Drug Monitor

TENS Linked to Aerosolized Pentamidine

Physicians from Kitasato University School of Medicine, Sagamihara, Japan report a case—the first to be published, to their knowledge—in which aerosolized pentamidine caused toxic epidermal necrolysis (TENS).

The case occurred in a 42-year-old man who was being treated for systemic lupus erythematosus and aspergilloma with prednisolone, sodium valproate, voriconazole, and lansoprazole. He began prophylactic treatment for *Pneumocystis* pneumonia with monthly inhalations of pentamidine 300 mg, and the day after his first dose, he developed generalized erythroderma and a fever of 104.4°F. More than half of the patient's body surface was covered with serum-filled blisters and bullae, and he had conjunctival erythema and blisters in the oral mucosa. A skin biopsy revealed ballooning keratinocytes and many individual necrotic keratinocytes.

The physicians subjected all the suspected drugs to the lymphocyte stimulating test, but only pentamidine showed positive results. They diagnosed the patient with TENS caused by pentamidine, reduced the dose of prednisolone to 50 mg/day after the first three days, and did not administer further aerosolized pentamidine. They treated the patient with plasma exchange for three days, and after the eruption continued, they treated him with methylprednisolone for three days and immunoglobulin for five days. Over the next three to four weeks, the eruption resolved slowly, and it has not recurred since.

The physicians note that inhaled pentamidine can remain in the tissue for more than two months, which may cause the symptoms of a pentamidine-related eruption to linger. They caution that pentamidine often is used to treat patients with underlying diseases, such as systemic lupus erythematosus and AIDS, in which drug eruptions are common. And they advise that patients whose eruptions persist despite plasma exchange therapy should be admitted to a burn unit—although such a transfer was not arranged in this case.

Source: *Am J Med.* 2009;122(1):e1–e2. doi:10.1016/j.amjmed.2008.08.022.

Can Oseltamivir Improve Cardiovascular Outcomes of Influenza?

Influenza is associated with adverse cardiac and cerebral vascular outcomes. Oseltamivir, an oral neuraminidase inhibitor, has been shown to decrease the severity of influenza. So does it follow that oseltamivir can reduce the recurrence of adverse vascular outcomes in patients with influenza and a history of cardiovascular disease (CVD)?

To find out, researchers from Health Affairs, TRICARE Management Activity, and Health Program Analysis and Evaluation, all in West Falls Church, VA, and Texas Heart Institute and Baylor College of Medicine, both in Houston, analyzed data on 37,482 patients enrolled in TRICARE. All of the patients were diagnosed with influenza between October 1, 2003 and September 30, 2007 and had previous histories of CVD. Patients who filled a prescription for oseltamivir within two days of influenza diagnosis were considered members of a "treated group," and all others were considered members of an "untreated group." The researchers looked at the patients' recurrent vascular outcomes (myocardial infarction, angina pectoris, stroke, or sudden cardiac death), as well as their mean days to recurrence of such outcomes, during the 30 days following influenza diagnosis.

Oseltamivir treatment was associated with a significant decrease in recurrent vascular event risk. The rate of any recurrent vascular event was 8.6% in the treated group, compared with 21.1% in the untreated group. Rates for each of the vascular events also were significantly lower in the treated group. In addition, the mean (SD) time to recurrence of vascular outcomes was 12.7 (8.6) days in the treated group and 8.1 (8.6) days in the untreated group. Oseltamivir treatment retained a significant protective effect when the researchers controlled for patients' gender, age, and military rank.

The researchers suggest that oseltamivir most likely provides protection "simply by reducing the severity and duration of influenza," which is associated with vascular outcomes. They add that future studies on oseltamivir and vascular outcomes would benefit from screening the medical and prescription medication history of participants in order to match the treated and untreated groups.

Source: *Circulation.* Epub March 5, 2009. doi:10.1161/CIRCOUTCOMES.108.820357/DC1.