

SUBSPECIALTY CONSULT

Dysmenorrhea and Irregular Uterine Bleeding

Dysmenorrhea and menorrhagia beyond the norm often overlap in adolescents and can occur in up to 15% of these young women.

The normal time period from breast development (thelarche) and development of pubic hair to menses in young girls is about 2 years. A longer time course is cause for investigation.

The maturation of the hypothalamic-pituitary-ovarian axis occurs over approximately 5 years. After initiation of menses (menarche), some adolescents have anovulatory cycles, i.e., no luteinizing hormone surge with subsequent lack of ovulation and dysfunctional estrogen effect on the uterine endometrial lining. This can present with irregular bleeding that can be very heavy when the endometrial lining sheds in an unsynchronized manner. If no other cause for this bleeding is established (for example, endocrine, anatomic, or underlying chronic disease), then it is considered dysfunctional uterine bleeding (DUB).

In the same time period of 5 years

from menarche, an estimated 15%-30% of young women will have primary dysmenorrhea strong enough to require pain medication, including nonsteroidal anti-inflammatory drugs (NSAIDs).

The vast majority of young adolescent girls experience some pain with their periods, ranging from discomfort to pain requiring medication to being unable to go to school.

When the pain is severe, these patients either miss school or just make it through the school day, but their attention and performance suffer. These girls with significant pain need more assistance because their dysmenorrhea may not sub-

side for several years, and a referral to a subspecialist is warranted.

In terms of differential diagnosis, menstrual pain (dysmenorrhea) is a crampy, focal phenomenon in the mid-lower quadrant, sometimes with radiation to the back and the lower extremities. It starts with the onset of menses. If the pain precedes menses, it may be endometriosis and not primary dysmenor-

rhea, although there is an overlap in the pain symptoms between these two entities. A nonleading question to ask is whether the patient experiences pain before, during, or after her cycle.

A gastrointestinal etiology is more likely if the pain is nonfocal and present in all four quadrants. Ruling out other GI etiologies, particularly constipation, is important. A trial of Miralax over 2-3 weeks with a cessation in the pain easily confirms constipation as the underlying cause. Constipation is very common in children and adolescents, and the pain is not related to the menstrual cycle.

Dysmenorrhea is a clinical diagnosis. Laboratory tests for this condition are not needed. Instead, a good history, detailed description of the pain, and ultrasound examination (transabdominal, not transvaginal) aid the differential diagnosis. Ultrasound is reassuring, as it can show normal uterine development

and no ovarian masses, including no benign childhood ovarian tumors. Rarely is a pelvic examination necessary.

Pediatricians are instrumental in terms of educating patients, encouraging these patients to keep a detailed menstrual and pain diary, and advocating appropriate use of NSAIDs.

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DR. MAMA is a pediatric and adolescent ob.gyn. at Cooper University Hospital in Camden, N.J. He said he had no relevant financial disclosures.



BY SAIFUDDIN T. MAMA, M.D., M.P.H.

Pataday™ (olopatadine hydrochloride ophthalmic solution) 0.2%

INDICATIONS AND USAGE

PATADAY™ solution is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

CONTRAINDICATIONS

Hypersensitivity to any components of this product.

WARNINGS

For topical ocular use only. Not for injection or oral use.

PRECAUTIONS

Information for Patients

As with any eye drop, 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.

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% should not be used to treat contact lens related irritation. The preservative in PATADAY™ solution, 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 PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% 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 and a 50 kg person, these doses were approximately 150,000 and 50,000 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 approximately 100,000 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 approximately 15,000 times the MROHD level.

Pregnancy:

Teratogenic effects: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 150,000 times the MROHD and rabbits treated at 400 mg/kg/day, or approximately 100,000 times the MROHD, during organogenesis showed a decrease in live fetuses. In addition, rats treated with 600 mg/kg/day of olopatadine during organogenesis showed a decrease in fetal weight. Further, rats treated with 600 mg/kg/day of olopatadine during late gestation through the lactation period showed a decrease in neonatal survival and body weight. 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 PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% 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 and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

The following adverse experiences have been reported in 5% or less of patients:

Ocular: blurred vision, burning or stinging, conjunctivitis, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, pain and ocular pruritus.

Non-ocular: asthenia, back pain, flu syndrome, headache, increased cough, infection, nausea, 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 once a day.

HOW SUPPLIED

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is supplied in a white, oval, low density polyethylene DROP-TAINER® dispenser with a natural low density polyethylene dispensing plug and a white polypropylene cap. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

NDC 0065-0272-25

2.5 mL fill in 4 mL oval bottle

Storage:

Store at 2°C to 25°C (36°F to 77°F)
U.S. Patents Nos. 4,871,865; 4,923,892; 5,116,863; 5,641,805; 6,995,186

Rx Only

References:

1. Abelson MB, Gomes PJ, Pasquine T, et al. Efficacy of olopatadine ophthalmic solution 0.2% in reducing signs and symptoms of allergic conjunctivitis. *Allergy Asthma Proc.* 2007;28:427-433.
2. PATADAY™ Solution Package Insert.
3. Vogelstein CT, Abelson MB, Pasquine T, et al. Preclinical and clinical antiallergic effect of olopatadine 0.2% solution 24 hours after topical ocular administration. *Allergy Asthma Proc.* 2004;25:69-75.
4. *Wolters Kluwer Health, Source®* Pharmaceutical Audit Suite. August 2009-September 2010.
5. *Wolters Kluwer Health, Source®* Pharmaceutical Audit Suite. September 2008-August 2009.

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