

Alternate Acetaminophen, Ibuprofen to Treat Fever

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Contributing Writer

A child's fever can be reduced more quickly and safely by alternating acetaminophen and ibuprofen instead of administering either agent alone, according to Dr. E. Michael Sarrell and his colleagues at Tel Aviv University in Israel.

About 19%-30% of all visits to primary care pediatricians are on account of fever, and acetaminophen and ibuprofen are the

most commonly prescribed therapeutics to bring elevated temperatures down. According to Dr. Sarrell and his colleagues, "Antipyretic use therefore plays a major role in daily pediatric practice, and it must be both effective and safe."

As a consequence, they designed a study to determine which agent—or if both intermittently—may be more effective.

In a double-blind, controlled clinical trial 464 children aged 6-36 months with a fever of at least 38.4° C presenting at one

of three pediatric centers in Israel were randomized to 12.5 mg/kg of acetaminophen syrup every 6 hours (154 patients), an ibuprofen suspension of 5 mg/kg every 8 hours (155 patients), or alternating acetaminophen/ibuprofen every 4 hours (155 patients) for a total of 3 days. Within each arm, one-half of the children received an initial loading dose of 25 mg/kg of acetaminophen or 10 mg/kg of ibuprofen to more quickly attain an effective drug serum concentration (Arch. Pediatr. Adolesc. Med. 2006; 160:197-202).

The type of loading medication had no effect on children's response, but the type of maintenance medication did—and significantly so. The alternating regimen reduced children's fevers more rapidly, led to less stress among children, and required less medication during the first 3 days of treatment than either acetaminophen or ibuprofen alone.

For example, 1 day after initiation of treatment, infants who received the alternating regimen had a 1.07° C drop in tem-

perature (vs. a drop of 0.19° C with acetaminophen and an increase of 0.02° C with ibuprofen), a 52.4% reduction in stress levels (vs. 39.6% with acetaminophen and 35.7% with ibuprofen), and required 22.6% fewer treatment doses from day 1 to day 2 (vs. 11.2% with acetaminophen and 2.2% with ibuprofen).

Moreover, only 10% of children who received the alternating treatment experienced a recurrence in fever on day 5 as opposed to 21% of children on acetaminophen and 17% of children on ibuprofen.

Because their treatment was more effective, children on acetaminophen/ibuprofen missed significantly fewer days of day care (which presumably meant that parents missed fewer days of work) than did children who were on acetaminophen or ibuprofen alone (1.76, 2.64, and 2.58 days, respectively).

No child experienced any serious adverse effects related to treatment, and there were no statistically significant differences between groups for abnormal laboratory values. ■

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Vigamox®

(moxifloxacin hydrochloride ophthalmic solution) 0.5% as base

DESCRIPTION: VIGAMOX® (moxifloxacin HCl ophthalmic solution) 0.5% is a sterile ophthalmic solution. It is an 8-methoxy fluoroquinolone anti-infective for topical ophthalmic use.

Clinical Studies: In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, VIGAMOX® solution produced clinical cures on day 5-6 in 66% to 69% of patients treated for bacterial conjunctivitis. Microbiological success rates for the eradication of the baseline pathogens ranged from 84% to 94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

INDICATIONS AND USAGE: VIGAMOX® solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic Gram-positive microorganisms:

*Corynebacterium species**, *Micrococcus luteus**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus warneri**, *Streptococcus pneumoniae*, *Streptococcus viridans* group

Aerobic Gram-negative microorganisms:

*Acinetobacter lwoffii**, *Haemophilus influenzae*, *Haemophilus parainfluenzae**

Other microorganisms:

Chlamydia trachomatis

*Efficacy for this organism was studied in fewer than 10 infections.

CONTRAINDICATIONS: VIGAMOX® (moxifloxacin HCl ophthalmic solution) is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS: NOT FOR INJECTION.

VIGAMOX® solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

PRECAUTIONS: General: As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemically administered quinolones including moxifloxacin have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions: Drug-drug interaction studies have not been conducted with VIGAMOX® solution. *In vitro* studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose for a 50 kg person, on a mg/kg basis). Moxifloxacin was not mutagenic in four bacterial strains used in the Ames *Salmonella* reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity *in vivo* in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 21,700 times the highest recommended total daily human ophthalmic dose. At 500 mg/kg orally, there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

Pregnancy:

Teratogenic Effects. Pregnancy Category C: Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose); however, decreased fetal body weights and slightly delayed fetal skeletal development were observed. There was no evidence of teratogenicity when pregnant Cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (approximately 4,300 times the highest recommended total daily human ophthalmic dose). An increased incidence of smaller fetuses was observed at 100 mg/kg/day.

Since there are no adequate and well-controlled studies in pregnant women, VIGAMOX® solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when VIGAMOX® solution is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of VIGAMOX® solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of VIGAMOX® has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS: The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% of patients. Nonocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash, and rhinitis.

Reference:

1. Data on file. Alcon Laboratories, Inc. 2005.

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Oral Cefdinir Found Safe for Penicillin-Allergic Patients

BY JANE SALODOF MACNEIL
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KAPALUA, HAWAII — Oral cefdinir is safe for the treatment of skin and soft-tissue infections in people who are allergic to penicillin, Dr. James Q. Del Rosso said in a poster presentation at the Winter Clinical Dermatology Conference, Hawaii.

Dr. Del Rosso reported that a review of the literature found virtually no cross-reactivity between cefdinir (Omnicef) and penicillin, despite concerns over the use of cephalosporins in patients with a history of penicillin allergy.

"All cephalosporin antibiotics are not created equal," said Dr. Del Rosso, who has a private dermatology practice in Las Vegas.

He asserted that differences in the seven-position side chain structure of selected cephalosporins make cross-reactivity with penicillin less likely in second- and third-generation cephalosporins such as cefdinir.

"A thorough review of available data indicates that the frequently cited risk of 8%-18% cross-reactivity to cephalosporins among penicillin-allergic patients is not accurate, is misleading, and requires revision," Dr. Del Rosso noted in his poster.

The increased risk of allergic reactions in penicillin-allergic patients is only 0.4% for first-generation cephalosporins and "nearly nil" for certain later-generation agents, which he defined as cefdinir, cefpodoxime, and cefuroxime.

"The one we use in dermatology [cef-dinir] appears to have essentially no cross-reactivity with penicillin," he said in an interview at the conference, which was sponsored by the Center for Bio-Medical Communications Inc.

Dr. Del Rosso noted that the American Academy of Pediatrics has endorsed the use of cefdinir, cefpodoxime, and cefuroxime in penicillin-allergic children, excluding those who have had life-threatening reactions such as anaphylaxis or toxic epidermal necrolysis.

He added that the American Academy of Family Physicians has taken a similar position.

"The risk of anaphylaxis associated with cephalosporin use has been cited to range from 0.1% to 0.0001%, with no cases of fatal anaphylaxis reported in children," according to the poster.

Medicis provided support for the production of the poster.

Dr. Del Rosso is a consultant to, and serves on the speakers' bureau of, Abbott Laboratories, which makes Omnicef. ■

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