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Review Article

Current Medications for Osteoarthritis

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Abstract

As an inflammatory-related condition, arthritis describes over 100 types of diseases that affect people of all age, sex, and races. Unfortunately, there are no safe and effective therapies for arthritis. Particularly, although a broad range of medications has been used in clinical practice or at least under experimental investigation, osteoarthritis, the most common form of arthritis remains an incurable. Consequently, the dreadful public health and economic burden roar for novel strategies to improve the life quality of patients suffering from osteoarthritis.

Keywords: Arthritis Osteoarthritis; Disease-Modifying Osteoarthritis Drugs; Disease-Modifying Antirheumatic Drugs; Non-Steroidal Anti-Inflammatory Drugs; Glucocorticoid, Anelgesics

Abbreviations

DMARDs: Disease-Modifying Antirheumatic Drugs; DMOADs: Disease-Modifying Osteoarthritis Drugs; IGF: Insulin-Like Growth Factor; IL: Interleukin; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; OARSI: Osteoarthritis Research Society International; OA: Osteoarthritis; RA: Rheumatoid Arthritis; TNFα: Tumor Necrosis Factor α; UK: The United Kingdom; US: The United States.

Introduction

Arthritis describes over 100 types of inflammatory diseases that damage nearly any joints in the body, causing pain, stiffness, swelling, and decreased the range of motion. Around 10 million people have doctor-diagnosed arthritis in the United Kingdom (UK) as acknowledged by the National Health Service [1], while the number is 54.4 million according to the Centers for Disease Control and Prevention of the United States (US) [2]. Particularly, arthritis is the leading cause of disability among adults in the US [3]. As arthritis affects people of all age, sex, and races, its prevalence is expected to increase sharply in the near future and turns to be a tremendous economic burden on patients and society [3-5]. Unfortunately, there is no simple cure for arthritis. The treatment of arthritis is very dependent on the type, severity, and impact of arthritis for each individual patient. As an illustration, according to the recent white paper published by the Osteoarthritis Research Society International (OARSI), osteoarthritis (OA), the most common form of arthritis that affects about 18% of women and 10% of men over 60 years of age, is still an incurable condition [4]. Unfortunately, unlike rheumatoid arthritis (RA), a systemic autoimmune disease for which multiple chemical or biological disease-modifying antirheumatic drugs (DMARDs) have been used clinically [6], there are currently no approved disease-modifying osteoarthritis drugs (DMOADs) that can prevent, stop, or even restrain the progression of OA [4,7,8].

Analgesics

Since pain in the affected joint(s) is the primary character of OA patients [9], the current guidelines for OA treatment are predominantly limited to pain release [4,10,11]. Indeed, patients

with generalized OA still have a high percentage of using analgesics or painkillers, such as hydrocodone or acetaminophen, and more than 1 type was frequently used [12]. Although analgesics are effective in pain relief, they may be palliative for arthritis therapy since they do not actively decrease inflammation and or minimize joint damages [13].

Glucocorticoids

Holding the anti-inflammation potency, glucocorticoids, such as prednisone and cortisone, are broadly used for current arthritis treatment [14-17]. However, glucocorticoid, particularly in cases with long-term and/or high-dose administration, is associated with increased incidence and earlier onset of bone mass loss, fracture, osteonecrosis, and osteoporosis [18-20]. Although the contribution of glucocorticoids to these adverse events in skeletal system is argued to be overestimated [21], their usage, particularly when administrated systematically, likely causes adverse side-effects in the musculoskeletal, cardiovascular, and gastrointestinal systems [18-20,22-25]. Even the intra-articular injection strategy that avoids most of the severe side effects of systematic glucocorticoid application is associated with intra-articular and periarticular calcification, skin atrophy or depigmentation, avascular necrosis, rapid destruction of the femoral head, acute synovitis, Charcot's arthropathy, tendinopathy, Nicolau's syndrome, and joint dislocation [25]. These undesirable side-effects challenge the use of glucocorticoids as safe arthritis treatments.

