JUVENILE IDIOPATHIC ARTHRITIS: A REVIEW

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Abstrac:t Inflammation of the joints causes arthritis. Arthritis causes pain, swelling, stiffness and loss of motion and most common arthritis in children is known as juvenile idiopathic arthritis (JIA). Juvenile idiopathic arthritis is heterogenous group of disease of uncertain origin characterized by arthritis that develops before the age of 16 years. It is the most common childhood chronic rheumatic disease and cause much disability. Juvenile idiopathic arthritis is considered as a multifactorial genetic and environmental risk factors. Juvenile arthritis is a rheumatic disease which causes loss of function due to an inflamed supporting structure. According to demographic characteristics, clinical features, treatment features, treatment modalities and disease prognosis, the disease is divided into many groups. Systemic juvenile arthritis which is characterized by recurrent fever and rash. Oligo juvenile idiopathic arthritis, which is common among young females patients. Then comes the seropositive polyarticular juvenile arthritis which is seen in less than 10% pediatric patients. New research of the disease pathogenesis is the basis for the development of new and better treatments for JIA. The goal of such treatments is not just to relieve pain, but also to control inflammation and stop irreversible joint damage and long-term disability. Biological agents have significantly improved the disease prognosis.

KEYWORDS- Juvenile arthritis, methotrexate, osteoporosis, joint pain.

1. INTRODUCTION

Juvenile idiopathic arthritis is not a single disorder, but a concept that includes all types of arthritis that begin before a patient is 16 years of age, and remains for more than 6 weeks and are of unknown origin. Juvenile idiopathic arthritis (JIA) is an array of biologically distinct types of chronic inflammatory arthritis that have not been thoroughly understood since childhood (Giancane et al., 2016). The main therapy for JIA patients with oligoarticular involvement is the injection of non-steroidal anti-inflammatory drugs (NSAID) and intra-articular corticosteroids (IAC). The most widely used disease-modifying anti-rheumatic drug (DMARD) in the management of JIAs is methotrexate, predominantly as a second-line agent in children with an ineffective response to intra-articular corticosteroids (IAC) injections or as injections initial care for patients with aggressive disease (Aslan et al., 2011).These advances have increased the expectation for disease control.The disease is divided into several subgroups, according to demographic characteristics, clinical features, treatment modalities and disease prognosis. In the past 5 years, pivotal experiments have contributed to significant advances in multiple fields, ranging from the classification of diseases to new treatments (Gowdie et al., 2012) New research of the disease pathogenesis is the basis for the development of new and better treatments for juvenile idiopathic arthritis. The goal of such treatments is not just to relieve pain, but also to control inflammation and stop irreversible joint damage and long-term disability. Biological agents have significantly improved the disease prognosis (Barut et al., 2017).

2. EPIDEMIOLOGY

JIA is the most common childhood chronic rheumatologic disorder.The annual occurrence is 2-20 cases per 100,000 people, with a rate of 16-50 cases per 100,000 people,which means there are an estimated 294,000 children in the United States who are affected (Prakken et al., 2011).The prevalence varies by ethnicity, but it is more common among norther Europeans (Eisenstien et al., 2014). According to a Turkish survey, 64 out of every 100,000 children have chronic arthritis (S ozen et al., 1998).Surprisingly, an Australian study found a prevalence of 400 in every 100,000 people (PJ Manners et al., 1996).

