

## Two cases of anticholinergic poisoning from transdermal scopolamine patch

### 東莨菪鹼經皮貼片引致抗膽鹼能中毒的兩個個案報告

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Scopolamine transdermal patch is a form of anticholinergic drug used to prevent motion sickness. We reported two cases of anticholinergic poisoning resulting from scopolamine transdermal patch. The first case experienced local toxicity and presented with right eye mydriasis for five days. The second case developed systemic anticholinergic toxidrome contributed by the scopolamine patch and presented with acute confusion. She was treated successfully by physostigmine, an anticholinergic antidote. The recommendation on physostigmine use was also discussed. We hope that these two case reports will raise the clinician awareness of the potential side effect of this kind of product. (*Hong Kong j.emerg.med.* 2006;13:221-224)

東莨菪鹼經皮貼片是一種抗膽鹼能藥物的形式，用於防止暈動病。我們報告東莨菪鹼經皮貼片引致抗膽鹼能中毒的兩個個案。第一個個案感受局部性中毒，有五天右眼顯示瞳孔放大。而第二個個案，東莨菪鹼經皮貼片促使全身性抗膽鹼能中毒綜合症的形成，而出現急性精神錯亂。她經抗膽鹼能解毒藥毒扁豆鹼的治療成功。本文還討論毒扁豆鹼在使用上的建議。我們希望這兩個個案報告會提高臨床醫生對這類產品潛在副作用的警覺性。

**Keywords:** Anticholinergic, physostigmine, poisoning, scopolamine

**關鍵詞：**膽鹼能對抗劑、毒扁豆鹼、中毒、東莨菪鹼

## Introduction

Scopolamine is an antimuscarinic agent commonly used to treat motion sickness and its efficacy was confirmed in a recent systematic review.<sup>1</sup> Anticholinergic poisoning resulting from oral and parenteral administration of scopolamine is well recognised. However, clinicians may not be aware of

the potential side effects of a topical transdermal scopolamine patch, which can be bought as an over-the-counter medication. We report two cases of anticholinergic poisoning resulting from the use of this medication and the use of physostigmine in managing one of the cases.

## Case one

A 27-year-old lady presented in February 2004 with blurring of vision in her right eye for two days. She enjoyed good past health and had just returned to Hong Kong after a trip to Korea. On examination, the right pupil was dilated and non-reactive. She did not have other symptoms and the rest of the examination was normal. There was no history of recent use of any local eye medication. However, on

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direct questioning, she gave the history of using a transdermal patch for motion sickness given by the tour guide in Korea. She used the patch for two days and her symptom started on the second day after applying the medication. She also recalled that she might rub the right eye after touching the patch and therefore possibly acquire local contamination. We made the diagnosis of scopolamine-induced mydriasis and treated her conservatively by reassurance and follow up. Her symptom gradually subsided in about three days.

### Case two

The second case was a 28-year-old healthy lady who presented with acute confusion in February 2005. She suffered from motion sickness after a travel from China and consulted a local general practitioner (GP) in Hong Kong. She received an intramuscular injection for vomiting, oral diphenhydramine (50 mg) and cinnarizine (25 mg). Four hours later, her husband brought her to our accident and emergency (A&E) department because of progressive confusion. Her vital signs, including blood pressure (112/77 mmHg) and pulse (78 bpm), were normal. On examination, the patient was disorientated, the neck was soft and there was no focal neurology. We found dilated pupils, dry mucosa, as well as decreased bowel sounds and made a provisional diagnosis of anticholinergic poisoning. The electrocardiogram, electrolytes and spot glucose were all normal. Although she had been given anticholinergic agents (diphenhydramine and cinnarizine) by the GP, the dose was normal and could not explain the clinical picture solely. Based on the experience of the first case, we looked particularly for the use of transdermal scopolamine patch and found it behind the patient's left ear, which was initially covered by hair. We removed the patch and treated her with slow intravenous injection of physostigmine. She responded promptly to normal mental status after 2 mg of physostigmine without any cholinergic side effects. She remained orientated and asymptomatic in the next eight hours and was discharged from our A&E uneventfully.

### Discussion

Motion sickness refers to the symptoms caused by repetitive angular and linear acceleration and deceleration. Its prevalence ranged from 7%<sup>2</sup> to 64%<sup>3</sup> in different studies. Scopolamine is an effective treatment against motion sickness and is usually in the forms of oral or parenteral preparations. Since scopolamine is also well-absorbed percutaneously, another route of its administration is by transdermal patch applied topically behind the ear. The transdermal scopolamine system consists of an outer layer of aluminised polyester, a reservoir of scopolamine, a microporous polypropylene membrane that controls the rate of diffusion, and a final adhesive layer. In Hong Kong, there is only one registered transdermal scopolamine patch (HK-52409), which is manufactured in Korea and contains 1.5 mg scopolamine.<sup>4</sup> Although we did not have samples of the patch used by the first patient, we made a reasonable assumption that the patch was of similar formulation as she was given the patch in Korea. For the second patient, the patch looked the same as the one shown in Figure 1, which was the transdermal scopolamine patch we bought in a local pharmacy store in Hong Kong.

