosing recommendations to distribute to team members participating in the drill.

Results: During the launch of the exercise, all clinicians involved reviewed the antidote-dosing tool with the pharmacy team members. Because of the ease of use, limited time was necessary to review the dosing tool before the start of the exercise. After the exercise, feedback regarding the use of the tool was very positive and participants appreciated the tool for use in a theoretical emergency that they have had limited experience managing.

Conclusions: Optimizing team preparedness with accessible and practical dosing tools may be a helpful addition to emergency preparedness for chemical and biological events with the potential for many casualties.

Acetylcholinesterase inhibitors (AChEIs) are xenobiotics that bind acetylcholinesterase, the enzyme responsible for breakdown of acetylcholine.[1] AChEIs chemical groups are classified as quaternary alcohols, carbamates, and organophosphates (OPs), with the latter having the most potential for human harm. With industrial exposures, intentional overdoses, or as a chemical weapon, AChEIs can lead to an overwhelming accumulation of acetylcholine in the peripheral and central nervous systems.[2]

Since World War I, there has been a significant expansion in the use of the subcategory of OPs referred to as nerve agents for the purpose of chemical warfare. Nerve agents began to be mass-produced as chemical weapons by Nazi Germany during World War II, and since then, second-, third-, and fourth-generation agents have been developed.[3] Fourth-generation agents are the most potent nerve agents known to date, and are sometimes referred to as Novichoks ("newcomer" in Russian).

The use of a nerve agent in a chemical attack, although rare, has the potential for catastrophic morbidity and mortality, as seen with the 1995 Tokyo sarin attack that injured over 5000 people.[4] The CHEMPACK program was created as part of the Strategic National Stockpile and was designed for the forward placement of the necessary antidotes in the setting of a potential large-scale nerve agent attack in the United States.[5] The possibility of terror attacks, particularly in New York City (NYC), proves the need for defense measures against chemical, biological, radiological, and nuclear (CBRN) agents. Since the 9/11 terror attacks occurred in NYC in 2001, NYC hospitals have prioritized CBRN planning across several sectors including law enforcement, fire department, emergency medical services, public health, and health-care stakeholders. Additionally, after several recent reports of poisoning using fourth-generation agents, health-care facilities renewed their interest in becoming better prepared for nerve agent exposure response.[3]

Because of the infrequency of CBRN events, preparation is critical and an ongoing challenge for health-care and emergency systems to ensure proper response to a mass casualty incident (MCI) involving hazardous agents.[4,6] One of the most well prepared countries for CBRN response due to previous and ongoing conflicts is Israel.[2] In a review of MCI emergency preparedness in 23 acute care hospitals in Israel, a high rate of staff knowledge was observed for responding to rare events such as toxicological and biological attacks.[6] This was despite most health-care workers in the system not having practical experience responding to such events. The review noted that each emergency department (ED) is supplied with information sheets

SDMPH
SOCIETY FOR DISASTER MEDICINE & PUBLIC HEALTH

with the management for each type of hazard immediately accessible to them to avoid clinicians having to recall from memory or spend time finding resources.

Effective hospital disaster preparedness should engage multiple stakeholders along with ancillary departments and external agencies. The pharmacy department may be an underused resource when engaging in MCI planning.[7] In addition to ensuring proper antidote stocking, storage, and dispensing in the event of an occurrence, pharmacy resources can be accessed to supplement clinical support for antidote management strategies. Because of the rarity of such an event, many institutions may not have a standardized dosing tool for OP incident management.

Methods

Our institution is a busy, 450-bed, academic Level 1 Trauma Center in NYC accustomed to unpredictable patient surges and multiple triage events including motor vehicle accidents, gunshot wounds, and multi-dwelling fires. Due to the urban location of the hospital, as well as proximity of the surrounding industrial areas, leadership has prioritized chemical event planning.

