REVIEW :TREATMENT ON RHEUMATOIDE ARTHIRITIS

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic autoimmune disorder characterized by symmetric inflammation of synovial joints leading to progressive erosion of cartilage and bone. The risk factors include age, gender, genetics, and environmental exposure (cigarette smoking, air pollutants, and occupational). As there is no cure for RA, the treatment goals are to reduce the pain and stop/ slow further damage. Here, we present a brief summary of various past and present treatment modalities to address the complications associated with RA. The clinical status of RA patients has improved in recent years due to medical advances in diagnosis and treatment, that have made it possible to reduce disease activity and prevent systemic complications. The most promising results were obtained by developing disease-modifying anti-rheumatic drugs (DMARDs), the class to which conventional synthetic, biologic, and targeted synthetic drugs belong. In the present work, we offer a comprehensive perspective on the management of RA, by centralizing the existing data provided by significant literature, emphasizing the importance of an early and accurate diagnosis associated with optimal personalized treatment in order to achieve better outcomes for RA patients. In addition, this study suggests future research perspectives in the treatment of RA that could lead to higher efficacy and safety profiles and lower financial costs.

Keyword: *Rheumatoid arthritis , NSAIDS, Tenosynovectomy, Radiosynovectomy, DMARDs etc.*

1.INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, inflammatory , systemic autoimmune disease, affecting the joints with varying severity among patients. The risk factors include age, gender, genetics, and environmental exposure (cigarette smoking, air pollutants, and occupational).[12] The prevalent and persistent form of autoimmune disorder that results in chronic inflammation of the other body components is rheumatoid arthiritis. This happens when a persons immune system unintentionally destroy their bodily tissues or joint lining capsule. Rheumatoide arthiritis (RA) has been discovered to affect certain people skin, lungs ,eyes, kidneys, and blood vessels[33].Especially RA affect hands and feet first ,but it can occur in any type of joint. It mainly involves the same joints on both sides of the body.Inflammation develops in the targeted tissues or organ as a result of the immune system's response in RA,the heart,eyes,lungs,and joints may all be affected. Many complications can follow, such as permanent joint damage requiring arthroplasty, rheumatoid vasculitis, and Felty syndrome requiring splenectomy if it remains unaddressed. As there is no cure for RA, the treatment goals are to reduce the pain and stop/slow further damage. Here, we present a brief summary of various past and present treatment modalities to address the complications associated with RA[12].Rheumatoid arthritis is a systemic disease that affects the synovial joints. It is a persistent chronic disease that spreads from joint to joint and affects about 0.5% of people worldwide. Not that long ago it was believed that anti term outcome of the disease.[19]

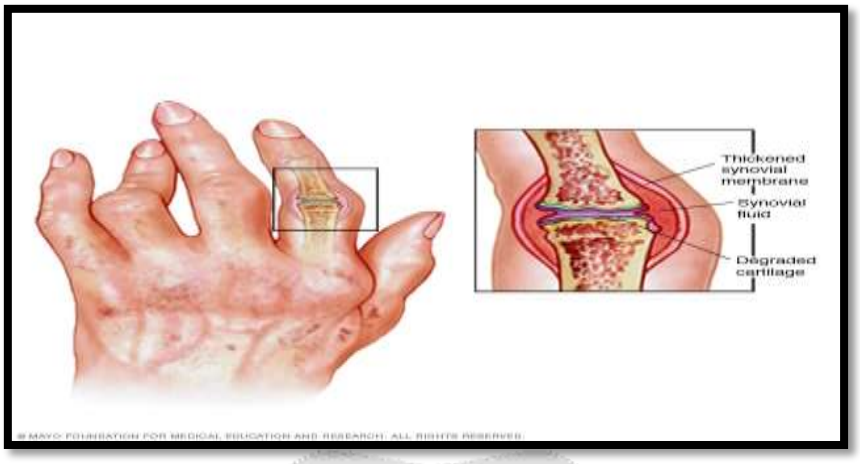

Fig 1:Rheumatoid arthiritis

1.1SIGNS AND SYMPTOMS OF RHEUMATOID ARTHRITIS

- Stiffness in more than one joint.
- Tenderness and swelling in more than one joint.
- The same symptoms on both sides of the body (such as in both hands or both knees)
- Pain or aching in more than one joint.
- Weight loss.
- Fever.
- Fatigue or tiredness.
- Weakness.[3]

2. RISK FACTOR OF RA:

Fig 2: Risk factors

Age:RA can begin at any age, but the likelihood increases with age. The onset of RA is highest among adults in their sixties.

