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Short Communication

Understanding and Managing Juvenile Arthritis: A Comprehensive Examination of Diagnosis, Treatment, and Long-Term Outcome

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Abstract

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of idiopathic inflammatory arthritis affecting children younger than 16 years of age and lasting six weeks or longer. Depending on the number of joints affected, presence of extra-articular manifestations, systemic symptoms, serology and genetic factors, JIA is divided into oligoarticular, polyarticular, systemic, psoriatic, enthesitis-related and undifferentiated arthritis. The illness can run in families but can also be caused by particular factors. Treatment of JIA requires anti-inflammatory and immunomodulatory drugs and physical therapy, and eventually, surgery, nutritional support, and psychosocial support may be needed. Patients 4 to 17 years of age with polyarticular-course juvenile rheumatoid arthritis who had active disease (at least five swollen joints and at least three joints with limitation of motion) that had not responded adequately to treatment with nonsteroidal antiinflammatory drugs (NSAIDs) are taken for the study.

Keywords: Juvenile Idiopathic Arthritis (JIA); Illness

The aim of this study is to compare the efficacy and safety of methotrexate and adalimubab in patents with juvenile arthritis (JA).

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of idiopathic inflammatory arthritis affecting children younger than 16 years of age and lasting six weeks or longer. The terminology of chronic arthritis in children has evolved from juvenile chronic arthritis (JCA) and juvenile rheumatoid arthritis (JRA) to JIA since 1995. Unlike adult rheumatoid arthritis, which is ongoing (chronic) and lasts a lifetime, children often outgrow JIA. But the disease can affect bone development in a growing child [1].

Children of all races and ethnic backgrounds can get the disease. It is very rare for more than one member of a family to have JIA,

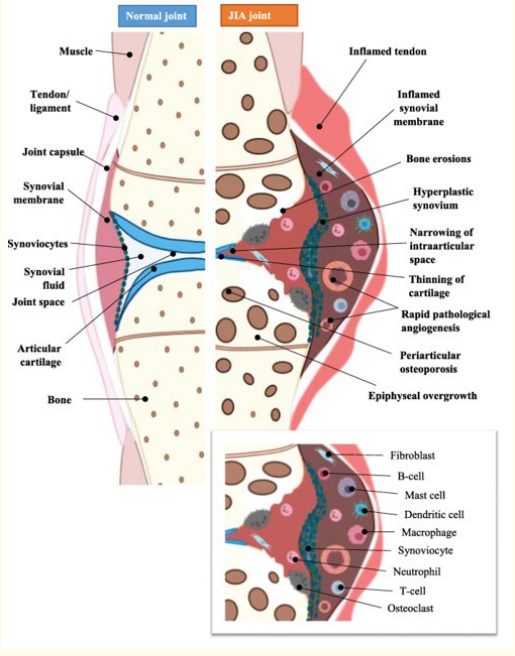

Figure 1

but children with a family member with chronic arthritis, including JIA, are at a slightly increased risk of developing it. Having a family member with psoriasis is a risk factor for a form of JIA called psoriatic JIA.

Types

The most typical types of juvenile arthritis are divided into groups based on the symptoms they produce, all of which result in chronic, or long-term, inflammation and pain in the joints and other areas of the body [2].

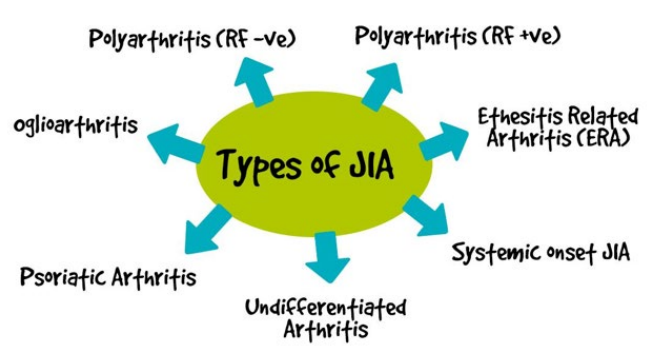

Figure 2

Oligoarticular

The word oligoarticular is characterized by "few joints." Only a small number of joints are affected by this kind of juvenile arthritis. The oligoarticular variant of juvenile arthritis affects about 50% of youngsters. It is more likely to appear in girls under the age of eight.

