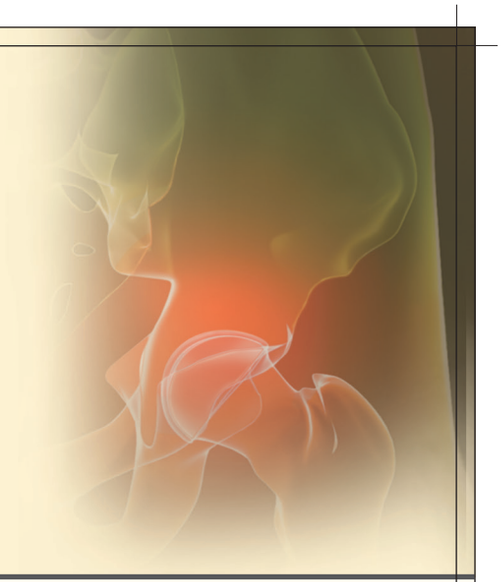


Rheuma Facts

A quarterly Magazine

3rd Issue, July 2013

Current News

Updated Rheumatoid Arthritis Management Recommendations Issued By EULAR

The European League against Rheumatism (EULAR) has released updated recommendations for the management of RA. According to this latest guidance, treatment with disease-modifying anti-rheumatic drugs (DMARDs) should be initiated as soon as a diagnosis of RA is made with the aim of reaching a target of remission or low disease activity in every patient

Main Category: Arthritis / Rheumatology Article Date: 07 Jul 2013 - 0:00 PDT

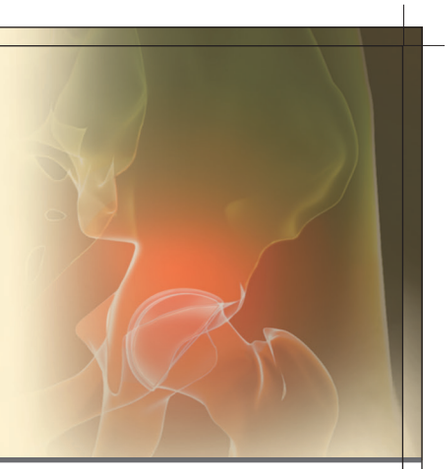
Vitamin D Deficiency Speeds Up Aging of Bones

The bones of people with vitamin D deficiency tend to age faster compared to those with healthy levels of “the sunshine vitamin”, American and German scientists found. The researchers also showed that low levels of vitamin D undermine bone quality

Written by Christian Nordqvist 15 Jul 2013

Rheuma Facts

A quarterly Magazine



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An approach to a patient with RA

Summarized by:
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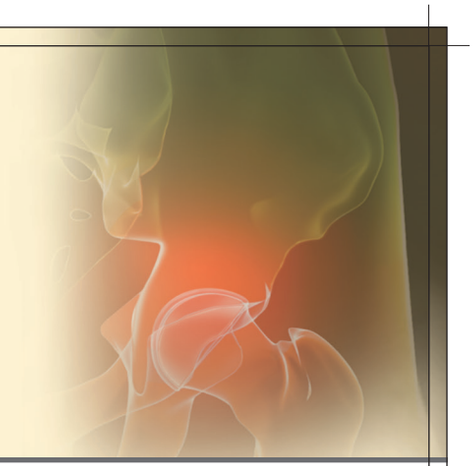


INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder of unknown etiology that primarily involves joints. The arthritis is symmetrical, may be remitting, but if uncontrolled may lead to destruction of joints due to erosion of cartilage and bone which leads to deformity. The disease usually progresses from the periphery to more proximal joints, and in patients who do not fully respond to treatment, results in significant locomotor disability within 10 to 20 years

Many of the clinical features that are discussed in this topic review are used in the clinical diagnosis of RA and also serve as classification criteria for RA. The latter are used to define patient populations with RA for clinical or other research purposes. The diagnosis and classification of RA are presented separately. (See "Diagnosis and differential diagnosis of rheumatoid arthritis".)

