

A case of malathion poisoning with prolonged cholinergic toxicity

一個馬拉硫磷中毒及有長時間膽鹼能毒性的個案

PKM Pang 彭繼茂 and FT Lee 李富達

A case of severe organophosphate poisoning in a woman who ingested malathion is presented. Pralidoxime was given for more than two weeks but the lady had a poor response and developed recurrent episodes of cholinergic symptoms. Further studies are required to validate the World Health Organization regimen of pralidoxime in organophosphate poisoning. (*Hong Kong j.emerg.med.* 2009;16:98-101)

本文表述一名婦人服下馬拉硫磷後的嚴重有機磷中毒個案。雖然給與兩星期多的碘解磷定，這女士的反應仍差及出現重覆的膽鹼能症狀發作。需要進一步的研究以確認世界衛生組織在有機磷中毒中使用碘解磷定的方案。

Keywords: Antidotes, cholinesterase inhibitors, organophosphorus compounds, pralidoxime compounds

關鍵詞：解毒劑，膽鹼酯酶抑制劑，有機磷化合物，碘解磷定化合物

Case presentation

A 37-year-old woman attended the emergency department at 6:38pm in September 2006. She was well when last seen at 1pm. Her housemaid reported that the patient vomited whitish fluid and lost consciousness at 6pm. When the ambulance men arrived, they noted a smell of insecticide from the vomitus. Her husband reported that she had history of depression and she might have taken a bottle of pesticide!

She was in coma with a Glasgow Coma Scale of 3 on arrival at the emergency department. The pupils were pin-point. Muscle fasciculation was noted in her lower limbs.

She was tachypnoeic and cyanotic with SpO₂ of 88% on room air. Lots of secretion was coming out from her mouth. Her blood pressure was 199/100 mmHg and her pulse rate was 92 per minute. Her body temperature was 34.6°C. Her blood sugar by glucoStix was 10.8 mmol/L. Her electrocardiogram was normal.

She was intubated under rapid sequence induction and etomidate, alfentanil, and rocuronium were given. Gastric lavage was performed and followed by instillation of 50 gm of activated charcoal. Atropine 9.6 mg were given intravenously until the bronchorrhoea dried up and pralidoxime iodide (2-PAM) 1 gm infusion was started. She was then admitted to the intensive care unit (ICU) for further management.

Correspondence to:

Pang Kai Mau, Peter, FHKCEM, FHKAM (Emergency Medicine)
Yan Chai Hospital, Accident and Emergency Department,
7-11 Yan Chai Street, Tsuen Wan, N.T., Hong Kong
Email: pangkmp@ha.org.hk

Princess Margaret Hospital, Accident and Emergency Department,
2-10 Princess Margaret Hospital Road, Kwai Chung, N.T.,
Hong Kong

Lee Fu Tat, FHKCEM, FHKAM (Emergency Medicine), MRCP (UK)

Pseudocholinesterase level was taken in the emergency department and the result came back as 0.3 kU/L (reference 4.88-12 kU/L). Toxicological screening of the gastric aspirate confirmed the presence of malathion. Three more doses of activated charcoal and 1 gm 2-PAM were given in the ICU. However, she had persistent cholinergic symptoms and continuous 2-PAM infusion at a rate of 0.5 gm in 100 ml normal

saline, 33 ml/hr (with a total dose of 56 gm in 14 days) and atropine infusion of 0.6 mg/ml, at a rate of 4 ml/hr were given. She also suffered from hypokalaemia (K^+ 2.1 mmol/L) and metabolic acidosis (pH 7.22, BE -7.3, HCO_3^- 20.3, pCO_2 6.7, pO_2 24).

A trial of weaning off atropine and extubation was done on Day 6. However, there was a recurrence of bronchorrhoea and salivation after stopping the atropine infusion for one day. She was then re-intubated and atropine infusion was resumed on Day 7. Tracheostomy was performed on Day 8. On Day 11, another trial of weaning off atropine and 2-PAM was made, but again the cholinergic symptoms recurred. 2-PAM (33 ml/hr) and atropine infusion (2 ml/hr) were resumed again on Day 13. Finally, atropine and 2-PAM were successfully stopped on Day 15 and Day 16 respectively without further recurrence of cholinergic symptoms.

She stayed in the ICU for 20 days and was discharged home on Day 22. She was re-admitted 4 days later with dyspnoea and subsequent CT neck showed severe tracheal stenosis at the T1 level.

Discussion

Different organophosphates (OP) have different properties in terms of toxicity onset time, aging rate and response to oxime. This patient presented with cholinergic toxidrome after malathion poisoning which belongs to the dimethyl group-organophosphate. The time of ingestion was within five hours. The classical combination of antidotes of atropine and 2-PAM was given. However the response was poor as evidenced by the repeated recurrences of cholinergic symptoms.

There are several possibilities for the poor response to 2-PAM in this patient.

First of all, the World Health Organization (WHO) recommends a 2-PAM regimen (>30 mg/kg bolus followed by >8 mg/kg/hr infusion) for organophosphate poisoning. We had given the patient 1 gm 2-PAM at the emergency department, and 1 gm

at the ICU (total 2 gm) as loading and, a maintenance infusion at a rate of "0.5 gm in 100 ml normal saline at 33 ml/hr i.e. 4 gm/day" with a total dose of 56 gm in 14 days. Assuming an average weight of 60 kg, one may argue that the maintenance dosage of 2-PAM (2.75 mg/kg/hr) for this woman was inadequate.

