



CURRENT PHARMACOLOGICAL INTERVENTIONS AND DEVELOPMENT OF INNOVATIVE TREATMENT TECHNIQUES FOR THE MANAGEMENT OF ARTHRITIS

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Abstract : Arthritis is chronic inflammatory disease affecting normally on joints, including those in hands and feet. In arthritis, the body's immune system attacks its own tissues, including joints. In severe cases, it attacks the internal organs. The techniques employed for the recognition of arthritis includes, laboratory findings and various imaging processes. Current Pharmacological interventions and life style adjustments are also recommended for the management of this disease. Researchers are actively involved in the field of modern scientific technologies to develop a suitable cost-effective pharmaceutical aid for the treatment and management of arthritis.

Index terms: Joints, Immune system, Medications, Arthritis, Interventions

1. INTRODUCTION

Arthritis is derived from the Greek term "disease of the joints." It is defined as an acute or chronic joint inflammation that often co-exists with pain and structural damage, Arthritis is not synonymous with arthralgia, which refers to pain localized to a joint, regardless of the origin of the pain (which may or may not be due to joint inflammation). More than 100 different types of arthritis have been described, the most common being osteoarthritis or degenerative arthritis which is non-inflammatory arthritis. Inflammatory arthritis can occur in several settings, and inflammation can be caused by autoimmune processes (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, etc.), crystal deposition induced inflammation (gout, pseudogout, basic calcium phosphate disease) or infections (septic arthritis, Lyme's arthritis). Inflammatory arthritis can also accompany other autoimmune connective tissue diseases such as systemic lupus erythematosus, Sjogren syndrome, scleroderma, myositis, inflammatory bowel disease, celiac disease, etc (Cranny et al, 2009).

There are several diseases where joint pain is primary and is considered the main feature. Generally when a person has "arthritis" it means that they have one of these diseases, which include: Osteoarthritis, Rheumatoid arthritis, Gout and Pseudo-gout, Septic arthritis, Ankylosing spondylitis, Juvenile idiopathic arthritis, Still's disease, Psoriatic arthritis (Reginate et al, 2003).

The etiology of arthritis varies with the type of arthritis. In osteoarthritis, the major contributory factors include advancing age, female sex, joint trauma, and obesity. Some genetic factors have been described such as mutations in genes encoding types II, IV, V, and VI collagens (Siva et al, 2003).

Rheumatoid arthritis (RA), on the other hand, is an autoimmune systemic inflammatory disorder. An interplay between several genetic factors (HLADRB1 and others) and environmental factors (smoking) leads to activation and dysfunction of the immune system leading to inflammation.

In Gout, prolonged hyperuricemia leads to uric acid deposition in joints, which then leads to joint inflammation. There are several genetic mutations that can cause hyperuricemia, although this accounts for less than 10% of gout. The majority of patients with gout are under-excretors i.e. they are not able to get rid of all the uric acid that is produced in them as a result of endogenous or exogenous purine metabolism. Male sex, advancing age, chronic kidney disease, alcoholism, and certain drugs such as the diuretics are additional risk factors for hyperuricemia and gout.

Arthritis can frequently be seen in patients with other autoimmune diseases and is one of the most common clinical features in patients with systemic lupus erythematosus (SLE) (Justiz et al,2021). Other diseases frequently associated with arthritis include inflammatory bowel disease, psoriasis, celiac disease, Sjogren syndrome, systemic sclerosis, dermatomyositis, mixed connective tissue disease (MCTD), etc.

Pain, which can vary in severity, is a common symptom in virtually all types of arthritis. Other symptoms include swelling, joint stiffness, redness, and aching around the joints. Arthritic disorders like lupus and rheumatoid arthritis can affect other organs in the body, leading to a variety of symptoms. Symptoms may include: Inability to use the hand or walk, stiffness in one or more joints, rash or itch, malaise and fatigue, weight loss, poor sleep, muscle aches and pains, tenderness, difficulty moving the joint. It is common in advanced arthritis for significant secondary changes to occur. For example, arthritic symptoms might make it difficult for a person to move around and/or exercise which can lead to secondary effects, such as: Illustration of gout affected foot, muscle weakness, loss of flexibility, decreased aerobic fitness. These changes, in addition to the primary symptoms, can have a huge impact on quality of life (Eustice et al,2012).

Physical examination is the most important tool in assessing arthritis and arthralgias. Inflammatory arthritis is associated with tenderness, swelling, effusion, erythema and warmth. These features are more obvious in an acute inflammatory arthritic process, but maybe less pronounced in chronic inflammatory arthritis. Osteoarthritis can also be associated with tenderness, swelling, and effusion, although erythema and warmth are usually lacking. Decreased range of motion and obvious joint deformity can also be observed in arthritis.

