

ACL Reconstruction Called Safe in Kids, Teens

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KEYSTONE, COLO. — Growing adolescents can undergo anterior cruciate ligament repair safely, and perhaps should have the surgery to avoid the possibility of later problems, George A. Paletta Jr., M.D., said at the annual meeting of the American Orthopaedic Society for Sports Medicine.

Recommendations for the management of anterior cruciate ligament (ACL) injury

in the skeletally immature patient have varied, but Dr. Paletta's thorough investigations, and case series of patients, have convinced him that it is possible to perform a reconstruction without compromising the tibial growth plate and creating a leg length discrepancy, he said.

The natural history of an ACL injury in a skeletally immature patient is that the majority continue to have knee instability and many develop meniscal tears, said Dr. Paletta, chief of sports medicine service at

Washington University, St. Louis. In one series of 38 junior high athletes with ACL injuries who did not have ACL surgery and were followed for a minimum of 2 years, 27 developed meniscal tears (*Am. J. Sports Med.* 1994;22:478-84).

That is to say nothing of what could be happening to these children's knees in the even longer term, Dr. Paletta said.

And keeping the child or adolescent out of hazardous sports is not really the answer because most who reinjure their

knees do so not during an organized activity but during recess or some other time when they are just being exuberant.

On the other hand, animal studies have shown that one needs to damage a greater proportion of the physal plates than is normally damaged during an ACL reconstruction to create growth arrest. And in a series of growing athletes who have undergone reconstruction, 90% or better have reportedly returned to sports.

In his own series of patients, yet to be published, Dr. Paletta performed ACL reconstruction in 29 patients aged 10-13 years by using either an over-the-top technique that spared the physal area of the

femur or a technique that drilled through the physal areas of the tibia and the femur.

At a minimum of 2 years' follow-up, none of the patients had any radiographic evidence of premature closure of the growth plates, and all

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but two patients (one from each group) had returned to sports participation at the same level as before their injury.

Though the results from both techniques were similar, pivot-testing suggested the complete transphyseal technique produced somewhat better stability, Dr. Paletta said.

In another series of Dr. Paletta's patients, 49 preadolescents (Tanner stage 0, 1, or 2) with ACL tears were treated with complete transphyseal reconstruction, he said.

Again at a minimum follow-up of 24 months (with an average follow-up of 40 months), none of the patients had a leg length discrepancy greater than 1 cm and none had an angular deformity of more than 5 degrees.

Twenty-seven of the patients had reached skeletal maturity by the time of the last examination.

Forty-seven of the 49 patients reported no instability, and 45 of the patients had returned to sports at or above the same level as before their injury. Only one patient had a rerupture, an injury that occurred 6 years after the surgery.

On the basis of his experience, Dr. Paletta said his recommendations for management would be to perform transphyseal hamstring reconstruction for isolated ACL insufficiency for male patients who are Tanner stage 1, 2, or 3, and for premenarcheal females, if there is functional instability.

If there is no functional instability, Dr. Paletta would recommend treating patients conservatively.

For older patients with isolated ACL insufficiency—males Tanner stage 4 or 5, and postmenarcheal females—he would recommend reconstruction.

He would also recommend reconstruction for any patient if there also was meniscus damage. ■

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* Shorter duration of episode: in study 1, acyclovir (n=324) 4.3 days vs vehicle (n=346) 4.8 days (P=0.010). In study 2, acyclovir (n=328) 4.6 days vs vehicle (n=343) 5.2 days (P=0.007). Shorter duration of pain: in study 1, acyclovir (n=334) 2.9 days vs vehicle (n=352) 3.2 days (P=0.024). In study 2, acyclovir (n=348) 3.1 days vs vehicle (n=351) 3.5 days (P=0.027).

Reference: 1. Spruance SL, Nett R, Marbury T, Wolff R, Johnson J, Spaulding T, for The Acyclovir Cream Study Group. Acyclovir cream for treatment of herpes simplex labialis: results of two randomized, double-blind, vehicle-controlled, multicenter clinical trials. *Antimicrob Agents Chemother.* 2002;46:2238-2243.

ZOVIRAX® (acyclovir) Cream 5%

INDICATIONS AND USAGE

ZOVIRAX Cream is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and adolescents (12 years of age and older).

CONTRAINDICATIONS

ZOVIRAX Cream is contraindicated in patients with known hypersensitivity to acyclovir, valacyclovir, or any component of the formulation.

