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The Oxime Cost-Effective Stockpile: Lessons Learned from Iran and Japan

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CAUTION:
This presentation includes Tetsu Okumura's private opinion as a researcher, NOT the official statements of the JAPANESE GOVERNMENT.

Introduction

- During the Iran-Iraq war from 1981 to 1987, tabun and sarin were used.
- The details of the nerve agent attacks remained unknown, but in 2004, Newmark et al. translated a report by Dr. Syed Abbas Foroutan who responded to the nerve agent attacks and treated victims in Iran.

whether oxime therapy for organophosphate poisoning was either harmful or effective

- The atropine, pralidoxime , and diazepam have historically been used as golden standard of antidotes for nerve agents.
- These recommendations have followed reports of organophosphate (agricultural chemical) poisoning in efficacy of oximes in treating subjects were questioned.
- For example, Peter et al., reevaluated the efficacy of oxime therapy for organophosphate poisoning using meta-analytic techniques and warned that oxime therapy was not only ineffective, but also potentially harmful.
- In the Cochrane Review, well known for its assessments of clinical practice with an emphasis on evidence-based medicine, one study found that although there was no evidence to conclude whether oxime therapy for organophosphate poisoning was either harmful or effective, further investigations would be required.

Therapy for nerve agents in Iran

- In Iran, early therapy using atropine sulfate was the basis for responding to nerve agent attacks.
- Oximes were not used at the scene and diazepam was only administered at aid stations.
- Iranian soldiers carried auto-injectors filled with atropine sulfate (not diazepam or PAM).

Tokyo Subway Sarin Attacks

- In Tokyo, PAM administration did not save a single life, and none of the victims who died could have been saved by administering PAM.
- Therefore, when analyzing survival as the endpoint, there is no evidence to support the efficacy of PAM.
- When considering long-term prognosis, the usefulness of oxime therapy was not ruled out.

Evidence-based responses to nerve agent attacks

- Chemical terrorism involving nerve agents is not only a threat to advanced countries with economic resources, but also developing countries in Africa and Asia with fewer economic resources. It is also difficult for developing countries to stockpile drugs.
- From the viewpoint of life-saving measures, the significance of oximes is not necessary high, and as a result, stockpiling of expensive oximes is a low priority.
- However, it may be prudent to encourage stockpiling of oximes among first responders with the basic knowledge of chemical weapons who are likely to be exposed to nerve agents, such as, fire fighters and police officers.

cost-effective responses to nerve agent attacks

- It is necessary to stockpile cost-effective drugs: atropine sulfate first and diazepam second. Atropine sulfate has a No1 priority, diazepam a No 2 priority, and PAM a No 3 priority.
- When stockpiling drugs, shelf life is an important issue. However, atropine sulfate and diazepam are used for a wide variety of applications, and cost performance is relatively high given that they can be stockpiled in a running stock fashion.
- As far as atropine sulfate is concerned, it acts faster using an auto-injector because of the spraying effect when compared to conventional intramuscular injection. However, from the viewpoint of cost performance, because auto-injectors are expensive and cannot be used multiple times in clinical settings, pre-filled syringes and conventional ampoules are more useful.
- Advanced countries have a responsibility of developing more effective oximes and mass-producing them in a cost effective manner. Different countries are conducing research on oximes with some international collaboration, but advanced countries should collaborate with each other to minimize duplication and waste and maximize oxime research and development.

Conclusion

- The drug of choice is atropine sulfate, and how quickly atropine sulfate can be administered is key to saving lives.
- After atropine sulfate, Diazepam is the second important drug.
- At present, if economic resources are lacking, then it is not necessary to stockpile oximes.
- Advanced countries need to collaborate with each other to conduct research to develop more effective oximes and mass produce them to bring their costs down.

THANK YOU