

ARTHRITIS: GOUT

OBJECTIVES

At the conclusion of this course, the learner will be able to:

1. List several types of arthritis.
2. Briefly describe rheumatoid arthritis and osteoarthritis.
3. Detail gouty arthritis in terms of its etiology, prevalence, pathophysiology, signs and symptoms, complications, diagnosis, prevention and treatment, including pharmacological interventions and the latest research about the cardiovascular side effects of the COX-2 inhibitors and the effect of this research on the withdrawal some medications from the market and stronger warnings.

ARTHRITIS: GOUT

INTRODUCTION

Arthritis is an inflammatory disease of the bone joints that is marked with a limitation of movement, swelling and pain. It can be caused by an infection in the joint, a buildup of uric acid or simply with the degeneration of a joint or joints as an individual grows older.

Arthritis is the number one chronic disorder that leads to disability in our country among people 15 years of age and older. In 2005, it was estimated that 66 million people, that is, one out of every 3 adults in our nation is affected by arthritis. Nationally, it affects about 300,000 children and it is estimated that it costs the United States in excess of \$86.2 billion every year. Women are more affected than males. (Arthritis Foundation, 2004)

TYPES OF ARTHRITIS

There are more than 100 different types of arthritis. Some of these types include the below.

- *Osteoarthritis*- is the most common form of arthritis. It is a degenerative joint disease in which the cartilage that covers the ends of bones in the joint deteriorates, causing pain and a loss of movement as a result of the bone rubbing against bone rather than cartilage.
- *Rheumatoid arthritis*- is one of the most disabling forms of arthritis. It affects primarily women. This form is an autoimmune disease where the joint lining becomes inflamed as a result of the person's immune system.
- *Gout*- primarily affects mostly men. This form of arthritis affects small joints, specifically the great toe. A defect in body chemistry, that is, a buildup of uric acid leads to gout. This form can be successfully controlled with dietary changes and medications.
- *Ankylosing spondylitis*- when the bones of the spine become inflamed they fuse together, thus leading to ankylosing spondylitis which affects the spine.
- *Juvenile arthritis*- this term encompasses all types of arthritis that can occur among the pediatric population. Some of these types are ankylosing spondylitis, juvenile rheumatoid arthritis and juvenile lupus among other types.
- *Systemic lupus erythematosus (lupus)*- is serious systemic disorder that inflames and damages joints as well as other connective tissue throughout the entire body.
- *Scleroderma*- is a disease that attacks the body's connective tissue. It causes a hardening and thickening of the skin.
- *Fibromyalgia*- affects primarily women. It leads to widespread pain that affects muscles and their attachments to the bone. (Arthritis Foundation, 2004)
- *Septic arthritis*- develops when a bacteria such as streptococcus (pneumoniae), staphylococcus, group B streptococcus, Mycobacterium tuberculosis and candida albicans. It occurs most often among children less than 3 years of age and primarily affects the hip. The onset is generally quite rapid with a low grade fever, severe joint pain and joint swelling.
- *Psoriatic arthritis*- can be mild affecting only a couple of joints or it can be more severe affecting the spine. Genetics may play a role in this form of arthritis. Generally, people with psoriasis have a greater incidence of arthritis than those without this skin disorder.

- *Fungal arthritis*- this rare form of arthritis is also referred to as mycotic arthritis. Fungi that lead to this form include blastomycosis, histoplasmosis, candidiasis, coccidioidomycosis, sporotrichosis, and cryptococcosis. The infection typically begins in the lungs and then progresses. The knees are most often affected. Immunocompromised patients are at greatest risk. (MDchoice, Inc., 2005)

OSTEOARTHRITIS, RHEUMATOID ARTHRITIS AND GOUT

Osteoarthritis, known as degenerative joint disease, is the most commonly seen form of arthritis among the elderly population. Osteoarthritis results from the wearing out or deterioration of the smooth cartilage lining of the joint. This loss of cartilage makes the joints rougher than they had been when the cartilage was in place. Although it can also affect the hands, degenerative osteoarthritis is most often seen in the knees, spine and hips, the weight bearing joints of the body. This form of arthritis cannot be cured but those that suffer from it rarely become bedridden or crippled as a result of it. Post menopausal osteoarthritis is the result of the depletion of hormonal estrogen after menopause. It is a variation of the larger diagnosis of osteoarthritis from other causes.

Rheumatoid arthritis also involves painful swelling of the joints but it is usually associated with the smaller, non weight bearing joints of the body. Also, it is not usually associated with old age onset, but instead, it primarily begins in the young adult from ages 30 to 40 from unknown causes. It can also develop in young child. This form of rheumatoid arthritis is referred to as Still's disease or juvenile rheumatoid arthritis. Unlike osteoarthritis, rheumatoid arthritis is associated with physical deformities and crippling.

