CASE REPORT

Transdermal Scopolamine and Transient Psychosis

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INTRODUCTION

Transdermal scopolamine (Transderm V®, CIBA Pharmaceuticals) has been marketed in Canada for several years for the prevention of nausea and vomiting associated with motion sickness in adults.[1] Due to its antinauseant/anticholinergic properties, this product has also been used in the treatment of vertigo, reduction of gastric acid secretion, prevention of chemotherapy-induced emesis, premedication before surgery, and post-operative nausea. While scopolamine is available for oral or parenteral use, the transdermal delivery system has the advantage of providing a sustained duration of action permitting dosing every 72 hours. In addition, although side effects are similar with systemic administration, they are reported to occur less frequently with the transdermal system.[2,3] The incidence of reported central nervous system adverse effects from transdermal scopolamine is becoming more apparent with the growing use of this dosage form.[2-5] We present three cases of suspected transdermal scopolamine-induced psychosis at this hospital to illustrate the importance of this potentially overlooked adverse effect.

CASE 1

SC, a 57 year-old female, was admitted with a dilated cardiomyopathy and underwent a cardiac transplant on 08/04/92 (DD/MM/YY). Post-operative medications, which were continued until discharge, were prednisone, azathioprine, isoproterenol, cotrimoxazole, ranitidine, furosemide, aspirin, and cyclosporine. Muromonab-CD3 was ordered post-operatively until 18/04/92. Metoclopramide 10mg four times daily was administered from 14/04/92 until discharge. She also received two doses of oxazepam 15 mg at bedtime on 15/04/92 and 16/04/92, but it was stopped as the patient complained this drug gave her nightmares. The patient was started on transdermal scopolamine every three days at 0400 hours 18/04/92 for treatment of nausea. On 20/04/92 the patient was confused, spoke inappropriately, and suffered visual hallucinations but was easily re-oriented. The patch was subsequently removed at 1100 hours 20/04/92, and on 21/04/92 the patient was oriented x 3 with no complaints of hallucinations. There were no other significant changes made to the medications received. Whole blood cyclosporine levels ranged from 187 to 382 mcg/L at discharge. Renal function parameters remained within normal limits throughout the hospital stay.

CASE 2

VB, a 64 year-old male, was admitted with unstable angina and underwent quadruple coronary artery bypass graft surgery on 15/04/92. Post-operative medications included ranitidine, dimenhydrinate, oxazepam, aspirin, Amphojel®, and acetaminophen with codeine 30 mg. The patient was "allergic" to morphine claiming it caused itchiness and hallucinations. VB received oxazepam 15 mg at bedtime from 15/04/92 to 17/04/92, 45 doses of acetaminophen with codeine 30 mg between 16/04/92 and 20/04/92, six doses of dimenhydrinate 50 mg between 16/04/92 and 19/04/92, and six doses of metoclopramide 10mg every six hours which terminated at 2200 hours 18/04/92. The patient was

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started on transdermal scopolamine one patch every 48 hours at 1000 hours 19/04/92. At 0200 hours 20/04/92 the patient was awake and reported to be talking to himself; at 0020 hours 21/04/92 the patient was awake, paranoid and trying to leave his room; at 0300 hours he claimed he could see his daughter and son in his room; at 0500 hours he was found sitting on the floor washing his dentures in the toilet and calling out. He was disoriented x 3. The scopolamine patch was removed at 0925 hours 21/04/92. Confusion and hallucinations continued until 0825 hours the next morning. At that point, the patient was noted to be coherent and oriented x 3. Throughout hospitalization, renal function remained slightly reduced at 0.70-0.77mL/sec.

CASE 3

DW, a 74 year-old male, was admitted with left main stenosis and triple coronary artery disease. He underwent quadruple bypass surgery on 12/03/92. Post-operative medications included vancomycin, aspirin, digoxin, ranitidine, and sotolol which were continued until discharge. The patient also received oxazepam 15 mg at bedtime on 11/03/92 and 14/03/92 through 17/03/92. He received only one dose of dimenhydrinate 50mg orally on 15/03/92. At 2200 hours 15/03/92, the patient was started on oral metoclopramide 10 mg four times daily, and transdermal scopolamine every three days for control of nausea. On 18/03/92, DW experienced bad dreams and hallucinations. A digoxin serum level taken on this day was within normal limits at 1.0 nmol/L as was serum creatinine. On 19/03/92, he reported to staff that he saw crabs running around the room and under the bed. He also claimed to have spoken to his wife who had passed away over a year ago. He then began to report seeing spiders and on 20/03/92 hallucinations were more vivid. DW otherwise appeared lucid, alert, and oriented. Both the metoclopramide and scopolamine were stopped at 2200 hours 20/03/92. Upon waking at 0700 hours 21/03/92, the patient was oriented with no further episodes of hallucinations.