3. PATHOPHYSIOLOGY

Juvenile idiopathic arthritis(JIA) appears to be a complex genetic trait involving the effects of several genes linked to immunity and inflammation, despite the fact that the causes of the disease are unknown.Infections, along with stress and trauma, are thought to be the primary aetiological causes (JE Weiss et al., 2005).According to recent research, the gut microbiota is emerging as a significant factor in autoimmune diseases, like JIA (A Verwoerd et al., 2016). The increased occurrence of autoimmune disorders in JIA patients indicates that the condition has a genetic basis (S Prahalad et al., 2002). The most widely mentioned genetic factors are human leukocyte antigen (HLA) B27 and other HLA tissue types (E Ross et al., 2016)(ED Ferrucci et al., 2005)(A Hinks et al., 2016). JIA pathogenesis is thought to be caused by a variety of infections, including enteric infections, parvovirus B19 (B Gonzalez et al., 2007), rubella, mumps, and hepatitis B (A Aslan et al., 2011) because rubella virus stays on in lymphocytes and develops a persistent infection site in the synovium, causing chronic inflammation (BA Lang et al., 1990).The connection between HLA class I and II alleles with JIA is well known, suggesting that T cells and antigen presentation are likely involved in the pathogenesis of JIA. Joint destruction is caused by potential trigger-induced T-lymphocytes and secreted cytokines. Chronic inflammation is mediated by T lymphocytes, and T cells are the most common mononuclear cells found in synovial fluid(H Mangee et al., 1998).Macrophages, induced by secreted mediators, develop pro-inflammatory cytokines [interleukin (IL) 1, IL-6, and tumour necrosis factor (TNF)-alpha] (TL Moore et al., 1999). As a result, acute phase markers such as [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)] rise, and acute joint inflammation occurs with an increase in synovial fluid. Villous hypertrophy and hyperaemia of the sub synovial tissue are both symptoms of

synovial inflammation (synovitis). The percentage of T-lymphocytes in synovial fluids differs between JIA subtypes, which may explain the differences in treatment response among JIA subgroups(J Zhou et al., 2016).

4. RISK FACTORS

Osteopenia and osteoporosis: Children with JIA are more likely to develop osteopenia and osteoporosis, which increases the risk of fracture.Chronic active arthritis and persistent inflammation, decreased physical activity, inadequate sunlight exposure, and corticosteroid use are all risk factors for decreased bone mineral density.

Uveitis: As seen in acute anterior uveitis, uveitis may present with overt symptoms. Eye pain, redness, headaches, photophobia, and visual changes are all common symptoms (LN Sarah et al., 2016).

5. SYMPTOMS:

Joint pain: The most common symptom of JIA is joint pain and it's possible that the joints will swell and become tender.They have the ability to turn red and become warm to the touch.This results in a loss of fine dexterity, especially in the hands.

Eye problems: Some types can cause inflammation in the eyes. If left untreated, this disorder can lead to cataracts, glaucoma, and even blindness.

Swollen lymph nodes and internal organs: Lymph nodes can swell and become inflamed as a result of systemic JIA. Lymph nodes are tiny glands that serve as filters in your body. They can be found in a variety of places on the body, including the corners of the jaw, the armpit, and the inside of the thigh.Internal organs such as the heart, liver, and spleen, as well as the tissue surrounding the organs, may be affected by swelling (serositis).

6. CLASSIFICATION

Oligoarticular JIA:During the first six months of illness, patients with arthritis in less than five joints are diagnosed with oligoarticular JIA. The large joints of the lower extremities, such as the knees and ankles, are commonly involved in these patients (JT Cassidy et al., 1986).Half of all patients have monoarticular onset, which only affects the knee (JJ Calabro et al., 1969). It is further divided into two subgroups: persistent (no more than four joints affected during the course of the disease) and extended (the total number of affected joints reaches four after the initial 6-month period) (RE petty et al., 2001).Patients with oligoarticular disease, especially ANA-positive girls, are at an increased risk of developing uveitis, which is typically their most severe clinical issue.

Polyarticular Juvenile Idiopathic Arthritis: Polyarticular JIA is characterized as arthritis affecting at least five joints in the first six months of the disease. According to RF positivity, the disorder is divided into two subgroups (Weiss et al., 2007).The disease's prevalence varies by geographical area, with RF-negative polyarticular JIA accounting for 11-30 percent of cases and RF-positive cases accounting for 2-10 percent (Kumar et al., 2016).Both disease subgroups are more prevalent in girls. The onset of RF negative polyarticular JIA is biphasic, with peaks between 2 and 4 years and 6 and 12 years (Ravelli et al., 2007). The RF-positive subgroup is more commonin later childhood and adolescence.In both disease subgroups, mild fever, weight loss, and anaemia are normal.In both disease subgroups, mild fever, weight loss, and anaemia are normal (Demirkaya et al., 2011).

