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A Comprehensive Review of Treatment Approaches and Perspectives for Management of Rheumatoid Arthritis

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ABSTRACT

Rheumatoid arthritis (RA) is an inflammatory illness that mostly affects the joints, although it can also affect other organs and limit movement. This symmetrical, chronic illness typically manifests between the ages of 35 and 60 and causes joint degradation, pain, and systemic symptoms. Because of their different clinical manifestations, RA and osteoarthritis must be distinguished from one another. Osteoarthritis is caused by wear and tear, whereas RA is symmetrical and involves an immunological response. The goals of RA management are to lessen discomfort, reduce inflammation, and avoid joint deformities and destruction because there is currently no known treatment for RA. A combination of medication, specialized exercise, education, and rest are used in treatment plans, taking into account the disease's course, the joints that are impacted, and the patient's general health. The two main forms of treatment are corticosteroids and nonsteroidal anti-inflammatory medications (NSAIDs), which reduce inflammation and discomfort but frequently present varying side effects. Disease modifying anti-rheumatic medications commonly called DMARDs, provide a backup plan by delaying the deterioration of joints and easing associated symptoms. Modern treatment options include methotrexate, hydrochloroquine, and more recent drugs like leflunomide and biologics like interleukin inhibitors and tumor necrosis factor (TNF) inhibitors, each with unique advantages and disadvantages. In order to improve joint function and reduce discomfort, surgical interventions—which have become less common as a result of medical advancements are taken into consideration for severe cases or end-stage RA. Physcial and occupational therapy, nutritional supplements, complementary therapies, and current molecular mechanism research provide further options for controlling RA symptoms and enhancing the quality of life for patients. This review offers a thorough analysis of both traditional and contemporary RA treatments, emphasizing the need for a multimodal strategy to effectively manage the disease and pointing out possible directions for future research and development.

Keywords: Autoimmune disease, Rheumatoid arthritis, Disease-modifying drugs, Joint degradation, Osteoarthritis, Joint pain.

INTRODUCTION

RA is a chronic symmetrical, inflammatory, autoimmune disease, rheumatoid arthritis (RA) first affects tiny joints before moving on to larger joints and eventually the skin, eyes, heart, kidneys, and lungs. Joint bone and cartilage are frequently damaged, and ligaments and tendons deteriorate [1]. Deformities and bone erosion result from

all of this joint deterioration, which is typically extremely painful for the patient. Rheumatoid nodules beneath the skin, tiredness, fever, weight loss, and morning stiffness of the afflicted joints lasting more than thirty minutes are typical signs of RA. This condition typically manifests itself between the ages of 35 and 60, with periods of remission and aggravation. Juvenile RA (JRA), which is comparable to RA but does not have the rheumatoid factor, can also affect young children before the age of 16 [2]. It is estimated that the prevalence of RA is 1% globally [3] and 1-2% in the West [1]. Osteoarthritis (OA) usually affects the distal interphalangeal (DIP) joint, whereas RA mostly affects the proximal interphalangeal (PIP) and metacarpophalangeal (MP) joints. Based on clinical differences, RA can be diagnosed differently from OA. The most prevalent kind of arthritis, OA, is not an autoimmune disease but rather the result of wear and tear. It doesn't affect the immune system, heart, or lungs. Furthermore, RA is symmetrical, whereas OA usually affects only one side of the body. Another way RA patients are different is that they experience morning stiffness that lasts for at least sixty minutes. Patients with osteoarthritis frequently have morning stiffness, although it normally goes away or improves after 20 to 30 minutes [4]. The goals of RA treatment include minimizing joint inflammation and pain, maximizing joint function, and preventing joint deformity and destruction. Treatment methods include medicine, weight-bearing exercise, education about the illness, and rest. Individualized treatment regimens are frequently developed in response to the needs of the patient and their overall health status. This covers things like how quickly the illness advances, which joints are afflicted, age, overall health, kind of employment, compliance, and awareness of the issue [5]. This study provides a brief summary of both conventional and contemporary treatments for RA symptoms.