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs; which block prostaglandin synthesis to present their analgesic effects [26]), such as ibuprofen and naproxen, have been widely used in the clinic for arthritis treatment. Over 10 years ago, published guidelines and experts opinions are divided over the relative role of acetaminophen and NSAIDs as first-line pharmacologic therapy for OA, and the data has been shown to suggest that NSAIDs are superior to acetaminophen for reducing knee and hip pain in people with OA but have not been shown to be superior in improving function [27,28], while in a recent systematic review and meta-analysis, acetaminophen was found to have a similar effect as oral NSAIDs, but lower than topical NSAIDs [29]. In 2018, a network meta-analysis included 28 randomized controlled trials with 7,372 participants indicates that topical NSAIDs in licensed doses were statistically superior to placebo overall in OA management [30]. Meanwhile, numerous researches have been done to improve the efficiency of NSAIDs for the treatment of arthritis. For example, Pawar *et. al.* currently investigated to use drug-fortified liposomes as carriers for sustained release of NSAIDs in a rat arthritis model [31]. However, the effectiveness of NSAIDs is not always satisfied [9]. NSAIDs reduce pain and inflammation in the short- term but do not effectively control arthritis progression [32]. For example, in a recent 6-week randomized trial in 31 US centers with 367 Asian knee OA patients, only slight improvement was led by NSAIDs application in comparison with placebo control [9,33]. Moreover, most NSAIDs have been associated with increased risk of adverse events, such as myocardial infarction, stroke, or cardiovascular death [34-36], and thus the safety concerns of NSAID usage cannot be neglected.

DMARDs

Disease-modifying antirheumatic drugs (DMARDs) comprise a diversity of drugs that slow or suppress inflammation and thus postpone the progression of arthritis, in which methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide are the most commonly used [37]. However, DMARDs do not directly achieve analgesia, and it often takes a considerable time to display their benefits [32,37]. More importantly, although DMARDs has been broadly and effectively used to control the RA progression, their efficacy has not been replicated in OA conditions. For instance, adalimumab, a human monoclonal antibody against tumor necrosis factor α (TNFα), failed to show effects in randomized, double-blind, placebo-controlled trials of hand OA [38,39]; while in another randomized, double-blind, placebo- controlled multicenter study in 170 patients with painful knee OA, anakinra, an interleukin (IL)-1 receptor antagonist, was not superior to placebo in regard to OA symptom improvement and cartilage turnover after 4 weeks [40].

Combo treatment

All these currently available choices have their own challenges, and often used in combination. For example, in RA treatment, analgesics and NSAIDs are used for temporary pain relief until DMARDs take effects for long-term maintenance [6]. However, it is worth noting that both DMARDs and NSAIDs can increase the risk of blood clots, heart attack, stroke, heart failure, gastrointestinal disorder, and kidney dysfunction [23,32,41-45]. The combo treatment may combine the advantages of each individual drug, but it may augment the risk for severe adverse events significantly when taking the account of drug- drug interaction.

Conclusion

All the currently available medication choices for arthritis have their own challenges. Further, although articular cartilage destruction is the primary concern of OA, none of these current medications actively promote the bioactivities of chondrocytes to battle against the degeneration of cartilage tissue. Therefore, as desired for a long time, there are urgent demands and a worldwide competition to discover safe and effective alternative therapies

that can reduce the incidence and retard the progression of OA and help cartilage recovery from the arthritic damages.

Conflict of Interest

All authors declare no conflict of interest.