Systemic juvenile idiopathic arthritis: This disease subtype, which is characterized by systemic symptoms, affects both males and females equally and can strike at any time during childhood (Barut et al., 2015).The disorder is characterized by the occurrence of arthritis, intermittent fever, and one of the following symptoms for at least two weeks:rash, lymphadenopathy, hepatosplenomegaly, or severe, hypoalbuminaemia, and hyponatraemia (Sahin et al., 2016).Cardiac disease is well-known, and pericardial effusions are seen in around 10% of children with Systemic juvenile idiopathic arthritis (J Goldenberg et al., 1992). In the differential diagnosis of Systemic juvenile idiopathic arthritis, there are a variety of factors to consider:Septicemia, bacterial endocarditis, brucellosis, typhoid fever, leishmaniasis, viral infections), cancer (leukaemia, lymphoma, neuroblastoma), rheumatic fever, connective tissue disorders, Kawasaki disease, Castleman's disease, and autoinflammatory diseases (Ravelli et al., 2007).Osteopenia, osteoporosis, growth retardation, erosive arthritis, and amyloidosis are all possible complications ofSystemic juvenile idiopathic arthritis. Around 5-8 percent of cases, macrophage activation syndrome (MAS), a serious, life-threatening sJIA complication, is seen. It's associated to a serious mortality and morbidity.

Psoriatic arthritis: Psoriatic arthritis is a form of chronic inflammatory arthritis that first occurs in the middle of childhood. Psoriatic arthritis is a difficult diagnosis to make because the arthritis can manifest itself several years before the rash appears (Shore et al., 1982). Psoriatic arthritis is a form of asymmetric arthritis that most commonly affects the knees and ankles, as well as the small joints of the hands and feet (Hussien et al., 1989). Inflammation of the proximal interphalangeal joints, distal interphalangeal joints, and the tendon sheath causes a diffuse swelling of the digit known as "sausage digit."Rashes, nail changes (including pitting, onycholysis, and the oil-drop sign), and uveitis are examples of extra-articular symptoms.By the age of 15, one-third of psoriatic arthritis patients have developed the rash. Since asymptomatic anterior uveitis can be observed in up to 17% of psoriatic arthritis patients, all children with the disease should have a slit-lamp examination every 6 months (Zisman et al., 2017).

7. DIAGNOSIS

1. Clinical diagnosis

Juvenile idiopathic arthritis has a wide range of clinical symptoms. Several signs that are associated with arthritis are not always indicative of Juvenile idiopathic arthritis , and can have several etiologies that can be distinguished with a thorough review of the patient's medical history (Boros et al., 2010). Polyarticular joint disease has a complex etiology and can occur as a viral infection or the start of a chronic illness. Furthermore, the underlying etiological pathway of a rheumatological disorder or a manifestation of systemic disease may be

infectious or post-infectious.This disease can progress over days or even weeks, making it difficult to diagnose at the time of presentation.To correctly diagnose JIA, the first step is to rule out arthritis with established causes (Singh et al., 2010). Trauma may result in a short-term painful joint effusion. JIA may be the most common cause of chronic oligoarthritis, according to some studies. The affected joint in a child with oligoarticular JIA is swollen and sometimes wet, but it is rarely painful, tender, or red (Petty et al., 2001). Septic arthritis is more likely to be the right diagnosis if a joint is particularly sore and erythematous, or if the child is febrile (Fink et al., 1977). To rule out septic arthritis and osteomyelitis, such patients should have a fast joint aspiration examination.Polyarthritis in a preadolescent or teenage girl could indicate the existence of systemic lupus erythematosus (SLE). SLE arthritis may resemble JIA arthritis, but without serologic testing, a correct diagnosis may be difficult to make before the more typical clinical symptoms of SLE are known.The differential diagnosis of a child with systemic JIA may be challenging, particularly at the onset or early stages of the disease, when the child may have a high spiking fever with evidence of systemic inflammation but no arthritis or other specific indications that allow for a definitive diagnosis (Miller et al., 1996).Children with systemic JIA can initially be misdiagnosed as having an acute infection or septicemia. The appearance of arthritis and/or a rheumatoid rash, on the other hand, assists in developing a proper diagnosis of systemic JIA. Laboratory examinations, on the other hand, may be ineffective in diagnosing systemic JIA.The septic form of fever occurs in children with infectious diseases; this type of fever is more clinically perplexing because it does not return to baseline every day, as does the fever associated with JIA. A strong spiking fever is the diagnostic symptom of systemic JIA (McMinn et al., 1959).