First-Line Treatment: Corticosteroids and NSAIDs

Fast-acting nonsteroidal anti-inflammatory medications (NSAIDs) such as aspirin, naproxen, ibuprofen, and lodine are used as first-line treatment for RA. Although aspirin has adverse effects like tinnitus and hearing loss, it is beneficial for treating joint pain. Celecoxib is one of the newer, less potent NSAIDs that inhibits cyclo-oxygenase, although it can induce nausea, abdominal pain, ulcers, and bleeding in the gastrointestinal tract [6].

Strong anti-inflammatory drugs called corticosteroids are used to treat RA, but they come with a lot of adverse effects. During exacerbations or flares, they should be taken for brief periods of time at low doses. They function by stopping the release of phospholipids and reducing the actions of eosinophils; nonetheless, they can weaken bones, increase body weight, induce diabetes, and impair immunity [7].

Opioid Painkillers

The issue of whether or not to provide opiate analgesics to individuals suffering from RA pain was evaluated by Whittle and colleagues [8]. Based on their results, mild opioids like codeine, dextropropoxyphene, and tramadol might be useful in the short term for treating RA pain, but the risks outweigh the benefits. They advise looking into other analgesics initially [9].

Disease-Modifying Antirheumatic Drugs (DMARDs) for Second-Line Management

Slow-acting drugs take weeks or months to become effective as second-line treatment, with the goal of slowing joint degradation and deformity progression. DMARDs can lower the risk of lymphoma in people with RA [10].

Methotrexate

The immunosuppressive medication methotrexate (MTX) inhibits dihydrofolic acid from binding to the enzyme that converts dihydrofolic into folinic acid. The synthesis of amino acids and polyamine is hampered and the metabolism of purines and pyrimidines is compromised in the absence of folinic acid. It is flexible in dosage, less likely to cause side effects, and effective. Synthetic DMARD combinations have proven to be more beneficial than MTX monotherapy;

nevertheless, although the combination of biological and synthetic DMARDs is superior, it is more expensive and has more adverse effects [7].

Hydrochloroquine

An antimalarial medication called plaquenil (hydrochloroquine) is used to treat RA over the long run by reducing the release of proinflammatory cytokines. GI tract, skin, and central nervous system problems are typical side effects [11].

Sulfasalazine (Azulfidine)

When used with anti-inflammatory drugs, Sulfasalazine is used to treat RA and irritable bowel illness. Although it has negative effects and should be avoided in people with sulfa allergies, it lowers interleukin IL-8 and monocyte chemoattractant protein productions [12].

Gold salts

While more potent therapies like MTX have replaced gold salts like aurothioglucose, auranofin, myochrysine, and D-penicillamine in the treatment of RA, other immunosuppressive drugs are saved for severe cases of the illness or its consequences [13].

More Recent Drugs Used in RA Management

Leflunomide: Oral drug leflunomide is transformed into malononitrilamide, which prevents uridine monophosphate pyrimidine ribonucleotide synthesis from occurring. It lessens RA symptoms and delays the course of the illness. While it is recommended to be used in combination with MTX, it can also be used as a monotherapy in patients who do not react to MTX. The side effects include dermatitis, hypertension, gastrointestinal distress, liver damage, leukopenia, interstitial lung disease, neuropathy, and loss of bone marrow [14].

Tumor necrosis factor (TNF) inhibitors

Biologic drugs such as certolizumab pegol, adalimumab, etanercept, infliximab, and adalimumab inhibit TNF, a protein that causes inflammation in joints. These medications offer quick symptom relief and are typically taken alongside other DMARDs, particularly MTX. Patients with demyelinating disorders or congestive heart failure should not take these medications [15]. Tocilizumab: For patients who have not received standard DMARD treatment, tocilizumab, a biologic that inhibits IL-6, is administered [16]. Tofacitinib: is a JAK inhibitor, is used to treat cells that are not responsive to MTX by inhibiting Janus kinases (enzymes of inflammation) within the cell. It is taken orally twice a day, either by itself or in combination with MTX but not with traditional biologic medications or other potent immunosuppressants [17]. Biologic drugs such as Anakinra, Rituximab, and Abatacept are used to treat RA. Every day subcutaneous injections of Anakinra target IL-1, while Rituximab depletes B cells that cause inflammation and aberrant production of antibodies. It is utilized when TNF inhibitors are ineffective and has demonstrated efficacy in the treatment of conditions such as cryoglobulinemia and vasculitis [18, 19]. Monthly or subcutaneous administration of abatacept prevents T cell activation. Patients who have not responded well to conventional DMARD treatment are prescribed it [20].