In the planning stage for a chemical incident MCI drill, it was proposed that medical staff would benefit from having a succinct antidote-dosing tool to rapidly disseminate during the drill. While the Centers for Disease Control and Prevention (CDC) maintains a job aid website for initial emergency department treatment, the algorithm does not differentiate between mild/moderate and severe manifestations, or provide detailed administration instructions and guidance.[8] Moreover, in a true nerve agent attack, it is reasonable to anticipate that medical staff may be overwhelmed with the additional task of locating an antidote dosing guide, while attempting to manage an unpredictable patient volume and acuity level under extreme psychological stress. Furthermore, in a catastrophic attack, Internet or online resources may be inaccessible. In collaboration with the full-scale exercise (FSE) planning team, the clinical pharmacist developed an antidote-dosing guide to use for the planned MCI chemical agent drill.

The dosing guide was created to be a 2-sided 1-page tool (Figure 1). Information provided on the first side included examples of nerve agents, personal protective equipment warnings, and pharmacy contact numbers. The tool included antidote-related pharmacotherapy information such as mechanisms of action, concentrations supplied, and administration instructions and goals of therapy for the primary used antidotes and therapies including atropine, pralidoxime, and benzodiazepines.

The second page was modeled after dosing guidance provided by the NIH (National Institutes of Health) and CDC, with additional therapeutic considerations added to the dosing guide.[2,8–10] Treatment recommendations were stratified by level of toxicity and symptomology, as well as by age and weight. The pharmacy department maintains a 24/7 decentralized pharmacy satellite in the ED. Physical copies of the dosing guide were kept with stocked antidotes in the ED satellite, and as a supplement to the MCI Response Toolkit.

Antidote supplies were reviewed and doses calculated for an estimated initial patient influx to treat such an incident. Based off this review, our pharmacy department optimized par levels of stored antidotes to ensure adequate amounts for emergent treatment before the receipt of a theoretical authorized CHEMPACK distribution.

This exercise did not involve patient subjects and was exempt from Institutional Review Board (IRB) review.

Results

Per the internal MCI standard drill protocol, an interdisciplinary pre-event huddle was completed, where all required personnel received known and pertinent casualty information. Delineation of clinical, nursing, pharmacy, security, and other leadership roles were discussed. Clinical pharmacists and other members of the pharmacy team were deployed to the ED for the drill to serve as subject matter experts and facilitate medication dosing, preparation, and pharmacotherapy questions. All clinicians, nursing, and pharmacy team members reviewed and discussed the OP nerve agent tool with the developers of the dosing tool in advance of patient arrival to determine theoretical treatment plans for exercise patients. Because of the self-explanatory nature of the guide, limited training time was necessary for team members to familiarize themselves with the treatment algorithm. To assess the key objectives of the exercise, evaluators were strategically placed at the entrance to the emergency department, the pharmacy, and within treatment areas.

After the drill, a debriefing was performed and participants were queried for feedback, including specifics of using the nerve agent antidote tool. Clinician and nursing feedback specified that having a concise algorithmic tool expedited antidote dosing and provided medication administration clarity, as most were unfamiliar with management. After the exercise, some modifications were made to the antidote dosing tool, including clarification of dilution and administration instructions and highlighting mg/kg for pediatric weight-based dosing.

Limitations

The limitation of this report is that it was performed at a single center with a small cohort of staff in a single exercise. No comparison of the outcome of this MCI drill was made to any previous drills without the resource of an antidote-dosing tool. Feedback on using the dosing tool was only received from the team members participating in this MCI drill. Although an MCI drill is designed to mimic real life experiences, a true catastrophic MCI can be unpredictable and may transpire differently.

Discussion and Conclusions

To our knowledge, this is the only publication detailing an MCI drill for nerve agent chemical exposure using an antidote-dosing tool for adult and pediatric patients. In a survey by Madsen and Greenberg of 89 ED directors in 12 highly populated US cities, only 18.3% of respondents reported being very confident that their training for MCIs had prepared their departments to respond to a chemical attack.[5] This survey also highlighted major deficiencies in knowledge regarding antidote stocking and treatment capabilities for a theoretical nerve agent incident.

