PATHOPHYSIOLOGICAL AND THERAPEUTIC EFFECT OF ARTHRITIC AILMENTS-
A BRIEF REVIEW

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ABSTRACT

The word “arthritis” is derived from Greek words: arthon, meaning a joint, and –itis, meaning inflammation. Typically involves redness, heat, swelling, and tenderness. So, arthritis describes a joint that is red, hot, swollen, and tender. Arthritis is a condition in which joints are painful and stiff. If the joints are actually red, hot, swollen and tender. Arthritis is not a single disease with a single cause. There are dozens of different types of arthritis, each with its own cause. Arthritis is a systemic inflammatory process which rheumatoid arthritis, These pathological conditions leads to joint destruction and extra articular symptoms, having significant effect on morbidity and mortality. Rheumatoid arthritis is a subset of arthritis which is an autoimmune disease that is characterized by inflammation of the joints and destruction of cartilage and bone, often compromising both the quality and duration of life. The disease pathology is complex, involving the infiltration and activation of various populations of immune cells along with the release of destructive inflammatory mediators into the synovial fluid of affected joints. This review will summarize the factor responsible for vital development, vital biomarker, diagnostic technique and therapeutic agent for guided intervention into Rheumatoid arthritis.

KEYWORDS- Arthritis, inflammation, joint destruction, cartilage, biomarker.

1. INTRODUCTION

Rheumatoid arthritis is a chronic autoimmune disorder that is characterized by destructive inflammation of both internal organs and joints, latter typically manifested as damage to cartilage, bone, tendons and ligaments (Chrystal M. Paulosetal., 2003). Statistics show that RA and related musculoskeletal disorders affect greater than 0.5–1% of the population worldwide, and it is predicted that one out of every five Americans will suffer from one of these disorders by 2020 (R.C. Lawrence et al., 1998). RA affects females three times more often than males, and the disease can start at any age, with a peak incidence at 50–60 years of age (A.J. Silman etal., 1994). Tragically, female 80% of the affected population becomes disabled within 20 years of symptom onset, making RA the most common cause of disability in the workforce(D. L. scottetal., 1998). Not surprisingly, the total social and medical costs attributed to Rheumatoid arthritis are predicted to exceed US$100 billion by 2020 (E. Yelinetal., 1996). While several anti-arthritic drugs are now available, many of these are very costly and have limited efficacy and is not desirable due to side effects. The role of obesity in clinical course of Rheumatoid arthritis is very clear. We investigated the association of obesity and adiposity with disease activity with disease activity and clinical response to combination therapy in Rheumatoid arthritis patients.

Classification of arthritis

A. Rheumatoid arthritis
B. Osteoarthritis
C. Juvenile arthritis
D. Psoriasis arthritis

(A) Rheumatoid arthritis

Rheumatoid arthritis is an autoimmune disease that is characterized by inflammation of the joints and destruction of cartilage and bone, often compromising both the quality and duration of life. The disease pathology is complex, involving the infiltration and activation of various populations of immune cells along with the release of destructive inflammatory mediators into the synovium of affected joints. Although it is still debatable whether activated macrophages are the primary promoters of Rheumatoid arthritis, emerging data clearly show that the biological activity of this subset of inflammatory cells greatly contributes to both the acute and chronic stages of the disease. The further discovery of folate receptor expression on these activated (but not quiescent) macrophages in both animal models and human patients with naturally occurring Rheumatoid
arthriti has opened the possibility of exploiting folic acid to target attached drugs to this population of pathologic cells. Indeed, recent studies have shown that folate-linked imaging and therapeutic agents can be selectively delivered to arthritic joints, allowing both visualization and treatment of Rheumatoid arthritis, with little or no collateral toxicity to normal tissues.

![Diagram of a joint](image)

**Fig-1.1 A diagram showing how rheumatoid arthritis affects a joint (Hasty KA et al., 1990)**

### B. Osteoarthritis

Osteoarthritis is first and foremost the ongoing destruction of the articular cartilages of joints. Therefore, the extracellular matrix and the cells of the articular cartilages are the primary targets of osteoarthritis therapy. This tries to inhibit enzymatic destruction of the extracellular cartilage matrix as well as the modification of the cellular phenotype of the chondrocytes: cell degeneration and cell death are alongside anabolic activation and stabilization of the cellular phenotype of major interest. However, apart from the cartilage and its cells, other tissues of the joints are also important for the symptoms of the disease, which basically all originate outside the articular cartilage. In addition, changes in the sub-chondral bone as well as the synovial capsule and membrane are important at least for the progression of the disease process (T. Aigner et al., 2006).

