A Review on Osteoarthritis

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Summary:

Osteoarthritis (OA) is a common musculoskeletal condition worldwide. In Bangladesh, it is also the most prevalent rheumatological disease. Recent research on the disease pathogenesis and treatment has stimulated new interest in OA. The previous "degenerative" and "wear and tear" concept of OA has been discarded. Diagnosis of difficult cases has already improved with new imaging techniques and improving further. Studies have emphasized the positive role of patient education and the multidisciplinary approach to the disease. Numerous new studies on the pharmacological modality of therapy of OA have shown paracetamol to be the most appropriate first line drug. Emphasis is also on the cautious use of NSAIDs, especially in at-risk patients. The cyclooxygenase-2 specific inhibitors also show less gastrointestinal toxicity in OA but there are warnings. Short-term benefit is found with intra-articular steroids and longer term with hyaluronic acid. Glucosamine is shown to be a safe drug in OA. Further studies are going on for the development of a disease modifying osteoarthritis drug but are not yet approved for prescribing. This review summarizes the current evidences on OA.

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Introduction:

Osteoarthritis (OA), a common, chronic, degenerative, musculoskeletal disorder of unknown etiology represents failure of the diarthroidal (movable, synovial lined) joint[1]. It is one of the most prevalent disease in our society, with a worldwide distribution. It ranks fourth in health impact in women and eighth in men in the western world[2]. The recently concluded Community Oriented Programme for Control of Rheumatic Diseases (COPCORD) study has determined the prevalence of OA in Bangladeshi population. According to this study, OA prevalence in rural, slum and affluent areas are 7.4%, 9.0% and 11.3% respectively and tops all other rheumatological diseases in Bangladesh.

The name "osteoarthritis" emerged from the observation of the striking overgrowth of marginal and subchondral bone by the pathologists and radiologists at the turn of the century[3]. It has been regarded as an age related "wear and tear" phenomenon for many years until now. There are claims that this attitude led to the negative approach to research and treatment in OA. Some authors have also argued that the descriptor "degenerative" for OA is erroneous[4]. Recent research on the disease have led to newer concepts in pathogenesis and non-pharmacological and pharmacological modalities of management of the disease.

Classification:

Osteoarthritis is grossly classified into primary and secondary groups. The primary is again divided into localized and generalized forms. The latter is more prevalent in post-menopausal women with development of Heberden's nodes. Secondary OA is pathologically identical to the primary variety and here an underlying cause, such as trauma, obesity, Paget's disease or inflammatory arthritis, is present. Table-I gives a detailed description of the classification of the disease.

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Table-I

Classification of osteoarthritis[5]

I. Idiopathic/ Primary:
- A. Localized OA:
  1. Hands: Heberden's and Bouchard's nodes (nodal), erosive interphalangeal arthritis (nonnodal), first carpometacarpal joint
  2. Feet: hallux valgus, hallux rigidus, contracted toes (hammer/cock-up toes), talonavicular
  3. Knee:
     - a. Medial compartment
     - b. Lateral compartment
     - c. Patellofemoral compartment
  4. Hip:
     - a. Eccentric (superior)
     - b. Concentric (axial, medial)
     - c. Diffuse (coxae senilis)
  5. Spine:
     - a. Apophyseal joints
     - b. Intervertebral joints (discs)
     - c. Spondylosis (osteophytes)
     - d. Ligamentous (hyperostosis, Forestier's disease, diffuse idiopathic skeletal hyperostosis)
  6. Other single sites, e.g., glenohumoral, acromioclavicular, tibiotalar, sacroiliac, temporomandibular
- B. Generalized OA includes 3 or more of the areas listed above (Kellgren-Moore)

