Availability of Nerve Gas Antidotes at Emergency Pharmacy in Taiwan

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Abstract

Incident chemical attack was one of the devastating man-made disasters. To investigate the hospital stockpiling for nerve agent antidote, we studied the safety deposit of atropine as an indicator in 10 emergency response hospitals in Taipei. Two of them were tertiary medical center, and the remaining eight secondary referral hospitals. The average amount of safe deposit was calculated from January 2002 to December 2003 for each hospital. The amount of stockpile in the two medical centers was higher than that of the other 8 response hospitals (1650±110 mg v. 230±45 mg, P<0.01). The average amount of atropine in all hospitals was 380±50 mg. In addition, the average time needed to supply additional antidotes was 3±1 hours. The capacity of the treatment during attack was estimated to be 2.6±0.2 persons per hour for each hospital. Although the stockpile of these hospitals fulfilled the requirements from Department of Health, they could not afford an adequate capacity for a sarin event. In conclusion, our study revealed that the hospital stockpiling of atropine is insufficient for incidental chemical attack in Taiwan, the increase of hospital stockpile or the implementation of in situ rapid synthesis method might be a resolution. (Ann Disaster Med. 2003;2:20-25)

Key words: Incidental Chemical Attack; Nerve Agents; Atropine; Hospital Stockpile

Introduction

In recent years, the terrorism attacks occurred again and again.[1-4] Attacks by biological, chemical and radiological agents were considered the most possible and devastating methods for such man-made disasters.[4-6] Of chemical weapons, nerve gases such as sarin are well known as the threatening means.[1,4,7-9] Because of the possible involvement of numerous people, the antidote atropine may be rapidly depleted.[10,11] The condition remains to be elucidated in Taiwan. Although the Department of Health requested all the hospitals had three-month safety reserve for all medical logistics, the real reserve may be not the same as what is expected. Most of the hospitals maintain zero stockpiles and have their needs satisfied by certain logistic companies. Although it allows for the requests provided by the Department of Health, the situation will be very different when a terrorist attack such as a sarin event occurs.

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To solve the problem, Dr. Kozak ever provided a simple method to compounding a large volume of injectable atropine from powder with good results.[11] In addition, there is a significant cost advantage to using powered atropine as a hospital stockpile. Before we tested if the method can be applied to our system, the first issue we have to clarify is the availability of injectable atropine in the hospitals in Taiwan. We therein underwent the following investigation to evaluate the availability of atropine and its corresponding response capacity for a possible chemical terrorist attack.

Methods

The emergency response hospitals have to be evaluated annually by the bureau of Health, Taipei City Government. The amount of safe deposit for medical supply was one of the checklists. We therein collected the data about the amount of atropine safe deposits in 10 emergency response hospitals in Taipei City. Two of them were tertiary medical center, and the remaining eight secondary referral hospitals. The average amount of safe deposit was calculated from January 2002 to December 2003 for each hospital.

For the hospitals that maintained zero hospital deposits, we investigated furthermore the operation of medical supply logistics. The average time needed from the notice or ordering of the hospitals to the arrival of medical supply were studied and recorded.

For estimation of the average victims that could be treated in the first hour, we assumed the average use of intravenous atropine being 2 mg per 5 min or totally 24 mg in the first hour.

Results

The safe deposit for atropine was requested as 100 mg for medical center and 50 mg for other response hospitals by the definition of the Department of Health. All of the hospitals in this study could fulfill the criteria. The amount of stockpile in the two medical centers was higher than that of the other 8 response hospitals (1650±110 mg v. 230±45 mg, P<0.01). The average amount of atropine in the hospitals enrolled for investigation was 380±50 mg. In other words, each hospital could treat 16±2 persons for one hour.

In addition, the average time needed to supply additional antidotes was 3±1 hours. In consideration of the average stockpiles, the capacity of the treatment during a nerve agent attack would be 2.6±0.2 persons per hour for each hospital. Because Taiwan still had no experience of the chemical attack, the number of possible victims could not be estimated. However, if we took Tokyo Sarin attack as an example, the affected person was more than 5,000. If the similar attack occurs in Taipei where there are 64 emergency response hospitals, the capacity of treatment will be 1,000 persons totally. The shortage of atropine will be the problem for such an event.