### C. Juvenile arthritis

Juvenile idiopathic arthritis, also known as juvenile rheumatoid arthritis, is the most common form of arthritis in children and adolescents. (Juvenile in this context refers to an onset before age 16, idiopathic refers to a condition with no defined cause, and arthritis is the inflammation of the synovium of a joint.) JIA is an autoimmune, non-infective, inflammatory joint disease of more than 3 months duration in children less than 16 years of age. The disease commonly occurs in children from the ages of 7 to 12, but it may occur in adolescents as old as 15 years of age, as well as in infants. It is a subset of arthritis seen in childhood, which may be transient and self-limited or chronic. It differs significantly from arthritis commonly seen in adults (osteoarthritis, rheumatoid arthritis) and other types of arthritis that can present in childhood which are chronic conditions (e.g. psoriatic arthritis and ankylosing spondylitis). Aetio-pathology is similar to rheumatoid arthritis but with less marked cartilage erosion and joint instability and absent rheumatoid factor. JIA affects approximately 1 in 1,000 children in any given year, with about 1 in 10,000 having a more severe form.

### D. Infectious arthritis (Septic arthritis)

Septic, or infectious, arthritis is infection of one or more joints by microorganism. Normally, the joint is lubricated with a small amount of fluid that is referred to as synovial fluid or joint fluid. The normal joint fluid is sterile and, if removed and cultured in the laboratory, no microbes will be found. With septic arthritis, microbes are identifiable in an affected joint fluid most commonly. Septic arthritis affects a single joint, but occasionally more joints are involved.

### 2. Physiology of Rheumatoid arthritis

Rheumatoid arthritis synovia demonstrated classic Rheumatoid arthritis histopathology with thickening of the lining layer and mononuclear infiltration of the sublining including formation of perivascular infiltrates. Non-Rheumatoid arthritis synovia were obtained from arthroscopically non-inflamed sites and were histologically normal in appearance. Rheumatoid arthritis is a chronic inflammatory disease that affects approximately 1% of the population. Rheumatoid arthritis is characterized by irreversible joint damage accompanied by destruction of bone and cartilage. In addition, the chronic inflammation associated with Rheumatoid arthritis often damages the skin, subcutaneous tissue, and lungs. Moreover, inflammatory reactions in the arterial endothelium, which occur independently of atherosclerosis risk, promote endothelial dysfunction and increase the risk of cardiovascular disease, thereby diminishing quality of life and survival time (A.J. Silman et al., 1994).

Although the etiology is unknown, Rheumatoid arthritis is certainly associated with autoimmune disorders, and its pathogenesis has been well investigated. Auto-reactive T cells that infiltrate the synovial tissue promote the immune response and lead to overproduction of pro-inflammatory cytokines, such as tumor necrosis factor-α (TNFα) and interleukin-6 (IL-6). Thus, early RA therapy is based on aggressive biologic modification of the disease through controlling synovial T cells and/or suppressing the levels of cytokines implicated in the disease. In addition to these immunogenic factors, reactive oxygen species (ROS) are also important therapeutic targets because they are upstream of the cytokine-mediated inflammatory cascades. Activation of nuclear factor (NF)-κB by excess ROS production leads to increased production of pro-inflammatory cytokines, thereby creating a positive feedback loop and promoting sustained RA inflammation (E. Yelin et al., 1995). Hydroxyl radicals, a particular ROS, are harmful because of their rapid and indiscriminate reactivity and they are thought to play a certain role in the pathogenesis of RA (J.M. Greene et al., 1992).
rats intra-peritoneal, and its bio distribution was assessed 4 h later by nuclear scintigraphy. Resulting images revealed accumulation of EC20 in the articular extremities, as well as in the livers and spleens of diseased rats, but not in the joints or organs of healthy rats. (C.P. Leamon et al., 2002).