The next step shall be assessing the arthritis onset, the number of joints involved, symmetry, distribution, and pattern.

1. Onset: Acute onset arthritis is typical of septic arthritis, crystalline arthropathies, and reactive arthritis. Osteoarthritis, on the other hand, is almost always insidious onset. Rheumatoid arthritis and psoriatic arthritis are of insidious onset in most cases, although occasionally they can be acute onset as well. Arthritis associated with underlying autoimmune disorders is usually insidious onset.

2. Number of involved joints: Arthritis can be monoarticular (single joint), oligoarticular (2-4 joints) or polyarticular (several joints). Bacterial, Lyme's, mycobacterial and Neisseria infections present with acute monoarthritis. It is also seen in patients with gout (especially early in the disease), pseudogout, hydroxyapatite disease, and trauma. Rarely, psoriatic arthritis can have an initial presentation as monoarthritis, which may later evolve into oligo or polyarthritis. Chronic monoarthritis can be seen in patients with untreated infections (Bacterial, Lyme's, mycobacterial and fungal), gout, pseudogout, osteoarthritis, Pigmented villonodular synovitis, hemarthrosis, tumors, osteonecrosis, early oligoarticular juvenile idiopathic arthritis (JIA) and rarely in rheumatoid or psoriatic arthritis.

In general, diseases with monoarticular or polyarticular involvement can also present as oligo arthritis. However, oligo arthritis predominantly of the lower extremity joints (knees or ankles) is characteristic of HLA-B27 associated seronegative spondylo arthritis. A subgroup of patients with psoriatic arthritis present with oligoarticular involvement of small joints of the hands including the distal interphalangeal (DIP), proximal interphalangeal (PIP), and metacarpophalangeal (MCP) joints.

3. Symmetry: Polyarticular symmetrical inflammatory arthritis involving the small joints of hands and feet is the hallmark of RA. Other causes of symmetrical polyarthritis include psoriatic arthritis, pseudogout (pseudo-RA type), Adult-onset Still disease, arthritis associated with underlying autoimmune diseases such as SLE and MCTD and osteoarthritis, especially erosive osteoarthritis, nodal osteoarthritis, and primary generalized osteoarthritis. Asymmetrical polyarthritis can be seen in psoriatic arthritis, ankylosing spondylitis, reactive arthritis, IBD associated arthritis, juvenile idiopathic arthritis, undifferentiated spondylo arthritis, gout, pseudogout, and osteoarthritis. As noted above, asymmetrical oligoarthritis of lower extremity joints can be seen in HLA-B27 associated seronegative spondyloarthritis.

Several patterns on peripheral involvement can give a clue to the diagnosis. RA is typically associated with polyarticular symmetrical inflammatory arthritis involving the small joints of hands (MCP, PIP) and feet (MTP). Wrist, ankle and knee involvement is also common. However, DIP joints of the hands are usually spared in RA. DIP joint involvement can be seen in osteoarthritis, psoriatic arthritis, and gout. Knee, wrist and 2nd and 3rd MCP joints are the commonly involved joints in pseudogout. Pain, stiffness and limited range of motion of bilateral shoulders and hips due to underlying inflammatory arthritis and peri-arthritis is the hallmark of Polymyalgia rheumatica, although rarely, RA can have a similar presentation.

4. Pattern: Progressive additive pattern with the ongoing involvement of more joints can be seen in RA, psoriatic arthritis and polyarticular osteoarthritis. A migratory pattern where arthritis moves from one joint to another with complete resolution in the previously involved joint can be seen in Whipple disease, neisserial arthritis, and rheumatic fever. An intermittent pattern can be seen in palindromic rheumatism, gout, pseudogout, familial Mediterranean fever, Adult-onset Still disease and Muckle-Wells syndrome, This is characterized by complete resolution of symptoms in the previously involved joints with the asymptomatic period lasting varying amount of time before arthritis recurs in the same or other joints.

There is no known cure for arthritis and rheumatic diseases. Treatment options vary depending on the type of arthritis. The goal of this activity is to provide a general overview of the current innovative and future advancement in treatment of arthritis.

2. PATHOPHYSIOLOGY

Osteoarthritis is characterized by a degenerative cascade of progressive cartilage loss which leads to bone damage. Characteristic findings include subchondral cysts, osteophytes, and subchondral plate thickening. Interleukin-6, interferon-induced protein-10, and macrophage chemotactic protein induce proteolytic enzymes such as matrix metalloproteinases, serine proteases, and cysteine proteinases and result in the degradation of collagen (Struglics et al,2015). Calcification of the surrounding articular cartilage reduces the thickness of and eventually destroys the cartilaginous matrix. Old age also is associated with a decrement in chondrocyte function, enhancing susceptibility to osteoarthritic degeneration.