The following is a summary of characteristic clinical features, some of which are also useful for diagnostic and/or classification purposes:

Morning stiffness for at least one hour and present for at least six weeks

- Swelling of three or more joints for at least six weeks
- Swelling of wrist, metacarpophalangeal, or proximal interphalangeal joints for at least six weeks
- Symmetric joint swelling
- Hand x-ray changes typical of RA that include erosions or bony decalcification
- Rheumatoid subcutaneous nodules
- Rheumatoid factors or anti-citrullinated peptide/protein antibodies
- Elevated acute phase reactants (erythrocyte sedimentation rate or C-reactive protein)

EVALUATION FOR SUSPECTED RA

RA should be suspected in the adult patient who presents with inflammatory polyarthritis. The initial evaluation of such patients requires a careful history and physical examination, along with selected laboratory testing to identify features characteristic of RA or which suggest an alternative diagnosis

We focus especially on the following for the purposes of diagnosis:
We perform a thorough medical history, with particular attention to joint pain and reported swelling and the presence, location (peripheral joints rather than low back), and duration (at least 30 minutes) of morning stiffness. The absence of other conditions or symptoms suggesting an alternative diagnosis, such as psoriasis, inflammatory bowel disease, or a systemic rheumatic disease such as systemic lupus erythematosus (SLE) helps to exclude other disorders

Symptoms of arthritis that have been present for a short time, for example less than six weeks, may well be due to an acute viral polyarthritis rather than to RA. The longer symptoms persist, the more likely the diagnosis of RA becomes. Thus, in patients presenting very early, close observation with frequent follow-up appointments are required, with repeated serologic analysis for anti-cyclic citrullinated peptide (CCP) antibodies, rheumatoid factor and acute-phase reactants. In a minority of patients, several such visits are required before the differential diagnosis between RA and viral arthritis becomes established

A complete physical examination is indicated to assess for synovitis, including the presence and distribution of swollen or tender joints and limited joint motion; extraarticular disease manifestations, such as rheumatoid nodules; and signs of diseases, such as systemic lupus erythematosus or psoriasis, included in the differential diagnosis

We perform the following laboratory tests, which support the diagnosis if positive and/or elevated:

- Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibodies

We perform both RF and anti-CCP antibody testing when initially evaluating a patient with suspected RA. The results of both tests are informative, since a positive result for either test increases overall diagnostic sensitivity, while the specificity is increased when both tests are positive. Despite this, both tests are negative on presentation in up to 50 percent of patients, and remain negative during follow-up in 20 percent of patients with RA. It is important to note that anti CCP is 90 percent specific for the diagnosis of RA

- Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) levels—both the ESR and CRP are typically elevated in RA

We perform the following testing in all patients, which may be helpful in the differential diagnosis of RA and as baseline testing for monitoring of disease activity or progression and medication safety:

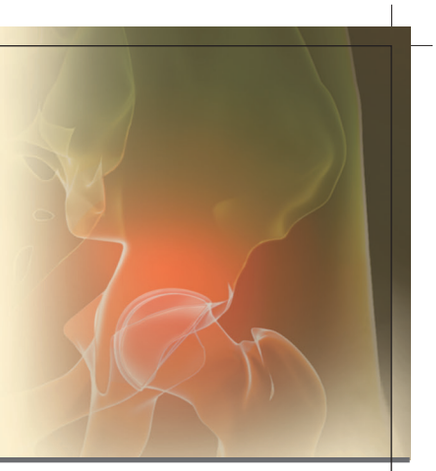
- Antinuclear antibody (ANA) testing — A negative ANA helps exclude SLE and other systemic rheumatic diseases; the ANA may be positive in up to a third of patients with RA. In patients with a positive ANA, anti-double stranded DNA and anti-Smith antibody testing should also be performed; these antibodies have high specificity for SLE

- Complete blood count (CBC) with differential and platelet count, tests of liver and kidney function, serum uric acid, and a urinalsis—The CBC is often abnormal in RA, with anemia and thrombocytosis consistent with chronic inflammation. Liver and kidney testing abnormalities indicate a disorder other than RA; if caused by comorbid conditions, they may affect therapeutic choices or drug dosing. Hyperuricemia may prompt additional efforts, including arthrocentesis and crytal search, to exclude gout; polyarticular gout can infrequently be mistaken for RA

- Radiographs of the hands, wrists, feet — We obtain radiographs during the initial evaluation primarily as a baseline for monitoring disease progression. However, characteristic joint erosions may be observed in patients presenting with symptoms for the first time and hence aid in diagnosis. Additionally, in patients with other disorders, such as psoriatic arthritis, spondyloarthropathy, gout, or chondrocalcinosis, radiographic changes more characteristic of these conditions may point to an alternative diagnosis

