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Research article

Psychological Effects and Management of Rheumatoid Arthritis

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ABSTRACT

Rheumatoid arthritis (RA) is a common long-term inflammatory condition that can affect physical, psychological and social wellbeing. RA is an ailment which arises due to the immune system of the humans itself, influencing the joints of the patients. Ample difficulties can follow, for example, lasting joint harm requiring rheumatoid vasculitis, arthroplasty, and Felty syndrome necessitating splenectomy, if it remains untreated. Patients may also experience psychological challenges due to that the fact that RA has no permanent treatment. Nevertheless, the treatment areas are to diminish the pain and arrest additional harm. The aim of treatment is to suppress the activity (inflammation) of rheumatoid arthritis and to optimize patients' physical, psychological and social functioning. This review presents a brief summary on psychological implications of living with rheumatoid arthritis, pathogenesis, diagnosis, causes, sign and symptoms and treatments associated with RA.

Keywords: Rheumatoid arthritis, Inflammation, Autoimmune disease, Anxiety, Depression.

INTRODUCTION

Rheumatoid arthritis, a chronic illness that affects the joints which causes pain, swelling, and stiffness. People suffering from this disease may feel sick and tired, and they sometimes get fevers, this disease can last for many years or a lifetime[1]. Since there is no cure, patients require help and support from healthcare professionals to manage the symptoms, which can affect their everyday function. Anyone can get this disease, though it occurs more often in women. RA often starts in middle age and is most common in older people, children and young adults are also prone to it.[2] As there are a variety of systemic manifestations, the characteristic feature of RA is persistent inflammatory synovitis, usually involving peripheral joints in a symmetric distribution. Synovial inflammation leads to cartilage destruction and bone erosions, joint disease affects the mobility of the joint and may be associated with deformities of joints that seriously affect the quality of life[1, 3].

RHEUMATOID ARTHRITIS AND MENTAL HEALTH

The World Health Organization (WHO) (2003) refers to psychological wellbeing as a state in which every individual realises his or her own potential, can cope with the usual stresses of life, can work productively and is able to make a contribution to his or her community[4].Chronic illness is specified by the WHO as the principal cause of premature death in the world. According to WHO's estimations, it is responsible for 63% of all mortalities[5]. In addition, mental health problems such as depression or anxiety can worsen RA symptoms[6]. Anxiety is characterized by feelings of tension, worry and irritability along with physical changes like increased blood pressure. Depression is characterized by sadness, a lack of interest in daily activities, weight loss or gain, sleeplessness or excessive sleeping, lack of energy, inability to concentrate, feelings of worthlessness or excessive guilt, and recurrent thoughts of death or suicide[7, 8]. Rates of depression and anxiety in people with arthritis-related diseases vary depending on the population, the size of the study, and the measurement tools used. But data shows that the rates can be between two- and ten-times greater than the rates of the general population, depending on the type of arthritis. Studies also show that anxiety and depression can lower your pain threshold. And then the chronic pain aggravates your anxiety and depression. Furthermore, people with arthritis and depression tend to have more functional limitations, are less likely to adhere to their treatment regimens, and have increased odds of developing other health problems. The vicious cycle of pain, poor health and negative mood can significantly change the course and management of your arthritis[9]..

Pain and Depression

Many studies have shown clearly that people with RA with the highest pain levels are the most likely to be anxious or depressed. Exactly why higher pain severity is associated with depression is not clear. It seems to be a two-way street. Pain incites depression. Living with daily pain is physically and emotionally stressful. Chronic stress is known to change your levels of brain and nervous system chemicals. These stress hormones and neurochemicals – like cortisol, serotonin and norepinephrine – affect your mood, thinking and behaviour. Disrupting your body's balance of these chemicals can bring on depression in some people. Depression makes pain worse. Depression weakens a person's ability to deal and cope with pain. A person's perception about their condition, for example back pain, might become more negative when compared with individuals who are not depressed[6, 10, 11].