Symptoms of rheumatoid arthritis are typically more severe than those of osteoarthritis. Rheumatoid arthritis is a systemic and chronic inflammatory state caused by an autoimmune response to an environmental trigger. The degradation of cartilage and, eventually, bone is preceded by endothelial cell activation and synovial cell hyperplasia. The pathology occurs following the aberrant production of inflammatory mediators (such as tumour necrosis factor, interleukins 1, 6 and 8 and others following exposure to an antigenic pathogen) (De Hair et al,2014).

The monosodium urate salts of gout precipitate as needle-shaped crystals. This crystallization is more likely to occur in cooler body parts and with acidic conditions. Destabilization of these deposited intraarticular uric acid crystals leads to IL-1 mediated inflammatory response leading to the typical acute gouty arthritis flare. The process is different in pseudogout where the inorganic pyrophosphate from chondrocytes combines with calcium to form calcium pyrophosphate dihydrate. This crystal is deposited in joint spaces that have a predilection to osteoarthritic changes. Pseudogout crystal damage includes the fragmentation of bone and cartilage and the formation of osteophytes and subchondral cysts. Metabolic disorders such as hemochromatosis, hyperparathyroidism, or hypomagnesemia increase the likelihood of calcium pyrophosphate deposition (Kleiber et al,2017).

Septic arthritis is typically an inflammatory response to a monobacterial infection. Bacterial entry into the synovial fluid triggers a release of cytokines, chemokines, and proteases that degrade cartilage and trigger hyperplasia of the synovial membrane. Toxins produced by bacteria play an additional destructive role within the joint space itself. In adults, *Staphylococcus aureus* is the most common pathogen (with streptococci strains also being common). Infection by gram-negative bacteria is more commonly seen as a result of trauma, intravenous drug use, immunosuppression, or in the elderly or very young.

3. CURRENT EPIDEMIOLOGICAL STATUS OF ARTHRITIS

Arthritis is predominantly a disease of the elderly, but children can also be affected by this disease. Arthritis is more common in women than men at all ages and affects all races, ethnic groups and cultures. Over one-third of the American population has arthritis on imaging, and this number is bound to increase with the mean population age. Between 19% and 30% of adults over the age of 45 years have knee osteoarthritis, 27% have osteoarthritis of the hand, and 27% have osteoarthritis of the hip (Heliovaara et al,1993). It is estimated that 40% of men and 47% of women will develop osteoarthritis in their lifetime, with the incidence increasing to 60% if they have a body mass index greater than 30.

Gout is the most common inflammatory arthritis in the United States, affecting more than 8 million individuals in the United States with a prevalence of 3.9%, with a prevalence of more than 9% in individuals over 60 years of age. The incidence of gout is more than 45 per 100,000. Notably, both the incidence and prevalence of gout is on the rise with more than 2-fold increase in over the past few decades. The prevalence of pseudogout in the adult population is between 4% and 7% with over half of patients suffering from knee arthritis.

Rheumatoid arthritis is found in approximately 1% of Caucasians, with females being affected more frequently than males (lifetime risk of 3.6% in women vs. 1.7% in men). Disease onset is typically in early adulthood, with a disease prevalence of 5% in women over the age of 65 (Crowsan et al,2011).

Septic arthritis is typically caused by bacterial seeding of an already arthritic joint via the hematogenous spread, most often from skin or urinary tract infection. Septic arthritis has a prevalence of 0.01% in the general population and 0.7% in patients with rheumatoid arthritis (Kaaandrop et al,1997).

4. DIAGNOSIS AND EVALUATION OF ARTHRITIS

Diagnosis is made by clinical examination from an appropriate health professional and may be supported by other tests such as radiology and blood tests, depending on the type of suspected arthritis. Pain patterns may differ depending on the arthritis and the location. Rheumatoid arthritis is generally worse in the morning and associated with stiffness lasting over 30 minutes. However, in the early stages, patients may have no symptoms after a warm shower. Osteoarthritis, on the other hand, tends to be associated with morning stiffness which eases relatively quickly with movement and exercise. In the aged and children, pain might not be the main presenting feature; the aged patient simply moves less, the infantile patient refuses to use the affected limb (Nancy Garick et al,2019).