Incorporating dosing tools has the potential to empower providers to efficiently make treatment determinations during a potential catastrophic event when time, experience, and resources are limited. All participating providers in our MCI drill used the dosing guide while treating exercise patients, and a positive response was reported in anonymous post exercise surveys.

https://doi.org/10.1017/dmp.2023.5 Published online by Cambridge University Press

MANAGEMENT OF SUSPECTED NERVE AGENT TOXICITY IN THE EMERGENCY DEPARTMENT

Nerve agents affect the body's ability to process acetylcholine causing a cholinergic toxidrome.
Examples include pesticides, as well as chemical warfare agents (tabun, sarin, soman, VX, VE, Novichok)

Pharmacy Contact Numbers:

- ED Satellite Phone Number: XXX-XXX-XXXX
- Main Pharmacy Number: XXX-XXX-XXXX
- ED Clinical Pharmacotherapy Specialist Number (available weekdays): XXX-XXX-XXXX

*numbers redacted for publication

Sequence of Initiating Treatment:

- STEP 1: All **staff must use proper personal protective equipment** when in contact with patients per Emergency Management Protocol
- STEP 2: **Patient decontamination must be performed** as appropriate
- STEP 3: **Provide antidotal therapy**. Initial doses are located in the ED satellite. Contact pharmacy and/or Emergency Management for supply restock in case of Mass Casualty Incident

Medication	Mechanism of Action	Concentrations Supplied	Administration Instructions and Goal in Therapy
Atropine	Blocks acetylcholine effects by competitive antagonism at muscarinic receptors	Atropine sulfate 0.4 mg/mL (20 mL multi-dose vials)	IV administration: **Undiluted rapid IV push** Continue until secretions have diminished and breathing is comfortable or airway resistance has returned to near normal *Note: Atropine doses are significantly higher than for other conditions* • Mild/moderate: Repeat atropine interval is 5 – 10 minutes • Severe: Repeat atropine interval is 2 – 5 minutes
Pralidoxime (2-PAM)	Oxime acetylcholinesterase reactivator	Pralidoxime 1000 mg/vial	IV administration: Reconstitute 1000 mg vial with 20 mL SWFI for concentration of 50 mg/mL. **IV push dose slowly over ≥ 5 minutes** • Repeat dose may be given about one hour after first dose if muscle weakness not improved. Additional doses may be given every 10-12 hours if muscle weakness has not improved and atropine still required in previous 12 – 24 hours IM administration: Reconstitute 1000 mg vial with 3.3 mL SWFI for concentration of 300 mg/mL • Mild: 1 injection of 600 mg; wait 15 minutes. If after 15 minutes symptoms persist, repeat with 2nd dose of 600 mg. If after additional 15 minutes symptoms persist, repeat with 3rd dose of 600 mg for total of 1800 mg. • Severe symptoms: 3 injections of 600 mg in rapid succession for total dose of 1800 mg • Persistent symptoms after 3 injections of 600 mg: May repeat the series about 1 hour after first series
Benzodiazepines	Terminates seizure activity associated with severe nerve agent toxicity	Diazepam 5 mg/mL (10 mL multi-dose vials) Midazolam 5 mg/mL vial	IV administration: Undiluted, slow IV push IM administration: Undiluted, deep into muscle mass Administer to all severe toxicity patients; repeat as needed for seizures