Figure 3

When a child has oligoarticular juvenile arthritis, only one joint—usually the knee or ankle—is affected in half of the cases. Juvenile monoarticular arthritis is what this is. This arthritis may only need slight treatment in some circumstances.

Polyarticular

The polyarticular variant of juvenile arthritis affects about 30% of youngsters. Girls than boys are more likely to develop this type of arthritis. Five or more joints, including both bigger (such as the knees and ankles) and smaller (such as the hands and feet), are affected by polyarticular juvenile arthritis. Both sides of the body are frequently impacted.

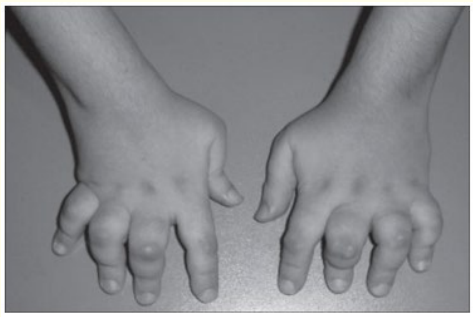

Figure 4

Children who have elevated levels of IgM rheumatoid factor (RF), a specific blood marker or antibody, may have a more severe version of the illness.

Psoriatic

Children who with psoriatic arthritis experience either:a condition known as psoriasis or a psoriatic parent or sibling. These kids may also experience nail alterations and dactylitis, a generalized swelling of the toe or finger. Occasionally, just a few joints are damaged; other times, several joints, including both tiny and major joints, are impacted.

Enthesitis-related Arthritis

A kind of juvenile arthritis called enthesitis-related arthritis usually involves inflammation of tendons, ligaments, and joints. The spine may also be affected. Children with this form of arthritis might have back pain as well as joint pain occasionally without any

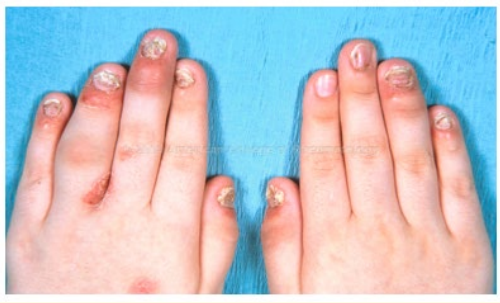

Figure 5

visible swelling. Back inflammation can happen later in life. Boys above the age of 6 are most frequently affected with enthesitis-related arthritis.

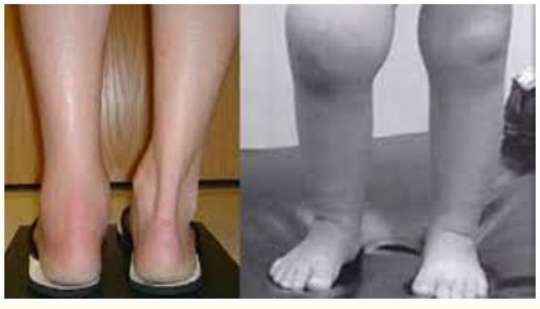

Figure 6

Systemic

The systemic form of juvenile arthritis affects about 20% of youngsters. Juvenile systemic arthritis affects movement in at least one joint and produces swelling. Rash and inflammation of internal organs like the heart, liver, spleen, and lymph nodes are further symptoms. This diagnosis is supported by a temperature of at least 102° every day for at least two weeks.

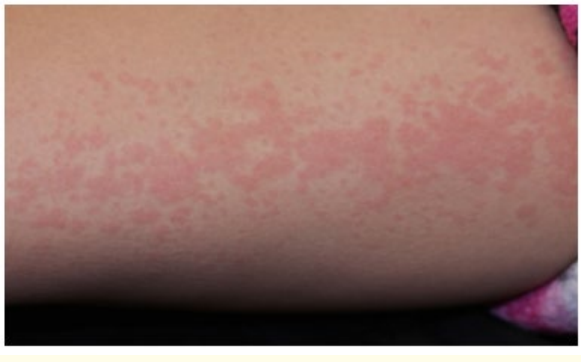

Figure 7

Children with systemic juvenile arthritis who are not appropriately treated may develop macrophage activation syndrome, a serious illness that affects several organ systems. This disorder can be lethal if left untreated.