Gout is quite different from osteoarthritis and rheumatoid arthritis. Gout is a disease or disorder that occurs when the body cannot excrete the uric acid it produces because the body is overproducing it or the kidneys have a diminished ability to filter it out and excrete it. When uric acid builds up in the body the joints, as well as soft tissues, become affected by it. The buildup of uric acid in gout causes very painful attacks of arthritis and it is accompanied by a high concentration of uric acid in the bloodstream and the formation of uric acid crystals in the affected joints.

ETIOLOGY AND PREVALENCE

The cause of gout is unknown but a number of things appear to lead to the under secretion and the over production of uric acid, those things that lead to and characterize this form of arthritis.

Some of these factors include:

- genetics (fructose intolerance, increased activity of hypoxanthine guanine phosphoribosyl transferase and the hyperactivity of phosphoribosyl pyrophosphate);
- environment (diuretics, ethanol abuse, a diet high in purines, and extreme muscular exertion);
- some diseases (sickle cell anemia, diabetes mellitus, hypertension, polycythemia, renal disease and leukemia) and;
- the absence of the enzyme uricase.

The more developed nations of the world have a greater incidence of gout than undeveloped nations and men are affected with gout more than women. It is rare in women prior to menopause and its appearance in women after menopause appears to be associated with the use of diuretics. More severe symptoms are found among those that have had a bout of gout before the age of 30. (Langford & Thompson, 2000; Merck & Co., 2005)

PATHOPHYSIOLOGY

An overproduction of uric acid and an undersecretion of uric acid lead to gout. Crystals of monosodium urate form when uric acid builds up in the system. When these crystals are deposited into tissues surrounding peripheral joints, such as tendons, cartilage and ligaments and in other tissue, such as the ear, the person is affected by gout. These crystals are then periodically released from time to time, for some unknown reason, during an acute attack of inflammation. Over time, the monosodium urate crystals can also be deposited in organs, such as the kidney, and in larger joints. (Langford & Thompson, 2000; Merck & Co., 2005)

SIGNS AND SYMPTOMS

An acute attack of gout can occur at any time without any warning but it sometimes follows a stressor (physical or emotional), surgery, an overabundance of foods high in purines, alcohol, an infection and fatigue.

The first sign is usually nocturnal pain in one or more peripheral joints. The great toe is affected most often, however, it can also affect the knee, ankle, instep, wrist, and elbow.

Other signs and symptoms include:

- acute pain which can be very severe,
- redness,
- swelling,
- tenderness,
- warm, shiny, tense purple or red skin color over the affected joint(s),
- tachycardia,
- malaise,
- chills,
- fever,
- leukocytosis, and
- limited joint movement. (Langford & Thompson, 2000; Merck & Co., 2005)

THE COMPLICATIONS OF GOUT

Acute attacks of gout can occur several times a year unless prophylactic treatment is given. Eventually, without treatment, chronic arthritis, chronic joint pain, erosive, permanent joint deformity, and limitations of joint mobility and function can occur.

The joints that are most often affected are those of the feet and hands, however, the shoulder, cervical spine, sacroiliac, hip and sternoclavicular joints can also be affected with gout. Cyclosporine induced gout typically begins in the larger central joints, like the sacroiliac, hands and hip. It can also damage the renal tubules.

Urolithiasis (uric acid or calcium oxalate stones) occurs in approximately 20% of people with gout. Obstruction, infection, renal dysfunction can follow. (Langford & Thompson, 2000; Merck & Co., 2005)

DIAGNOSIS

The diagnosis of gout is based on the following data:

- physical exam

- elevated serum uric acid (although about 30% of patients have normal levels)
- the presence of urate crystals in the synovial fluid
- the presence of crystals on compensated polarized light microscopy
- a response to colchicines in 24 hours or less during an acute attack
- visible tophi on an x-ray (tophi less than 5 mm in diameter are not visible on an x-ray)
- the presence of subcutaneous tophi (Langford & Thompson, 2000; Merck & Co., 2005)

PREVENTION

Daily prophylactic doses of colchicine and allopurinol are used to prevent recurring attacks of gout when the patient is affected with chronic gout. (Langford & Thompson, 2000; Merck & Co., 2005)

TREATMENT

The goals of treatment include:

- the prevention of acute attacks,
- ending an acute attack when it does occur,
- the prevention of further crystal deposits and
- eliminating existing tophi.