Discussion

Logistics is usually one of the critical steps for determining successful disaster relief and rescue. Effective logistics management ensures that all functions are executed in a unified time-efficient and cost-effective manner. According to FEMA, individual logistics functions and associated subfunctions include:

[12] (a) materiel management including requisitioning, ordering, and sourcing; acquisition; resource tracking; receipt; storage and handling; security; accountability; inventory; deployment; issue and distribution; recovery; reutilization; and disposition; (b) property management including accountability, inventory, disposal, and record processing; (c) facility management including facility selection and acquisition, building services, information systems, communications, fleet management, safety and health, and physical security; (d) transportation management including transportation prioritizing, ordering, sourcing, and acquisition; time-phasing plans; and movement coordination and tracking. In the viewpoint of chemical disasters, immediate supply of the antidotes is always the essential step for effective treatment for the victims exposed to the chemical agents.

Intentional chemical disasters are one of the types of terrorism in the world. The organophosphate nerve agents tabun (GA), sarin (GB), soman (GD), and cyclosarin (GF) are among the most toxic chemical warfare agents known.[1,4,7-9,13,14] Together they comprise the G-series nerve agents, thus named because German scientists first synthesized them, beginning with GA in 1936. Sarin was developed in 1938, followed by GD in 1944 and finally GF in 1949. The only other known nerve agent is O-ethyl S-(2-diisopropylaminoethyl) methylphosphonothioate (VX). Besides decontamination and emergency care including airway maintenance and circulation support, reversal of nerve agent toxicity depends on the prompt parenteral administration of the antidotes such as atropine and pralidoxime. In general, Nerve agents act by first binding and then irreversibly inactivating acetylcholinesterase, producing a toxic accumulation of acetylcholine at muscarinic, nicotinic, and central nervous system synapses.[15] At muscarinic receptors, nerve agents cause miosis and glandular hypersecretion (salivary, bronchial, lacrimal, bronchoconstriction, vomiting, diarrhea, urinary and fecal incontinence, bradycardia). At nicotinic receptors, they cause sweating and initial defasciculation followed by weakness and flaccid paralysis. At cholinergic receptors of central nervous system, these agents produce irritability, dizziness, lethargy, amnesia, ataxia, seizures, coma, and respiratory depression. Nerve agents also cause tachycardia and hypertension via stimulation of the adrenal medulla. They also appear to bind nicotinic, cardiac muscarinic, and glutamate N-methyl-d-aspartate receptors. Nerve agents also antagonize gamma-aminobutyric acid neurotransmission, which in part may mediate seizures and neuropathy.

In 1995, sarin attack in Tokyo subway that killed 12 victims and affected over 5,000 people.[4,7-9] Although the event might be not considered as an intentional chemical disaster by definition in consideration of the maintenance of intact society in Japan, it still disclosed the shortcomings in disaster preparedness. The shortage of the antidote atropine for such a mass casualty was an example. The antidotes including atropine are usually deposited in the hospital's pharmacy. The amount of the antidotes available at hand is always not sufficient for a large number of the victims exposed to the nerve gases. In the United States, disaster response organizations are stockpiling the antidotes, but still consume much time to make the latter available.[16] The same situation could occur in Taiwan.

Our study demonstrated that the reserve of the antidotes for nerve agents is low for a mass casualty caused by intentional or accidental chemical incidents. The possible reason for the above observation is that most of the hospitals keep zero deposit under the concept of hospital management. The medical supply companies take over most of the logistics work for medical institutes. It of course has its own cost-effective benefits in the usual time, but may sacrifice the efficiencies during a chemical incident. We think the resolutions may include two major ways. The first is to establish disaster response hospitals that are mainly responsible for the management of specific types of the disasters. This resolution needs full and long-standing financial support from the government. The other way is to develop the alternative method to make the antidotes available. For this purpose, the medical supply companies should have the ability to keep the antidotes immediately available at any time. Otherwise, the hospitals have to have the ability to synthesize the antidotes immediately in situ.

Dr. Kozak provided recently a method of rapid atropine synthesis in situ.[11] With their method, a large amount of atropine could be provided in less than 1 hour for emergency personnel to treat hundreds of victims. On average, 10 to 20 mg is needed per patient. A single 2-g bottle could therefore be applied to the treatment of more than 100 victims. As they stated, rescue personnel could even use the hand-fill method to reconstitute antidote at the scene of the chemical attack. Although the safety (or quality control) and the authorization may be two major problems for us to use the model, the rapid synthesis method is still a good way in recent situation here. As Dr. Kozak mentioned, several potential candidates for rapid synthesis include pralidoxime, diazepam, beta-agonists, and cyanide antidotes.