Bibliography

1. N.o. UK, Arthritis, NHS of UK.
2. C.o. US, Arthritis Types, Arthritis, CDC of US.
3. A Foundation, Understanding Arthritis, Arthritis Foundation.
4. O.R.S. International, Osteoarthritis: A serious Disease, Osteoarthritis Research Society International (2016): 1-103.
5. JM Hootman., *et al*. "Updated Projected Prevalence of Self- Reported Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation Among US Adults, 2015-2040". *Arthritis and Rheumatology* 68 (2016): 1582-1587.
6. P Kumar and S Banik. "Pharmacotherapy options in rheumatoid arthritis". *Clinical Medicine Insights: Arthritis and Musculoskeletal Disorder*s 6 (2013): 35-43.
7. J Sokolove and CM Lepus. "Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations". *Therapeutic Advances in Musculoskeletal Disease* 5 (2013): 77-94.
8. MA Karsdal., *et al*. "Disease-modifying treatments for osteoarthritis (DMOADs): of the knee and hip: lessons learned from failures and opportunities for the future". *Osteoarthritis Cartilage* 24 (2016): 2013-2021.
9. CT Appleton. "Osteoarthritis year in review 2017: biology". *Osteoarthritis and Cartilage* 26 (2018): 296-303.
10. TE McAlindon., *et al*. "OARSI guidelines for the non-surgical management of knee osteoarthritis". *Osteoarthritis and Cartilage* 22 (2014): 363-388.
11. AE Nelson. "Osteoarthritis year in review 2017: clinical". *Osteoarthritis and Cartilage* 26 (2018): 319-325.
12. JJ van den Driest., *et al*. "Analgesic Use in Dutch Patients with Osteoarthritis: Frequent but Low Doses". *Clinical Rheumatology* (2018).
13. M van Laar., *et al*. "Pain treatment in arthritis-related pain: beyond NSAIDs". *Open Rheumatology* 6 (2012): 320-330.
14. L Caplan., *et al*. "Corticosteroid use in rheumatoid arthritis: Prevalence, predictors, correlates, and outcomes". *Journal of Rheumatology* 34 (2007): 696-705.
15. M Hammer., *et al*. "Intra-articular injection of cortisone". *Zeitschrift Fur Rheumatologie* 74 (2015): 774.
16. M Chandrappa and S Biswas. "Glucocorticoids in Management of Adult Rheumatoid Arthritis-Current Prescribing Practices and Perceptions of Physicians in India: GLUMAR Survey". *Rheumatology: Current Research* 7 (2017): 1000220.
17. H Yamanaka., *et al*. "Infection rates in patients from five rheumatoid arthritis (RA): registries: contextualising an RA clinical trial programme". *RMD Open* 3 (2017): e000498.
18. F Seguro., *et al*. "Dutch Lipid Clinic Network low-density lipoprotein cholesterol criteria are associated with long-term mortality in the general population". *Archives of Cardiovascular Diseases* 108 (2015): 511-518.
19. C Cooper., *et al*. "Balancing benefits and risks of glucocorticoids in rheumatic diseases and other inflammatory joint disorders: new insights from emerging data. An expert consensus paper from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)". *Aging Clinical and Experimental Research* 28 (2016): 1-16.
20. J Compston. "Glucocorticoid-induced osteoporosis: an update". *Endocrine* 61 (2018): 7-16.
21. JWG Jacobs., *et al*. "Glucocorticoids Are Always Under Suspicion - Is the Perception of Their Risks Unbiased?" *Journal of Rheumatology* 45 (2018): 293-296.
22. JN Hoes., *et al*. "EULAR evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases". *Annals of the Rheumatic Diseases* 66 (2007): 1560-1567.
23. A Jagpal and JR Curtis. "Gastrointestinal Perforations with Biologics in Patients with Rheumatoid Arthritis: Implications for Clinicians". *Drug Safety* 41 (2018): 545-553.
24. JB Rice., *et al*. "Quantitative characterization of the relationship between levels of extended corticosteroid use and related adverse events in a US population". *Current Medical Research and Opinion* (2018): 1-9.