PRECAUTIONS

General: ZOVIRAX Cream is intended for cutaneous use only and should not be used in the eye or inside the mouth or nose. ZOVIRAX Cream should only be used on herpes labialis on the affected external aspects of the lips and face. Because no data are available, application to human mucous membranes is not recommended. ZOVIRAX Cream has a potential for irritation and contact sensitization (see ADVERSE REACTIONS). The effect of ZOVIRAX Cream has not been established in immunocompromised patients.

Drug Interactions: Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with ZOVIRAX Cream.

Carcinogenesis, Mutagenesis, Impairment or Fertility: Systemic exposure following topical administration of acyclovir is minimal. Dermal carcinogenicity studies were not conducted. Results from the studies of carcinogenesis, mutagenesis and fertility are not included in the full prescribing information for ZOVIRAX Cream due to the minimal exposures of acyclovir that result from dermal application. Information on these studies is available in the full prescribing information for ZOVIRAX Capsules, Tablets, and Suspension and ZOVIRAX for Injection.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Acyclovir was not teratogenic in the mouse, rabbit, or rat at exposures greatly in excess of human exposure. There are no adequate and well-controlled studies of systemic acyclovir in pregnant women. A prospective epidemiologic registry of acyclovir use during pregnancy was established in 1984 and completed in April 1999. There were 749 pregnancies followed in women exposed to systemic acyclovir during the first trimester of pregnancy resulting in 756 outcomes. The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects

or to permit reliable or definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. Systemic acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether topically applied acyclovir is excreted in breast milk. Systemic exposure following topical administration is minimal. After oral administration of ZOVIRAX, acyclovir concentrations have been documented in breast milk in 2 women and ranged from 0.6 to 4.1 times the corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Nursing mothers who have active herpetic lesions near or on the breast should avoid nursing.

Geriatric Use: Clinical studies of acyclovir cream did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Systemic absorption of acyclovir after topical administration is minimal (see CLINICAL PHARMACOLOGY).

Pediatric Use: Safety and effectiveness in pediatric patients less than 12 years of age have not been established.

ADVERSE REACTIONS

In 5 double-blind, placebo-controlled trials, 1,124 patients were treated with ZOVIRAX Cream and 1,161 with placebo (vehicle) cream. ZOVIRAX Cream was well tolerated; 5% of patients on ZOVIRAX Cream and 4% of patients on placebo reported local application site reactions.

The most common adverse reactions at the site of topical application were dry lips, desquamation, dryness of skin, cracked lips, burning skin, pruritus, flakiness of skin, and stinging on skin; each event occurred in less than 1% of patients receiving ZOVIRAX Cream and vehicle. Three patients on ZOVIRAX Cream and 1 patient on placebo discontinued treatment due to an adverse event.

An additional study, enrolling 22 healthy adults, was conducted to evaluate the dermal tolerance of ZOVIRAX Cream compared with vehicle using single occluded and semi-occluded patch testing methodology. Both ZOVIRAX Cream and vehicle showed a high and cumulative irritation potential. Another study, enrolling 251 healthy adults, was conducted to evaluate the contact sensitization potential of ZOVIRAX Cream using repeat insult patch testing methodology. Of 202 evaluable subjects, possible cutaneous sensitization reactions were observed in the same 4 (2%) subjects with both ZOVIRAX Cream and vehicle, and these reactions to both ZOVIRAX Cream and vehicle were confirmed in 3 subjects upon rechallenge. The sensitizing ingredient(s) has not been identified.

The safety profile in patients 12 to 17 years of age was similar to that observed in adults.

Observed During Clinical Practice: In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of acyclovir cream. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to acyclovir cream.

General: Angioedema, anaphylaxis.

Skin: Contact dermatitis, eczema, application site reactions including signs and symptoms of inflammation.

OVERDOSAGE

Overdosage by topical application of ZOVIRAX Cream is unlikely because of minimal systemic exposure (see CLINICAL PHARMACOLOGY).

DOSAGE AND ADMINISTRATION

ZOVIRAX Cream should be applied 5 times per day for 4 days. Therapy should be initiated as early as possible following onset of signs and symptoms (i.e., during the prodrome or when lesions appear). For adolescents 12 years of age and older, the dosage is the same as in adults.

HOW SUPPLIED

Each gram of ZOVIRAX Cream 5% contains 50 mg acyclovir in an aqueous cream base. ZOVIRAX Cream is supplied as follows:
2-g tubes (NDC 64455-994-42).
5-g tubes (NDC 64455-994-45).

Store at or below 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) (see USP Controlled Room Temperature).

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