Elements of the history of the disorder guide diagnosis. Important features are speed and time of onset, pattern of joint involvement, symmetry of symptoms, early morning stiffness, tenderness, gelling or locking with inactivity, aggravating and relieving factors, and other systemic symptoms. Physical examination may confirm the diagnosis or may indicate systemic disease. Radiographs are often used to follow progression or help assess severity.

Blood tests and X-rays of the affected joints often are performed to make the diagnosis. Screening blood tests are indicated if certain arthritis is suspected. These might include rheumatoid factor, antinuclear factor (ANF), extractable nuclear antigen, and specific antibodies.

Laboratory tests:

The analysis of different types of body fluids can help pinpoint the type of arthritis you may have. Fluids commonly analyzed include blood, urine and joint fluid. To obtain a sample of joint fluid, doctors cleanse and numb the area before inserting a needle in the joint space to withdraw some fluid.

Imaging:

These types of tests can detect problems within the joint that may be causing your symptoms. Examples include:

X-rays: Using low levels of radiation to visualize bone, X-rays can show cartilage loss, bone damage and bone spurs. X-rays may not reveal early arthritic damage, but they are often used to track progression of the disease.

Computerized tomography (CT): CT scanners take X-rays from many different angles and combine the information to create cross-sectional views of internal structures. CTs can visualize both bone and the surrounding soft tissues.

Magnetic resonance imaging (MRI): Combining radio waves with a strong magnetic field, MRIs can produce more-detailed cross-sectional images of soft tissues such as cartilage, tendons and ligaments.

Ultrasound: This technology uses high-frequency sound waves to image soft tissues, cartilage and fluid-containing structures near the joints (bursae). Ultrasound is also used to guide needle placement for removing joint fluid or injecting medications into the joint.

5. CURRENT TREATMENT METHODS FOR MANAGING ARTHRITIS

Arthritis treatment focuses on relieving symptoms and improving joint function.

Medications:

The medications used to treat arthritis vary depending on the type of arthritis. Commonly used arthritis medications include:

NSAIDs: Nonsteroidal anti-inflammatory drugs (NSAIDs) can relieve pain and reduce inflammation. Examples include ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve). Stronger NSAIDs can cause stomach irritation and may increase your risk of heart attack or stroke. NSAIDs are also available as creams or gels, which can be rubbed on joints.

Counterirritants: Some varieties of creams and ointments contain menthol or capsaicin, the ingredient that makes hot peppers spicy. Rubbing these preparations on the skin over your aching joint may interfere with the transmission of pain signals from the joint itself.

Steroids: Corticosteroid medications, such as prednisone, reduce inflammation and pain and slow joint damage. Corticosteroids may be given as a pill or as an injection into the painful joint. Side effects may include thinning of bones, weight gain and diabetes.

Disease-modifying antirheumatic drugs (DMARDs): These drugs can slow the progression of rheumatoid arthritis and save the joints and other tissues from permanent damage. In addition to conventional DMARDs, there are also biologic agents and targeted synthetic DMARDs. Side effects vary but most DMARDs increase your risk of infections.

Therapy:

Physical therapy: In general, studies have shown that physical exercise of the affected joint can noticeably improve long-term pain relief. Furthermore, exercise of the arthritic joint is encouraged to maintain the health of the joint and the overall body of the person.

Individuals with arthritis can benefit from both physical and occupational therapy. In arthritis the joints become stiff and the range of movement can be limited. Physical therapy has been shown to significantly improve function, decrease pain, and delay the need for surgical intervention in advanced cases. Exercise prescribed by a physical therapist has been shown to be more effective than medications in treating osteoarthritis of the knee. Exercise often focuses on improving muscle strength, endurance and flexibility. In some cases, exercises may be designed to train balance. Occupational therapy can provide assistance with activities. Assistive technology is a tool used to aid a person's disability by reducing their physical barriers by improving the use of their damaged body part, typically after an amputation. Assistive technology devices can be customized to the patient or bought commercially.

Surgery: If conservative measures don't help, doctors may suggest surgery, such as:

Joint repair: In some instances, joint surfaces can be smoothed or realigned to reduce pain and improve function. These types of procedures can often be performed arthroscopically — through small incisions over the joint.

Joint replacement: This procedure removes the damaged joint and replaces it with an artificial one. Joints most commonly replaced are hips and knees.

Joint fusion: This procedure is more often used for smaller joints, such as those in the wrist, ankle and fingers. It removes the ends of the two bones in the joint and then locks those ends together until they heal into one rigid unit.

Lifestyle and home remedies: In many cases, arthritis symptoms can be reduced with the following measures:

Weight loss: Excess weight puts extra stress on weight-bearing joints. Losing weight may increase your mobility and limit future joint injury.

