

Interscience Conference on Antimicrobial Agents and Chemotherapy
 American Epilepsy Society
 Masters of Pediatrics Conference
 Miami Children's Hospital Conference
 American Academy of Allergy, Asthma and Immunology Annual Meeting
 American Academy of Child & Adolescent Psychiatry:
 Psychopharmacology Update

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Patanol[®]
 (olopatadine hydrochloride
 ophthalmic solution) 0.1%

Clearly ahead

DESCRIPTION

PATANOL[®] (olopatadine hydrochloride ophthalmic solution) 0.1% is a sterile ophthalmic solution containing olopatadine, a relatively selective H₁-receptor antagonist and inhibitor of histamine release from the mast cell for topical administration to the eyes.

INDICATIONS AND USAGE

PATANOL[®] (olopatadine hydrochloride ophthalmic solution) 0.1% is indicated for the treatment of the signs and symptoms of allergic conjunctivitis.

CONTRAINDICATIONS

PATANOL[®] is contraindicated in persons with a known hypersensitivity to olopatadine hydrochloride or any components of PATANOL[®].

WARNINGS

PATANOL[®] is for topical use only and not for injection or oral use.

PRECAUTIONS

Information for Patients: To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Patients should be advised not to wear a contact lens if their eye is red. PATANOL[®] should not be used to treat contact lens related irritation. The preservative in PATANOL[®], benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red should be instructed to wait at least ten minutes after instilling PATANOL[®] before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size, these doses were 78,125 and 31,250 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay, or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of 62,500 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of 7,800 times the maximum recommended ocular human use level.

Pregnancy: Pregnancy Category C. Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day or 93,750 times the MROHD and rabbits treated at 400 mg/kg/day or 62,500 times the MROHD during organogenesis showed a decrease in live fetuses. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers: Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATANOL[®] is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

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

ADVERSE REACTIONS

Headaches have been reported at an incidence of 7%. The following adverse experiences have been reported in less than 5% of patients: Asthenia, blurred vision, burning or stinging, cold syndrome, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, nausea, pharyngitis, pruritus, rhinitis, sinusitis, and taste perversion. Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye two times per day at an interval of 6 to 8 hours.

HOW SUPPLIED

PATANOL[®] (olopatadine hydrochloride ophthalmic solution) 0.1% is supplied as follows:

- 5 mL in plastic DROP-TAINER[®] dispenser.
- 5 mL NDC 0065-0271-05.

Rx Only

U.S. Patents Nos. 4,871,865; 4,923,892; 5,116,863; 5,641,805.
 Revised: December 2003

References:

1. Rosenwasser LJ, O'Brien T, Weyne J. Mast cell stabilization and anti-histamine effects of olopatadine ophthalmic solution: a review of pre-clinical and clinical research. *Curr Med Res Opin.* 2005;21:1377-1387.
2. PATANOL[®] solution prescribing information.
3. Yanni JM, Stephens DJ, Miller ST, et al. The *in vitro* and *in vivo* ocular pharmacology of olopatadine (AL-4943A), an effective anti-allergic/antihistaminic agent. *J Ocul Pharmacol Ther.* 1996;12:389-400.
4. Brockman HL, Momen MM, Knudtson JR, Miller ST, Graff G, Yanni JM. Interactions of olopatadine and selected antihistamines with model and natural membranes. *Ocul Immunol Inflamm.* 2003;11:247-268.
5. Berger W, Abelson MB, Gomes PJ, et al. Effects of adjuvant therapy with 0.1% olopatadine hydrochloride ophthalmic solution on quality of life in patients with allergic rhinitis using systemic or nasal therapy. *Ann Allergy Asthma Immunol.* 2005;95:361-371.

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Staged Diagnostic Testing Proposed for Encephalitis

BY JANE SALODOF MACNEIL
 Southwest Bureau

ASPEN, COLO. — Dr. Mark J. Abzug has proposed a three-staged diagnostic approach to testing a child ill with encephalitis.