Etiology

Abnormal immune responses triggered by the interactions between environmental factors in a genetically susceptible individual are speculative. Some environmental factors such as antibiotic exposure and C-section deliveries are potential risks. The immune system of the body targets its own healthy cells and tissues. JIA occurs by various factors. Genes and the environment are two of these. This indicates that the illness can run in families but can also be caused by particular factors [1].

Treatment

Treatment of JIA requires anti-inflammatory and immunomodulatory drugs and physical therapy, and eventually, surgery, nutritional support, and psychosocial support may be needed. The choice of pharmacological treatment depends on the disease subtypes, disease severity and damage, associated disease, and family acceptance. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the mainstay of initial symptomatic treatment for all subtypes. The NSAID use in JIA has decreased over time with modern aggressive treatment, including methotrexate and biologics [1].

Treatment will rely on childs symptoms, age, and general health. Moreover, it will depend on how serious the problem is.

Medicines like,

- NSAIDs, or nonsteroidal anti-inflammatory drugs, are used to treat pain and inflammation.
- Disease-modifying antirheumatic medicines (DMARDs), like methotrexate, used to control inflammation and control JIA.
- Corticosteroid medications can be used to treat severe symptoms and inflammation.
- Biologic medications that prevent the body from responding in an inflammatory way. When other treatments don't work, they are tried.

Statistics

About 14% of Indians seek medical attention each year for this joint issue. In India, more than 180 million people suffered

Drug	Mechanism of Action	Therapeutic Options	Adverse Event
Methotrexate	MTX is a structural analogue of folic acid that inhibits dihydrofolate reductase and DNA synthesis Acts in different pathway: cytokine production, arachidonic acid metabolism and cell apoptosis	Polyarticular JIA Oligoarticular JIA JIA-related uveitis refractory to topical treatment sJIA with predominant joint inflammation and without active systemic symptoms Psoriatic JIA	Nausea Oral ulceration Infections (herpes zoster) Severe complications in less than 1% of cases include:- Cirrhosis- Pneumonitis- Leucopenia- Thrombocytopenia- Anaemia
Leflunomide	Inhibition of T-cell proliferation by blocking pyrimidine synthesis	Polyarticular JIA patients who cannot tolerate MTX Used rarely in pediatric patients because of its teratogenicity and long half-life	Diarrhoea, Rashes, Cytopenia, Abnormal liver-function test, Teratogenicity
Sulfasalazine	Immune-suppressive effect not fully established	ERA with moderate activity, but not in other types of JIA	Gastrointestinal toxicity, Sulphonamide allergy, Neuropsychiatric complications (headache, anxiety), Pancytopenia, Pneumonitis, Myelosuppression, Hypogammaglobulinaemia
Adalimumab	Subcutaneous recombinant human IgG1κ monoclonal antibody Neutralises TNFα by binding with soluble and membrane-bound TNF	JIA patients with resistance or intolerance to MTX Polyarticular JIA JIA with uveitis	Risk of reactivation of latent infections such as tuberculosis, and new infections caused by viruses, fungi, or bacteria Rare reports of:- Lymphoma- Demyelinating central nervous system disorders- Cardiac failure
Infliximab	Intravenous chimeric monoclonal antibody against TNFα Binding with soluble and transmembrane TNFα, that mediates complement and antibody-dependent cytotoxicity of expressed TNFα cells (macrophages and monocytes)	Polyarticular JIA where there has been the use of MTX for at least 3 months with poor response Uveitis Psoriatic JIA	Opportunistic infections: herpes, tuberculosis, pseudomonas pneumonia, reactivation of hepatitis B, fungal infection
Etanercept	Fusion protein consisting of the extracellular domain of the human p75 TNFα receptor Linked to the Fc region of human IgG1, binds and inhibits soluble TNFα	Polyarticular JIA with resistance or intolerance to MTX ERA Psoriatic JIA	Central nervous system events (headache, neuritis) Varicella infections Rare:- Malignancy

Table 1

from arthritis in 2017. Additionally, statistics showed that 14% of Indians visited a doctor each year for this joint ailment. Even though these figures may have increased significantly over the last five years, arthritis still has a higher prevalence than conditions like diabetes, AIDS, and cancer [3].

