

Three Factors Spell Trouble in JIA-Related Uveitis

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VERSAILLES, FRANCE — A multi-center chart review of children whose uveitis was associated with juvenile idiopathic arthritis has identified three factors to help physicians target patients at risk of poor ocular outcomes.

"Sometimes the ophthalmologists are a little shy about pushing stronger immunomodulatory drugs. We were looking

for predictors at onset so that ... maybe we would know which kids are likely to have trouble and maybe get them started on stronger medications earlier," the study's lead investigator, Richard J. Mier, M.D., said during a poster presentation at the 12th European Pediatric Rheumatology Congress.

Of the 44 children studied, 17 (39%) had serious eye problems during the 3 years after uveitis was detected. Despite the dual diagnosis, just 35% of the children who

had poor ocular outcomes were receiving systemic immunomodulatory drugs.

The surprising finding was that "only a third was getting treatment," Dr. Mier, director of pediatric services at Shriners Hospital for Children in Lexington, Ky., said in an interview.

"Our bottom line," he added, "is that we are undertreating these kids, and what we really need to do is treat them more aggressively earlier."

Dr. Mier and his coinvestigators defined

poor ocular outcomes 36 months after diagnosis as acuity of 20/50 or less in one eye, three or more complications, or the need for ocular surgery. The study narrowed 17 potential risk factors at uveitis diagnosis to the following three predictors of poor ocular outcomes:

- ▶ Moderate or severe inflammation in one or both eyes.
- ▶ Eye inflammation symptoms such as pain, redness, photophobia, and tearing.
- ▶ Visual acuity of 20/50 or less in one or both eyes.

While uveitis is an eye inflammation, most children with juvenile idiopathic arthritis (JIA) do not present with eye symptoms, according to Dr. Mier. Typically, they are referred to an ophthalmologist for an eye exam after JIA is diagnosed because uveitis is a known comorbidity.

The children in the study were diagnosed with arthritis at 53 months of age on average and with uveitis more than a year later at 69 months.

At 36 months of follow-up, the most common ocular complications were synechiae, cataracts, glaucoma, and band keratopathy. About a third of the children (34%) required eye surgery.

Different centers use a variety of strategies for managing uveitis associated with JIA, according to Dr. Mier. The ideal is to have the pediatric rheumatologist collaborate with the ophthalmologist in treating the child, he said. ■



BRIEF SUMMARY

Please consult package insert for full Prescribing Information.

INDICATION

EUFLEXXA™ (1% sodium hyaluronate) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen).

CONTRAINDICATIONS

- Do not use EUFLEXXA™ to treat patients who have a known hypersensitivity to hyaluronan preparations
- Do not use EUFLEXXA™ to treat patients with knee joint infections, infections or skin disease in the area of the injection site

WARNINGS

- Mixing of quaternary ammonium salts such as benzalkonium chloride with hyaluronan solutions results in formation of a precipitate. EUFLEXXA™ should not be administered through a needle previously used with medical solutions containing benzalkonium chloride. Do not use disinfectants for skin preparation that contain quaternary ammonium salts
- Do not inject intravascularly because intravascular injection may cause systemic adverse events

PRECAUTIONS

General

- Patients having repeated exposure to EUFLEXXA™ have the potential for an immune response; however, this has not been assessed in humans
- Safety and effectiveness of injection in conjunction with other intra-articular injectables, or into joints other than the knee has not been studied
- Remove any joint effusion before injecting
- Transient pain or swelling of the injected joint may occur after intra-articular injection with EUFLEXXA™
- Do not use after expiration date
- Protect from light
- Do not re-use—dispose of the syringe after use
- Do not use if the blister package is opened or damaged

Information for Patients

- Transient pain and/or swelling of the injected joint may occur after intra-articular injection of EUFLEXXA™
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within 48 hours following intra-articular injection
- The safety and effectiveness of repeated treatment cycles of EUFLEXXA™ have not been established

ADVERSE EVENTS

Adverse event information regarding the use of EUFLEXXA™ as a treatment for pain in OA of the knee was available from two sources; a multicenter clinical trial conducted in Germany and a single center clinical trial that was conducted in Israel.