4. ANIMAL MODEL
Adjuvant-induced arthritis (AA) in Lewis rats is a model of T-cell mediated autoimmune disease resembling human rheumatoid arthritis (RA). AA can be induced by a single intradermal (i.d.), injection of complete Freund’s adjuvant (CFA) consisting of Mycobacterium tuberculosis (Mt) and incomplete Freund’s adjuvant (IFA) but AA cannot be induced by injection of IFA alone in the Lewis rats, suggesting the importance of Mt as an antigen and IFA as a co-adjuvant. However, an i.d. injection of IFA alone was able to induce polyarthritis in DA rats, known as oil-induce polyarthritis in DA rats, known as oil induced arthritis (OIA) (Kleinau S et al., 1991). Similarly, it was also reported that pristane a well-defined synthetic mineral oil, could induce severe and chronic arthritis in various rats or in mice, known as pristane –induced arthritis (PIA) and lipoidal amine (avridine), a strong interaction inducer, could induce polyarthritis in Lewis rats, known as avridine –induced arthritis (AIA). The clinical course and histology of OIA, PIA and AIA are indistinguishable from those of AA (C.Vingsbo et al., 1996). The fact that OIA and AIA as well as AA can be passively transferred in the naïve rats by the lymph node cells (LNCS) or spleen cells derived from arthritic rats suggests involvement of immunological mechanism for induction of these forms of arthritis. (L.Zhang et al., 1999).

Different type arthritis model- 4.1 Collagen-antibody-induced arthritis
Rheumatoid arthritis is associated with auto-antibody production against self-type II collagen, citrullinated proteins (ACPA) and IgG (rheumatoid factor). Similarly, in CIA, in which anti-type II collagen IgG antibodies are detectable, transfer of serum from an immunized mouse into a non-immunized recipient can induce arthritis demonstrates a role for humoral immunity in the development of arthritis in which type II collagen is thought to be the predominant epitope. Furthermore, anti-collagen antibody cocktails have been shown to induce the development of arthritis. Similar protocols are now commonly used for the induction of collagen-antibody induced arthritis (CAIA). Identification of auto-antibody collagen epitopes allows the development of more arthritogenic antibody cocktails that may better represent the humoral auto-immunity in RA. This could also lead to the identification of conserved regions in type II collagen between species which may be central to driving disease pathology. Although the clinical development of arthritis is similar to that in CIA and Rheumatoid arthritis, CAIA is characterized by macrophage and polymorphonuclear inflammatory cell infiltrate, but is not associated with a T- and B-cell

Fig 1.2 Schematic diagram of an activated macrophage and the pro-inflammatory that it produces.

3. Diagnosis and treatment of rheumatoid arthritis
3.1 TECHNIQUE
Magnetic resonance imaging (MRI) can directly visualize the bone and soft tissues in three dimensions, and has the potential to measure inflammatory activity and joint destruction.

MRI is a reliable technique for the evaluation of the rotator cuff tendons, but it provides only a static evaluation of the shoulder joint and can only indirectly suggest the diagnosis of sub-acromial impingement.

Ultrasound is an effective and established technique in musculoskeletal imaging; its role in diagnostic imaging is continuing to expand with the development of further clinical applications and with the advancement of ultrasound technology.

Sonography is well suited for examinations of the musculoskeletal system because structures are often superficial, examinations may be done in a position that is comfortable for the patient, and comparisons with the contra-lateral side are possible. Real-time imaging capability of sonography is a particular advantageous feature, permitting dynamic evaluation of a system on movement. Dynamic sonography is a useful tool for the evaluation of a wide variety of musculoskeletal disorders that are best or only shown dynamically—that is, during motion, muscle contraction, probe compression, or position change of the patient. Many of these disorders cannot be diagnosed by many other imaging method (Nevien El-Liethy et al., 2014).

3.2 Diagnostic imaging of rheumatoid arthritis using folate-targeted radiopharmaceuticals
As inferred above, we have recently shown that FR expression on activated macrophages can be exploited to selectively target imaging agents to sites of inflammation in rats with adjuvant-induced arthritis (M.J. Turke et al., 2002).

Thus EC20, a folate-conjugated radiopharmaceutical complexes with 99mTc, was administered to diseased
response; although the administration of type II collagen reactive T cells has been shown to enhance disease severity. Therefore, CAIA can provide insight into the separate roles of innate and adaptive immune response in the development of arthritis. Furthermore, as disease develops within 48 h of antibody administration with 100% penetrance and is inducible regardless of the MHC class II haplotype, CAIA is well suited for studying the development of arthritis in genetically modified strains of mice.