II. Secondary:
- A. Trauma:
  1. Acute
  2. Chronic (occupational, sports)
- B. Congenital or developmental:
  1. Localized diseases: Legg-Calve-Perthes, congenital hip dislocation, slipped epiphysis
  2. Mechanical factors: unequal lower extremity length, valgus/varus deformity, hypermobility syndromes
  3. Bone dysplasias: epiphyseal dysplasia, spondyloepiphyseal dysplasia, osteonychondystrophy
- C. Metabolic:
  1. Ochronosis (alkaptonuria)
  2. Hemochromatosis
  3. Wilson's disease
  4. Gaucher's disease
- D. Endocrine:
  1. Acromegaly
  2. Hyperparathyroidism
  3. Diabetes mellitus
  4. Obesity
  5. Hypothyroidism
- E. Calcium deposition diseases:
  1. Calcium pyrophosphate dihydrate deposition
  2. Apatite arthropathy
- F. Other bone and joint diseases:
  1. Localized: fracture, avascular necrosis, infection, gout
  2. Diffuse: rheumatoid (inflammatory) arthritis, Paget's disease, osteopetrosis, osteochondritis
- G. Neuropathic (Charcot joints)
- H. Endemic:
  1. Kashin-Beck
  2. Mseleni
- I. Miscellaneous:
  1. Frostbite
  2. Caisson's disease
  3. Hemoglobinopathies

Clinical Features:
Typical feature is pain that worsens on weight bearing and activity, which improves with rest. Morning stiffness of less than 20-30 minutes and gelling of the involved joints after periods of inactivity may also be present. Physical examination may reveal localized tenderness and bony or soft tissue swelling. Bony crepitus is a characteristic feature. Synovial effusion, if present, is not large. On palpation, presence of some warmth is not unusual. Periarticular muscle atrophy due to prolonged disuse, gross joint deformity, bony hypertrophy, subluxation and marked loss of range of movement may be the features of advanced cases. Systemic symptoms are absent in OA and erythrocyte sedimentation rate is usually normal. The American College of Rheumatology has produced a criterion for diagnosis of OA (Tables-II, IV-VI). But as it was developed for epidemiological purpose, its use in routine clinical practice is not recommended. A comprehensive list of differential diagnosis is shown in Table-III.

Table-II

Clinical features of osteoarthritis

Symptoms:
- Joint pain
- Morning stiffness lasting less than 30 minutes
- Joint instability or buckling
- Loss of function

Signs:
- Bony enlargement at affected joints
- Limitation of range of motion
- Crepitus on motion
- Pain with motion
- Malalignment and/or joint deformity

Pattern of joint involvement*:
- Axial: cervical and lumbar spine
- Peripheral: distal interphalangeal joint, proximal interphalangeal joint, first carpometacarpal joints, knees, hips

*Disease with multiple joint involvement is a subtype of osteoarthritis; most commonly, osteoarthritis affects the hands, hips, knees and/or spine.

Table-III

Clinical findings differentiating osteoarthritis from other causes of painful joints

Condition	History	Physical findings
Bursitis/ Tendonitis;	Pain increased with movement Pain worse at night No systemic symptoms Pain on some maneuvers, not others	No joint abnormality or swelling Certain passive maneuvers produce pain Pain on resisted active range of motion of affected muscles
Mechanical intra-articular Conditions;	Recurrent joint swelling Joint locks Joint “gives way” Intermittent pain with pain-free intervals	Pain and limitation at certain points of flexion or extension Pain on combined rotation and extension of the knee
Rheumatoid arthritis	Often insidious onset Morning stiffness of 1 hour Systemic symptoms Associated symptoms (e.g., Raynaud’s syndrome, skin rash)	Involvement of MCP, wrist, elbows, ankles Synovial thickening Classical deformities: Swan neck Boutonniere Ulnar deviation Loss of range of motion of wrist, elbows

MCP denotes metacarpophalangeal joint
Adapted from: E, Bjelle A, Eden S, Svanberg A. A longitudinal study of the occurrence of joint complaints in elderly people. Age Ageing 1992; 21: 160-7.

Table-IV

Combined clinical (history, physical examination, laboratory) and radiographic classification criteria for osteoarthritis of the Hip [6]*

Hip pain and at least 2 of the following 3 features:
ESR<20 mm/hour
Radiographic femoral or acetabular osteophytes
Radiographic joint space narrowing (superior, axial, and/or medial)

ESR denotes erythrocyte sedimentation rate (Westergren)
*This classification method yields a sensitivity of 89% and a specificity of 91%

Table-V

Classification criteria for osteoarthritis of the Hand[7]*

Hand pain, aching, or stiffness and 3 or 4 of the following features:
Hard tissue enlargement of 2 or more of 10 selected joints
Hard tissue enlargement of 2 or more DIP joints
Fewer than 3 swollen MCP joints
Deformity of at least 1 of 10 selected joints

DIP denotes distal interphalangeal; MCP, metacarpophalangeal
*The 10 selected joints are the 2nd and 3rd DIP, the 2nd and 3rd proximal interphalangeal and the 1st carpometacarpal joints of both hands. This classification method yields a sensitivity of 94% and a specificity of 87%.