We perform the following studies in selected patients:

Serologic studies for infection — In patients with a very short history, for example less than six weeks, particularly those who are seronegative for anti-CCP and rheumatoid factor, we perform serologic testing



for human parvovirus B19, hepatitis B virus (HBV), and hepatitis C virus (HCV). In areas endemic for Lyme disease we perform serologic studies for Borrelia as well

Synovial fluid analysis — We perform arthrocentesis and synovial fluid analysis for the diagnosis or exclusion of gout, pseudogout, or an infectious arthritis if a joint effusion is present and there is uncertainty regarding the diagnosis, particularly in the setting a monoarthritis, oligoarthritis, or asymmetric joint inflammation. Synovial fluid testing should include a cell count and differential, crystal search, and Gram stain and culture. Synovial fluid analysis should also be obtained to exclude infection or crystalline arthropathy in patients who undergo glucocorticoid injections for symptomatic relief

Magnetic resonance imaging (MRI) studies and ultrasonography do not have an established role in the routine evaluation of patients with polyarthritis. However, MRI and ultrasound are more sensitive than radiography at detecting changes resulting from synovitis and may be helpful in establishing the presence of synovitis in patients with normal radiographs and uncertainty regarding either the diagnosis or the presence of inflammatory changes, such as patients with obesity or subtle findings on examination

DIAGNOSIS

The diagnosis of RA can be made when the following clinical features are all present:

- Inflammatory arthritis involving three or more joints
- Positive rheumatoid factor (RF) and/or anti-citrullinated peptide/protein antibody (such as anti-CCP) testing
- Elevated levels of C-reactive protein (CRP) or the erythrocyte sedimentation rate (ESR)

Diseases with similar clinical features have been excluded, particularly psoriatic arthritis, acute viral polyarthritis, polyarticular gout or calcium pyrophosphate deposition disease, and systemic lupus erythematosus

- The duration of symptoms is more than six weeks

These criteria are consistent with the 2010 ACR/EULAR classification criteria for RA

CLASSIFICATION CRITERIA

The 2010 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria focus on features that would identify patients at an earlier stage of disease than would the previously used criteria that had been last revised in 1987. The 1987 ACR criteria were formulated to distinguish patients with established RA from patients with other defined rheumatic diseases; the 2010 ACR/EULAR criteria for RA focused on identifying the factors, among patients newly presenting with undifferentiated inflammatory synovitis, which could allow for the identification of patients for whom the risk of symptom persistence or structural damage is sufficient to be considered for intervention with disease-modifying antirheumatic drugs classification as definite RA is based upon the presence of synovitis in at least one joint, the absence of an alternative diagnosis better explaining the synovitis, and achievement of a total score of at least 6 (of a possible 10) from the individual scores in four domains. The highest score achieved in a given domain is used for this calculation. These domains and their values are:

- 2 to 10 large joints (from among shoulders, elbows, hips, knees, and ankles) = 1 point
- 1 to 3 small joints (from among the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists) = 2 points
- 4 to 10 small joints = 3 points
- Greater than 10 joints (including at least one small joint) = 5 points
- Serological abnormality (rheumatoid factor or anti-citrullinated peptide/protein antibody)
- Low positive (above the upper limit of normal, ULN) = 2 points
- High positive (greater than 3 times the ULN) = 3 points
- Elevated acute phase response (erythrocyte sedimentation rate or C-reactive protein) (above the ULN = 1 point)
- Symptom duration (at least six weeks = 1 point)

DIFFERENTIAL DIAGNOSIS

A variety of conditions must be considered in the differential diagnosis of RA. Features of some disorders that are included in the differential diagnosis of RA are shown in the table

Acute viral polyarthritis A number of viral infections may cause an acute viral polyarthritis

Viral infections such as rubella, parvovirus B19, and HBV can cause an acute polyarthritis syndrome that may be mistaken for the inflammatory polyarthritis of RA. However, the syndrome is usually short-lived, lasting only from a few days to several weeks, and rarely beyond six weeks. HCV can cause a polyarthritis or oligoarthritis in a minority of patients, but is more commonly associated with arthralgias