Exercise: Regular exercise can help keep joints flexible. Swimming and water aerobics may be good choices because the buoyancy of the water reduces stress on weight-bearing joints.

Heat and cold: Heating pads or ice packs may help relieve arthritis pain.

Assistive devices: Using canes, shoe inserts, walkers, raised toilet seats, and other assistive devices can help protect joints and improve your ability to perform daily tasks.

Alternative medicine: Many people use alternative remedies for arthritis, but there is little reliable evidence to support the use of many of these products. The most promising alternative remedies for arthritis include:

Acupuncture: This therapy uses fine needles inserted at specific points on the skin to reduce many types of pain, including that caused by some types of arthritis.

Glucosamine: Although study results have been mixed, some studies have found that glucosamine works no better than placebo. However, glucosamine and the placebo both relieved osteoarthritis pain better than taking nothing, particularly in people who have moderate to severe pain from knee osteoarthritis.

Chondroitin: Chondroitin may provide modest pain relief from osteoarthritis, although study results are mixed.

Fish oil: Some preliminary studies have found that fish oil supplements may reduce the symptoms of some types of arthritis. Fish oil can interfere with medications, so check with your doctor first.

Yoga and tai chi: The slow, stretching movements associated with yoga and tai chi may help improve joint flexibility and range of motion.

Massage: Light stroking and kneading of muscles may increase blood flow and warm affected joints, temporarily relieving pain. Make sure your massage therapist knows which joints are affected by arthritis.

6. RECENT ADVANCES AND FUTURE DIRECTIONS IN BIOPSYCHOSOCIAL ASSESSMENT IN TREATMENT OF ARTHRITIS

Francis J. Keefe et.al. proposed an article which provides an overview of the emerging literature on biopsychosocial assessment and treatment for two of the most common forms of arthritis: osteoarthritis and rheumatoid arthritis. The article is divided into 3 parts. In the 1st part, the basic elements of the biopsychosocial approach to assessing and treating persons having arthritis is described. In the 2nd part, the authors evaluate studies of biopsychosocial approaches to the assessment of arthritis pain and disability. Six research areas are reviewed: learned helplessness, depression, stress, pain coping, self-efficacy, and the social context of arthritis. The 3rd part of the article reviews studies that testing the efficacy of biopsychosocial treatment approaches for persons having osteoarthritis and rheumatoid arthritis.

Arthritic disorders such as OA and RA are particularly appropriate diseases in which to apply the biopsychosocial model. These diseases are among the most common forms of arthritis, are chronic in nature, cannot be cured using current biomedical treatments, and can produce high levels of pain and disability. The biopsychosocial model continues to be a very useful approach to understanding both pain and disability. The biopsychosocial model provides a systems perspective on arthritis. Changes in one part of the system can produce changes in another part of the system. For example, increases in disease activity (a biological change) can lead to increases in anxiety and depression (psychological changes) and decreases in the ability to work or perform household chores (social changes), both of which, in turn, can increase pain and disability. Alternatively, improvements in a person's self-efficacy about controlling arthritis symptoms (a psychological change) can lead to enhanced compliance with medications (producing biological changes) or increased interaction with supportive friends and family (a social change), both of which can reduce pain and disability (Keefe et al,1999).

Biopsychosocial Approaches to Treating Arthritis: Since the initial application of cognitive-behavioural treatment interventions for rheumatoid arthritis in the early to mid-1980s, there has been growing evidence that psychosocial interventions may be helpful in the management of arthritis pain (Bradely et al,1999). Newer protocols encourage persons having arthritis to use coping skills and cognitive-behavioural interventions not only to manage pain but also to address psychological disturbance, interpersonal distress, and physical function.

Psychosocial Interventions for Osteoarthritis: The studies based on persons having OA showed that cognitive-behavioral treatment protocols focused on teaching pain coping skills were effective in decreasing pain and reducing psychological disability when compared with arthritis education or standard care control conditions. More recent direction for intervention research in OA has been studies testing effects of involving spouses in pain coping skills training. Studies, revealed that persons in the spouse-assisted coping skills training condition and the conventional coping skills training condition showed significant immediate improvements in pain, psychological disability, self-efficacy, and marital satisfaction. These studies suggest that more intensive treatment may be needed to produce clinically significant benefits in persons undergoing surgical procedures for arthritis. In addition, the timing of intervention may be critical. Working with persons on the day prior to surgery may not be effective, whereas educating and training persons over several weeks prior to surgery may be much more effective in enhancing learning and mastery of coping skills.

