

Current Medications for Osteoarthritis

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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, Analgesics

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; TNF α : 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 (TNF α), 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.

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