Inflammation and Depression

Pain and disability are linked to depression in RA, but a developing theory is that inflammation also plays a role. A 2016 study published in The Journal of Clinical Psychiatry reviewed levels of C-reactive protein – a marker of inflammation – in 10,036 people who responded to the National Health and Nutrition Examination Survey. Those with symptoms of depression had CRP levels that were 31% higher than those with no depressive symptoms. There are many studies recognizing depression as an inflammatory state. "There is a well-documented event called cytokine-induced depression, where cytokines are increased, and depression occurs," explains Patricia Katz, PhD, professor of medicine at University of California San Francisco. Specific cytokines, such as interleukin-1, interleukin-6, and tumour necrosis factor-α, are involved in the pain and inflammation process in RA[11].

Lifestyle and Depression

Having RA is painful and exhausting. Inflammation and the fatigue that goes with it further drag you down. Add a co-occurring condition like diabetes or a heart condition, and the active life you once knew may have disappeared. These health challenges may cause you to not exercise, become less social and more isolated, and have worse sleep quality. These negative changes in your lifestyle can increase your pain and dampen your overall mood – bringing on the blues and depression. Although what causes depression in people with RA may differ, the link is real and potentially life changing. Treating not only your RA but also specifically treating your anxiety or depression is key to living your fullest life[11, 12].