Psychosocial Interventions for Rheumatoid Arthritis: A much larger number of controlled studies of psychosocial interventions have been conducted in RA populations than in OA populations. These studies have addressed a variety of questions regarding treatment efficacy. Radojevic, Nicassio, and Weisman et al 1992 tested whether the addition of a family support component could enhance the efficacy of a cognitive-behavioural therapy intervention for controlling RA symptoms and he concluded that cognitive-behavioural interventions are effective in managing RA disease-related symptoms and underscored the potential use of involving family members in cognitive-behavioural treatments for RA. Another recent study of persons having RA conducted by (Leibing, et. al. (1999). compared the effects of a comprehensive cognitive-behavioral treatment protocol with a routine care control condition. When compared with persons in the control condition, persons in the cognitive-behavioral treatment condition showed significant improvements in pain affect, coping, and emotional stability. They focused primarily on pain management. With the increasing emphasis on cost control in health care, investigators have begun exploring the effects of briefer psychosocial interventions for managing RA and the findings suggest that brief psychosocial protocols might be beneficial for persons having arthritis. A promising new area of intervention research in arthritis management involves the study of the emotional disclosure paradigm developed by Pennebaker and colleagues. The review indicated that emotional disclosure is associated with significant improvements in physical health, psychological well-being, physiological functioning, and general functioning.

7. CURRENT FRAMEWORK OF RHEUMATOID ARTHRITIS THERAPY:

Two overriding concepts guide early RA treatment: early aggressive therapy and treat to target. Early aggressive therapy is the prompt institution of agents to decrease inflammation and thereby prevent the joint destruction that leads to pain and disability. In general, agents to treat RA can reduce inflammation by blocking immune mediators or by modulating the number or functional properties of immune cells (Stoffer et al,2016). Agents that can ameliorate the signs and symptoms of RA and reduce the progression of damage are known as disease modifying anti-rheumatic drugs. Methotrexate and TNF blockers are 2 of the most used agents. For RA, the target is disease activity. While a number of different indices for assessing disease activity has been developed, in general, they include only a few clinical or laboratory parameters. A sample of joints (e.g., 28 or 44 joints) frequently suffices for assessing disease activity. Each of the indices has a defined target value for remission or for low disease activity. The goal of treatment is therefore to achieve that target as quickly and safely as possible and continue therapy for as long as necessary to sustain remission or low disease activity (Burnmester et al,2017).

Early Diagnosis and Treatment: The key to improving RA outcomes is early diagnosis and treatment. While RA is a common disease in the population. Patients developing joint symptoms from RA often believe that they are experiencing the expected symptomatology that occurs with OA and aging. Patients may self-medicate, and time frequently passes before they seek medical attention. At that point, the disease may have progressed to the stage of damage. Education directed at the public is therefore essential to convey the messages that arthritis occurs in different forms and that joint pain is not an inevitable consequence of life. At present there is a severe shortage of rheumatologists, physicians with specialized training in RA This shortage is likely worldwide, and even in locations where there are rheumatologists, access may be limited due to a variety of factors. The solution to this problem is the development of better systems for patient triage and the creation of early arthritis clinics (Deal CL et al,2007).

Treat to Target: Early aggressive therapy with treat to target approaches is designed to reduce inflammation, prevent damage, and alter the course of disease to limit late complications. As shown in many clinical studies, numerous agents alone or in combination can achieve this goal. In general, an agent to rapidly reduce inflammation is an important element in early aggressive therapy and provides a foundation for other disease modifying anti rheumatoid drugs (DMARDs) to act with methotrexate as the anchor drug for most patients. Another approach to early aggressive therapy involves the use of biologic therapy, specifically tumour necrosis factor (TNF) blockers, in association with methotrexate. Early aggressive therapy is therefore a junction point in RA treatment where cost considerations become very real. While biologic therapies are effective, they are expensive (Durez et al, 2007). The alternative approach of combination therapy with conventional DMARDs, such as hydroxychloroquine and sulfasalazine together with methotrexate (so-called "triple therapy") and the use of glucocorticoids as bridge therapy, is also effective. It is much less expensive, but it involves several agents and the inclusion of glucocorticoids and their associated side effects (Jalal H et al,2016).

8. FUTURE OUTLOOK

The literature survey was conducted to analyse the recent advances and treatment methods used in treating arthritic condition. Arthritis is a disease that affects the joints. There are many types of arthritis, all of which can cause pain and reduce mobility. Some forms of arthritis result from natural wear and tear. Other types come from autoimmune diseases or inflammatory conditions. There are a variety of treatments for arthritis, ranging from physical or occupational therapy to joint surgery. Your healthcare provider will assess your symptoms and recommend the right treatment plan for your needs. Most people can successfully manage arthritis and still do the activities they care about.