Coexisting conditions, such as hyperlipidemia, diabetes, obesity and hypertension must be controlled and managed.

Surgery

At times, large crystal deposits, referred to as tophi, are surgically removed. (Merck & Co., 2005)

Medications

Colchicine

Colchicine is a uricosuric medication used for both acute attacks of gouty arthritis and chronic gout that is accompanied by recurrent and frequent acute attacks. Its mechanisms of action lower serum uric acid levels by inhibiting the reabsorption of uric acid.

When used for the treatment of acute gout attacks, the response to colchicine is typically quite dramatic in terms of its effect. Joint pain usually subsides after only 12 hours of treatment and the joint pain may disappear completely in 48 hours or less. Although colchicine does not retard the progressive joint damage of gout that is produced by tophi, it can prevent it by lowering and maintaining the serum urate concentration at or near its normal level.

Colchicine is contraindicated with a hypersensitivity to it. It is also contraindicated with high dose aspirin therapy and among patients that have severe gastrointestinal, hepatic or renal impairment. It should be used with caution when a patient has a blood dyscrasia, is pregnant or lactating and among the elderly and pediatric populations. The elderly may be adversely affected with electrolyte imbalances if they experience vomiting as a result of the colchicine therapy.

Some of the side effects and adverse drug reactions associated with colchicines are:

- oliguria,
- renal impairment,
- hematuria,
- nausea,
- vomiting,
- anorexia,
- peripheral neuritis,
- peptic ulcer,
- myopathy, and
- hematological changes (thrombocytopenia, aplastic anemia, agranulocytosis and pancytopenia).

The usual adult dosage of colchicine is 0.5 mg to 1.2 mg (usually 1 mg) by mouth every 2 hours for acute attacks of gout until the therapeutic response is obtained or diarrhea or vomiting occur. The maximum dosage is 7 mg over 48 hours. The prophylactic dosage is 0.5 to 1.8 mg every day for long term therapy.

This medication should be taken on an empty stomach to enhance absorption. Intravenous colchicine can be given when the patient's

gastrointestinal tract is not tolerating po colchicine. (Merck & Co., 2005; Skidmore-Roth, Linda, 2004)

Probenecid

Probenecid (Benemid) another uric acid lowering medication, is used for the prevention of hyperuricemia and gouty arthritis. Specifically, it lowers the reabsorption of uric acid, therefore and reduces serum uric acid levels by promoting its excretion.

This medication is contraindicated with renal and hepatic disease, hypersensitivity and among patients who have uric acid calculi. It must be used cautiously during pregnancy.

Some of the side effects and adverse effects of probenecid are:

- nausea, vomiting and anorexia,
- bradycardia,
- gastric irritation,
- drowsiness,
- headache,
- dermatitis, pruritus, and rash,
- glycosuria, frequency and thirst,
- hypokalemia,
- acidosis,
- hyperchloremia, and
- hyperglycemia.

More serious side effects and adverse reactions include hepatic necrosis, nephrotic syndrome and apnea.

The usual adult dosage of probenecid for hyperuricemia is 250 mg two times a day for one week which can be increased by 250 mg to 500 mg a day or bid until the uric acid level normalizes. The maximum daily dosage is 2 g. The maintenance dose is 500 mg per day.

Patients taking probenecid should be instructed to drink plenty of fluids (2 to 3 liters per day) to decrease their risk of uric acid stones. They should also be advised to take the medication with food or milk and to take an antacid to decrease the risk of gastrointestinal side effects.

When a patient is taking probenecid, the following have to be monitored and assessed.

- uric acid levels,
- urinary pH, glucose and output,
- electrolytes,
- respiratory status,
- mobility and joint pain,
- central nervous system status.

An overdose can be signaled with confusion, hyperreflexia, twitching and headache. (Skidmore-Roth, Linda, 2004)

Allopurinol

Allopurinol is another uricosuric agent used for the treatment of chronic gout, calcium oxalate calculi, and Chagas' disease. Its mechanism of action decreases the amount of uric acid that is synthesized. It is used to prevent an attack of gout and to treat hyperuricemia.

It is contraindicated in patients who have had a prior severe allergic reaction to it. It should be used cautiously with pregnancy, lactation and among children. Cautious use is also advised when the patient has had a prior mild allergic reaction to it and for those with renal insufficiency or hepatic disease. Baseline and ongoing liver function studies should be done because this medication is hepatotoxic.

Some of the adverse reactions associated with allopurinol are GI irritation, neuritis, fever, drowsiness, pruritic rash, leukocytosis, thrombocytopenia, eosinophilia, leukocytosis, bone marrow suppression, hepatitis, cataracts and renal impairment.