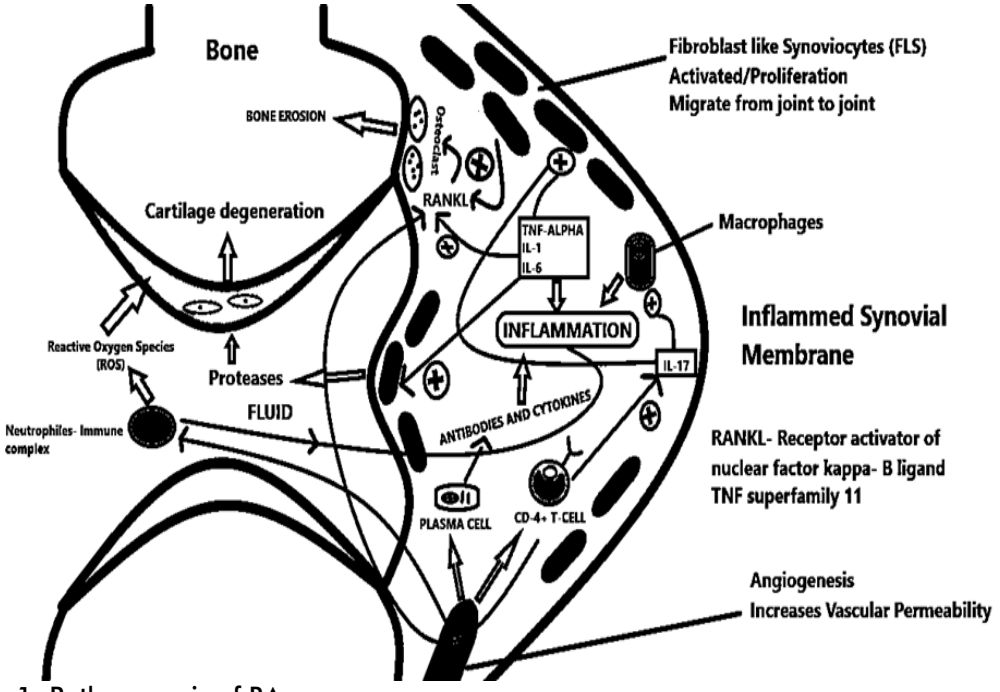

Figure 1: Pathogenesis of RA

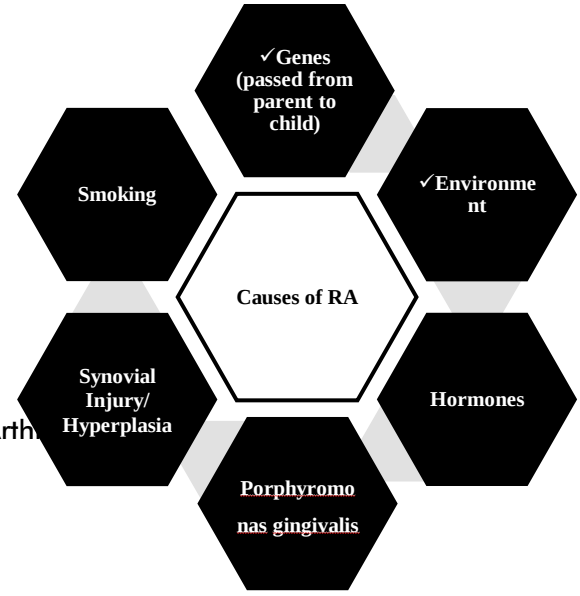

Figure 2: Causes of Rheumatoid Arth

Effects on work

Patients often express concerns at the time of their diagnosis about their ability to work. The unpredictability of their symptoms can make it difficult to remain in occupations that have a fixed starting time. Joint stiffness can be heightened in the morning, and patients might find they have to get up two or three hours before starting work to enable their joint stiffness to ease. Occupations and employers that endorse flexitime can make it easier for an individual to manage their symptoms. Part-time work, if available and financially viable, can provide the patient with the opportunity for rest periods throughout the week. It can be challenging for people with rheumatoid arthritis to remain in physically demanding work, such as that involving manual labour, where there is daily stress and repetitive strain on joints and muscles. Patients with continual pain, fatigue, functional disability or high levels of disease activity often have to leave the workforce[13].

Effects on partners

A diagnosis of a long-term condition such as rheumatoid arthritis has the potential to affect not only individuals with the condition but also partners, resulting in emotions such as anger, guilt, helplessness, feelings of loss, and worry and fear of the future[14]. Participants in one study described the frustration of seeing partners in pain and being unable to help as well as having to forego enjoyable activities[14]. Another study identified significant financial, physical and psychological strain on spouses. Partners employed coping strategies such as maintaining a positive outlook and planning short recreational activities[15]. Many couples developed a sense of shared ownership of the illness over time[15]. Most partners wished to be involved in every aspect of care and to be recognised by healthcare professionals as an essential source of support for the patient. They also identified the need for partner support groups[13, 14].

SOCIAL SUPPORT

Social support is a major factor of wellbeing. A diagnosis of rheumatoid arthritis can be a strain on the whole family. Roles within the family unit many have to change and not every family member may be receptive to enforced changes. For example, a mother with rheumatoid arthritis may find it difficult to join in physical activities with her children because of physical discomfort in her joints. Thus, instead of engaging in physical activities with her children, the mother could spend time with her children, taking them to the cinema or going out for a meal. Problems are likely to occur when the person with rheumatoid arthritis feels guilty that the condition is causing changes in the family, and stops communicating or sharing the management of the condition with the family. Being married is not in itself associated with better health in rheumatoid arthritis, but being in a well-adjusted

or non-distressed marriage is linked with less pain and better functioning [13, 16].

PATHOGENESIS OF RHEUMATOID ARTHRITIS

Pathogenesis of Rheumatoid Arthritis is shown in Figure 1.

The earliest event in RA pathogenesis is activation of the innate immune response. Antigen-presenting cells, including dendritic cells, macrophages and activated B cells, present arthritis-associated antigens to T cells. Concurrently, CD4+ T cells that secrete IL-2 and IFN-g infiltrate the synovial membrane[17]. B cells contribute to RA pathogenesis not only through antigen presentation, but also through the production of antibodies, autoantibodies and cytokines. In addition to antigen presentation, macrophages are involved in osteoclastogenesis and are a major source of cytokines, including TNF-α, IL-1 and IL-6. Within the synovial membrane there is a great increase in activated fibroblast-like synoviocytes, which also produce inflammatory cytokines[17]. Synoviocytes contribute to the destruction of cartilage and bone by direct invasion into these tissues[18].