Systemic rheumatic diseases

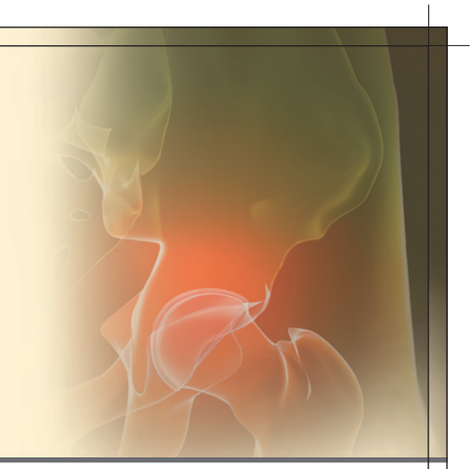
Early RA may be difficult to distinguish from the arthritis of systemic lupus erythematosus (SLE), Sjögren's syndrome, dermatomyositis, or overlap syndromes, such as mixed connective tissue disease. In contrast with RA, these disorders are generally characterized by the presence of other systemic features, such as rashes, dry mouth and dry eyes, myositis, or nephritis, and by various autoantibodies not seen in RA. Additionally, the relative responses of the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) can be less well correlated with each other in other diseases, particularly SLE, than in RA. Whereas both are commonly raised in RA, the CRP is often normal or only minimally elevated in patients with active SLE even when the ESR is elevated

Palindromic rheumatism

Palindromic rheumatism is characterized by episodes of joint inflammation sequentially affecting one to several joint areas for hours to days, with symptom-free periods that may last from days to months Some patients presenting with this syndrome eventually develop a well-defined rheumatic disease, the most common being RA (ranging from 28 to 67 percent); some of the remaining patients develop SLE and other systemic disorders. Patients with anti-CCP antibodies appear more likely to progress to definite RA. Close follow-up and specific serologic evaluation can help distinguish among these disorders

Hypermobility syndrome and fibromyalgia

Pain, rather than stiffness or swelling, is the dominant symptom of the two common disorders: hypermobility syndrome and fibromyalgia. Although the hypermobility syndrome and fibromyalgia can both bear superficial resemblances to RA due to the presence of polyarthralgia, there are important distinguishing features:



The hypermobility syndrome is associated with hyperextensible joints, and patients lack signs of synovitis

Fibromyalgia is associated with tender points at nonarticular sites such as the medial portions of the elbows, across the trapezius muscle, and down the spine; there is no evidence of synovitis on examination, such as swelling, warmth or diminished joint range of motion, although patients may exhibit joint line tenderness on exam

Reactive arthritis and arthritis of IBD

Reactive arthritis often presents as a monoarthritis or oligoarthritis in large joints, such as the knees, and RA may occasionally present in this fashion as well. The physical signs of both reactive arthritis and RA can be identical in the knees

The arthritis associated with inflammatory bowel disease (IBD) or other gastrointestinal disorders is also part of the differential diagnosis. Patients with IBD may develop a peripheral polyarthritis with prominent involvement of the metacarpophalangeal joints that can be mistaken for RA; other presentations include predominantly large joint oligoarticular involvement or a spondyloarthropathy with sacroiliitis. This disorder may be missed if abdominal symptoms or symptoms of diarrhea and/or blood or mucus in the stool are not prominent, or not specifically sought in the history

Lyme arthritis

Lyme arthritis, a late manifestation of Lyme disease, occurs primarily in individuals who live in or travel to Lyme disease endemic areas. Lyme arthritis is characterized by intermittent or persistent inflammatory arthritis in a few large joints, especially the knee. The most commonly involved joints, after the knee, are the shoulder, ankle, elbow, temporomandibular joint, and wrist. Migratory arthralgias without frank arthritis may occur during early localized or early disseminated Lyme disease

Psoriatic arthritis

Psoriatic arthritis can be difficult to distinguish from RA because a symmetric polyarthritis can be observed in both disorders. We generally make the diagnosis of psoriatic arthritis in such patients who also have psoriasis and are seronegative for RF and anti-CCP. However, we diagnose RA in those with a symmetric polyarthritis who are seropositive for at least one of these antibodies since skin psoriasis is so common. However, serologic testing and skin findings may not be informative since patients with RA may not have RF or CCP antibodies (eg, seronegative RA) and the joint symptoms of psoriatic arthritis may precede the onset of skin disease by many years. Such patients should be evaluated and monitored for other signs more characteristic of psoriatic arthritis, such as nail changes or enthesitis; occasional patients exhibit overlapping features of both disorders