Encephalitis has an extraordinary number of possible causes for which an ever-increasing number of tests are available, he said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

Under the banner of broad differential diagnoses, he listed more than 100 viruses; more than a dozen bacteria; parasites; fungi; parameningeal focus, autoimmune conditions, metabolic disorders; toxins; drugs; malignancy; and hemorrhage.

Even with extensive investigation, the etiology is elusive, according to Dr. Abzug, a professor of pediatrics at the University of Colorado, Denver.

Studies find a cause in only 25%–65% of cases.

"Encephalitis is one of the most frustrating, if not the most frustrating, infectious disease consults," Dr. Abzug commented.

"Here is a child who was well, usually up to a day or two before. By the time you see the child, he or she may now be neurologically devastated," he said.

Few therapeutics are available, he added, and the damage is often irreversible in children who survive.

With so many possible causes and such poor results, Dr. Abzug offered his proposal, presented as "arguable," as an answer to a fundamental question for clinicians: Where do you start?

A reasonable approach begins with patient history, he said. It often provides more valuable information than diagnostic tests.

Dr. Abzug urged clinicians to ask about respiratory and gastrointestinal symptoms, vaccinations, family exposures to infectious diseases, recent travel, animal and insect exposures, consumption of unpasteurized dairy products, recreational activities such as spelunking and hiking, and pica/geophagia.

Seasonal outbreaks and diseases prevalent in the community also should be considered, he said.

Physical examination is not very helpful, as the findings do not usually point to a specific etiology, according to Dr. Abzug.

Focal, in particular, is almost always—although not uniformly—present in herpes simplex infections, but also can suggest other diseases.

"All that is focal is not herpes simplex disease."

His staged approach begins with first-line testing for the most likely causes. Dr.

Abzug recommended cerebrospinal fluid (CSF) polymerase chain reaction (PCR) testing for herpes simplex virus and enterovirus.

The former accounts for 10%-20% of cases in the United States, the latter for up to 80% of encephalitis cases in which etiology is proved, he said.

Another 8%-10% of encephalitis cases with proven etiology are attributed to influenza virus.

In enterovirus season, do a viral culture or PCR of throat and rectal specimens, Dr. Abzug said.

During respiratory season, do a nasal wash with direct fluorescent antibody/viral culture testing for influenza, adenovirus, and other known respiratory viruses.

First-line testing also should include evaluation of symptomatic body sites and, if suggested clinically or by epidemiologic history, tests for exposure-related pathogens requiring specific treatments, such as tuberculosis.

In immunocompromised patients, do a CSF test for cryptococcal antigen and CSF PCR for varicella zoster, cytomegalovirus, Epstein-Barr virus, and (possibly) human herpesvirus 6. Always save CSF and serum, he said.

If this does not produce a diagnosis, Dr. Abzug proposed engaging in a second line of testing.

This would include Epstein-Barr serology; *Mycoplasma pneumoniae* CSF and throat PCR; testing for animal-related pathogens for which there have been relevant exposures; and tests for vector-borne pathogens, such as West Nile virus and other arboviruses, and for Lyme disease, if the epidemiology suggests possible exposures.

As a third line, Dr. Abzug recommended tests for miscellaneous pathogens if they fit the clinical context, such as parvovirus PCR and serology; human immunodeficiency virus PCR and serology; and tests for other specific exposure-related pathogens.

He also said to look for parasitic disease in the presence of a subacute course and/or eosinophilia in a child presenting with encephalitis.

"You can spend lots and lots of money, and not find anything," Dr. Abzug said, warning that no etiology will be identified in many cases.

In response to an audience question, he said he would start acyclovir treatment early on, and would continue it until herpes is ruled out or an alternate diagnosis is reached.

"Starting acyclovir until you know [the right diagnosis] is the right thing to do because the sooner you start therapy for herpes encephalitis, the better your outcome" if it turns out to be the culprit, Dr. Abzug emphasized. ■

The staged approach begins with first-line testing for the most likely causes, using CSF PCR testing for herpes simplex virus and enterovirus.