DIAGNOSIS OF RHEUMATOID ARTHRITIS

People can go to a family doctor or rheumatologist to be diagnosed. A rheumatologist is a doctor who helps people with problems in the joints, bones, and muscles. RA can be hard to diagnose because there is no single test for the disease. The symptoms can be the same as other kinds of joint disease. The full symptoms can take time to develop. To diagnose rheumatoid arthritis, doctors use medical history, physical exam, x-rays, and lab tests[19, 20].

Indications of Rheumatoid Arthritis

Primary indications can be mirrored by other diseases, the signs and symptoms are very characteristic of rheumatoid disease which may include tiredness, pain, swelling, tenderness and redness of the joints, eventually leading to limiting the motion of the joints and then leading to limping and joint deformity and finally loss of joint function [21].

TREATMENT AND MANAGEMENT OF RHEUMATOID ARTHRITIS

First-Line Management of Rheumatoid Arthritis: NSAIDS and Corticosteroids

The general objective of first-line treatment is to lessen pain and decreasing aggravation. NSAIDS like Aspirin, Naproxen, ibuprofen, etodolac etc are fast acting drugs which relieve the pain. NSAIDs mechanism of action includes inhibiting the enzyme cyclo-oxygenase which stops the synthesis of prostaglandins, prostacyclin, and thromboxane. Side effects like nausea, ulcers, etc. can be reduced if taken alongside food. Antacids, can be used to reduce these symptoms as well[22-24]. Corticosteroids are a more potent anti-inflammatory drug 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 [23, 25].

Whittle et al. tended to the subject of the utilization of narcotic analgesics for patients with pain because of RA. From their inferences, weak opioids such as tramadol, codeine, and dextropropoxyphene 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[23, 26].

Second-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. Drugs 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[27].The foremost second line drug is Methotrexate (MTX) which is an immunosuppressive drug. It inhibits the binding of dihydrofolic acid to folinic acid as it is an analogue to folic acid. The use of MTX necessitates consistent blood tests due to its adverse effects, i.e., liver problems, bone marrow erosion etc. Folic acid supplementation can reduce the risk of side effects. It is an effective DMARD, has a lesser incidence of side effects and has dosage flexibility[23, 27]. Hydroxychloroquine (Plaquenil) is an antimalarial drug and can be used for long-term treatment of RA. This drug decreases the secretion of monocyte-derived proinflammatory cytokines. Common side effects include problems in the GI tract, skin, and central nervous system. The eyes, in particular, can be affected when this drug is taken at high doses. Patients on this drug require routine consultation with an ophthalmologist. Sulfasalazine (Azulfidine) is a DMARD typically used in the treatment of irritable bowel disease. Combined with anti-inflammatory drugs, this DMARD can be used to treat RA. The mechanism of action of this drug in the treatment of RA has not been identified. This drug has side effects of GI and central nervous system symptoms as well as rash. It is usually well-tolerated among patients, but should be avoided in patients with sulfa allergies since it contains sulfa and salicylate compounds[23, 28]. Gold salts had been used previously but now their use has become limited due to emergence of more effective drugs like Methotrexate. Drugs like cyclosporine

,cyclophosphamide, azathioprine can be used with patients suffering from aggressive Rheumatoid arthritis symptoms [23, 29].