In conclusion, our study revealed that the hospital stockpiling of atropine is insufficient for incidental chemical attack in Taiwan although its amount still fulfilled the requirements defined by the Department of Health.

References

1. Sidell FR. Chemical agent terrorism. Ann Emerg Med 1996;28:223-4
2. Laquer W. Post-modern terrorism. Foreign Affairs 1996;76:24-36
3. Bentura S. Chechen leader threatens Moscow with nuclear terrorism. Agence France Presses English Wire Service, November 8, 1991
4. Okumura T, Takasu N, Ishimatsu S, et al. Report on 640 victims of the Tokyo subway sarin attack. Ann Emerg Med 1996; 28:129-35
5. Carter A, Deutch J, Zelikow P. Catastophic terrorism-Tackling the new danger. Foreign Affairs 1998;77:80-94
6. Roberts B. Has the taboo been broken? In Roberts B (ed): Terrorism with Chemical and Biological Weapons: Calibrating Risks and Responses. Alexandria, VA: Chemical and Biological Arms Control Institute, 1997:121-40
7. Nozaki H, Hori S, Shinozama Y, et al. Secondary exposure of medical staff to sarin vapor in the emergency room. Intensive Care Med 1995;21:1032-35
8. Kon M, Suzuki T, Ishikawa M. A case of

fatal sarin poisoning: management problems. Jap J Disast Med 1996;1:12-14
9. Suzuki T, Morita H, Ono K, et al. Sarin poisoning in Tokyo subway. Lancet 1995;345:980
10. Goldsmith MF. Preparing for medical consequences of terrorism. JAMA 1996; 275:1713-4
11. Kozak RJ, Siegel S, Kuzma J. Rapid atropine synthesis for the treatment of massive nerve agent exposure. Ann Emerg Med 2003;41:685-8
12. Federal Emergency Management Agency (FEMA). Logistic Management Support Annex. Available at http://www.uscg.mil/d13/retco/pdf/frplm.pdf/ Accessed on May 31, 2003
13. Brennan RJ, Waeckerle JF, Sharp TW, et al. Chemical warfare agents: emergency medical and public health issues. Ann Emerg Med 1999;34:191-204
14. Centers for Disease Control and Prevention. Biological and chemical terrorism: strategic plan for preparedness and response. Recommendations of the CDC strategic planning workgroup. MMWR Morb Mortal Wkly Rep. 2000; 49(RR-4):1-14
15. Arnold JL. CBRNE - Nerve Agents, G-series: Tabun, Sarin, Soman. eMedicine. Available at http://www.emedicine.com/emerg/topic898.htm/ Accessed on May 31, 2003
16. Geller RJ, Lopez GP, Cutler S, et al. Antidote availability: reformulation of bulk atropine for nerve agent casualties. Presented at: National Disaster Medical System Conference; May 1999, Washington, D.C.

台灣神經解毒劑的緊急藥物儲備能量

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摘 要

化學恐怖攻擊事件是最具毀滅性的人為災難之一。為了解醫院神經解毒劑的儲備能量，我們研究了台北市十所責任醫院，以Atropine為指標的安全存量。其中兩家醫院是三級醫學中心而其他為二級轉診醫院。各醫院平均安全計量的計算期程為2002年1月至2003年12月。兩家醫學中心的儲備量高於其他八家(1650±110 mg v. 230±45 mg, P<0.01)。所有醫院的Atropine平均存量是380±50 mg。此外，額外解毒劑的平均供應時間為3±1小時。遭遇攻擊期間各家醫院的治療容量預估為每小時2.6±0.2人。雖然這些醫院已達到衛生署的要求標準，它們仍無法負荷沙林毒氣事件。總之，我們的研究發現台灣醫院atropine的儲備能量不足以應付化學恐怖攻擊，而增加儲備量或醫療院所本身快速合成的能力，是可能的解決方案。(Ann Disaster Med. 2003;2:20-25)

關鍵詞：化學恐怖攻擊；神經毒劑；Atropine；醫院儲備量

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