2. Laboratory examination:

As previously described, the diagnosis of JIA is primarily clinical. There is no way to confirm the diagnosis of JIA without a lab test or a combination of tests. The laboratory experiments, on the other hand, can be used to provide proof of inflammation, help the clinical diagnosis of JIA, control therapy toxicity, and better understand the disease's pathogenesis.

The count of blood cells (CBC) and inflammatory markers such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are useful laboratory tests (CRP).The levels of ESR and CRP in active JIA, on the other hand, are variable. ESR is a useful measure of active disease at onset and during follow-up visits with a child with JIA, particularly when the disease is polyarticular or systemic.A CBC may show anemia of chronic disease if there has been longstanding inflammation.Chronic disease (low serum iron, low total iron-binding capability, adequate hemosiderin store) is the primary cause of JIA-associated anaemia, though iron deficiency can also play a role. It has been identified that in people with systemic disease, plasma iron transport and the amount of iron available for erythropoiesis decreases.In children with active disease, leukocytosis is normal, and their platelet count can increase in cases of serious systemic or polyarticular involvement (Cassidy et al., 1973) (Hoyeraal et al., 1974).RF tests were found to be possibly positive in children with both JIA and diseases other than JIA in a review of the diagnostic utility of rheumatoid factor (RF) serology in children (Eichenfield et al., 1986). In patients with polyarthritis, an RF examination should be performed because its existence has prognostic significance (Shin et al., 2005). The presence of anti-nuclear antibody (ANA) increases the risk of developing asymptomatic uveitis, particularly in those with oligoarticular onset disease, while ANA testing should be done in all JIA patients (Petty et al., 2003). Conventional radiographs are the most accessible, fast, and cost-effective way to assess a joint. Ultrasonography is often the most effective method of detecting intra-articular fluid, particularly in joints like the hip and shoulder, where fluid can be difficult to detect clinically (Fedrizzi et al., 1997). Over the last decade, the increased use of conventional magnetic resonance (MR) imaging and developments in more practical MR techniques have enhanced the assessment of joint disease in JIA.MR imaging is more effective than ultrasonography or plain radiography at detecting inflammatory changes in the joint and cartilage injury. Later symptoms of JIA, such as erosions, loss of joint space, cartilage injury, and ligamentous involvement, can also be accurately evaluated using MR imaging (Lamer et al., 2000).In addition, technetium-99m bone scans are useful for identifying the early stages of inflammatory arthritis.Unfortunately, no single imaging modality currently meets all imaging requirements, but methods for detecting JIA are rapidly improving (Mckay et al., 2010).