Newer Drugs

Leflunomide, a ribonucleotide uridine monophosphate pyrimidine inhibitor cuts the progression of RA and its effect is enhanced if used synergistically with methotrexate. Inside the body, Lefluonaminde is converted to malononitrilamide. Another advantage of this drug is that it can be used in the form of a monotherapy in case resistance to methotrexate is observed. Side effects include GI upset, hypertension, leukopenia, liver damage, neuropathy, rash, and bone marrow damage[23, 30].Biologics, also known as Biological DMARDs, commonly referred to as Biologics, are more accurate and targeted in their approach and rapidly limit the ascent of the joint damage [31]. The downside of using Biologics is the frequency of encountering infections, lymphoma and multiple sclerosis [23, 30]. The approach to take in case the second line agents fail or do not respond, is inhibiting the Tumour Necrosis Factor, a protein which promotes inflammation, by drugs such as etanercept, infliximab, adalimumab etc. Depression of TNF leads to reduced recruitment of cells that lead to inflammation[31]. Unfortunately, these drugs tend to be very expensive and their role in treating patients at various stages of RA and with various mechanisms of action is a matter of continuous investigation[23, 32]. Anakinra, binds to Interleukin-1 which causes inflammation. It is injected subcutaneously but is not used quite frequently as its response rate is low. Rituximab diminishes the B cells which is an agent of inflammation. It is used when the patient does not respond to TNF inhibitors. Abatacept works in a similar way as Rituximab the difference being blocking the T cell activation which again, is an agent of inflammation. This is administered subcutaneously weekly or monthly through IV infusion [23]. Tocilizumab which works by blocking Interleukin 6 has a similar dose as Abatacept. Lastly, tofacitinib has a different mechanism of action and acts by inhibiting Janus kinases within cells due to which it is known as a JAK inhibitor [23, 32, 33].

Surgery

Joint surgery in patients with RA reached a peak in the 1990s. However, a 2010 study showed decreased rates of joint surgery in RA patients 40–59 years of age. In contrast, patients older than 60 years had increased rates of surgery[34]. Surgery is a final alternative for the management of RA. Indications include intractable joint pain or functional decline due to joint degradation. Different sorts of surgeries are performed such as eliminating the damaged joint and swapping it with a metallic, plastic, or ceramic prosthesis. This is most frequently done in the shoulder, elbow, wrist, hip, knee, and ankle[35]. The major contraindication for surgical joint replacements is the presence of active systemic articular infection[23].

Other Therapies

The idea that diet can "intensify" symptoms is no longer accepted as true in sharp contrast to the earlier beliefs[36]. Intake of supplements like Fish oils,omega-3 fatty acid are advantageous for managing short-term RA symptoms. Cumin has anti-inflammatory effects in patients whereas calcium and vitamin D3 prevents osteoporosis. Folic acid is beneficial in preventing side effects of drugs[37]. Patients with RA also benefit from physical and occupational therapies can also benefit patients as they preserve joint mobility and strengthen muscles[38]. Swimming, Yoga and Tai Chi are good for the muscles and not too stern on the joints. Excersise should be followed by applying hot and cold packs. Lastly, with the scientific advancements and enhanced understanding of the molecular mechanisms, newer and better treatment options should become available in the near future[23, 39].

Alternative therapies for psychological distress

A number of alternative therapies exist to combat psychological distress, and they can be encompassed into a stress management programme. Treatments include cognitive behavioural therapy (CBT), meditation and relaxation, biofeedback, patient education and exercise. Cognitive behavioural therapy (CBT) is recommended as a first-line treatment for mild-to-moderate anxiety and depression.[40] CBT is problem and solution focused, encouraging self-management and promoting self-efficacy. It specifically addresses misconceptions, errors in thinking, unhelpful beliefs and maladaptive patterns of behaviour (e.g. non-compliance with conventional therapy, including drugs, chronic pain management, joint protection and planning and pacing principles)[41].