Both our patients suffered from anticholinergic symptoms, antimuscarinic to be precise, after the use of the patch. The first one was a local contamination that resulted in mydriasis only. A similar case was

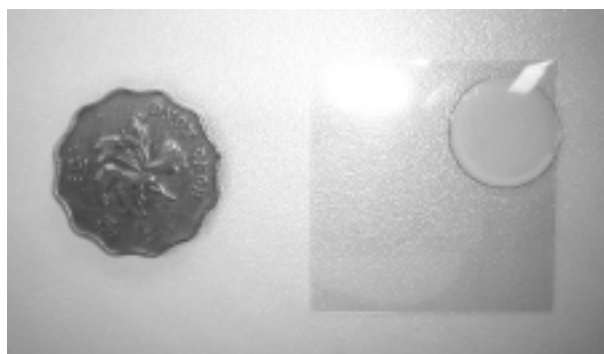


Figure 1. Transdermal scopolamine patch available in Hong Kong, comparing with the size of a 2-dollar coin.

reported in the literature<sup>5</sup> and it could cause diagnostic confusion if the clinician did not ask for the use of the patch. Scopolamine is a very potent mydriatic agent when applied locally and its effect may last up to two weeks. Treatment is mainly conservative.

In our second patient, she developed both central (confusion) and peripheral (dilated pupils, decreased bowel sounds and dry mucosa) signs of anticholinergic poisoning. The full blown anticholinergic toxidrome is reflected by the well known mnemonic "blind as a bat, mad as a hatter, dry as a bone, full as a flask, hot as a hare" which translate into the clinical findings of dilated and non-reactive pupils, confusion and delirium, dry skin and mucosa, urinary retention and hyperthermia; as well as tachycardia and decreased bowel sounds. However, symptoms and signs are variable and dilated pupils, dry mucosa and tachycardia are more sensitive findings than the others.<sup>6</sup> As hyperthermia and confusion are part of the anticholinergic toxidrome, failure to make the correct diagnosis may lead to the use of unnecessary invasive investigations such as lumbar puncture. In our patient, the history of using transdermal scopolamine patch and the prescribed medications from the GP plus the clinical diagnosis of anticholinergic toxidrome and her prompt response to physostigmine made the diagnosis definite. These eliminate the need of hospital admission and further investigation.

Since our second patient was exposed to a number of drugs having anticholinergic properties (scopolamine, diphenhydramine, cinnarizine and an unidentified anti-emetic injection), it is more likely that the combination of all these drugs causes a "supra-therapeutic" anticholinergic status of the patient, resulting in the clinical presentation. Unfortunately, we did not have a quantitative analysis of the patient's specimen concerning the relative amount of the above-mentioned drugs. Since all the drugs were given within their own dosage recommendation, it is reasonable to assume that our patient suffered from the poisoning as a result of the synergistic interaction of all those drugs.

Concerning physostigmine, it was first described in 1846 and subsequently used as an anticholinergic antidote, as well as an analeptic in the 1970s. Pharmacologically, it is a reversible cholinesterase inhibitor and can pass through the blood brain barrier and therefore able to counteract both the central and peripheral features of anticholinergic poisoning. It was reported in literature that physostigmine was dangerous to be used in patients with tricyclic antidepressants (TCA) poisoning,<sup>7,8</sup> as it was associated with seizure and asystole. This made TCA poisoning an absolute contraindication to the use of this antidote. History of asthma, cardiovascular disease and widened QRS (>100 ms) in ECG were relative contraindications to the use of physostigmine. On the other hand, physostigmine was found to be effective and safer than benzodiazepines for the treatment of anticholinergic delirium.<sup>9</sup> Balancing the risks and benefits, we recommend the use of physostigmine when all of the following three criteria are met: (1) a clinical diagnosis of anticholinergic poisoning; (2) the patient requires either restraint or invasive investigations if not treated promptly; and (3) no absolute or relative contraindications to the use of physostigmine. The initial dose is 0.5-2 mg in adults or 0.02 mg/kg (maximum 0.5 mg) in children and it should be given via the intravenous route slowly (at least 5-10 minutes) with close monitoring and atropine standby. We may need to repeat the dose if the response is inadequate in 10-15 minutes and the endpoints will either be adequate clinical response or onset of cholinergic side effects. In our second patient, she was given a total of 2 mg of physostigmine in about 15 minutes and she became orientated without any cholinergic side effect.

## Conclusion

In summary, we reported two cases of anticholinergic poisoning resulting from scopolamine transdermal patch and the successful use of physostigmine in treating the anticholinergic delirium. We hope that this case report will raise the clinicians' awareness of this over-the-counter product and its potential adverse effects.

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