Polymyalgia rheumatica

Polymyalgia rheumatica (PMR) can sometimes be mistaken for RA in patients presenting with more limited arthritis over the age of 50 who are seronegative or only have a low RF titer. Unlike RA, PMR is usually associated with marked myalgias in the shoulders and hips, and joint involvement tends to be milder, more limited, and more often asymmetric

Crystalline arthritis

Crystalline arthritis (gout and pseudogout) can become chronic and even assume a polyarticular distribution. The diagnosis is established by the finding of urate or calcium pyrophosphate crystals, respectively, in synovial fluids. The presence of tophi on physical examination, the detection of serological markers of RA, and the characteristic appearance of gouty erosions are also useful in distinguishing RA from polyarticular gout

Infectious arthritis

Infectious arthritis is usually monoarticular, but polyarthritis can occur. The diagnosis is established by culturing the pathogen from the synovial fluid or from the blood. Patients with septic arthritis may or may not appear toxic on examination, depending upon the stage of their infection, the presence of medications that can mask infection (eg, glucocorticoids), and other clinical variables. Peripheral blood leukocytosis with a left shift is common, but not invariably present

Osteoarthritis

Osteoarthritis (OA) can be confused with RA in the middle aged or older patient when the small joints of the hands are involved. However, different patterns of clinical involvement usually permit the correct diagnosis

Paraneoplastic disease

Joint pain or frank polyarthritis can occur in association with cancer. The following are some examples:

Sarcoid arthropathy

Chronic arthritis in sarcoidosis may be oligoarticular or polyarticular and can appear similar to RA in some patients; it most frequently affects the ankles, knees, hands, wrist, metacarpophalangeal and proximal interphalangeal joints, and is frequently associated with parenchymal pulmonary disease

Treatment

Patient should be referred to Rheumatologist for the confirmation of diagnosis

Baseline LFT Creatinine CBC is needed for initiation of DMARD like Methotrexate, Salazopyrine, and Hydroxycholoroquine

Biologics are reserved for patients who are non responder to first line therapy

SUMMARY AND RECOMMENDATIONS

RA should be suspected in the adult patient who presents with inflammatory polyarthritis. The initial evaluation of such patients requires a careful history and physical examination, along with selected laboratory testing to identify features characteristic of RA or which suggest an alternative diagnosis. The following components of the medical evaluation are helpful in making a clinical diagnosis of RA, both for the identification of characteristic findings and for the exclusion of other diagnoses

- A thorough medical history, with particular attention to joint pain, stiffness, and associated functional difficulties
- A complete physical examination to assess for synovitis, limited joint motion, extraarticular disease manifestations, and signs of diseases included in differential diagnosis
- Basic and selected laboratory testing, including assays for acute phase reactants (erythrocyte sedimentation rate and C-reactive protein), rheumatoid factor, anti-cyclic citrullinated peptide (CCP) antibodies, and antinuclear antibodies
- Selected imaging studies, including bilateral radiographs of the hands, wrists, and feet
- Arthrocentesis is needed if there is diagnostic uncertainty

The Benefits of Vitamin D for Bone Health

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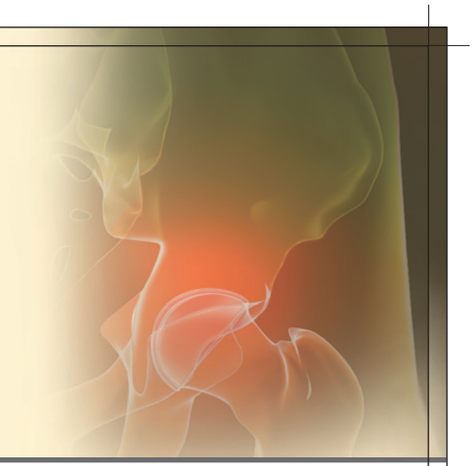
London



We often take our health for granted, specially the health of our bones. These are what we usually say:

"Who needs to worry about their bones?"