CONCLUSION

Psychological well-being is a fundamental part of normal daily life. Although the physiological effects associated with RA are well characterized, it is becoming increasingly important to address the psychological well-being of the patient. The negative effects that RA can have on psychological well-being are becoming increasingly apparent, with depression, anxiety and low self-esteem all associated with the condition. The recent developments in the

management strategies for rheumatoid arthritis have made significant contribution to reducing the disease progression and improving outcomes of the patients. Identifying the candidates early in 'window of opportunity" and aggressive target-oriented approach can prove to be a boon to the patients in long run. With judicious use of drugs and careful monitoring quality of life of patients with RA can be surely improved. The benefits of therapies such as CBT, meditation and exercise for patients with RA are clear and should be actively encouraged. A role for the use of antidepressants in some patients to improve well-being may also exist. By applying this approach, greater improvements in the well-being of patients with RA may be achieved, enabling them to live fulfilling lives without the psychological burden associated with this chronic disease.

REFERENCES

1. Firestein GS, Evolving concepts of rheumatoid arthritis, Nature, 2003;423(6937):356.
2. Joshi P, S Dhaneshwar S, An update on disease modifying antirheumatic drugs, Inflammation & Allergy-Drug Targets (Formerly Current Drug Targets-Inflammation & Allergy), 2014;13(4):249-61.
3. Gabriel SE, The epidemiology of rheumatoid arthritis, Rheumatic Disease Clinics, 2001;27(2):269-81.
4. Huppert FA, Psychological well-being: Evidence regarding its causes and consequences, Applied Psychology: Health and Well-Being, 2009;1(2):137-64.
5. Code P, Simultaneous determination of curcumin and berberine in their pure form and from the combined extracts of Curcuma longa and Berberis aristata, International Journal of Applied Science and Engineering, 2010;8(1):19-26.
6. Frank RG, Beck NC, Parker JC, Kashani JH, Elliott TR, Haut AE, et al., Depression in rheumatoid arthritis, J Rheumatol, 1988;15(6):920-5.
7. Bishop D, Green A, Cantor S, Torresin W, Depression, anxiety and rheumatoid arthritis activity, Clinical and experimental rheumatology, 1987;5(2):147-50.
8. Matsukawa Y, Suicides in persons suffering from rheumatoid arthritis, Rheumatology, 2003;42(12):1571-2.
9. Organization WH, Noncommunicable diseases country profiles 2018, 2018.
10. Cadena J, Vinaccia S, Pérez A, Rico MI, Hinojosa R, Anaya J-M, The impact of disease activity on the quality of life, mental health status, and family dysfunction in colombian patients with rheumatoid arthritis, JCR: Journal Of Clinical Rheumatology, 2003;9(3):142-50.
11. Kojima M, Kojima T, Suzuki S, Oguchi T, Oba M, Tsuchiya H, et al., Depression, inflammation, and pain in patients with rheumatoid arthritis, Arthritis Care & Research, 2009;61(8):1018-24.
12. Kurtze N, Gundersen KT, Svebak S, Quality of life, functional disability and lifestyle among subgroups of fibromyalgia patients: the significance of anxiety and depression, British Journal of Medical Psychology, 1999;72(4):471-84.
13. Ryan S, Psychological effects of living with rheumatoid arthritis, Nursing Standard (2014+), 2014;29(13):52.
14. Matheson L, Harcourt D, Hewlett S, 'Your whole life, your whole world, it changes': partners' experiences of living with rheumatoid arthritis, Musculoskeletal care, 2010;8(1):46-54.
15. Mann C, Dieppe P, Different patterns of illness-related interaction in couples coping with rheumatoid arthritis, Arthritis Care & Research: Official Journal of the American College of Rheumatology, 2006;55(2):279-86.
16. Reese JB, Somers TJ, Keefe FJ, Mosley-Williams A, Lumley MA, Pain and functioning of rheumatoid arthritis patients based on marital status: is a distressed marriage preferable to no marriage?, The Journal of Pain, 2010;11(10):958-64.
17. Choy E, Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis, Rheumatology, 2012;51(suppl_5):v3-v11.
18. Smolen JS, Aletaha D, Koeller M, Weisman MH, Emery P, New therapies for treatment of rheumatoid arthritis, The Lancet, 2007;370(9602):1861-74.
19. Yadav, G., Kumar, P., Kumar, Y., Singh, P.K.Dolutegravir, second generation integrase inhibitor: A new hope for HIV patient(2018) European Journal of Molecular and Clinical Medicine, 5, pp. 20-29. DOI: 10.5334/ejmcm.252
20. Majithia V, Geraci SA, Rheumatoid arthritis: diagnosis and management, The American journal of medicine, 2007;120(11):936-9.
21. PATEL MM. BASIC PATHOMECHANISMS OF AUTOIMMUNE DISORDERS & AN EPIDEMIOLOGICAL STUDY.. IN NGUJ. POP. SK Patel College of Pharmaceutical Education & Research, 2006.
22. McCabe CJ, Akehurst RL, Kirsch J, Whitfield M, Backhouse M, Woolf AD, et al., Choice of NSAID and management strategy in rheumatoid arthritis and osteoarthritis, Pharmacoeconomics, 1998;14(2):191-9.
23. Bullock J, Rizvi SA, Saleh AM, Ahmed SS, Do DP, Ansari RA, et al., Rheumatoid arthritis: a brief overview of the treatment, Medical Principles and Practice, 2018;27(6):501-7.
24. Ong C, Lirk P, Tan C, Seymour R, An evidence-based update on nonsteroidal anti-inflammatory drugs, Clinical medicine & research, 2007;5(1):19-34.
25. Combe B. SP0183 2016 update of the EULAR recommendations for the management of early arthritis. BMJ Publishing Group Ltd; 2016.