Table-VI

Criteria for classification of idiopathic osteoarthritis of the Knee[8]

Clinical and laboratory	Clinical and radiographic	Clinical†
At least 5 of following 9: Age > 50 years Stiffness < 30 minutes Crepitus Bony Tenderness Bony enlargement No palpable warmth ESR <40 mm/hour RF <1: 40 SF OA	Knee pain and at least 1 of following 3: Age > 50 years Stiffness < 30 minutes Crepitus and Osteophytes	At least 3 of following 6: Age > 50 years Stiffness < 30 minutes Crepitus Bony tenderness Bony enlargement No palpable warmth
92% sensitive 75% specific	91% sensitive 86% specific	95% sensitive 69% specific

ESR denotes erythrocyte sedimentation rate (Westergren); RF, rheumatoid factor; SF OA, synovial fluid signs of OA (clear, viscous, or white blood cell count <2,000/mm3).
† Alternative for the clinical category would be 4 of 6, which is 84% sensitive and 89% specific.

Natural history:

The natural history of OA is a slow process. In the knee, progression may take many years. Once established however, the joint may remain in a stable condition for many years. Spector *et al* found that in a cohort of 63 patients, radiographic deterioration occurred in approximately one third[9]. In another study of 31 patients with established knee OA followed up for eight years, 20 patients got worse and seven remained the same. Changes in symptoms, disability, and radiographs do not correlate[10]. In the hip, natural history is variable. In a Danish study, two thirds of hips studied deteriorated radiographically over 10 years, however symptomatic improvement was common[11]. Other studies have shown clinical deterioration to be more common. Unlike knee OA, symptomatic and radiological recovery is possible. Avascular necrosis of the femoral head occurs late in disease and is a major problem. In the hand, it is initially a relapsing and remitting disease with episodic inflammatory phases associated with joint redness and swelling. Bony swellings form at this time. The frequency of disease flares then reduces and the joint swellings become hard and fixed. This is associated with a reduction in pain.[11]

Pathogenesis:

Traditionally, OA was viewed as an inexorably progressive degenerative disease. The notion may be incorrect as many OA patients the disease stabilizes. Recent research suggests that it is a dynamic process and may progress in an episodic manner.

Cartilage is made of water (70%) and a type II collagen framework with proteoglycans and glyco-saminoglycans (consisting mainly of aggrecan and also chondroitin), produced by chondrocytes. Proteoglycans in turn bind to hyaluronate which stabilizes the macromolecule. Chondrocytes receive nutrition from the synovium by diffusion and the synovial fluid is circulated by joint movement. It has been postulated that if the joint stops moving (as a result of a fracture or immobility) and chondrocytes lose their source of nutrition, they go into shock and cartilage repair ceases. Metalloproteinases are produced, which catalyse collagen and proteoglycan degradation. The synovium has been shown to be variably inflamed in OA producing increased levels of interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α), cytokines that induce nitric oxide and metalloproteinase production. Interleukin-6 (IL-6) and mechanical loading of the joint also induce catabolic cytokine receptors. These bind IL-1 and TNF-α within cartilage causing more destruction.

It is thought that the osteophytes and subchondral sclerosis seen in OA may be the body's way of trying to compensate for lack of cartilage, although some researchers have found bony changes before cartilage changes in animal models[12]. This sort of abnormal bone is also thought to lead to further degradation of the cartilage surrounding it. Poor synthesis of cartilage building blocks may be caused by dysfunctional forms of insulin-like growth factor-1 and transforming growth factor-beta, agents that normally promote new cartilage formation[12].

Pathology:

Macroscopically, the osteoarthritic process results in cystic degeneration of the bone surrounding the joint, with loss of cartilage and irregular, abnormal bone formation at the edges of the joint (osteophytes) and narrowing of the joint space. Microscopically, there is flaking and fibrillation of the articular cartilage surface and destruction of the cartilage microarchitecture with formation of holes within it, as well as bony cysts[13].

Variations in the cellularity and vascularity of subchondral bone leads to sclerosis in some areas and new bone and callous formation where the synovium is continuous with the periosteum. The cartilage itself has three discrete zones within it: a surface layer adjacent to the synovium consisting of collagen aligned parallel to the surface; a middle zone consisting of thicker, wider spaced collagen molecules arranged randomly; and an inner zone adjacent to bone, consisting of collagen arranged perpendicular to the surface[13].