Standard drug - Methotrexate

It is a type of disease-modifying anti-rheumatic drug (DMARD). For those suffering from particular illnesses, it is used to lower immune system activity.

Due to its great potency and effectiveness in treating rheumatoid arthritis in these patients, methotrexate is a folic acid antagonist that has received FDA approval. It can also be helpful for treating juvenile idiopathic arthritis [7].

Brands - BIOTREXATE

Figure 8

Mechanism of action

Methotrexate inhibits dihydrofolate reductase, preventing the reduction of dihydrobiopterin (BH2) to tetrahydrobiopterin (BH4), leading to nitric oxide synthase uncoupling and increased sensitivity of T cells to apoptosis, thereby diminishing immune responses [4].

By modulating cell-specific signalling pathways, methotrexate inhibits important pro-inflammatory properties of major cell lineages involved in rheumatoid arthritis pathogenesis, including T cells, macrophages, endothelial cells and fibroblast-like synoviocytes [4].

Uses

- Certain bodily cells, particularly those that divide quickly like cancer cells, bone marrow cells, and skin cells, are inhibited from growing by methotrexate.

- Leukemia and some forms of breast, skin, head & neck, lung, uterine, and other cancers are all treated with methotrexate.

- Adults with rheumatoid arthritis and severe psoriasis are also treated with methotrexate. Juvenile rheumatoid arthritis of the polyarticular course that is active in youngsters is also treated with it [7].

Side effects

- Nausea and vomiting,
- Leading to anticipatory nausea in some children,
- And fear of injections or blood tests [6].

Drug interactions

As methotrexate is highly plasma protein bound, any drug that displaces methotrexate from proteins can increase its blood levels [5].

Dosage and administration

Methotrexate can be given either as a tablet by mouth or by a subcutaneous (under the skin) injection. Methotrexate is given once a week. In general, child will be on methotrexate for at least 12 months. After being stable (without flare-ups) for a while, your child's rheumatologist may wean your child's methotrexate dose. If your child continues to be stable over a period of time on less frequent or smaller methotrexate doses, it will then be stopped.

Usual pediatric dose for juvenile rheumatoid arthritis

Usual dose: 10 mg/m^2 once weekly administered subcutaneously/intramuscularly/orally, with escalation to achieve optimal response

- Dosages exceeding 30 mg/m^2 once weekly elevate the risk of severe adverse reactions, including myelosuppression.ost responses are typically observed within 3 to 6 weeks after initiating treatment, although responses have also been reported up to 12 weeks after starting treatment.
- To minimize the risk of adverse reactions, it is advisable to administer folic acid or folinic acid.

Missed dose

This medicine needs to be given on a fixed schedule. If you miss a dose or forget to use your medicine, call your doctor or pharmacist for instructions.

New drug - adalimumab

Adalimumab is a human IgG1 monoclonal antibody used to treat rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, Crohn disease [8].

Brand Name - HUMIRA

Figure 9

Mechanism of action

It inhibits the binding of TNF alpha (both soluble and membrane-bound) to its receptor. TNF blockade thus inhibits subsequent destruction of cartilage and bone [8].

Uses

- Rheumatoid arthritis
- Ankylosing spondylitis
- Crohn disease
- Ulcerative colitis
- Hidradenitis suppurativa
- Juvenile idiopathic arthritis
- Plaque psoriasis [8]

Adverse effects

The most common adverse effects of adalimumab are:

- Injection site reactions
- Headache
- Rash
- Risk of serious infections, in particular, reactivation of latent tuberculosis [8].

Serious infections

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue HUMIRA if a patient develops a serious infection or sepsis.

Reported infections include

- Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.
- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.

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