26. 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, 2012;51(8):1416-25.
27. Smolen JS, Landewé R, Breedveld FC, Buch M, Burmester G, Dougados M, et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update, Annals of the rheumatic diseases, 2014;73(3):492-509.
28. Sailaja AK, An overall review on rheumatoid arthritis, Current Pharma Research, 2014;4(2):1138.
29. Kumar P, Banik S, Pharmacotherapy options in rheumatoid arthritis, Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders, 2013;6:CMAMD. S5558.
30. Fox RI, Herrmann ML, Frangou CG, Wahl GM, Morris RE, Kirschbaum BJ, How does leflunomide modulate the immune response in rheumatoid arthritis?, BioDrugs, 1999;12(4):301-15.
31. Breedveld F, New tumor necrosis factor-alpha biologic therapies for rheumatoid arthritis, European cytokine network, 1998;9(3):233-8.
32. Gibofsky A, Combination therapy for rheumatoid arthritis in the era of biologicals, HSS Journal, 2006;2(1):30-41.
33. Cada DJ, Demaris K, Levien TL, Baker DE, Tofacitinib, Hospital pharmacy, 2013;48(5):413-24.
34. Louie GH, Ward MM, Changes in the rates of joint surgery among patients with rheumatoid arthritis in California, 1983–2007, Annals of the rheumatic diseases, 2010;69(5):868-71.
35. Paget SA. The hospital for special surgery rheumatoid arthritis handbook: Wiley; 2002.
36. Halstead J, Stoten S, Orthopedic Nursing: Caring for Patients with Musculoskeletal Disorders, Bridgewater: Western Schools, 2010.
37. Escott-Stump S. Nutrition and diagnosis-related care: Lippincott Williams & Wilkins; 2008.
38. Hammond A, The use of self-management strategies by people with rheumatoid arthritis, Clinical rehabilitation, 1998;12(1):81-7.
39. Gonzalez-Alvaro I, Ortiz AM, Seoane I, Garcia-Vicuna R, Martínez C, Gomariz RP, Biomarkers predicting a need for intensive treatment in patients with early arthritis, Current pharmaceutical design, 2015;21(2):170-81.
40. Health NCCfM, Health NIf, Excellence C, Society BP, Psychiatrists RCo. Common mental health disorders: identification and pathways to care: RCPsych Publications; 2011.
41. Health NCCfM, editor Antenatal and postnatal mental health: the NICE guideline on clinical management and service guidance2007: British Psychological Society.