Drug Monitor

Lithium for Patients with HIV?

Antiretroviral therapy has helped reduce the incidence of both minor and major HIV-associated neurocognitive impairment. Now, a small study suggests that adding lithium could help even more. Researchers from the University of California, San Diego say oral lithium, given daily for 12 weeks, improved neuropsychological performance in eight patients with HIV infection. Six improved enough to reduce their Global Deficit Score to normal.

Patients were given lithium 300 mg PO once daily to start. Doses were titrated to levels ranging from 600 to 1,200 mg/day. Improvements were observed in the domains of executive functions and information processing speed. It is these domains that are often impaired by HIV infection and associated with deficits in daily functioning, such as medication management, the researchers say. The improvements were statistically significant even though the sample size was small and the lithium dosage was low.

The lithium was well tolerated, with no grade 3 or 4 adverse events. Three patients experienced reversible erectile dysfunction and one reported mild worsening of a preexisting acneiform rash. The extra medication was not associated with changes in HIV RNA or CD4 cell counts. None of the patients stopped treatment prematurely.

Source: *AIDS.* 2006;20:1885–1888.

Acute Renal Failure Linked to Inhaled Tobramycin

Giving aminoglycosides in a nebulized form, such as tobramycin inhalation solution, is thought to reduce the risk of kidney damage. But a case reported by pharmacists from The University of Kansas Hospital, Kansas City suggests the risk still may be there.

A 62-year-old woman, with a history of chronic renal insufficiency and diabetes mellitus, was transferred to a surgical intensive care unit with reduced urine output and sepsis secondary to *Pseudomonas aeruginosa* infection. Prior to her transfer, she had been treated with antibiotics but no aminoglycosides.

After one month at the surgical unit, she was diagnosed with multidrug resistant *P. aeruginosa.* She was started on piperacillin-tazobactam 250 mg IV every six hours and tobramycin 2 mg/kg IV when trough serum concentrations dropped below 1 µg/mL. The antibiotic was changed to equal dosing of imipenem-cilastin, with the tobramycin being continued. Treatment lasted for three weeks and her serum creatinine concentration (SCr) remained steady throughout this time.

A month after the antibiotic regimen was stopped, she again was diagnosed with *P. aeruginosa* pneumonia. She was given imipenem-cilastatin 250 mg IV every six hours and vancomycin 1 g IV based on serum concentrations, as well as inhaled tobramycin 300 mg twice daily.

At the time, her SCr was 2 mg/dL. The imipenem-cilastatin was discontinued, but the inhaled tobramycin was not. After four weeks, her SCr rose steadily, to a peak of 4.5 mg/dL. The inhaled tobramycin was discontinued on day 28 and she was placed on hemodialysis. Her SCr never returned to normal and she never regained renal function. The patient remained on hemodialysis until she died six months later.

Although the researchers have no conclusive evidence that inhaled tobramycin was the offending agent, they say the patient's Naranjo adverse drug reaction probability score indicated a possible association. In addition, results of a mercapto-acetyl-glycyl-glycyl-glycine (MAG-3) scan and a urine sediment analysis were consistent with acute tubular necrosis (ATN). They cite a previous report of tobramycin nebulized solution causing acute renal failure, as well as a report of a patient with cystic fibrosis developing nephrotoxicity while receiving inhaled tobramycin 300 mg twice daily. The latter patient's histopathology studies also were consistent with ATN, and two weeks after the tobramycin was discontinued, her renal function returned to baseline.

Most of the available reports on inhaled tobramycin show no risk for nephrotoxicity, the researchers say. They note, however, that the majority of safety data exclude patients with reduced renal function. Another factor to consider, they say, is that inhaled tobramycin has been studied most often in patients with cystic fibrosis, whose altered pharmacokinetics may allow for increased drug clearance, thus reducing the risk of nephrotoxicity. As the drug is used more in patients without cystic fibrosis, its risk profile may be expanded.

