



# Drug Monitor

## Antibiotic Treatment of Acute Pyelonephritis

When acute pyelonephritis is treated with antibiotics, are short courses (seven to 14 days) just as safe and effective as long courses (14 to 42 days)? There has been no consensus on this question, although the Infectious Diseases Society of America recommends 10- to 14-day treatment for women with the disease.

Researchers from Alfa Institute of Biomedical Sciences, Marousi, Athens University School of Medicine, Athens, Henry Dunant Hospital, Athens, all in Greece, and Tufts University School of Medicine, Boston, MA, set out to help answer the question through a meta-analysis of randomized controlled trials. To be eligible for inclusion, the trials needed to compare short-course and long-course regimens of the same antibiotic administered at the same daily dosage to adult or adolescent patients with acute pyelonephritis. The trials also needed to report data on clinical success, bacteriologic efficacy, relapses, recurrences, and adverse events or patient withdrawals due to adverse events.

The researchers found four trials—one double-blind and three open-label—that met these criteria. The trials' short-course treatment arms included seven-day, 10-day, and 14-day treatment regimens, and their long-course treatment arms included 14-day, 21-day, and 42-day regimens. The antibiotics used in the trials included pivampicillin, pivmecillinam, trimethoprim and sulfamethoxazole, ampicillin, cephalexin, and fleroxacin.

The meta-analysis "failed to identify any significant differences with regard to the effectiveness and safety" between the short courses and long

courses, according to the researchers. They note that shortening treatment regimens could reduce the risk of antimicrobial resistance—an increasing problem in regard to *Escherichia coli*, which causes more than 80% of acute pyelonephritis cases.

The researchers add that the meta-analysis has some limitations, including the fact that the studies had different definitions of "short course" and "long course"—14 days was considered a short course in one study and a long course in another. And the generalizability of the meta-analysis may be limited by the fact that over 80% of the studies' patients were women, the researchers say, although female patients are almost 500% more likely than male patients to be hospitalized for acute pyelonephritis.

Source: *Clin Ther.* 2008;30(10):1859-1868.  
doi:10.1016/j.clinthera.2008.10.007.

## Statins and Pneumonia

A 2006 study suggested that statins' apparent antipneumonia benefits may be due to a "healthy user effect." Researchers from Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, however, say they have "powerful evidence" that statins fight pneumonia by reducing inflammation.

The researchers studied 1,009 patients with community-acquired pneumonia who were admitted consecutively to a hospital between January 2005 and November 2007. They hypothesized that if the healthy-user theory was correct, then all classes of cardiovascular drugs also would appear to have similar antipneumonia benefits for these patients and statin use would have no effect on the patients' levels of C-reactive protein—a marker of systemic inflammation.

Therefore, the researchers recorded the patients' use of four cardiovascular drugs: statins, aspirin, beta-blockers, and angiotensin II converting enzyme (ACE) inhibitors. And they looked at the outcomes of 30-day mortality, patients' levels of C-reactive protein upon hospital admission and at day four, development of complicated pneumonia, and need for mechanical ventilation or inotropic support.

Multivariate logistic regression indicated that, of all the cardiovascular drugs, only statins were associated with reduced 30-day mortality or with reduced incidence of complicated pneumonia. Statin use had no effect on requirement for mechanical ventilation or inotropic support, but it was associated with significantly lower C-reactive protein levels on admission and with the reduction of these levels by 50% or more at day four. In contrast to statins, beta-blockers were associated with increased 30-day mortality and an increased need for mechanical ventilation or inotropic support. There were no significant differences in the frequency of antibiotic therapy before admission between patients who were prescribed cardiovascular drugs and those who were not.

These findings indicate that the healthy-user theory is incorrect and that statins' anti-inflammatory effects are their mechanism of action against pneumonia, according to the researchers. They note that their study is the first to investigate the effects of multiple cardiovascular drugs on community-acquired pneumonia and to find that statins reduce the incidence of complicated pneumonia. It also is the first to find that beta-blockers are associated with increased 30-day mortality and need for mechanical ven-

tilation or inotropic support in pneumonia, they say, and further studies are needed to confirm these associations.

Source: *Am J Med.* 2008;121(11):1002–1007.e1. doi:10.1016/j.amjmed.2008.06.030.

## Boosting Blood Cells for Transplant Patients

Plerixafor (Mozobil, Genzyme Corporation, Cambridge, MA), an injectable drug that helps speed the process of gathering blood stem cells for bone marrow transplants, has been approved by the FDA.

Plerixafor is intended to be used with granulocyte-colony stimulating factor (G-CSF) for treatment of adults with non-Hodgkin lymphomas (NHLs) or multiple myeloma. Combined with G-CSF, plerixafor “mobilizes” the number of hematopoietic stem cells released from the bone marrow, thus making it more likely that the patient can proceed to transplant. A minimum of about 2 million stem cells/kg body weight must be collected for a transplant to take place. For many patients, the apheresis process can take three to four hours over several days, and even then some may not have enough cells.

In a randomized, clinical trial involving 298 patients with NHL, 59% of the patients who received plerixafor with G-CSF collected the target number of at least 5 million stem cells/kg body weight in four or fewer apheresis sessions, compared with 20% of the patients who received G-CSF and placebo. The median number of days to reach the target cell count was three days in the plerixafor group; in the placebo group it was not evaluable.

In another randomized trial, which involved 302 patients with multiple myeloma, 72% of the patients who received plerixafor with G-CSF collected the target number of at least 6 million stem cells/kg body weight

in two or fewer apheresis sessions (median, one day), compared with 34% of the patients who received G-CSF and placebo (median, four days).

The most commonly reported adverse reactions in the clinical studies were diarrhea, nausea, fatigue, infection site reactions, headaches, joint pain, dizziness, and vomiting.

Sources: FDA press release. December 18, 2008.

PharmaLive news release. December 15, 2008.

Mozobil [package insert]. Cambridge, MA: Genzyme Corporation; 2008.

## Timing Parecoxib Administration with Colorectal Surgery

The effectiveness of pre-emptive analgesia has been supported by animal studies, but clinical trials on its use have been controversial. To learn more, researchers from Queen Mary Hospital, Hong Kong compared the effectiveness of the only parenteral selective cyclooxygenase 2 inhibitor available, parecoxib, when it is administered before or after colorectal surgery.

The researchers randomly assigned 60 patients undergoing colorectal surgery to a presurgery group, a postsurgery group, or a control group. The presurgery group received parecoxib 40 mg IV before skin incision and received normal saline intravenously at skin closure, the postsurgery group received normal saline before skin incision and received parecoxib 40 mg IV at skin closure, and the control group received normal saline at both times. After surgery, the patients' morphine consumption through patient-controlled analgesia, pain scores on a numerical rating scale, and opioid adverse effects were recorded.

During the 24 hours following surgery, there was no statistical difference in the amount of morphine consumed by the presurgery group and the post-

surgery group—although both groups consumed 55% to 66% less morphine than the control group. The two parecoxib groups also had lower total pain scores sooner after surgery than did the control group. Although parecoxib's effect was slightly more pronounced in the postsurgery group than in the presurgery group, this difference was clinically insignificant. It might be due to parecoxib's effects lasting longer for the postoperative group because it was administered two and a half hours later, say the researchers. The opioid sparing effect in the postsurgery group lasted for 48 hours after surgery.

The researchers conclude that parecoxib is as effective after surgery as it is before surgery. When intraoperative dehydration or significant blood loss is possible, they say, providers can withhold parecoxib until surgery is completed without diminishing its significant analgesic effect. ●

Source: *Acute Pain.* 2008;10(3–4):123–130.

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