Risk factors:

Several risk factors may predispose to the development of OA. Table-VII summarizes some of the factors. Among these, age is the most powerful unmodifiable risk factor. The Framingham Study found that 27% of those aged 63-70 years had radiographic evidence of knee OA, increasing to 44%

Table-VII

Risk factors for osteoarthritis

Age
Female sex
Race
Genetic factors
Major joint traumaa
Repetitive stress, e.g., vocational
Obesitya
Congenital/developmental defects
Prior inflammatory joint disease
Metabolic/ endocrine disorders

[a] Potentially modifiable

SOURCE: Adapted from M Hochberg: J Rheumatol 18: 1438, 1991.

in the over 80 years age group.[14] Studies of proprioception in OA have found that it is reduced in an elderly patient group with knee OA[15]. Obesity is the strongest modifiable risk factor. Three to six times the body weight is transferred across the knee joint during walking. Any increase in weight should be multiplied by this factor to estimate the excess force across the knee joint when an overweight patient walks. The Chingford Study showed that for every two unit increase in body mass index (approximately 5 kg), the odds ratio for developing radiographic knee OA increased by 1.36[16]. Increasing weight increases the risk of contralateral OA of the knee in women with established OA of one knee. Being overweight at an average age of 36–37 years is a risk factor for developing knee OA in later life (>70 years of age). Losing 5 kg of weight reduced the risk of symptomatic knee OA in women of average height by 50%[12]. Also, increased risk of developing progressive OA seems to be apparent in overweight people with localized disease[17]. Bone density has an inverse relationship with OA. Increasing subchondral bone density may lead to increased loading through weight bearing joint cartilage[18].

Laboratory findings:

Table-VIII shows a summary of the laboratory methods proposed for diagnosis of OA. Radiographs

Table-VIII

Laboratory investigations suggested for diagnosis of osteoarthritis

Imaging:
Plain radiographs
Magnetic resonance imaging
Computed tomography
Radionucleotide imaging
Ultrasound
Arthroscopy
Biochemical markers
Marker of Cartilage Destruction
Cartilage Ologometric Matrix (COMP)
Markers of synovial inflammation
C Reactive Protein
Hayaluronan
YKL-40
Metalloproteases
Markers of bone turnover
Pyridinoline
Bone Sialoprotein

though cheap, provide a permanent record and are easily available, are not a precise measure of disease progression. Disease progression is measured by joint space narrowing which occurs at the rate of <0.1 mm per year and so it is difficult to measure accurately. Plain radiograph shows the following changes in OA:

- Joint space narrowing
- Osteophytes
- Bony cysts
- Subchondral sclerosis

Table-IX shows the radiographic differentiating features of OA and other causes of painful joints. The relationship between symptoms and radiographic findings has always been under debate and results are conflicting in different studies, partly due to the differences in population studied and radiographic and clinical criteria used. The presence of osteophytes has a very strong association with knee pain. However, absence or presence of joint space narrowing was not associated[19]. Knee pain severity was a more important determinant of functional impairment than radiographic severity of OA.[20, 21] There was no correlation between joint space narrowing and a disability score (Western Ontario and McMaster Universities Osteoarthritis index, WOMAC) at a single time point[21].

Magnetic resonance imaging (MRI) is already established for assessment for ligament and meniscal tears of the knee. It has no role in routine clinical practice. However, it is sensitive in quantifying cartilage loss (change in surface morphology and full thickness cartilage defects). It is not yet sensitive enough to detect preclinical OA, as it cannot evaluate cartilage fibrillation[22, 23]. Ultrasound is also good for assessing cartilage integrity and destruction but cartilage is not easily accessible in most weight bearing joints.

Current diagnosis of OA relies on a clinical history and radiography. Radiographic changes occur late in the disease and are largely irreversible. Molecular markers may theoretically be able to detect osteoarthritic changes at an early stage. Ideally, these markers would be sensitive to change, reliable, and quantitative[24]. Table-VIII outlines some of the proposed markers of OA.