"I've never had a broken bone, so my bones must be healthy"

"I don't really like the taste of milk"

"I take a vitamin, so I don't need calcium or vitamin D"

All of these comments are routinely heard each and every day in a physician's clinic. Disturbingly, these comments portray a potentially significant problem in this country. By not understanding the importance of developing many young women are not optimizing their bone health when they are able. An increase in bone thinning around the time of menopause will occur. It will be much worse in women who have not developed peak bone mass and strength in their 20's and 30's. This, in turn, can lead to osteoporosis and a higher risk of fractures later in life. Over the past few years, much more information has become available regarding bone health, calcium intake and vitamin D

Bone development occurs very early in life and peak bone density occurs by 25-30 years of age. The development of bone requires adequate building blocks to form a firm foundation for the skeletal system. In a very simple way

The bone is constantly undergoing change or remodeling. Bone building by cells called osteoblasts and bone breakdown by cells called osteoclasts, commonly occur within major bones. When a bone is being built, more bone is added for strength, while less bone is broken down. In general, bone building predominates until approximately age 30. Gradual bone loss begins to occur between age 40 and 50, and progresses rapidly after menopause

One of the building blocks used by osteoblasts for bone development is calcium. Calcium is so important during development that a fetus extracts calcium from the mother through the placenta to aid in development. Each and every living cell in the body requires calcium to function properly and your body cannot make calcium

Vitamin D has many functions in the body

Normally, it is produced by the skin when exposed to sunlight and aids in the absorption of calcium by the GI tract. In recent years, vitamin D research has revealed many exciting findings. Reports of new and promising studies seem to emerge almost weekly, including the potential for reduced rates of colorectal cancer, heart disease, diabetes, breast cancer and depression. Perhaps not surprisingly, in light of the other studies, one recent review of the health records of more than 13,000 Americans found that individuals with the lowest vitamin D levels were 26% more likely in an eight-year period to die than those with the highest levels

According to the National Osteoporosis Foundation recommendations, adults under age 50 need 1,000 mg of calcium and 400-800 IU of vitamin D daily. Adults 50 and over need 1,200 mg of calcium and 800-1,000 IU of vitamin D daily. However, many leading experts believe that vitamin D levels should guide intake amounts of vitamin D. Aiming for a vitamin D level of greater than 30 to obtain the optimal health benefits of this important vitamin should be considered

Therefore, achieving adequate nutrition, including calcium and vitamin D during childhood and beyond is vital for skeletal development, bone structure and overall health and well-being. Bone strength and density remain relatively constant until one approaches menopause, when bone loss will begin to occur. After menopause, bone loss accelerates during the first 3-5 years. This bone loss leads to more fragile bones and places a woman at greater risk for fracture. Routine counseling for all patients and their health care provider should encourage adequate calcium and vitamin D intake

Anti Depressant and Osteoarthrosis....

Dr. Ahmed Iqbal Mirza Consultant Rheumatologist
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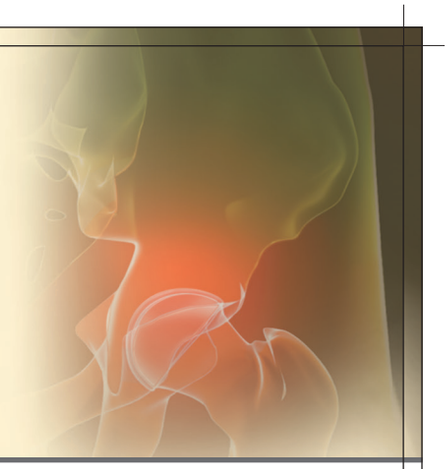
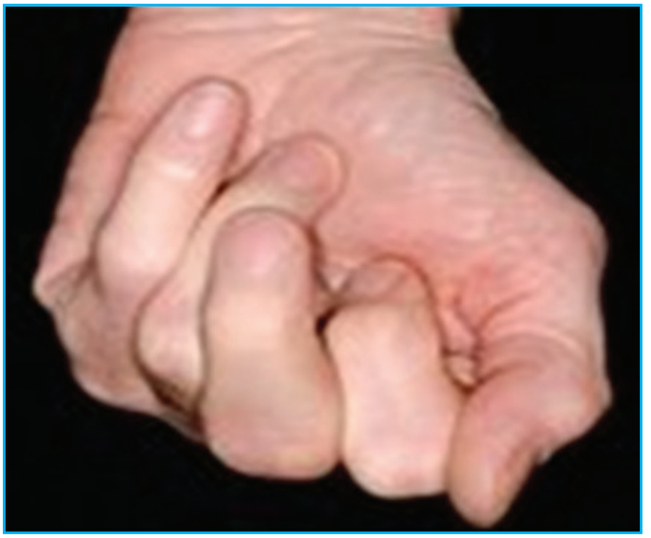