4.2 Zymosan-induced arthritis
Zymosan is a polysaccharide from the cell wall of *Saccharomyces cerevisiae* with repeating glucose units connected by b-1,3-glycosidic linkages. It binds to TLR2 in macrophages leading to the induction of pro-inflammatory cytokines, arachidonate mobilization, protein phosphorylation and also activates complement via the alternative pathway. Injection of zymosan intra-articularly into the knee joints of mice results in a proliferative inflammatory arthritis with mononuclear cell infiltration, synovial hypertrophy and pannus formation with the peak of disease at about day 3 and inflammation subsiding by day 7. Recent data, however, demonstrate that the model is in fact biphasic, with both bearly (oday 7) and late phases (4day 25). The main limitation of this model is the monoarthritis nature of the disease and the technical skill required for an intra-articular injection in mice. Furthermore, an intra-articular injection model precludes analysis of the systemic component of the disease.

4.3 Antigen-induced arthritis
Various strains of mice develop inflammatory arthritis when primed with an antigen (e.g. methylated BSA in complete Freund’s adjuvant) and subsequently challenged by intra-articular injection of the same antigen. Such models are useful in that mice of several strains can be investigated to establish a hierarchical role for given factors in adaptive immunemediated articular damage. Subsequent pathology comprises immune complex mediated inflammation followed by articular T-cell-mediated responses. The model does not however recapitulate the endogenous breach of tolerance that is typical of RA pathogenesis and as such the model has limitations in applicability to RA. A recent development of this model comprises of prior adoptive transfer of transgenic albumin–specific T cells followed by albumin priming and later intra-articular challenge. The recipient mice develop arthritis, which is followed by the emergence of auto-reactivity to collagen and the presence overtime of rheumatoid factors. This model has the advantage of facilitating imaging of the pathogenic T cells that in turn promote breach of self-tolerance to articular antigens.

4.4 Other induced models of arthritis
A single subcutaneous injection of small amounts of pristane (a natural saturated terpenoid alkane) leads to the development of an acute severe followed by a chronic relapsing phase in rats and mice. The model is largely T-cell dependent and the main pathological features include edema accompanied by an acute phase response, infiltration into the joint of mononuclear and poly-morphonuclearells, pannus formation, and the erosion of cartilage and bone. The proteoglycan-induced arthritis model involves immunization of genetically susceptible mouse strains, such as BALB/c, with human cartilage-derived proteoglycans. These mice develop severe polyarthritis and spondylitis.

Genetically manipulated spontaneous arthritis models

4.5 TNF-a transgenic mouse model of inflammatory arthritis
A transgenic mouse over-expressing human TNF-a was developed by Kollias and co-workers in 1991. The mouse develops chronic inflammatory erosive polyarthritis and treatment with a monoclonal antibody against human TNF-a completely prevents the disease. In contrast to CIA and adjuvant-induced arthritis, which are acute and self-limiting, the chronic progressive nature of the arthritis in this model bears close resemblance to the human disease. Since then multiple lines of TNF transgenic mice have highlighted the importance of TNF-a in the cytokine hierarchy of RA and given the success of anti-TNF-a therapy in humans the TNF transgenic mice provide a useful tool for evaluating the efficacy of novel therapies in RA, particularly in which novel targets are considered to operate downstream of TNF. Moreover, the model has proven particularly useful in defining the distinct contribution of effector cytokines that regulate inflammation and those that regulate cartilage and bone destruction, e.g. RANKL. K/B_N model A variety of insights have emerged with the advent of sophisticated transgenic murine models. The K/B_N spontaneous mouse model of arthritis was first described by Kouskoff et al. in 1996. These mice were generated by crossing the TCR transgenic KRN line with mice expressing the MHC class II molecule Ag7. K/B_N mice develop severe and destructive inflammatory arthritis. They have high titers of autoantibodies recognizing glucose-6-phosphate isomerase and serum from these mice induces arthritis in a wide range of normal recipient mouse strains (serum transfer model). The mechanism of action involves complement activation and mast cell degranulation and is mediated not only by TNF but also by IL-1. The discovery of this model led to several studies investigating titers of pathogenic anti-glucose-6-phosphatase isomerase antibodies in RA patients; however, to date the data remain controversial. Although this somewhat limits the utility of the model, it remains useful for the study of initial events involved in the induction of arthritis and in particular is in valuable in elucidating the contribution of discrete innate immune pathways in articular tissue damage.

4.5 SKG model
A point mutation in ZAP-70 induces inflammatory arthritis in part reflecting altered thymic T-cell selection.
This SKG model is dependent upon environmental stimuli and is absent in germ-free mice but can be induced by injection of zymosan in a derctin-1- dependent manner.