Sex: New cases of RA are typically two-to-three times higher in women than men.

Genetics/inherited traits: People born with specific genes are more likely to develop RA. These genes, called HLA (human leukocyte antigen) class II genotypes, can also make your arthritis worse.

Smoking: Multiple studies show that cigarette smoking increases a person's risk of developing RA and can make the disease worse.

History of live births: Women who have never given birth may be at greater risk of developing RA.

Obesity: Being obese can increase the risk of developing RA. Studies examining the role of obesity also found that the more overweight a person was, the higher his or her risk of developing RA became.[3]

Childhood trauma: People who grew up with abuse, neglect, or other household dysfunction may be more likely to develop an autoimmune disease.[26]

3.PATHOPHYSIOLOGY OF RHEUMATOID ARTHIRITIS

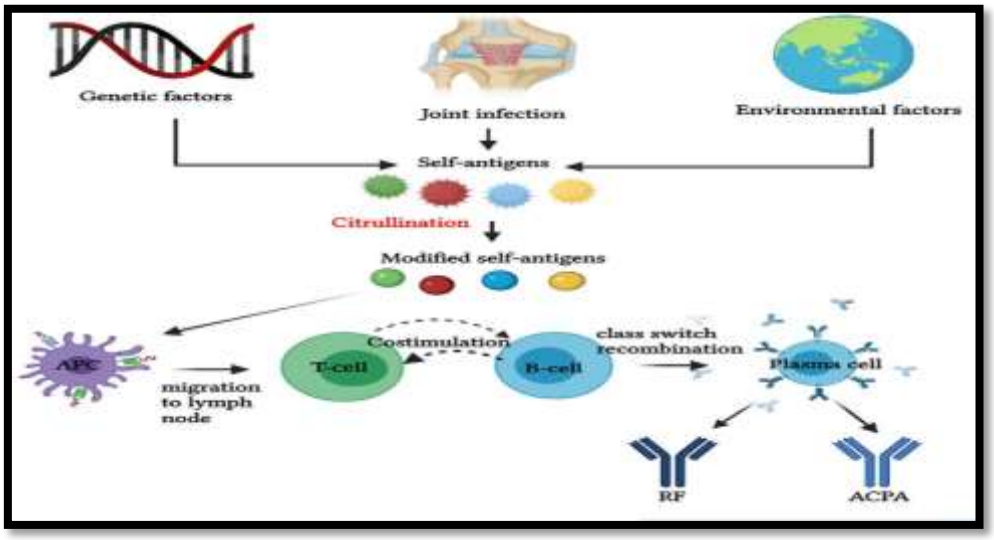

Fig 3 :Immunological process in the RA

The mechanisms underlying the involvement of air pollutants and gut microbiota in the pathogenesis of RA are shown in Figure

Although the pathophysiological mechanisms for RA are not fully elucidated, several hypotheses have been postulated. It has been reported that immunological processes can occur many years before symptoms of joint inflammation are noticed, the so-called pre-RA phase [28]

- The interactions between epigenetic modifications on the genomic structure and environmental factors can lead to modified self-antigens as in the case of immunoglobulin G (IgG), type 2 collagen and vimentin. These proteins with arginine residues can be converted to citrulline by peptidyl arginine deiminases in a post-translational modification called citrullination .Moreover, joint disorders like synovial hyperplasia or synovial infections can trigger cytokine release that may cause joint inflammation and also modified self-antigens.[28]

- Another important element with major implications in the pathogenesis of RA is the gut microbiota, the most densely colonized bacterial population within the human body.[1]
- It has been demonstrated that immunological, metabolic, and neurobehavioral features are influenced by gut microorganisms. When compared to healthy controls, RA patients showed significant

differences in the gut microbiota composition, being associated with an increase or a decrease in certain bacterial populations.[2]

- RA is generally characterized by an insidious onset of symptoms, but over time the disease progresses and gradually worsens. The trigger for RA symptoms is unknown, but the immunological processes that take place in the synovium and in the synovial fluid have been described.[29]

4.HOW RHEUMATOID ARTHRITIS DIAGONISED ?

RA is diagnosed by reviewing symptoms, conducting a physical examination, and doing X-rays and lab tests.Diagnosis and effective treatments, particularly treatment to suppress or control inflammation, can help reduce the damaging effects of RA.