Antidepressants can play a key role in alleviating painful conditions like osteoarthritis and may result in fewer side effects than traditionally prescribed drug regimes, such as anti-inflammatories and opioids, according to a perspective paper published online ahead of print publication by the *International Journal of Clinical Practice*



American doctors Leslie Citrome and Amy Weiss-Citrome analysed the latest clinical evidence on duloxetine, a well-established antidepressant that received US Food and Drug Administration (FDA) approval in 2010 for use with chronic musculoskeletal pain, including osteoarthritis

"It is not uncommon to treat osteoarthritis with a combination of drugs that work in different ways", explains Dr Leslie Citrome, Clinical Professor of Psychiatry and Behavioural Sciences at New York Medical College, Valhalla, New York, USA. "Our review supports this approach and confirms that antidepressants are not just for depression and can play a key role in relieving this painful condition"

The authors looked at studies exploring the effects of duloxetine being used on its own or in combination with non-steroidal anti-inflammatory drugs (NSAIDs). These included the two randomised double-blind, placebo controlled clinical trials that formed the basis of FDA approval for duloxetine for the treatment of chronic pain associated with osteoarthritis

Study results were analysed using number needed to treat (NNT) and number needed to harm (NNH). These quantify how many patients need to be treated with one intervention versus another before encountering one additional patient who experiences a desired outcome (NNT) or undesired disadvantage, such as a side-effect (NNH). A smaller number indicates greater advantages for NNT and greater disadvantages for NNH

"Applying these simple methods to often complex research gives us a real indication of whether a drug will benefit or harm our patients, which is what we as clinicians are most interested in", explains Dr Citrome

When duloxetine was compared with a placebo tablet containing no active ingredients, using data from the two FDA approval studies, the NNT was six. This means that six patients would need to be treated with duloxetine instead of receiving the placebo before encountering one additional patient experiencing an improvement in pain using a composite measure that brings together a number of indicators of efficacy. Such a low NNT makes a compelling case for this treatment approach

The authors say that this finding, over 13 weeks, compared favourably with other studies of NSAIDs – the NNT was five for etodolac after four weeks and four for tenoxicam after eight weeks When the side effects of the various drugs were taken into account, this showed that when duloxetine was used on its own for 13 weeks it provided a number of advantages over NSAIDs, which can lead to gastrointestinal bleeding, and opiates such as morphine, which can cause constipation

The most common side effects of duloxetine – nausea, fatigue and abdominal discomfort were small when compared to the placebo, resulting in NNHs of 16, 17 and 19 respectively. This means, for example, that 16 patients would need to be treated with duloxetine instead of receiving the placebo before encountering one additioal patient experiencing nausea

The studies used to gain FDA approval also showed that pain reduction using duloxetine on its own was not dependent on an improvement in depressive symptoms

"Although the use of duloxetine as a monotherapy for pain has been approved by the regulatory agencies, it is quite common for patients to receive a combination of drugs and NSAIDs are the most frequently prescribed drugs for the pain associated with osteoarthritis", says co-author Dr Amy Weiss-Citrome, a specialist in Physical Medicine and Rehabilitation

For that reason the authors also examined the findings of a recent study that showed the potential synergy of duloxetine and NSAIDs

The study, a ten-week double-blind trial of 524 patients with osteoarthritis of the knee, found that those who took a combination of duloxetine and NSAIDs reported greater pain reductions than the control group who took a NSAID with a placebo

The NNT for the outcome of substantial improvement in pain with combination treatment versus NSAIDs alone was six, underlining the benefits of this approach

"We believe that our analysis of these studies demonstrate that clinicians managing patients suffering from osteoarthritis should also consider prescribing adjunctive antidepressants that can effectively impact on central pain pathways", concludes Dr Leslie Citrome

Quiz

What is your Diagnosis