See chart on reverse for dosage recommendations

Patient Age	Antidote Recommendations: Mild/Moderate Toxicity	Antidote Recommendations: Severe Toxicity	Additional Treatment Considerations
Symptoms	Localized swelling, muscle fasciculations, nausea/vomiting, shortness of breath	Unconsciousness, convulsions, apnea, flaccid paralysis, severe respiratory distress requiring assisted ventilation	**Benzodiazepines should be administered in severe cases whether seizures are witnessed or not** • Diazepam IV is preferred and FDA-approved for this indication, but midazolam and lorazepam are acceptable alternatives • If diazepam and midazolam are unavailable, lorazepam is dosed at 0.1 mg/kg IV/IM/IO up to a max of 4 mg/dose **Assisted ventilation should be started as needed after antidote administration** • If possible, if patient is hypoxic secure airway prior to atropine administration **Respiratory distress refractory to maximal anticholinergic therapy can consider:** • Albuterol 2.5 mg/3 mL INH • Methylprednisolone 1 – 2 mg/kg IV • Magnesium 2 g IV **Antidotes should be administered to pregnant women at adult doses** if there is a true concern for toxicity and should not be withheld because of concerns for teratogenicity SWFI = sterile water for injection IV = intravenous IM = intramuscular IO = intraosseous INH = inhalation *2-PAM = Pralidoxime = Prototam
Infant (0-2 years; 3 – 12 kg)	Atropine 0.05 mg/kg (min: 0.1 mg, max 5 mg) IV/IO/IM AND 2-PAM* 15-30 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM	Atropine 0.1 mg/kg (min: 0.1 mg, max 5 mg) IV/IO/IM AND 2-PAM 45 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM; AND Diazepam 0.2-0.5 mg/kg (max 10 mg) IV/IO/IM OR Midazolam 0.15 mg/kg (max 10 mg) IV/IO/IM/IN	
Child (3-7 years; 13-25 kg)	Atropine 1 mg IV/IO/IM AND 2-PAM 15-30 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM	Atropine 2 mg IV/IO/IM or Atropine 0.1 mg/kg (min: 0.1 mg, max 5 mg) IV/IO/IM AND 2-PAM 45 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM; AND Diazepam 0.2-0.5 mg/kg (max 10 mg) IV/IO/IM OR Midazolam 5 mg IV/IO/IM/IN	
Child (8-14 years; 26-50 kg)	Atropine 2 mg IV/IO/IM AND 2-PAM 15-30 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM	Atropine 4 mg IV/IO/IM AND 2-PAM 45 mg/kg (max 1000 mg IV; 2000 mg IM) IV/IO/IM; AND Diazepam 0.2-0.5 mg/kg (max 10 mg) IV/IO/IM OR Midazolam 5 mg IV/IO/IM	
Adolescent (>14 years)/Adult/Pregnant	Atropine 2-4 mg IV/IO/IM AND 2-PAM 600 mg IV/IO/IM	Atropine 6 mg IV/IO/IM AND 2-PAM 1800 mg IV/IO/IM; AND Diazepam 10 mg IV/IO/IM OR Midazolam 10 mg IV/IO/IM/IN	
Elderly/Frail	Atropine 2 mg IV/IO/IM AND 2-PAM 10 mg/kg (max 2000 mg) IV/IO/IM	Atropine 2-4 mg IV/IO/IM AND 2-PAM 25 mg/kg (max 2000 mg) IV/IO/IM; AND Diazepam 10 mg IV/IO/IM OR Midazolam 10 mg IV/IO/IM/IN	

References:
https://www.cdc.gov/nceh/demil/articles/initialtreat.htm
https://chemm.hhs.gov/na_hospital_mmg.htm
https://chemm.hhs.gov/nerveagents/FGA_Medical_Management_Guidelines_508.pdf
Markenson D, Redlener I. Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidence-based consensus process. *Biosecur Bioterror*. 2004;2(4):301-19.
Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e. McGraw Hill; Accessed July 28, 2021.