It's best to diagnose RA early within 6 months of the onset of symptoms so that people with the disease can begin treatment to slow or stop disease progression (for example, damage to joints).[15]

5.HOW IS RA MANAGED?

Medication(s) and self-management strategies can effectively treat and manage RA. Disease-modifying antirheumatic drugs (DMARDs) are medications that slow disease progression and prevent joint deformity; biological response modifiers (biologicals) are medications that are an effective second-line treatment for RA.

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6.TREATMENT OF RHEUMATOID ARTHIRITIS

Rheumatoid arthritis treatments can help reduce joint inflammation, relieve pain, prevent or slow joint damage, reduce disability, and allow you to be as active as possible.

Diet and Nutrition
While there is no single arthritis-curing diet, diet and nutrition can play an important role in preventing or minimizing arthritis symptoms and flares.

Exercise
Exercise is used to keep the joint structures sturdy and can slow the rate of deterioration. Physical therapy is used to rehabilitate a joint or joints after an injection or surgery procedure.

Injections
Injections for arthritis can reduce pain symptoms to allow for a window of opportunity during which the patient can participate in physical therapy, exercise, and everyday activities.

Joint Aspiration
Joint aspiration, also known as arthrocentesis, is a procedure where a needle and syringe are used to remove fluid from a joint. The fluid is removed for diagnostic lab testing, and/or to alleviate pressure and relieve joint pain.

Medications
Medication treatments for arthritis may be over-the-counter medicines such as ibuprofen or aspirin, or doctor-prescribed medicines such as opioids. Each option has its own benefits and risks.

Specialists
Doctors with specialties benefiting people with a type of arthritis include rheumatologists, physiatrist, and orthopedic surgeons along with other specialists to diagnose or treat joint problems.[7]

6.1First-Line Management:

- NSAIDS

The overall goal of first-line treatment is to relieve pain and decrease inflammation. Medications, considered to be fast-acting, are nonsteroidal anti-inflammatory drugs (NSAIDs) including acetylsalicylate (Aspirin), naproxen (Naprosyn), ibuprofen (Advil and Motrin), and etodolac (Lodine).

Aspirin is an effective anti-inflammatory for RA when used at high doses, due to the inhibition of prostaglandins. It is one of the oldest NSAIDs used for joint pain. Side effects of aspirin at high doses include tinnitus, hearing loss, and gastric intolerance.

There are other NSAIDs that are newer on the market than aspirin and just as effective. In addition, these drugs require fewer doses per day.NSAIDs work by inhibiting cyclo-oxygenase to prevent the synthesis of prostaglandins, prostacyclin, and thromboxanes. Common side effects are nausea, abdominal pain, ulcers, and gastrointestinal (GI) bleeding.

These symptoms can be reduced if taken with food, antacids, proton pump inhibitors, or misoprostol (Cytotec), An even newer NSAID called celecoxib (Celebrex) is a selective Cox-2 inhibitor that has less risk of GI side effects[4]

2.Cortecosteroids

Corticosteroids are a more potent anti-inflammatory medication than NSAIDs, but they come with greater side effects. For this reason, they are only indicated for a short period of time at low doses, during exacerbations or flares of RA. Intra-articular injections of corticosteroids can be used for the local symptoms of inflammation[5]

They work by preventing the release of phospholipids and decreasing the actions of eosinophils, thereby decreasing inflammation. Their side effects include bone-thinning, weight gain, diabetes, and immunosuppression. Advising the patient to take calcium and vitamin D supplementation can prevent thinning of the bone. Side effects can be reduced by gradually tapering doses as a patient's condition improves. It is important to not abruptly discontinue injected or oral corticosteroids as this can lead to suppression of the hypothalamic-pituitary-adrenal axis (HPA) or flares of RA[6]

Opioid Analgesics

the use of opioid analgesics for patients with pain due to RA. From their conclusions, weak opioids such as codeine, dextropropoxyphene, and tramadol may play an effective role in the short-term management of pain caused by RA, but the adverse effects outweigh the benefits. They recommend that other analgesics be considered first[8]

6.2Second-Line Management:

Disease-Modifying Antirheumatic Drugs The overall goal of second-line treatment is to promote remission by slowing or stopping the progression of joint destruction and deformity. Medications are considered to be slow-acting because they take from weeks to months to be effective. Disease-modifying antirheumatic drugs (DMARDs) can also reduce the risk of developing lymphoma that can be associated with RA[10]