DISCUSSION

The main actions and side-effects of scopolamine given by the transdermal or systemic route are related to its anticholinergic activity. At therapeutic doses, tachycardia, mydriasis, inhibition of visual accommodation, reduced sweating, and reduced mucous membrane secretion have been reported. With the transdermal system, these peripheral side-effects are usually mild but common, with dry mouth occurring in 67% of patients[6]. Aside from drowsiness, which occurs in approximately 17% of patients[6], the central nervous system (CNS) effects occur infrequently and are more variable in presentation. The CNS effects usually resemble an agitated toxic delirium[7] including symptoms of disorientation, restlessness, confusion, hallucinations, and memory disturbances. Patients considered to be at increased risk of adverse CNS effects are the elderly, patients with pre-existing psychiatric disease, and patients receiving concurrent treatment with medications which possess anticholinergic activity, particularly antihistamines.[3]

The Transderm V® patch contains 1.5 mg scopolamine and this dosage form is designed to gradually release 1 mg of scopolamine over a three-day period. Maximum blood concentrations are achieved approximately 12 hours after application, and urinary excretion continues for up to 12 hours after removal of the system.[1] Psychotic symptoms may not appear for one to three days after applying the patch[6], and may take 24 to 36 hours to resolve after patch removal.[4,5] This may cloud the ability to establish a relationship between an adverse reaction and the use of the patch. It should also be noted that CNS symptoms may be present despite the absence of peripheral signs of anticholinergic toxicity.

The treatment of scopolamine-induced psychosis is mainly supportive. Removing the patch and washing the underlying skin to decrease further absorption should result in the resolution of symptoms within 24 to 36 hours. During this period, the patient should be provided with an environment which minimizes sensory stimulation. Physostigmine has been used to treat anticholinergic toxicity, but use of this drug for this indication is controversial and not without complications.[3]

In the case of the three patients which we have presented, other factors may have influenced the potential association between scopolamine and the CNS psychosis. No patient had a history of pre-existing psychiatric illness or cognitive impairment prior to hospital admission. However, all patients were elderly. In case 2, the patient was noted to have had a history of morphine-associated hallucinations although the patient had received 45 doses of acetaminophen with codeine over five days prior to the use of the patch without apparent adverse reactions. This patient also received six doses of dimenhydrinate (a strongly anticholinergic drug) prior to the scopolamine. Other drugs the patients received which have also been implicated in caus-

ing neurological toxicity include ranitidine (all cases), metoclopramide (all cases), cyclosporine (case 1), and digoxin (case 2). As ranitidine was continued throughout each patient's hospital stay, even after hallucinations resolved, it is unlikely this drug was involved in causing this toxicity, although it could potentially have enhanced this effect from scopolamine. Metoclopramide was administered throughout the hospital stay for case 1, discontinued 12 hours prior to scopolamine administration in case 2, and prescribed concurrently with scopolamine in case 3. Metoclopramide is known to cause extrapyramidal side-effects, drowsiness, dizziness, and anxiety; however, it is not reported to cause confusion and hallucinations[6,8]. Case 2 had reduced renal function and it is possible metoclopramide was still present in the patient's system at the time the scopolamine patch was applied; however, it is unlikely it was present three days later when hallucinations were occurring. Considering the lack of confusion and/or hallucinations being documented side-effects with metoclopramide and the variation in the use of metoclopramide when these symptoms occurred and resolved, the authors feel that metoclopramide is an unlikely contributing factor. A serum digoxin level determined the day patient 2 presented with hallucinations was in the low end of the normal range. Although there is an overlap between toxic and therapeutic serum digoxin levels[9], it is unlikely digoxin was contributing to the patient's CNS symptoms as this drug was continued until discharge, after hallucinations had ceased. Finally, cyclosporine-induced neurotoxicity, including visual hallucinations, is generally associated with toxic cyclosporine levels.[10] The blood cyclosporine levels in case 1 were well within the normal limits. The presence of concurrent medications and the range in onset of CNS symptoms, (24 to 72 hours after start of scopolamine therapy) demonstrate the difficulty in identifying a relationship between the CNS symptoms and the patch application. A psychiatric consult was requested in all three cases and symptoms resolved within 24 hours after removing the patch.

While transdermal scopolamine-induced psychosis is not highly reported, we can expect to see more cases of this adverse drug reaction in parallel with the increased use of this dosage form. The clinician should remember that the elderly are particularly susceptible to this side-effect and should be monitored accordingly.

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