### 4.6 Human/SCID chimeric mice

Several investigators have exploited the ability of SCID mice to tolerate xenografts by implanting them with human synovial tissue. In the first model, human synovial tissue from RA patients and normal cartilage were implanted under the renal capsule of SCID mice. After 35 days, focal erosions occurred at sites of synovial attach mento the cartilage. After 105 days, activated synovial fibroblast cells invaded the cartilage leading to cartilage destruction. Thus, this model allows the pathology of the human synovium with cartilage invasion and destruction mediated by the synovial fibroblast to be studied in an animal model.

### 4.7 Human DR4-CD4 mice

Genetic susceptibility to Rheumatoid arthritis is associated with a group of HLA class II alleles, which all share a similar stretch of positively charged amino acids at theHLA-DRB1 locus. A mouse model that included four separate transgenes: HLA-DR_0401 and human CD4 molecules, a RA-related human auto-antigenic protein (HCgp-39), and a TCR (TCR-ab) transgene specific for an important HCgp-39 epitope, allowed the analysis of strong Th1 responses in the context of HLA-DR_0401. This mouse has been particularly useful for the study of the mechanisms involved in the breach of self-tolerance that occurs in Rheumatoid arthritis. Other spontaneous transgenic models of arthritis Several other spontaneous models have also been reported. For example, mice with deficiency of IL-1 receptor antagonist similarly develop spontaneous arthritis that is dependent upon environmental stimuli and is mediated through a strong Th17-polarized response. A homozygous mutation in the gp130 receptor results in enhanced STAT3 activation and the emergence of an inflammatory destructive arthritis.[34] The foregoing provides opportunities to explore the interface of T-cell mediated and innate immunity in inducing arthritis. A recent model further implicates DNA recognition in this process.[35] DNase II_/_/IFN-1R_/_ mice and mice with an induced deletion of the DNase II gene develop an inflammatory polyarthritis associated with high levels of anti-CCP antibody and rheumatoid factor. The model is in part TNF-a-dependent, suggesting that incomplete DNA disposal by macrophages may lead to the dysregulated cytokine release.

## 5. THERAPY AND CURRENT ROLE OF BIOLOGICAL AGENT

### 5.1. TNF-α blockers

Three TNF-a antagonists are approved for use in rheumatoid arthritis in the USA: Etanercept, a construct of two P75 TNF receptors linked together by an IgG1 molecule; infliximab, a chimeric anti-TNF monoclonal antibody; and Adalimumab, a completely humanized anti-TNF monoclonal antibody. Two head-to-head trials compared methotrexate (MTX) and Etanercept; another compared MTX to a combination of MTX and infliximab (J.S Smolen et al., 2003). In the ERA trial (early Rheumatoid arthritis), patients with less than 2-year disease duration were randomized to rapidly escalating MTX of up to 20 mg/week, or to etanercept 25 mg, twice a week (J.M. Bathon et al., 2000) Both medications led to similar clinical responses at 6 and 12months; however, a more rapid onset of improvement was observed with Etanercept. The progression of radiographic damage was also evaluated: patients treated with MTX deteriorated at 2years by 2.5 units on the Sharp score versus 1 unit for Etanercept. The significance of such a small difference over 2years is unknown. In the TEMPO trial, similar observations were made in patients with established RA (average disease duration of 6years)/(L.Klareskog et al., 2004). This trial included a third arm combining MTX and Etanercept, which proved to be superior to the other 2 regimens both clinically and radio-graphically at 1year. In the ASPIRE trial, MTX was compared to a combination of MTX and infliximab at 2 different doses (3 mg/kg and 6 mg/kg) in patients with early RA (J.S.Smolen et al., 2003). Both combination groups showed superior improvement over MTX alone. Adalimumab, has also been studied in patients who have been on long-term stable doses of MTX.[21] Patients who received Adalimumab had greater improvement in ACR 20, 50 and 70 scores at 24weeks. Etanercept has also been approved for the treatment of psoriatic arthritis (PsA), based upon two placebo-controlled trials. In the first study, patients on stable doses of MTX were allowed to remain on MTX and were randomized to Etanercept or placebo. ACR 20 responses were achieved by 73% of the Etanercept patients and 13% of the placebo patients. In addition, skin lesions also showed improvement. The Etanercept patients showed a 46% mean improvement of skin score (PASI) versus 9% in the placebo patient.(P.J.Mease et al., 2000).