Arthritis may be a disease of the joint, but it also has systemic repercussions. There is no cure for osteoarthritis, and it can severely diminish the quality of life and lead to depression. Depending on the type of arthritis, there may also be other organs involved. The management of arthritis is ideally done by an interprofessional team that includes a nurse, dietitian, rheumatologist, physical therapist, orthopaedic surgeon, pain specialist, pharmacist, and an internist. Polypharmacy is a major concern in these patients because of the need to resolve the pain, hence the pharmacist should closely monitor the medications to prevent serious drug interactions and if narcotics are required, monitor for overuse. Almost all patients may benefit from physical rehabilitation and physical therapy. Sample evidence indicates that water-based exercise can diminish pain and improve joint function. Further, loss of weight also decreases the stress on the joint. In addition, a dietitian can help educate the patient on a healthy diet. The nursing team should assist the clinician in educating the patient on medication compliance, abstaining from alcohol, and discontinuing smoking. Since arthritis is a progressive disease, all patients should be urged to have close follow up with the primary care provider. A referral to a pain consultant early in the course may help prevent abuse of narcotics and other prescription-strength pain medications.

Recognition of arthritis is a complex disease with multifactorial nature, and the whole joints are involved in the degenerative process is crucial for cartilage repair. Therefore, it is necessary to increase our knowledge in basic sciences to comprehensively understand the mechanism of different joint components in arthritic pathology. Until now, in the clinics, conservative management, including physical measures and pharmacological therapy are still the first choices offered for arthritic patients. Joint arthroplasties or total replacement surgeries are served as the ultimate therapeutic option to rehabilitate the joint function of patients who withstand severe arthritis. However, these approaches are not able to induce healing processes or halt the degenerative processes in the joints. Demand for cartilage regeneration remains a big challenge both for clinicians and researchers thanks to the innovations and advances in biomaterials and biotechnology, more and more research efforts have been devoted to studying cartilage repair through non-surgical approaches.

Rheumatology is a dynamic field in the midst of a treatment revolution that is leading to dramatically improved outcomes for patients with RA. Along with all other providers, rheumatologists are well aware of cost issues and look forward to working with other stakeholders to assure that the benefits of modern treatment can extend to as many patients as possible in a way that meaningfully balances costs and outcomes.