Source: *Am J Health-Syst Pharm.* 2006;63: 1858–1861.

Treating Cancer During Pregnancy

Because the incidence of breast cancer rises with age, and because more women are having children later in life, it's been hypothesized that more women will be pregnant and have cancer at the same time. Researchers, from the Medical School and the

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M.D. Anderson Cancer Center of the University of Texas in Houston, found that it's possible to treat breast cancer during the second and third trimesters without significant short-term complications for the child.

Since 1992, they've treated 57 pregnant women with breast cancer, diagnosed at a mean gestational time of 17 weeks, with a combination of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC). Beginning in the second or third trimester, the women received FAC IV every 21 to 28 days through gestational week 35. At a median follow-up of 38.5 months, 40 women were alive and disease free. (Three were alive with recurrent breast cancer; 13 had died, 12 from breast cancer; and one had been lost to follow-up.)

The majority of the women were diagnosed with advanced-stage, poorly differentiated ductal carcinoma, including regional lymph node metastases. Neoadjuvant chemotherapy was used in attempts to downstage the cancer of 25 patients, and it was successful in 19. With "careful, multidisciplinary planning," the researchers found that 37% of these patients were able to undergo breast conservation therapy. They therefore offer that neoadjuvant chemotherapy with breast conservation is an option when a large tumor is present and there is regional lymph node involvement.

As the majority of patients had estrogen or progesterone receptor–negative tumors, the researchers say their data do not support the hypothesis that the hormonal milieu of pregnancy contributes to the development and progression of breast malignancy.

Most of the children were exposed to chemotherapy beginning in the second trimester (median of 23 gestational weeks). None were exposed to other systemic chemotherapeutic, hormonal, or biologic therapies in utero. All women who delivered had live babies. One baby had Down syndrome; two had congenital anomalies, including club foot and bilateral ureteral reflux; and one had a subarachnoid hemorrhage of unclear etiology at two days old. The latter child had neutropenia and thrombocytopenia despite a normal complete blood count in the mother. Although difficulty breathing occurred neonatally 28% of the time, the researchers say this complication and others were similar to reported norms in the general population.

Of the children who were school-aged at follow-up, only two required special attention in school: the child with Down syndrome and another with attention deficit disorder. Except for the parents of the child with Down syndrome, all 43 parents responding to follow-up felt their child was developing normally in comparison to siblings or other similar-aged children.

The researchers say their short-term data are "reassuring," though more follow-up is needed. They also note that, based on the child who had neutropenia, they are reluctant to administer dose dense chemotherapy to pregnant patients with breast cancer.

Source: *Cancer.* 2006;107:1219–1226.

Do Patients in the ED Overuse OTC Analgesics?

About 6% (34) of 546 patients seeking care at an emergency department (ED) reported exceeding the manufacturer's recommended daily dose of an over-the-counter (OTC) analgesic during the three days before their ED visit, in a study conducted by researchers from Denver Health and the University of Colorado, both in Denver, and Washington University, St. Louis, MO.

Over half of all the patients surveyed reported using a medication containing ibuprofen, acetaminophen, naproxen, or aspirin. The drugs most likely to be overused were ibuprofen and naproxen. In addition to exceeding a recommended dose, a number of patients were taking more than one product containing an analgesic. Most were taking acetaminophen and a nonsteroidal anti-inflammatory drug (NSAID), but several reported taking two NSAIDs concurrently.

Patients aged 30 to 39 were most likely to overuse an OTC analgesic, with those aged 50 to 59 least likely (10% versus 2%, respectively). The rates of overuse were similar for men and women. Among the reasons stated for taking an OTC analgesic were musculoskeletal pain, headache, cold symptoms, and fever.

The researchers found that 85% of the overusers agreed with the statement, "You could become ill from taking too much pain medication." The investigators say it was not clear whether these patients were just disregarding the risks of overuse or were not aware that the dose they were taking was beyond the limit. ●

Source: *Ann Emerg Med.* 2006;48:315–318.