### 5.2 IL-1 antagonists

The IL-1 receptor antagonist (IL-1Ra) is a naturally occurring regulatory molecule, which has structural homologies to IL-1. IL-1Ra binds to the IL-1 receptor but does not signal, and therefore acts to block IL-1 actions. Recombinant IL-1Ra (Anakinra) has been approved for the treatment of Rheumatoid arthritis, and has been used as monotherapy or in combination with other DMARDs. Studies have also shown that the combination of Anakinra, etanercept and MTX is no more effective in RA treatment than Etanercept plus MTX alone, and increases the risk of bacterial infection. Although studies have indicated that Anakinra retards radiographic progression, its moderate symptom control compared to TNF-a inhibitor therapies has led to its infrequent use in RA treatment. The disappointing clinical effectiveness of Anakinra has led to the speculation that either TNF-a plays a more important role as a dominant cytokine in RA than does IL-1; or,
that IL-1Ra is not as biologically active as alternative anti-IL-1 antagonists might be. (M.C. Genovese et al., 2004)

6. Combination therapy

A new therapeutic concept for the management of rheumatoid arthritis is strongly required since most traditional methods have failed to introduce remission. This paper attempted to review over novel therapeutic approaches based on the advanced program especially on early stage of Rheumatoid arthritis. Clinical improvement has been observed with triple combined therapy using such as bucillamine, methotrexate, and sulphasalzopryidine. Here the future development of therapeutic approach including targeting immunosuppression or gene targeting on proliferated synovium has been discussed. (K. Nishioka et al., 1992)

Despite significant cost differences, the comparative effect of combination treatments of disease modifying anti-rheumatic drugs (DMARDs) with and without biologic agents has rarely been examined. Thus we performed a network meta-analysis on the effect of combination therapies on progression of radiographic joint erosions in patients with rheumatoid arthritis (RA). The following combination drug therapies compared versus single DMARD were investigated: Double DMARD: 2 DMARDs (methotrexate, sulfasalazine, lefluonamide, injectable gold, cyclosporine, chloroquine, azathioprin, penicillamin) or 1 DMARD plus low dose glucocorticoid (LDGC); triple DMARD: 3 DMARDs or 2 DMARDs plus LDGC; biologic combination: 1 DMARD plus biologic agent (tumor necrosis factor α inhibitor (TNFi) or abatacept or tocilizumab or CD20 inhibitor (CD20i)) (N Graudaletal., 2014). Until late in the 20th century, the therapy of rheumatic diseases relied on the use of drugs that had been developed through empirical approaches without detailed understanding of the molecular mechanisms involved. That approach changed with the introduction of biologic therapeutics at the end of the 20th century and by the introduction of small-molecule inhibitors of intracellular signal transduction pathways. Treatment with initial high-dose prednisolone and a combination of methotrexate (MTX) and sulfasalazine (SSZ) according to the COBRA regimen (Dutch acronym for combination therapies rheumatoid arthritis, 'combination therapy for rheumatoid arthritis'), has repeatedly been demonstrated to be very effective in early rheumatoid arthritis. COBRA combination therapy is superior to initial monotherapy of SSZ and MTX, is also associated with a good long-term outcome, is as safe as other treatment regimes, and performs as well as the combination of high-dose MTX and the tumor necrosis factor antagonist infliximab. A pilot study with an intensified version of the COBRA combination therapy showed that strict monitoring and aggressive treatment intensification based on the Disease Activity Score can result in a remission rate of 90% in patients with active early. (LA Raschetal., 2014).

To determine whether order of medication withdrawal in children with juvenile idiopathic arthritis (JIA) on methotrexate (MTX) and tumor necrosis factor inhibitor (TNFi) combination therapy (CBT) affects flare-free survival (FFS). Methods: This retrospective observational study of 335 patients with polyarticular JIA or enthesitis related arthritis analyzed FFS off medications in 4 withdrawal arms: 1) TNFi plus MTX, off MTX first, 2) TNFi plus MTX, off TNFi first, 3) MTX monotherapy, or 4) TNFi monotherapy. Outcomes were evaluated based on order of medication withdrawal, clinical presentation, serologic parameters, and duration of clinically inactive disease (CID) on medications (Chang CY. et al., 2014).

7. CONCLUSION

Rheumatoid arthritis is a chronic inflammation of the joints. It can cause joint pain, deformities, and severe joint stiffness. In the past, many people with rheumatoid arthritis were confined to a wheelchair. Thanks to recent medical and surgical advances, managing rheumatoid arthritis is becoming more and more successful and patients continue to lead productive lives. There are several treatment options to choose from for rheumatoid arthritis, which include a range of medications and physical therapy. The patient's willingness to participate in their own treatment and self-care plays a big role in controlling rheumatoid arthritis.

8. REFERENCE


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