8. COMPLICATIONS

1. Uvietis

Anterior uveitis is one of the most severe complications of JIA.In up to 21% of patients with oligoarticular JIA and 10% of patients with polyarticular JIA, chronic anterior nongranulomatous uveitis (iridocyclitis) develops (Schnieder et al., 2002).Young girls with oligoarticular disease and a positive ANA confirmatory testing are more likely to develop uveitis (Petty et al., 1973).While conjunctivitis, unequal pupils, eye pain, and headache are common symptoms of uveitis, it may also cause conjunctivitis.Patients with JIA should be screened on a daily basis to reduce uveitis diagnosis delays.Back synechiae, cataracts, band keratopathy, glaucoma, and vision impairment are all uveitis complications (in up to 30 percent) (Yansey et al., 1993).The JIA subtype, age at disease onset, and ANA status all influence the risk of uveitis. Patients with oligoarticular JIA are at the highest risk, particularly if they are female, ANA-positive, and under the age of four. The frequency of ophthalmologic screening in children with JIA is summarized (Swantesson et al., 1983). One study shows that for a span of 1 to 5 years, researchers discovered that 4 percent of oligoarticular patients with uveitis had vision loss in one eye, and 17 percent had vision loss in both eyes (Bowyer et al., 2003).To alleviate inflammation and avoid posterior synechiae, uveitis is treated with topical steroids and mydriatics. When the child is awake, glucocorticoid ophthalmic drops can need to be given as often as every hour.In patients who do not respond to topical therapy, oral corticosteroids at a dose of 2 to 4 mg/kg/day with a maximum dose of 1 gramme may be needed, and pulse intravenous methylprednisolone (30 mg/kg) has been used with success in some cases. Patients who are unresponsive to glucocorticoids may benefit from methotrexate, cyclosporine A, and a sub-tenon injection of steroids.

2. Nutrition

Nutritional deficiencies are normal in children with rheumatoid arthritis. For the first year of life, a healthy child's daily caloric requirement is approximately 80 to 120 kcal/kg/day, with a decrease of approximately 10 kcal/kg for each subsequent three-year span (John.P et al., 2004).A cumulative caloric intake of less than 50% of expected needs was found in a random study of 33 JIA patients (Henderson et al., 1991). JIA causes a decrease in lean muscle mass and a rise in fat mass in children (Simon et al., 2003).Elevated levels

of IL-1 and TNF-a may be to reason for these impacts (Ostrov et al., 1992).It is important for the pediatrician to use dietary recommendations for healthy children based on sex and age rather than actual weight, and for a dietician or nutritionist to be part of the care team, particularly when there is severe malnutrition (Pepmuellar et al., 1996).

3. Growth disturbances

Patients with JIA also experience generalized growth retardation and delayed puberty (Bechtold et al., 2003).The causes are multifactorial such as metabolic, endocrinologic and malnutrition (Davies et al., 1997). Children who have had polyarticular disease for a long time are at the highest risk of diminished linear growth (Benedetti et al., 1991).Corticosteroid treatment on alternate days or at a daily dose of less than 0.5 mg/m2 can reduce the negative effects of corticosteroids on development (Ansell et al., 1994).In certain patients, growth hormone has been shown to be successful in treating extreme growth retardation (Saha et al., 2004). In a patient with chronic knee inflammation, overgrowth of a lower limb may occur as a result of hyperemia of inflammation (Calabro et al., 1969). Intra-articular steroid injections in the knee are beneficial since they minimize the occurrence of leg-length difference by controlling local inflammation (Sherry et al., 1999).

9. TREATMENT

The patient's functional capacity and efficiency in everyday life are hindered by chronic joint inflammation.The underlying cause of the above-mentioned complications is uncontrolled inflammation.In addition to joint-related complications, untreated patients can experience growth retardation, uveitis, blindness, and potentially life-threatening MAS. Drug side effects (e.g., osteoporosis, growth retardation due to glucocorticoids, etc.) should also be considered (Weiss et al., 2007).As a result, JIA treatment should be expedited and successful. The value of supportive measures like proper diet, calcium, and Vitamin D supplements should not be overlooked (Prakken et al., 2011)Controlling pain, preserving range of motion/muscle strength/muscle function, inducing disease remission, managing systemic complications, and facilitating normal physical and psychosocial growth should all be goals of therapy (Dağdeviren-Çakır et al., 2016) .Treatment time should be changed every three months before the treatment target is achieved.The severity of the disease should be monitored on a regular basis (every 1-6 months).Children and parents should be informed in detail aboutthe process and goals (Kasapçopur et al., 2015).