Surgery as a RA management strategy

The 1990s saw a peak in joint surgery for RA patients; however, rates of surgery rose for older patients while they declined for those in the 40–59 age range. With end-stage RA, surgery is a last resort that tries to reduce discomfort and improve joint function. Every patient requires a different course of treatment [21]. A tenosynovectomy is a surgical technique used to repair a ruptured tendon or remove inflammatory tendon sheaths [22]. While arthroscopy is used to repair ruptured tendons, radiosynovectomy is a more economical option than surgical synovectomy [23]. Osteotomy, joint fusion, soft-tissue release, small-joint implant arthroplasty, and metatarsal-head excision arthroplasty are further surgical

alternatives [24]. A significant contraindication to whole joint replacements is an active systemic articular infection. Whole joint replacements entail the removal of diseased joints and their replacement with prosthetics [25].

Additional Therapies for the Management of RA

Patients with RA don't need to avoid any particular foods, and eating doesn't make their symptoms worse. Complementary and alternative therapies such as fish oils, calcium, vitamin D, folic acid, cumin, omega-3 fatty acid supplements, and osteoporosis can help control transient symptoms and avoid MTX side effects [26]. Physical and occupational therapy, consistent exercise, and the use of hot and cold packs can help patients with RA preserve joint mobility and build muscle. Future developments in molecular mechanisms and research on collagen in connective tissue may result in novel therapy options [27].

CONCLUSION

The treatment of RA is a complex process with the goals of reducing joint deterioration, reducing pain, and improving the quality of life for those who are impacted. Given their diverse clinical presentations, it is imperative to distinguish between osteoarthritis and RA. The therapies used in current treatment paradigms range from corticosteroids and NSAIDs to biologics and DMARDs, each having unique advantages and drawbacks. Surgical operations are still reserved for the most severe cases of RA, despite the fact that these treatments have greatly improved RA care. Promising supplemental techniques include dietary supplements, continuous research into new treatment paths, and complementary therapies. Nevertheless, issues still exist, such as the adverse effects of medications and the requirement for individualized treatment regimens based on specific patient characteristics. A promising future lies in the ongoing investigation of molecular pathways and novel therapeutic approaches, which could completely transform the treatment of RA. To improve results and improve the lives of people with RA, a comprehensive strategy including medicinal, surgical, and complementary therapy is essential, as is a holistic understanding of the disease.

REFERENCES

1. Picerno V, Ferro F, Adinolfi A, Valentini E, Tani C, Alunno A. One year in review: the pathogenesis of rheumatoid arthritis. *Clin Exp Rheumatol.* 2015 Jul-Aug;33 (4):551–8.
2. Chaudhari K, Rizvi S, Syed BA. Rheumatoid arthritis: current and future trends. *Nat Rev Drug Discov.* 2016 May;15 (5):305–6.
3. Chopra A, Abdel-Nasser A. Epidemiology of rheumatic musculoskeletal disorders in the developing world. *Best Pract Res Clin Rheumatol.* 2008 Aug;22 (4):583–604.
4. McGonagle D, Hermann KG, Tan AL. Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. *Rheumatology (Oxford)* 2015 Jan;54 (1):29–38.
5. Staheli LT. Lower extremity management. In: Staheli LT, Hall JG, Jaffe KM, Paholke DO, editors. *Arthrogryposis: A Text Atlas.* Cambridge: Cambridge University Press; 1998. pp. pp. 55–73.
6. Ong CK, Lirk P, Tan CH, Seymour RA. An evidence-based update on nonsteroidal anti-inflammatory drugs. *Clin Med Res.* 2007 Mar;5 (1):19–34.
7. Liu D, Ahmet A, Ward L, Krishnamoorthy P, Mandelcorn ED, Leigh R, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol.* 2013 Aug;9(1):30.
8. Whittle SL, Colebatch AN, Buchbinder R, Edwards CJ, Adams K, Englbrecht M, et al. Multinational

