

Approach Sulfasalazine, MTX With Caution in JIA

BY TIMOTHY F. KIRN
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SNOWMASS, COLO. — Prescribing patterns for sulfasalazine and methotrexate in patients with juvenile idiopathic arthritis need fine tuning, Patience White, M.D., said at a symposium sponsored by the American College of Rheumatology.

The doctor's concerns: Sulfasalazine needs to be prescribed more cautiously,

and methotrexate dosages are often too high.

Although sulfasalazine is commonly prescribed for juvenile idiopathic arthritis (JIA), there are significant risks to weigh against the benefits in this population, said Dr. White, chair of pediatric rheumatology at Children's National Medical Center, Washington.

Reports have suggested that in late-onset pauciarticular juvenile arthritis, sulfasalazine decreases symptoms by 50% or

more. But "I would urge you to use caution here," Dr. White said. It may not be as effective in other subtypes of juvenile arthritis, and findings from double-blind trials have been mixed on the issue of whether it really is better than placebo.

Most important, 30% of patients with systemic onset JIA can have a febrile, serum-sickness-like reaction while taking sulfasalazine. This is a risk that deserves serious consideration before the drug is started, Dr. White stressed.

Methotrexate is an established second-line agent, yet the dosages used are of ten too high.

In a recent investigation comparing the safety and efficacy of parenteral methotrexate 15 mg/m² per week with higher dosages for patients with polyarticular-course JIA, researchers found that efficacy plateaued with the lower dose.

All participants had failed to improve while receiving standard dosages of methotrexate (8-12.5 mg/m² per week [Arthritis Rheum. 2004;50:2191-201]).

Dr. White said she considers 10 mg/m² per week the most effective and appropriate dose; when patients do not respond, she tends to try etanercept rather than increase the dose of methotrexate.

Etanercept clearly has a place in treat-

ment, she said. About 74% of polyarticular JIA patients respond to etanercept, and it can reduce the need for prednisone and methotrexate. The biologic has been shown to have no more toxicity in patients as young as 3 years old than it does in adults.

Various combination treatments have been tried in JIA with some success. However, these reports are based on small groups of patients, so combination therapy is not really evidence based, Dr. White said.

She added that sometimes when a JIA patient stops responding to a particular regimen that once was effective, it is not a failure of therapy. It may be that the patient has simply outgrown his or her dosage.

Children can be more susceptible than adults to certain types of toxicity, and these effects can be subtle. NSAIDs, for example, can make some children hyperactive. Naproxen can cause pseudoporphyria.

Because of their effects on growth, systemic corticosteroids should be avoided unless the diagnosis is absolutely certain, she said.

Intraarticular corticosteroid injections, on the other hand, work well in children. Several studies have demonstrated that triamcinolone is the agent of choice, Dr. White added.

Findings from double-blind trials have been mixed on the issue of whether sulfasalazine really is better than placebo.

ORTHOVISC® High Molecular Weight Hyaluronan

BRIEF SUMMARY. Please see full prescribing information.

INDICATIONS

ORTHOVISC® is indicated in the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and to simple analgesics, e.g. acetaminophen.

CONTRAINDICATIONS

- Do not administer to patients with known hypersensitivity (allergy) to hyaluronate preparations.
- Do not administer to patients with known allergies to avian or avian-derived products (including eggs, feathers, or poultry).
- Do not inject ORTHOVISC® in the knees of patients with infections or skin diseases in the area of the injection site or joint.

WARNINGS

- Do not concomitantly use disinfectants containing quarternary ammonium salts for skin preparation as hyaluronic acid can precipitate in their presence.
- Transient increases in inflammation in the injected knee following ORTHOVISC® injection have been reported in some patients with inflammatory osteoarthritis.

PRECAUTIONS

General

- Strict aseptic injection technique should be used during the application of ORTHOVISC®.
- The safety and effectiveness of the use of ORTHOVISC® in joints other than the knee have not been demonstrated.
- The effectiveness of a single treatment cycle of less than 3 injections has not been established. Pain relief may not be seen until after the third injection.
- The safety and effectiveness has not been established for more than one course of treatment.
- STERILE CONTENTS. The pre-filled syringe is intended for single use only. The contents of the syringe should be used immediately after opening. Discard any unused ORTHOVISC®. Do not resterilize.
- Do not use ORTHOVISC® if the package has been opened or damaged.
- Store ORTHOVISC® in its original package at room temperature (below 77°F/25°C). DO NOT FREEZE.
- Remove joint effusion, if present, before injecting ORTHOVISC®.
- Only medical professionals trained in accepted injection techniques for delivering agents into the knee joint should inject ORTHOVISC® for the indicated use.

ADVERSE EVENTS

ORTHOVISC® was investigated in 3 randomized, controlled clinical studies conducted in the U.S. An integrated safety analysis was conducted, pooling the ORTHOVISC® groups from the 3 studies and pooling the control groups, which were either intraarticular saline injections or arthrocentesis. In the integrated analysis, there were 562 patients in the groups treated with ORTHOVISC® (434 receiving 3 injections and 128 receiving 4 injections), 296 in the group treated with physiological saline, and 123 in the group treated with arthrocentesis.