However, clinical studies analysing human poisoning with organophosphate have entered into a controversy over the effect of 2-PAM.¹⁻⁸ A meta-analysis showed increased mortality rate, ventilation rate, and occurrence of intermediate syndromes.⁹ Another trial challenged the WHO 2-PAM recommendation as well.¹⁰

It is worth noting that a recent randomised control trial by Pawar et al¹⁰ with 200 subjects showed that a much higher dose regimen of continuous infusion of 1 gm/hr i.e. 24 gm/day for 48 hours after a 2 gm loading dose might be required to reduce morbidity and mortality in moderately severe cases.

Secondly, 2-PAM is not useful when aging of acetyl cholinesterase (AChE) has occurred. Aging $T^{1/2}$ of the inhibited AChE by dimethyl-OP is 3.7 hours. Time for complete ageing equals to 4 times of $T^{1/2}$ which should be around 13 hours. Since our patient presented within 6 hours after ingestion, aging of AChE should not have completed.

Thirdly, the recurrence of symptoms may be due to re-distribution of malathion from the body lipid storage. (Malathion is not as highly lipid soluble as compared to other organophosphates although it can stay in our body for more than two weeks.)

Conclusion

Current review of 2-PAM has entered into a controversy. It seems that a low-dose regimen of 2-PAM may be harmful. A recent randomised control trial by Pawar et al using high dose infusion of 24 gm/day had impressive result, and it challenged further the WHO recommended 2-PAM regimen (>30 mg/kg bolus followed by >8 mg/kg/hr infusion). There may be many theoretical

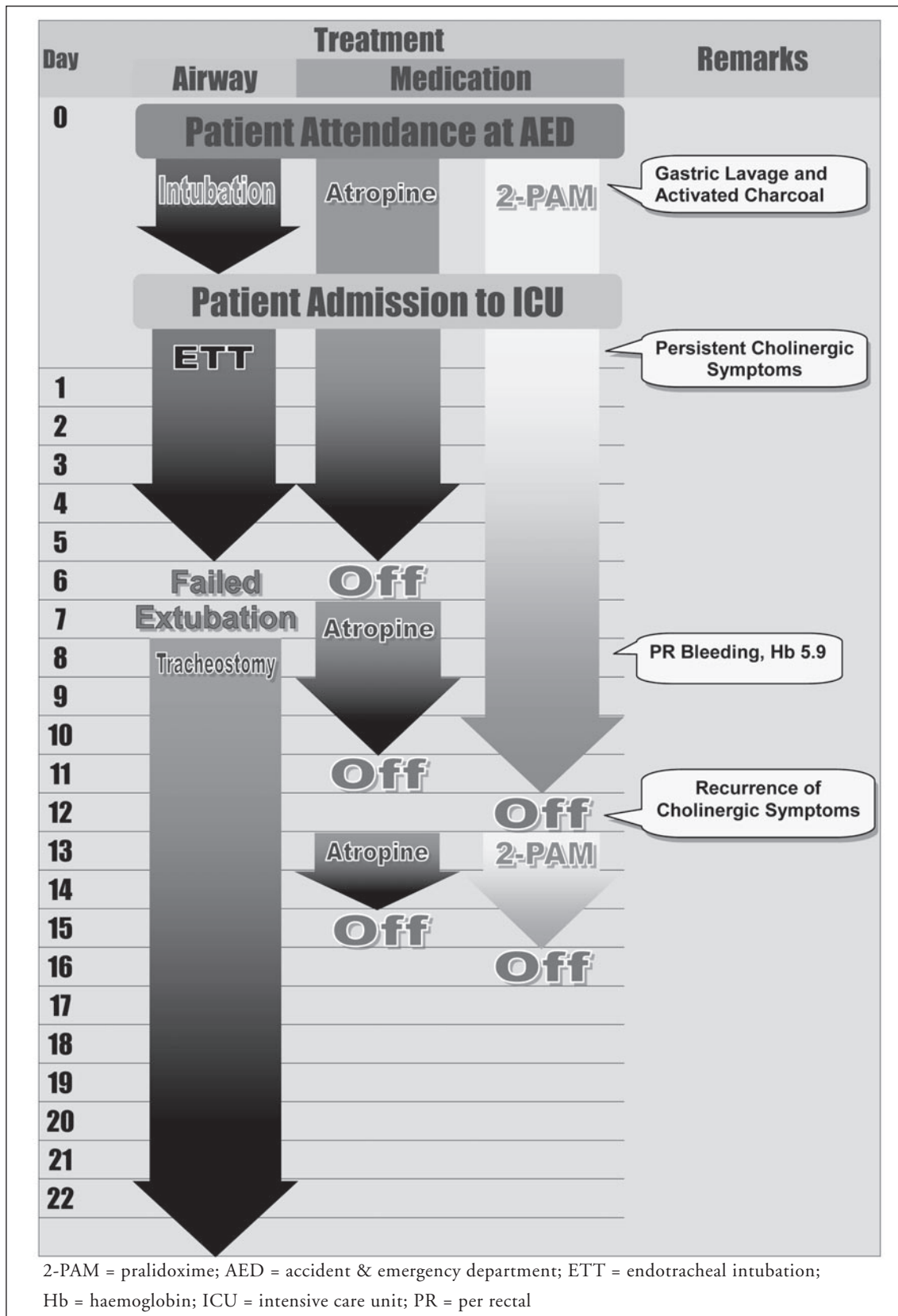


Figure 1. Timeline of events in the intensive care unit.

and practical reasons why 2-PAM works differently in patients with overwhelming self-poisoning. Future trials are required and they need to be well designed with pre-defined sub-group analysis. It may help to allow identification of particular patient groups that may benefit from 2-PAM.

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