NON-BIOLOGICAL MEDICAL TREATMENT

Non-Steroidal Anti-Inflammatory Drugs

The standard first line of treatment is nonsteroidal anti-inflammatory drugs (NSAIDs). The most widely used agents are ibuprofen, indomethacin, tolmetin, and naproxen.This class of drugs is most commonly used in children under the age of 12.NSAIDs have been shown to cause disease remission in patients with oligoarticular JIA.The drugs' key characteristics are their analgesic activity at low doses and their anti-inflammatory effect at higher doses.Pain relief is seen in the first 1-3 days of treatment. Despite the occasional side effects of abdominal pain and headache, this form of medication is considered tolerable in children (Makay et al., 2013).

Corticosteroids

This class of drugs is known for having the strongest anti-inflammatory properties.However, because of the various side effects and poor effectiveness in preventing joint damage, its use is limited.Even with a single injection, intra-articular administration (methylprednisolone acetate, triamcinolone hexacetonide) has been shown to be successful in inducing remission in oligoarticular JIA patients (Ravelli et al., 2011).In patients with the systemic type of the disease, oral or parenteral administration of steroids may alleviate systemic symptoms.Joint pain, swelling, sensitivity, or disease-related carditis, hepatitis, lung disease, and fever all respond positively to steroid treatment.In patients who have achieved disease control, however, low doses or alternate days of treatment are advised due to various side effects. Steroid doses of up to 1 mg/kg/day are commonly prescribed.In patients with cardiac insufficiency or tamponade caused by carditis or pericarditis, the dosage should be increased to 1-2 mg/kg/day. Patients with a serious clinical presentation of systemic JIA should be treated for three days with a high dose of steroids (30 mg/kg/day) (Kasapçopur et al., 2015).

DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

Methotrexate

Methotrexate is a folate antagonist that has been shown to be a highly effective, safe, and long-acting drug. 10-15 mg/m2/week (0.5-1 mg/kg/week) is the minimum treatment dose.The majority of patients respond within the first two to three weeks of treatment. It can take some time for a patient to respond to treatment (Giannini et al., 1992).Folic acid or folinic acid is given at a dosage of 1 mg/kg/day to help with side effects including bone marrow suppression, nausea, oral ulcers, and hair loss (woo P et al., 2000). It is important to remember that folinic acid reduces methotrexate activity (Takken et al., 2001).

Sulphasalazine

Sulphasalazine has been shown to be effective in patients with JIA, especially in the oligoarticular and enthesitis-related types of the disease, in several studies (Van Rossum et al., 1998).In general, a treatment response is achieved after 6-8 weeks of treatment (Imundo et al., 1996). Any of the potential side effects include headache, rash, gastrointestinal toxicity, myelosuppression, hypogammaglobulinemia, and allergic reactions (Joos et al., 1991).The initial dosage is 10-20 mg/kg per day, which is steadily increased to 50 mg/kg per day over the next few weeks (Brooks et al., 2001).

Leflunomide

Leflunomide is an immunosuppressive agent that reversibly inhibits de novo pyrimidine synthesis and is currently being investigated for use in JIA.Preliminary findings, presented show efficacy comparable to methotrexate (Silverman et al., 2004).Diarrhea, elevated liver enzymes, mucocutaneous defects, and teratogenicity are some of the side effects (Llowite et al., 2004).

BIOLOGICAL TREATMENTS

Over the last 15 years, biologic therapeutics have advanced significantlyresulted in a significant increase in JIA care.With an increase in the number of patients with inactive disease, the incidence of joint injury decreased and disease remission increased in the biological period.Biological agents, on the other hand, have been shown to be healthy in previous studies. The following text explains the effectiveness and safety of the biological agents used in JIA care.