Adverse events occurring at >5% of the overall integrated population included: arthralgia (12.6% in the ORTHOVISC® group, 17.2% in the saline group, and 0.8% in the arthrocentesis group); back pain (6.9% in the ORTHOVISC® group, 12.2% in the saline group, and 4.9% in the arthrocentesis group); and headache NOS (12.1% in the ORTHOVISC® group, 16.6% in the saline group, and 17.9% in the arthrocentesis group). Injection site adverse events (including erythema, edema, pain and reaction NOS) occurred at rates of 0.4%, 0.9%, 2.5% and 0.2%, respectively, in the ORTHOVISC® group, compared to 0.0%, 0.3%, 2.0%, and 0.7% in the saline group and 0.0%, 0.0%, 0.8% and 0.8% in the arthrocentesis group.

Local adverse events reported on a by-patient basis for the combined ITT populations of the three studies are presented in Table 1.

Table 1
Local individual adverse events reported on a by-patient basis for the combined ITT populations of the three studies.

Adverse Event	ORTHOVISC N = 562	Saline N = 296	Arthrocentesis N = 123
Any Adverse Event	349 (62.1%)	204 (68.9%)	65 (52.8%)
Injection site erythema	2 (0.4%)	0 (0%)	0 (0%)
Injection site edema	5 (0.9%)	1 (0.3%)	0 (0%)
Injection site pain	14 (2.5%)	6 (2.0%)	1 (0.8%)
Injection site reaction NOS ¹	1 (0.2%)	2 (0.7%)	1 (0.8%)
Pain NOS ¹	14 (2.5%)	11 (3.7%)	1 (0.8%)
Arthralgia	71 (12.6%)	51 (17.2%)	1 (0.8%)
Arthritis NOS ¹	4 (0.7%)	5 (1.7%)	0 (0%)
Arthropathy NOS ¹	5 (0.9%)	3 (1.0%)	0 (0%)
Baker's cyst	2 (0.4%)	2 (0.7%)	0 (0%)
Bursitis	6 (1.1%)	6 (2.0%)	2 (1.6%)
Joint disorder NOS ¹	2 (0.4%)	0 (0%)	0 (0%)
Joint effusion	2 (0.4%)	1 (0.3%)	1 (0.8%)
Joint stiffness	3 (0.5%)	2 (0.7%)	0 (0%)
Joint swelling	4 (0.7%)	2 (0.7%)	1 (0.8%)
Localized osteoarthritis	5 (0.9%)	1 (0.3%)	1 (0.8%)
Aggravated osteoarthritis	2 (0.4%)	0 (0%)	1 (0.8%)
Knee arthroplasty	3 (0.5%)	2 (0.7%)	0 (0%)

Notes: ¹NOS = Not otherwise specified.

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AML 530-220 01/04
08VSC1000B 2/04

Distributed by:

ORTHO BIOTECH
Ortho Biotech Products, L.P.
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Product Code 59676-360-01

WBC Count, Pain Severity Separate Leukemia From JIA

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SNOWMASS, COLO. — Elevated WBC count is the best indication that a pediatric patient presenting with joint pain has juvenile idiopathic arthritis rather than leukemia, but there are some subtle clinical differences, Patience White, M.D., said at a symposium sponsored by the American College of Rheumatology.

Joint pain in leukemia is usually much more severe than in JIA, and the patient with leukemia may also have bone pain and night pain, said Dr. White, chief of pediatric rheumatology at Children's National Medical Center, Washington.

In the child with JIA, fever will often be high and spiking; fever associated with leukemia tends to be low-grade.

In addition, 90% of patients with systemic onset JIA will have an associated rash, compared with 10% of leukemia patients.

Still, the two can look clinically similar,

and it's common for patients with leukemia to end up on a potentially harmful trial course of corticosteroids. In questionable cases, the white blood cell count is most revealing.

Dr. White noted the case of an 8-year-old boy referred to her for possible diagnosis of systemic onset JIA.

The patient had painful arthritis and a maculopapular rash over the trunk, wrist, and ankle and had been experiencing daily fevers for 4 weeks. He had lost 5% of his body weight.

Testing for infection, including blood and urine cultures and a Lyme disease assay, had been negative.

A course of treatment with an NSAID had been unsuccessful and, most importantly, the white blood cell count, at 9,000 cells/μL, was too low to be consistent with a diagnosis of JIA, Dr. White said.

If the patient had JIA, the WBC should have been at least 30,000 cells/μL.

She ordered a bone marrow biopsy rather than initiate a trial of corticosteroid therapy, and the diagnosis of leukemia was confirmed.

The two conditions can look clinically similar, and it's common for patients with leukemia to end up on potentially harmful corticosteroids.