Management:

The aims of management of patients with OA are:

- Patient education
- Pain control
- Improve function
- Alter the disease process

Table-IX

*Radiographic findings differentiating osteoarthritis from other causes of painful joints**

Condition	Bone density	Erosions	Cysts	Joint Space loss	Distribution	Bone production
OA	Normal overall	No, unless erosive OA	Yes, subchondral	Nonuniform	Unilateral and/or bilateral; asymmetric	Yes; osteophytes; subchondral sclerosis
RA	Decreased	Yes	Yes, synovial	Uniform	Bilateral; symmetric	No
Psoriatic arthritis	Normal	Yes	No	Yes	Bilateral; asymmetric	Yes
CPPD	Normal	No	Yes	Uniform	Bilateral	Yes; osteophytes; chondrocalcinosis; subchondral
AS	Early-normal Late-decreased	Yes	No	Yes	Bilateral; symmetric	Yes
DISH	Normal	No	No	No	Sporadic	Flowing osteophytes; ossification of tendon, ligaments

OA denotes osteoarthritis; RA, rheumatoid arthritis; CPPD, calcium pyrophosphate deposition disease; AS, ankylosing spondylitis; DISH, diffuse idiopathic skeletal hyperostosis

*Adapted from: Brower AC. Arthritis in black and white. Philadelphia: Saunders, 1998: 23-57.

The management strategies are:

- Education
- Exercise
- Weight Loss
- Physiotherapy
- Appliances
- Drugs
- Surgery

These recommendations are not meant to be rigid but should be flexible and customized according to the individual patient's needs and expectations. Comorbid conditions, such as cardiac disease, hypertension, peptic ulcer disease, renal disease, which are very likely to be present in the elderly age group, must be of prime importance.

Non-pharmacological modalities:

Non-pharmacological therapy is the mainstay of intervention. Table-X outlines the nonpharmacological therapies for patients with OA. Formal education should be an initial part of management of OA. A meta-analysis showed that patient education has a significant effect on pain and function, but that it was only 20% as effective as NSAIDs[25]. Exercise is the single most important intervention. There have been many studies showing the benefit of exercise in OA[26, 27]. Evidence suggests that while advice regarding exercise is important, being given a specific programme to do with "follow up" is probably more effective than advice alone. Table-XI shows the American Geriatrics Society protocol for an exercise programme[28]. A study of 21 obese elderly men and women with knee OA randomised to either a diet and exercise group or diet alone group found that the former group lost more weight but both groups had similar improvements in self reported disability, knee pain intensity, and frequency after six months[29]. In knee OA, shock absorbing footwear reduces the impact of a load on the knee. Heel wedging improves proprioception and reduces pain in OA of the knee. The occupational therapist can provide assessment for walking aids, for example, sticks and for providing a safe and functional environment at home and work. There is historical and anecdotal evidence for their benefit rather than from controlled trials. Therapeutic knee taping has also been effective in knee OA. A recently published study by Rana et al concluded that significant greater improvement in pain and disability was observed with knee taping[30].

Pharmacological therapies

Several modalities of pharmacological therapies exist. They are:

- Analgesics
- NSAIDs

Table-X

Nonpharmacological therapy for patients with osteoarthritis

Patient education
Self-management programs (e.g., Arthritis Foundation Self-Management Programme)
Personalized social support through telephone contact
Weight loss (if overweight)
Aerobic exercise programmes
Physical therapy range-of-motion exercises
Muscle-strengthening exercises
Assistive devices for ambulation
Patellar taping
Appropriate footwear
Lateral-wedged insoles (for genu varum) bracing
Occupational therapy
Joint protection and energy conservation
Assistive devices for activities of daily living

Table-XI

American Geriatrics Society recommendations for exercise[28]

Warm up: 5 min
Exercises:
Isometric strength training: daily
Isotonic strength training: 2-3 times/week
Flexibility training: daily
§Aerobic training (endurance): 3-5 times/week
Cool down: 5 min

Many patients need to concentrate on strength and flexibility training first before considering aerobic training. The exercise programme should be adapted to the patient's age and functional ability.