- **Entanercept-** Etanercept is a fusion protein that binds to soluble TNF and inhibits TNF receptor-mediated signaling downstream (Lowell et al., 2000).Etanercept is a biological agent that has shown to be effective in treating peripheral arthritis (Prince et al., 2007).In polyarticular JIA patients, it has proven to be the most effective treatment choice. The drug's weekly dosage is 0.8 mg/kg (Horneff et al., 2009).After the second or third dose, etanercept's efficacy becomes more noticeable.The local reaction at the injection site is the most common side effect.As a result, the medication should be given to various sections of the body (Halbig et al., 2009).
- **Infliximab-**Infliximab is a TNF-binding chimeric monoclonal antibody with a high affinity. Infliximab, unlike etanercept, binds to both soluble and membrane-bound TNF.Its effectiveness in JIA therapy has previously been demonstrated. 3-6 mg/kg/4-8 weeks is the current dosage (maximum dose 200 mg).Infliximab therapy is especially effective in spondyloarthropathies, inflammatory bowel disease, psoriatic arthritis, and uveitis (Burgos-vargas et al., 2007).The combination of infliximab and methotrexate significantly improves medication efficacy (Ruperto et al., 2007). The incidence of serious and opportunistic infections is unremarkable, apart from mild upper respiratory system infections.
- **Adalimumab**:Adalimumab is a TNF-binding monoclonal antibody that has been thoroughly humanized (Lovell et al., 2008).The standard dosage is 24 mg/m2 for 15 days (maximum 40 mg). The drug activity is increased when adalimumab and methotrexate are used together.As a first or second line of JIA therapy, it has been shown to be effective and healthy (Katsicas et al., 2009).
- **Anakinra:** Anakinra is a human IL-1 receptor antagonist that is recombinant. It's given subcutaneously in doses ranging from 2 to 10 mg/kg per day (maximum 200 mg) (Nigrovic et al., 2011). Since IL-1 is involved in the pathogenesis of sJIA, multicentric studies have demonstrated the efficacy and protection of anakinra in the treatment of Sjia (Quartier et al., 2011).Injection pain and local injection site reactions can make it difficult to use. In general, it is a well-tolerated medication, with serious infections occurring only in extreme cases.
- **Tocilizumab:**Tocilizumab is a humanized recombinant monoclonal antibody that binds to the interleukin-6 receptor. It's usually used in active sJIA patients over the age of two, either alone or with methotrexate.Doses of 12 mg/kg/2-4 weeks for children under 12 kg and 8 mg/kg/2-4 weeks for children over 12 kg are recommended. Tocilizumab is used to treat patients with unresponsive systemic JIA, particularly those with active arthritis who do not improve and those with polyarticular JIA.Because of tocilizumab's ability to reduce acute-phase markers and prevent fever reaction, some infections can go unnoticed in patients taking it (Yokota et al., 2008).
- **Abatacept:**Abatacept is a recombinant fusion protein that inhibits T-cell stimulation, causing B-cell and macrophage activation to decrease (Ruperto et al., 2008).The medicine is injected once a month at a dosage of 10 mg/kg. Previous studies have shown its efficacy and safety in patients with polyarticular JIA (Ravielli et al., 2018).Serious opportunistic infections have not been reported in patients treated with this medication, except for mild infections that do not require hospitalization.
- **Rituximab:** Rituximab is a human monoclonal antibody that boosts B-cell apoptosis while lowering mature B-cells that carry CD20.Since B-cells are its primary target, it has been shown to be effective in all conditions involving B lymphocytes. This drug's recommended dose is 375 mg/m2 given in three or four doses (Alexeeva et al., 2011).
- **Tofacitinib/CP-690.550**: Tofacitinib/CP-690.550 is a JAK inhibitor that inhibits JAK 1, JAK 2, and STAT 1 in a selective manner. Tofacitinib is currently used to treat adult RA patients. Tofacitinib is the subject of an ongoing open-label trial in the treatment of JIA.

10. CONCLUSION

JIA is a heterogeneous disorder with many unanswered questions about treatment options and clinical outcomes. Since a delay in diagnosis and care may result in permanent harm, early detection and appropriate, prompt treatment are critical.In terms of patient effectiveness and follow-up, disease activity measures are important.At times, care should be given to the patient while also sticking to general treatment guidelines.To prevent the negative effects of the medications, a multidisciplinary approach is essential.The primary aim of the treatment is to avoid disease-related complications and allow patients to live a healthier lifestyle.

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