Prepared by: Chanie Wassner, Pharm.D
Updated: November 2022

Figure 1. Nerve Agent Antidote-Dosing Tool

https://doi.org/10.1017/dmp.2023.5 Published online by Cambridge University Press

To best prepare for a nerve agent MCI, it is imperative that the ED work together with their disaster response teams and pharmacy management to establish antidote supply par levels and plans for distribution, as well as consider engaging clinical pharmacists to create an easy-to-use management guide. Maintaining such a guide in addition to functioning as a dosing tool for provider decision support, allows the pharmacy department to ensure specific drugs, available concentrations, and par levels are regularly updated on the institution level. In general, MCI drills focus on key operational competencies (eg, triage) and often do not provide a strong focus on methods for clinical treatment and acute stabilization of patients. With the threat of nerve agent attacks an ongoing concern, it is imperative to augment health-care institutional emergency preparedness and address the clinical knowledge and operational gaps for CBRN events by developing tools to maximize efficiency in times of crisis.

Author contributions. C.W., K.C., and I.W. conceived the idea for the manuscript. C.W., K.C., J.M., C.F., and I.W. participated in planning and carrying out the MCI exercise drill. C.W. took lead in preparing manuscript for submission. All authors contributed to writing the final manuscript.

Funding. The authors report no financial disclosures regarding the content of this manuscript.

Conflict of interests. The authors report no conflicts of interest regarding the content of this manuscript.

Content disclosure. This publication is not endorsed by the CDC, NIH, Strategic National Stockpile or CHEMPACK program.

Target learning audience. Emergency Medicine providers and management, Hospital pharmacists

References

1. **Vanderah TW, Pappano AJ.** Cholinoceptor-activating & cholinesterase-inhibiting drugs. In: Katzung BG, Vanderah TW. eds. *Basic & Clinical Pharmacology, 15e*. McGraw Hill; 2021. Accessed April 15, 2022. https://accessmedicine.mhmedical.com/content.aspx?bookid=2988&sectionid=250594730
2. **Suchard JR.** Chemical weapons. In: Nelson LS, Howland M, Lewin NA, *et al.* eds. *Goldfrank's Toxicologic Emergencies, 11e*. McGraw Hill; 2019. Accessed February 18, 2022. https://accessemergencymedicine.mhmedical.com/content.aspx?bookid=2569&sectionid=210264855.
3. **Vale JA, Marrs TC** OBE, Maynard RL CBE. Novichok: a murderous nerve agent attack in the UK. *Clin Toxicol (Phila).* 2018;56(11):1093-1097.
4. **Tokuda Y, Kikuchi M, Takahashi O, *et al.*** Prehospital management of sarin nerve gas terrorism in urban settings: 10 years of progress after the Tokyo subway sarin attack. *Resuscitation.* 2006;68(2):193-202.
5. **Madsen JM, Greenberg MI.** Preparedness for the evaluation and management of mass casualty incidents involving anticholinesterase compounds: a survey of emergency department directors in the 12 largest cities in the United States. *Am J Disaster Med.* 2010;5(6):333-351.
6. **Siman-Tov M, Davidson B, Adini B.** Maintaining preparedness to severe though infrequent threats – can it be done? *Int J Environ Res Public Health.* 2020;17(7):2385.
7. **Krajewski M, Sztajnkrycer M, Báez AA.** Hospital disaster preparedness in the United States: new issues, new challenges. *Int J Rescue Disaster Med.* 2004;4(2):1-6.
8. **Centers for Disease Control and Prevention**. Emergency room procedures in chemical hazard emergencies: a job aid. Updated May 31, 2013. Accessed February 4, 2022. https://www.cdc.gov/nceh/demil/articles/initialtreat.htm
9. **US Department of Health & Human Services**. Fourth generation agents: medical management guidelines. Updated January 2019. Accessed February 18, 2022. https://chemm.hhs.gov/nerveagents/FGA_Medical_Management_Guidelines_508.pdf
10. **Markenson D, Redlener I.** Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidence-based consensus process. *Biosecur Bioterror.* 2004;2(4):301-319.

https://doi.org/10.1017/dmp.2023.5 Published online by Cambridge University Press