- Corticosteroids
- Hyaluronic acid derivatives
- Topical treatments
- Glucosamine Sulfate

Possible DMOADs Pharmacologic therapy is considered as additional to the non-pharmacological modalities as drug therapy is most effective when combined with non-pharmacologic therapies.[31]

Table-XII

Risk factors for gastrointestinal complications occurring with NSAIDs

Patient related factors:
Age > 60 years
History of ulcer disease
Drug related factors:
Use of relatively toxic NSAID
High dose of NSAID (or two NSAIDs used concurrently)
Concurrent use of anticoagulant
Concurrent use of corticosteroids
Uncertain or possible risk factors:
Duration of NSAID treatment
Female sex
Underlying rheumatic disease
Cardiovascular disease
Helicobacter pylori infection
Smoking
Alcohol consumption

Analgesics and non-steroidal anti-inflammatory drugs.

Relief of mild to moderate joint pain can be achieved by simple analgesic like acetaminophen and it is comparable to non steroidal anti-inflammatory drugs (NSAIDs)[32-36]. Bradley and his colleagues failed to demonstrate differences in responses to acetaminophen and ibuprofen in knee OA patients with clinical features of joint inflammation[37]. However, Eccles and colleagues, in a metaanalysis of trials comparing simple analgesics with NSAIDs in patients with knee OA, did note that NSAID-treated patients had significantly greater improvement in both pain at rest and pain on motion[36]. In another study, acetaminophen and ibuprofen were comparably effective in patients with mild-to-moderate pain, but ibuprofen was statistically superior to acetaminophen in patients with severe pain[38] and in another study diclofenac was statistically superior to acetaminophen for both pain and function measured with several validated outcome measures[39]. Although a number of patients may fail to obtain adequate relief even with full doses of acetaminophen, this drug merits a trial as initial therapy, based on its overall cost, efficacy, and toxicity profile[36,40]. American College of Rheumatology (ACR) and European League Against Rheumatism guidelines recommend this as initial therapy[41, 42]. The daily dose of acetaminophen should not exceed 4 gm. Although it is one of the safest analgesics, acetaminophen can be associated with clinically important adverse events. Recent reports have highlighted long-recognized conditions in which increased awareness of potential toxicity is important. For example, because acetaminophen can prolong the half-life of warfarin sodium, careful monitoring of the prothrombin time is recommended in patients taking warfarin sodium who subsequently begin high-dose acetaminophen treatment[43, 44]. Hepatic toxicity with acetaminophen is rare with doses of ? 4 gm/day. Nonetheless, the drug should be used cautiously in patients with existing liver disease and avoided in patients with chronic alcohol abuse because of known increased risk in these settings[45-47]. Even though acetaminophen was reported to be weakly associated with end-stage renal disease, the Scientific Advisory Committee of the National Kidney Foundation

recommends it as the drug of choice for analgesia in patients with impaired renal function[48].

If acetaminophen fails to control symptoms adequately, alternative or additional pharmacological agents should be considered. The choice will depend on the presence of relevant risk factors. Table-XII shows some of the important risk factors that should be looked for. All NSAIDs are thought to have similar pain relieving effects, with a reduction in pain of around 30% and an improvement in function of around 15%[49,50]. If used, the dose should be titrated depending on response and side effect profile. Renal and gastrointestinal side effects are a major source of mortality and morbidity, especially in the elderly. If a patient is at risk of peptic ulceration, gastroprotection in the form of misoprostol or proton pump inhibitors should be prescribed. The new cyclo-oxygenase-2 (COX-2) specific inhibitors are increasingly used. They have equal efficacy to standard NSAIDs and thought to pose less gastrointestinal toxicity. However, they can still cause upper gastrointestinal adverse events along with increased predisposition to myocardial events[51] and renal toxicity. An increasing number of evidences also exist showing interaction of various NSAIDs and aspirin. It has been argued that aspirin loses its cardioprotective effect when given concomitantly with different NSAIDs[52, 53].

Intra-articular modalities[54]:
Corticosteroids (tiamcinolone hexacetonide and methyl prednisolone) show significant short-term benefit of 2-4 weeks in comparison to placebo in knee joints. Data on hip, thumb base and finger injections are lacking. Side effects of skin atrophy, dermal pigmentation, specially with long acting preparations and if soft tissues are injected, are reported. Infection is rarely reported. Though early studies suggested cartilage damage with excessive intra-articular injection use, now the damage is thought to be mostly due to the progression of the disease itself. However, intra-articular injection should be reserved for flare-ups only. Some studies describe a greater benefit in OA with knee effusions. American College of Rheumatology guidelines suggest no more than 3–4 knee joint injections per year. In patients needing more than this number, other therapeutic maneuvers should be considered.