25. GS Habib., *et al*. "Local effects of intra-articular corticosteroids". *Clinical Rheumatology* 29 (2010): 347-356.

26. RO Day., *et al*. "Non-steroidal anti-inflammatory drugs (NSAIDs)". *BMJ-British Medical Journal* 346 (2013).

27. TE Towheed., *et al*. "Acetaminophen for osteoarthritis". *Cochrane Database of Systematic Reviews* (2006): CD004257.

28. TE Towheed., *et al*. "Acetaminophen for osteoarthritis". *Cochrane Database of Systematic Reviews* (2003): CD004257.

29. M Stewart., *et al*. "Efficacy of commonly prescribed analgesics in the management of osteoarthritis: a systematic review and meta-analysis". *Rheumatology International* (2018).

30. MSM Persson., *et al*. "The relative efficacy of topical non-steroidal anti-inflammatory drugs and capsaicin in osteoarthritis: a network meta-analysis of randomised controlled trials". *Osteoarthritis Cartilage* (2018).

31. VA Pawar., *et al*. "Drug-fortified liposomes as carriers for sustained release of NSAIDs: The concept and its validation in the animal model for the treatment of arthritis". *European Journal of Pharmaceutical Sciences* 125 (2018): 11-22.

32. DL Scott., *et al*. "Brocklehurst's Textbook of Geriatric Medicine and Gerontology, SAUNDERS, ELSERVIER, Phiadelphia, (2010): 566- 576.

33. MN Essex., *et al*. "Efficacy and safety of nonsteroidal anti-inflammatory drugs in Asian patients with knee osteoarthritis: summary of a randomized, placebo-controlled study". *International Journal of Rheumatic Diseases* 19 (2016): 262-270.

34. S Trelle., *et al*. "Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis". *British Medical Journal* 342 (2011).

35. M Lindberg. "Use of NSAIDs in rheumatoid arthritis should be limited". *Ugeskr Laeger* 175 (2013): 1039- 1041.

36. C Roubille., *et al*. "The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis". *Annals of the Rheumatic Diseases* 74 (2015): 480-489.

37. A Foundation, DMARDs Overview: Understand these treatments for inflammatory arthritis, Athritis Foundation.

38. G Verbruggen., *et al*. "Tumour necrosis factor blockade for the treatment of erosive osteoarthritis of the interphalangeal finger joints: a double blind, randomised trial on structure modification". *Annals of the Rheumatic Diseases* 71 (2012): 891-898.

39. X Chevalier., *et al*. "Adalimumab in patients with hand osteoarthritis refractory to analgesics and NSAIDs: a randomised, multicentre, double- blind, placebo-controlled trial". *Annals of the Rheumatic Diseases* 74 (2015): 1697-1705.

40. X Chevalier., *et al*. "Intraarticular Injection of Anakinra in Osteoarthritis of the Knee: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study". *Arthritis and Rheumatism-Arthritis Care and Research* 61 (2009): 344-352.

41. M Schmidt., *et al*. "Non-steroidal anti-inflammatory drug use and risk of atrial fibrillation or flutter: population-based case-control study". *BMJ-British Medical Journal* 343 (2011).

42. JM Piper., *et al*. "Corticosteroid use and peptic ulcer disease: role of nonsteroidal anti-inflammatory drugs". *Annals of Internal Medicine* 114 (1991): 735-740.

43. SE Gabriel., *et al*. "Risk for serious gastrointestinal complications related to use of nonsteroidal anti-inflammatory drugs. A meta-analysis". *Annals of Internal Medicine* 115 (1991): 787-796.

44. PA Scott., *et al*. "Non-steroidal anti-inflammatory drugs and cardiac failure: meta- analyses of observational studies and randomised controlled trials". *European Journal of Heart Failure* 10 (2008): 1102- 1107.

45. Coxib., *et al*. "Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials". *Lancet* 382 (2013): 769-779.

Volume 1 Issue 3 December 2018