

Community, Nosocomial MRSA Forms Are Mixing

BY BARBARA J. RUTLEDGE
Contributing Writer

Methicillin-resistant *Staphylococcus aureus* (MRSA) strains that typically cause community-acquired infections are infecting patients in hospitals, and strains considered health care associated are infecting patients with no health care-related risk factors, reported Dr. R. Monina Klevens of the Centers for Disease Control and

Prevention (CDC) and her associates.

The Active Bacterial Core Surveillance program of the CDC is a population-based surveillance system for invasive organisms, including MRSA infections. The surveillance is ongoing in California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee (Emerging Infectious Diseases 2006;12:1991-3).

Surveillance reports are generated when positive MRSA cultures are detected in

normally sterile sites, such as blood or cerebrospinal fluid.

Laboratory reports are linked to the patient's medical record, and health care-related risk factors (HRFs) are abstracted from the medical record for inclusion in a surveillance database.

HRFs include the presence of an invasive device, history of MRSA infection or colonization, dialysis, hospitalization, residence in a long-term care facility, and surgery.

Obtaining a bacterial culture more than 48 hours after hospital admission also suggests infection with a health care-associated strain.

MRSA strains are empirically typed, based on the separation characteristics seen using pulsed-field gel electrophoresis. In earlier MRSA outbreaks, strains USA300 and USA400 were the predominant community-associated strains. USA100 and USA 500 were considered health care-associated strains.

From January 2004 through February 2006, more than 9,100 cases of invasive MRSA were reported and classified as

classic health care-associated infections, with cultures obtained more than 48 hours after admission; cases with one or more HRF but with community-onset infections (less than 48 hours); or cases with community-associated infections and no HRF.

Of the 9,147 cases, 2,535 (28%) were classic health care-associated infections, 5,353 (59%) were health care associated, but community acquired, and 1,259 (14%) were community-associated infections.

One hundred isolates were selected for typing by pulsed-field gel electrophoresis. Seven of 27 isolates (26%) from community-associated cases were USA100 or USA500, and 8 of 29 (28%) classic health care-associated cases were strain USA300. Overall, 18%-28% of patients with HRFs were infected with strains considered to be community-associated MRSA strains.

"The distinction between health care- and community-associated MRSA is rapidly blurring," Dr. Klevens and her associates wrote. ■

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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Sipping Granules Preferred for Taking 'Bitter' Clarithromycin

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Children with respiratory tract infection and their parents generally preferred treatment with clarithromycin granules sipped through a strawlike device than with conventional clarithromycin suspension syrup, Dr. Dieter Adam reported.

A randomized, open-label study in 263 children aged 2-12 years treated for 7-10 days found no significant difference in efficacy after completion of the therapy, with the bacterial organism eradicated in 93% by either formulation.

In the sipping group, however, 23% had clinical symptoms resolve in 3-5 days compared with 13% in the suspension group, he said in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Parents assessed the sipped formulation as easier to administer and better tasting to the child, compared with the suspension form.

Rates of adherence to therapy were significantly higher with the sipped form than with the suspension in the first 5 days of therapy (92% vs. 38%) and at the end of treatment (94% vs. 86%), said Dr. Adam, a pediatrician at the University of Munich, Germany, and his associates.

The study was funded by Grünenthal GmbH, which markets the Siptechnology formulation in Latin America and some

European countries. The company is pursuing U.S. approval, said Dr. Adam, who has no other affiliation with the company.

The Siptechnology consists of a plastic strawlike device loaded with a dose of drug granules with a film coating to mask the taste. The study randomized patients in a 2:1 ratio to the Siptechnology or suspension syrup. Children in the Siptechnology group used the device to sip their preferred soft drink through a liquid-permeable controller on the end of the "straw," ingesting both the soda and drug granules.

Patients or their parents reported the taste was good or very good in 62% of the Siptechnology group compared with 36% of the suspension group.

Both regimens delivered 15 mg/kg per day divided into two equal doses. Patients were treated for acute otitis media in 20% of cases, tonsillitis in 25%, pharyngitis in 30%, and acute bronchitis in 42%. (Some children had

more than one infection.) "Normally, clarithromycin has a bitter taste" that may interfere with adherence and might reduce cure rates in the real world compared with the Siptechnology, although efficacy was comparable in this trial setting, Dr. Adam said at the conference, sponsored by the American Society for Microbiology.

Patients or their parents reported the taste was good or very good in 62% of the Siptechnology group compared with 36% of the suspension group. Patients ingested the drug without resistance or resentment in 88% of doses in the Siptechnology group and 67% of doses in the suspension group. ■