Hyaluronic acid (HA) is a high molecular weight polysaccharide, and is a major component of synovial fluid and cartilage. The molecular weight and amount of HA decrease OA. It was postulated that supplementation with intra-articular HA could help to improve synovial fluid viscosity. Both high and low molecular weight HA have been studied. They have been shown to be superior to placebo in reducing pain and number of intra-articular corticosteroid injections needed for 12 months. Symptomatic effect started at week 3–5 and persisted up to 12 months. In comparison with intra-articular steroid, a double blind study found that hyaluronic acid and intra-articular corticosteroids had similar efficacy up to week 5, followed by superior efficacy of hyaluronic acid until the end of the six-month study. There is also evidence that hyaluronic acid injections have similar efficacy to NSAIDs for between 3–6 months.

Topical treatments:
Topical capsaicin (a derivative of hot chilli peppers) cream is often used on hands and knees in patients with moderate pain. Topically applied capsaicin is proposed to exert its action by stimulating a subpopulation of nociceptive pain neurons. Exposure to capsaicin depletes substance P that matter the neurons insensitive to all other exposures including the capsaicin itself. However, redness and burning is reported at the site of application[55]. There are trials showing the efficacy of capsaicin in OA[56, 57]. There is little evidence of efficacy of topical NSAIDs.

Glucosamine sulphate:
Glucosamine sulphate is a nutrient supplement available as over the counter in Europe and USA, and is used to relieve musculoskeletal symptoms. Many preparations are available, some of which also contain chondroitin sulphate. Both glucosamine sulphate and chondroitin sulphate are derivatives of glycosaminoglycans found in articular cartilage. Their mechanism of action is unclear, especially as they cannot be absorbed from the gut intact. Reginster *et al* studied 212 patients with primary knee OA and found that there was a 20%-25% improvement in symptoms and a reduction in knee medial compartment changes over three years in those taking glucosamine.[58] A meta-analysis has also shown that glucosamine sulphate has some analgesic efficacy[59].

Interestingly, a recent double blind placebo controlled trial found no clinical or statistical analgesic effect, and only a large placebo response (33%)[60]. This trial included patients with a wider spectrum of disease severity and higher pain and disability scores than the Reginster trial. Glucosamine sulphate has probably an analgesic effect in mild to moderate knee OA. There is little evidence for its use in OA at other sites.

In Search for disease modifying osteoarthritis drug (DMOAD):

DMOADs are drugs whose action is not aimed principally at the control of symptoms, but instead at the prevention of structural damage in normal joints at risk for development of OA, or at the progression of structural damage in joints already affected by OA. For the most part, such approaches have been aimed at inhibiting the breakdown of articular cartilage by matrix metalloproteinases, or at stimulating repair activity by chondrocytes. Although a number of agents are under study, including matrix metalloproteinase inhibitors and growth factors, no agent has been shown to have a DMOAD effect in humans, and none are available for this indication. The new interest in OA will hopefully allow the development of true DMOAD.

Diacerein is a drug that inhibits production and activity of metalloproteinases and interleukins and may have an effect in delaying progression of hip osteoarthritis as measured by minimum joint space measured visually[62]. There is also interest in the use of bisphosphonates and specific leukotriene antagonists as disease modifiers.

Local delivery of anti-inflammatory cytokines (for example, IL-1-Ra) or gene induction using gene transfer methods may provide a novel treatment regimen.

Further work on cartilage culture and transplantation for other joints is needed.

Large clinical trials to assess the efficacy of interventions are also necessary, using validated and reliable outcome measures that reflect disease activity, damage, and quality of life.

Surgery:

Surgery is used where medical therapy has reached its limits. Arthroscopic debridement and lavage can improve symptoms in degenerative meniscal tears, but does not halt progression. Autologous cartilage transplantation, where grafts of normal cartilage are taken from the edge of the diseased joint, cultured in-vitro and reimplanted into areas where the cartilage is denuded may be an effective technique, but it is expensive and is not currently recommended for first line treatment of knee joint articular cartilage defects[61].

Conclusion:

OA is a potentially treatable condition with positive patient benefit if the application of modalities of therapy is judicious and current evidence based. New insight into the disease process and advent of new drugs hold great promises for the OA patients and the treating physician. Though there are no DMOAD is available for therapeutic use presently, studies are going on for development of such a drug. Till then patients can rip the benefits of the current treatment.

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