REFERENCES

- 1.Ma L, Cranney A, Holroyd-Leduc JM. Acute monoarthritis: what is the cause of my patient's painful swollen joint? *CMAJ*. 2009 Jan 06;180(1):59-65. [PMC free article] [PubMed] [Reference list]
- 2.Reginato AM, Olsen BR. The role of structural genes in the pathogenesis of osteoarthritic disorders. *Arthritis Res*. 2002;4(6):337-45. [PMC free article] [PubMed] [Reference list]
- 3.Siva C, Velazquez C, Mody A, Brasington R. Diagnosing acute monoarthritis in adults: a practical approach for the family physician. *Am Fam Physician*. 2003 Jul 01;68(1):83-90. [PubMed] [Reference list]
- 4.Justiz Vaillant AA, Goyal A, Bansal P, Varacallo M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Oct 15, 2021. Systemic Lupus Erythematosus. [PubMed] [Reference list]
- 5.Eustice, Carol (2012). *Arthritis: types of arthritis*. Adams Media. ISBN 978-1-4405-4446-0. OCLC 808835849.
- 6."Arthritis and Rheumatic Diseases". NIAMS. October 2014. Archived from the original on 4 October 2016. Retrieved 31 March 2021.
- 7.Struglics A, Larsson S, Kumahashi N, Frobell R, Lohmander LS. Changes in Cytokines and Aggrecan ARGS Neoepitope in Synovial Fluid and Serum and in C-Terminal Crosslinking Telopeptide of Type II Collagen and N-Terminal Crosslinking Telopeptide of Type I Collagen in Urine Over Five Years After Anterior Cruciate Ligament Rupture: An Exploratory Analysis in the Knee Anterior Cruciate Ligament, Nonsurgical Versus Surgical Treatment Trial. *Arthritis Rheumatol*. 2015 Jul;67(7):1816-25. [PubMed] [Reference list]
- 8.de Hair MJ, van de Sande MG, Ramwadhoebe TH, Hansson M, Landewé R, van der Leij C, Maas M, Serre G, van Schaardenburg D, Klareskog L, Gerlag DM, van Baarsen LG, Tak PP. Features of the synovium of individuals at risk of developing rheumatoid arthritis: implications for understanding preclinical rheumatoid arthritis. *Arthritis Rheumatol*. 2014 Mar;66(3):513-22. [PMC free article] [PubMed] [Reference list]
- 9.Kleiber Balderrama C, Rosenthal AK, Lans D, Singh JA, Bartels CM. Calcium Pyrophosphate Deposition Disease and Associated Medical Comorbidities: A National Cross-Sectional Study of US Veterans. *Arthritis Care Res (Hoboken)*. 2017 Sep;69(9):1400-1406. [PMC free article] [PubMed] [Reference list]
- 10."Juvenile idiopathic arthritis: MedlinePlus Medical Encyclopedia". medlineplus.gov. Retrieved 2019-05-06.
- 11.Heliövaara M, Mäkelä M, Impivaara O, Knekt P, Aromaa A, Sievers K. Association of overweight, trauma and workload with coxarthrosis. A health survey of 7,217 persons. *Acta Orthop Scand*. 1993 Oct;64(5):513-8. [PubMed] [Reference list]
- 12.Crowson CS, Matteson EL, Myasoedova E, Michet CJ, Ernste FC, Warrington KJ, Davis JM, Hunder GG, Thorneau TM, Gabriel SE. The lifetime risk of adult-onset rheumatoid arthritis and other inflammatory autoimmune rheumatic diseases. *Arthritis Rheum*. 2011 Mar;63(3):633-9. [PMC free article] [PubMed] [Reference list]
- 13.Kaandorp CJ, Krijnen P, Moens HJ, Habbema JD, van Schaardenburg D. The outcome of bacterial arthritis: a prospective community-based study. *Arthritis Rheum*. 1997 May;40(5):884-92. [PubMed] [Reference list]
- 14."How is arthritis diagnosed? | Arthritis Research UK". www.arthritisresearchuk.org. Archived from the original on 2015-04-02. Retrieved 2015-06-09
- 15.Nancy Garrick, Deputy Director (2017-04-20). "Rheumatoid Arthritis". National Institute of Arthritis and Musculoskeletal and Skin Diseases. Retrieved 2019-05-06.
- 16.Keefe, F. J., & Bonk, V. (1999). Psychosocial assessment of pain in patients having rheumatic diseases. *Rheumatic Disease Clinics of North America*, 25, 81–103
- 17.Bradley, L. A., & Alberts, K. R. (1999). Psychological and behavioral approaches to pain management for patients with rheumatic disease. *Rheumatic Disease Clinics of North America*, 25, 215–232.

18. Keefe, F. J., Caldwell, D. S., Baucom, D., Salley, A., Robinson, E., Timmons, K., et al. (1996). Spouse-assisted coping training in the management of osteoarthritic knee pain. *Arthritis Care & Research*, 9, 279–291.
19. Radojevic, V., Nicassio, P. M., & Weisman, M. H. (1992). Behavioral intervention with and without family support for rheumatoid arthritis. *Behaviour therapy*, 23, 13–20.
20. Leibing, E., Pfingsten, M., Bartmann, W., Rueger, U., & Schuessler, G. (1999). Cognitive-behavioral treatment in unselected rheumatoid arthritis outpatients. *Clinical Journal of Pain*, 15, 58–66.
21. Stoffer MA, Scholes MM, Smolen JS, Aletaha D, Breedveld FC, Burmester G, et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search update. *Ann Rheum Dis*. NCMJ vol. 78, no. 5ncmedicaljournal.com 3402016;75(1):16-22.
22. Burmester GR, Pope JE. Novel treatment strategies in rheumatoid arthritis. *Lancet*. 2017;389(10086):2338-2348.
23. Deal CL, Hooker R, Harrington T, Birnbaum N, Hogan P, Bouchery E, et al. The United States rheumatology workforce: supply and demand, 2005-2025. *Arthritis Rheum*. 2007;56(3):722-729
24. Durez P, Malghem J, Nzeusseu Toukap A, Depresseux G, Lauwerys BR, Westhovens R, et al. Treatment of early rheumatoid arthritis: a randomized magnetic resonance imaging study comparing the effects of methotrexate alone, methotrexate in combination with infliximab, and methotrexate in combination with intravenous pulse methylprednisolone. *Arthritis Rheum*. 2007;56(12):3919-3927
25. Jalal H, O'Dell JR, Bridges SL, Jr., Cofield S, Curtis JR, Mikuls TR, et al. Cost-effectiveness of triple therapy versus etanercept plus methotrexate in early aggressive rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2016;68(12):1751-1757