Multicenter Clinical Investigation

This clinical investigation was a prospective randomized, double blinded, active control (commercially available hyaluronan product) study conducted at 10 centers. Three hundred twenty-one patients were randomized into groups of equal size to receive either EUFLEXXA™ (n=160) or the active control (n=161). A total of 119 patients reported 196 adverse events; this number represents 54 (33.8%) of the EUFLEXXA™ group and 65 (44.4%) of the active control group. There were no deaths reported during the study.

Incidences of each event were similar for both groups, except for knee joint effusion, which was reported by 9 patients in the active control group and one patient in the EUFLEXXA™ treatment group. A total of 160 patients received 478 injections of EUFLEXXA™. There were 27 reported adverse

events considered to be related to EUFLEXXA™ injections: arthralgia – 11 (6.9%); back pain – 1 (0.63%); blood pressure increase – 3 (1.88%); joint effusion – 1 (0.63%); joint swelling – 3 (1.88%); nausea – 1 (0.63%); paresthesia – 2 (1.25%); feeling of sickness of injection – 3 (1.88%); skin irritation – 1 (0.63%); tenderness in study knee – 1 (0.63%). Four adverse events were reported for the EUFLEXXA™ group that the relationship to treatment was considered to be unknown: fatigue – 3 (1.88%); nausea – 1 (0.63%).

Single Center Study

In a single-center, single-blinded, placebo controlled, prospective, two parallel treatment arm clinical trial a total of 49 (25 EUFLEXXA™, 24 placebo) patients were randomized into two treatment groups in a ratio of 1:1 EUFLEXXA™ or placebo. A total of 65 adverse events were reported by 17 (68%) of the patients in the EUFLEXXA™ group and 15 (63%) in the placebo group. Of the 65 total events reported, 20 were regarded as treatment related. Knee pain, hypokinesia of the knee, knee swelling, and rash were considered to be treatment related adverse events.

DETAILED DEVICE DESCRIPTION

Each syringe of EUFLEXXA™ contains:

Sodium hyaluronate	20 mg
Sodium chloride	17 mg
Disodium hydrogen phosphate dodecahydrate	1.12 mg
Sodium dihydrogen phosphate dihydrate	0.1 mg
Water for injection	q.s.

HOW SUPPLIED

EUFLEXXA™ is supplied in 2.25 ml nominal volume, disposable, pre-filled glass syringes containing 2 ml of EUFLEXXA™. Only the contents of the syringe are sterile. EUFLEXXA™ is nonpyrogenic.

CAUTION

Product contact parts of the syringe contain natural rubber latex, which may cause allergic reactions.

DIRECTIONS FOR USE

- Store refrigerated at 2°-8°C (36°-46°F). Protect from light.
- EUFLEXXA™ is administered by intra-articular injection into the knee synovial capsule using strict aseptic injection procedures. The full content of the syringe is injected into the affected knee at weekly intervals for 3 weeks, for a total of 3 injections.
- Twenty to thirty minutes before use, remove the product box from the refrigerator, remove the blister pack from the box and allow the syringe to come to room temperature. Be sure to return any syringes not intended for use to the refrigerator.

Toll free number for providers and patients to call with questions: 1-(888)-FERRING (1-(888)-337-7464).

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o-JIA Prognosis May Have New Genetic Marker

A gene polymorphism of the phosphorylated glycoprotein, osteopontin, appears to be associated with the prognosis of oligoarticular-onset juvenile idiopathic arthritis, but more data are needed before it is considered a reliable disease marker.

Recently proposed to be a new proinflammatory cytokine, osteopontin plays a role in bone resorption and angiogenesis and is known to mediate a number of inflammatory mechanisms.

The current study, led by Renato Marciano, M.D., of the G. Gaslini Institute and the University of Genova, Italy, involved 73 patients with persistent oligoarticular-onset juvenile idiopathic arthritis (o-JIA) and 46 with extended o-JIA (*Ann. Rheum. Dis.* 2005; doi:10.1136/ard.2005.040626).

Patients were genotyped for the biallelic insertion/deletion variant at +245 in the first intron of the osteopontin gene, which the researchers had previously found to be in strict linkage with molecular variants in the osteopontin promoter region.

The TG polymorphism in the first intron was identified as allele 1, and the TGTG allele as allele 2. The presence of allele 2 was significantly higher (47/73 or 64%) in the persistent oligoarticular group, compared with patients with the extended form (20/46 or 43%), suggesting a dominant effect of the TGTG allele in o-JIA patients.

—Patrice Wendling