evidence-based recommendations for pain management by pharmacotherapy in inflammatory arthritis: integrating systematic literature research and expert opinion of a broad panel of rheumatologists in the 3e Initiative. *Rheumatology (Oxford)* 2012 Aug;51(8):1416–25.
9. Richards BL, Whittle SL, van der Heijde DM, Buchbinder R. The efficacy and safety of antidepressants in inflammatory arthritis: a Cochrane systematic review. *J Rheumatol Suppl.* 2012 Sep;90(0):21–7.
10. Smolen JS, Landewé R, Breedveld FC, Dougados M, Emery P, Gaujoux-Viala C, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. *Ann Rheum Dis.* 2010 Jun;69(6):964–75.
11. Silva JC, Mariz HA, Rocha LF, Jr, Oliveira PS, Dantas AT, Duarte AL, et al. Hydroxychloroquine decreases Th17-related cytokines in systemic lupus erythematosus and rheumatoid arthritis patients. *Clinics (São Paulo)* 2013 Jun;68 (6):766–71.
12. Volin MV, Harlow LA, Woods JM, Campbell PL, Amin MA, Tokuhira M, et al. Treatment with sulfasalazine or sulfapyridine, but not 5-aminosalicyclic acid, inhibits basic fibroblast growth factor-induced endothelial cell chemotaxis. *Arthritis Rheum.* 1999 Sep;42(9):1927–35.
13. Kumar P, Banik S. Pharmacotherapy options in rheumatoid arthritis. *Clin Med Insights Arthritis Musculoskelet Disord.* 2013 Aug;6:35–43.
14. Gibofsky A. Combination therapy for rheumatoid arthritis in the era of biologicals. *HSS J.* 2006 Feb;2 (1):30–41.
15. Lis K, Kuzawińska O, Bałkowiec-Iskra E. Tumor necrosis factor inhibitors - state of knowledge. *Arch Med Sci.* 2014 Dec;10 (6):1175–85.
16. Gómez-Gómez GJ, Masedo Á, Yela C, Martínez-Montiel MP, Casís B. Current stage in inflammatory bowel disease: what is next? *World J Gastroenterol.* 2015 Oct;21 (40):11282–303.
17. Cada DJ, Demaris K, Levien TL, Baker DE. Tofacitinib. *Hosp Pharm.* 2013 May;48((5)):413–24.
18. Mann DL. Innate immunity and the failing heart: the cytokine hypothesis revisited. *Circ Res.* 2015 Mar;116 (7):1254–68.
19. Mok CC. Rituximab for the treatment of rheumatoid arthritis: an update. *Drug Des Devel Ther.* 2013 Dec;8:87–100.
20. Rosman Z, Shoenfeld Y, Zandman-Goddard G. Biologic therapy for autoimmune diseases: an update. *BMC Med.* 2013 Apr;11 (1):88.
21. Louie GH, Ward MM. Changes in the rates of joint surgery among patients with rheumatoid arthritis in California, 1983-2007. *Ann Rheum Dis.* 2010 May;69 (5) :868–71.
22. Chung KC, Pushman AG. Current concepts in the management of the rheumatoid hand. *J Hand Surg Am.* 2011 Apr;36 (4):736–47.
23. Knut L. Radiosynovectomy in the therapeutic management of arthritis. *World J Nucl Med.* 2015 Jan-Apr;14((1)):10–5.
24. Puddu G, Cipolla M, Cerullo G, Franco V, Giannì E. Which osteotomy for a valgus knee? *Int Orthop.* 2010 Feb;34((2)):239–47.
25. Pajarinen J, Lin TH, Sato T, Yao Z, Goodman SB. Interaction of Materials and Biology in Total Joint Replacement - Successes, Challenges and Future Directions. *J Mater Chem B Mater Biol Med.* 2014 Nov;2((41)):7094–108.
26. Escott-Stump S. *Nutrition and Diagnosis-Related Care.* Philadelphia: Lippincott Williams & Wilkins; 2011.

27. González-Álvaro I, Ortiz AM, Seoane IV, García-Vicuña R, Martínez C, Gomariz RP. Biomarkers predicting a need for intensive treatment in patients with early arthritis. *Curr Pharm Des.* 2015;21(2):170–81.

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