Methotrexate (MTX)

Is the initial second-line drug (also considered an anchor drug). It is an analog to folic acid that competitively inhibits the binding of dihydrofolic acid (FH2) to the enzyme that is responsible for converting FH2 to folinic acid (FH4). Without FH4, the metabolism of purine and pyrimidine is impaired, and the synthesis of amino acids and polyamine is inhibited. MTX is an immunosuppressive drug that requires regular blood tests due to its side effects, i.e., liver problems, cirrhosis, and bone marrow deterioration. Folic acid supplementation can reduce the risk of side effects. It is an effective DMARD, has a lower incidence of side effects than other DMARDs, and has dosage flexibility, meaning that doses can be adjusted as needed[11]

Until now, there is convincing data showing the benefits of combinations of conventional synthetic DMARDs over MTX monotherapy. However, biological and synthetic DMARDs in combination are reported to be better than MTX but with more side effects and greater costs[13,14,16]

Methotrexate may be given orally (in tablet or liquid form) or parenterally, by sc or im injection

.The following dose schedules are commonly used:

1. single weekly oral or im low dose 2. doses divided into two or three weekly doses at consecutive 12-h intervals If significant improvement is not noted, the dosage may be gradually increased. The usual starting dose in RA is 7.5–10 mg per week. If a positive response has not occurred within 4 to 8 weeks after MTX initiation and there has been no toxicity, the dose should be increased (by 2.5–5 mg/week each month) to 20–25 mg per week before considering the treatment a failure. To improve the efficacy of MTX at dosages of 20–25 mg weekly or more, a change to parenteral administration (sc) should be considered [30,31,32]

6.3Surgery:

Surgery is a last resort for the treatment of RA. Indications include intractable joint pain or functional decline due to joint destruction after all nonsurgical approaches have failed. At this point, the disease is considered "end-stage." A tenosynovectomy involves the excision of inflamed tendon sheaths or repairing a recent tendon rupture, most commonly in the hand[17] Radiosynovectomy is an alternative to surgical synovectomy; it involves intra-articular injection of small radioactive particles, is cost-effective, and can treat multiple joints simultaneously[13]. Calcium and vitamin D supplementation can be helpful in preventing osteoporosis. Lastly, folic acid can help to prevent the side effects of MTX[16]. Lastly, with the scientific advancements and enhanced understanding of the molecular mechanisms, newer and better treatment options should become available in the near future[21,22]

6.4Newer medication :

Tocilizumab (Actemra) is a biologic that works by blocking IL-6, a chemical messenger of inflammation. It is administered via intravenous infusion given monthly or via weekly subcutaneous injections. It is also used for patients who have not been effectively treated with traditional DMARDs.[24]The efficacy of using methotrexate monotherapy and the efficacy of TCZ monotherapy (8 mg/kg, every 4 weeks) in patients who had either never used methotrexate or who had not used it in the previous 6 months even though they had not been classed as having an inadequate response to methotrexate.

Anakinra (Kineret) is a drug that is injected subcutaneously daily. It works by binding to IL-1, a chemical messenger of inflammation. It can be used in combination with other DMARDs or as a monotherapy, but due its low response rate compared to other biologics, it is not used as frequently.[25,27].dose - 100mg/0.67mL. May use alone or in combo with DMARDs (not TNF-blocking agents).

Leflunomide is an oral medication that is converted to malononitrilamide, which inhibits the synthesis of ribonucleotide uridine monophosphate pyrimidine. It relieves symptoms and retards the progression of RA. It is recommended to be used in combination with MTX but can constitute a monotherapy if patients do not respond to MTX.Loading dose: 100 mg orally once a day for 3 days.

7.CONCLUSION:

RA is a debilitating, chronic, inflammatory disease, capable of causing joint damage as well as long-term disability. Early diagnosis and intervention are essential for the prevention of serious damage and loss of essential bodily functions. The treating physician should consider adhering to treat-to-target (T2T) recommendations, by first outlining the aims and then implementing the protocols to achieve and assess them. Furthermore, early referral to a specialist can help to ensure better treatment outcomes. With advances in the field of molecular medicine, we have a better understanding of disease mechanisms which can aid in the designing of more effective treatments.Many drugs Which are comes under the second line drugs and newer medicine are Effective against RA.

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