The adult dosage of allopurinol for gout may range from 200 to 600 mg/day in divided doses to inhibit uric acid synthesis and to control serum urate concentration. The maximum daily dosage is 800 mg a day. (Skidmore-Roth, Linda, 2004)

Sulfinpyrazone

Sulfinpyrazone, another medication used for gout, increases the excretion of uric acid by inhibiting the reabsorption of urates in the tubules. The recommended adult dosage for gout is 100 to 200 mg bid for a week and then 200 mg to 400 mg twice a day but not to exceed 800 mg per day

Sulfinpyrazone is contraindicated for patients with GI inflammation, active peptic ulcers, blood dyscrasias, hypersensitivity and a creatinine

clearance of <50 mL/min. It must be used with caution during pregnancy.

Some of the side effects of sulfinpyrazone are rash, flushing, headache, dizziness, tinnitus, polyuria, anemia, increased bleeding time, renal calculi and leukopenia. More serious adverse reactions include apnea, hepatic necrosis, GI bleeding, agranulocytosis and coma. (Skidmore-Roth, Linda, 2004)

Salicylates and nonsteroidal anti-inflammatory medications NSAIDs)

These medications serve as both anti-inflammatory agents and analgesics. Examples are aspirin, ibuprofen, diclofenac, fenoprofen, flurbiprofen, indomethacin, ketoprofen, meclofenamate, nabumetone, naproxen, oxaprofen, piroxicam, sulindac and tolmetin.

Some of the side effects and adverse drug reactions to the NSAIDs are GI irritation, cardiovascular complications, blood dyscrasias, nephrotoxicity (oliguria, azotemia, hematuria and dysuria), abdominal pain, cholestatic hepatitis, anorexia, dizziness and drowsiness. Antacids, H₂ blockers and sucralfate can be given between meals for mild GI side effects of aspirin. 100 to 200 µg bid to qid of misoprostrol or a proton pump inhibitor can be used with aspirin and other NSAIDs to reduce the risk of GI bleeding among high risk patients.

The NSAIDS are contraindicated among patients with asthma, severe liver and/or renal disease, and hypersensitivity. They can be used with caution among the elderly and children, during lactation and pregnancy and for patients with GI, cardiac and/or bleeding disorders.

The patient's blood, renal and hepatic function must be monitored when NSAIDS are used. Baseline hearing and eye exams are also recommended so that changes can be identified. Toxicity may be signaled with tinnitus and/or blurred vision. Current concerns about COX-2 inhibitors and NSAIDS are described below. (Skidmore-Roth, 2004)

Analgesics

In addition to the NSAIDs, other analgesics, such as codeine 30 mg to 60 mg may be used to manage the pain. (Merck & Co., 2005)

Sodium Bicarbonate

Sodium bicarbonate is used to alkalize urine for patients that have calculi formation. The usual adult dosage is 325 mg to 2 g four times a day or 48 mEq (4g) followed by 12 to 24 mEq q4h. (Skidmore-Roth, Linda, 2004)

RECENT NEWS ABOUT COX-2 INHIBITORS AND NSAIDS

In 2005, research indicated that some popularly used and intensely marketed COX-2 inhibitors, used for arthritis, increased the risk of cardiovascular events. On April 7, 2004 the U.S. Food and Drug Administration (FDA) asked Pfizer Inc. to voluntarily take Bextra off the market and to place strong warnings on Celebrex as a result of this research. This advice and news lead to the withdrawal of Bextra (valdecoxib) from the market and to the strong warning that Celebrex (celecoxib), too, is associated with cardiovascular complications. Vioxx (rofecoxib) had been previously taken off the market by Merck because of its cardiovascular disease risk as well.

The FDA has also asked the numerous manufacturers of over the counter NSAIDs, other than aspirin and acetaminophen, to include additional information about the potential for gastrointestinal and cardiovascular side effects and risks.

At the current time it appears that the cardiovascular side effects are dose dependent, therefore, decisions about whether or not to take available NSAIDs and Celebrex should be up to the patient and their physician. Additionally, if the decision is to use or continue to use one of these medications, the dosage should be the lowest possible to achieve the desired effect. (Arthritis Foundation, 2005)

Diet

People that have gout should:

- avoid alcohol,
- eat a nutritious diet without purine rich foods, and
- increase their fluid intake to decrease urate crystal precipitation and to decrease the risk of dehydration. (Merck & Co., 2005; Skidmore-Roth, Linda, 2004)

Other Interventions

The patient should lose weight, as indicated, to avoid additional stress on the joints. At times, splinting the inflamed joint may be beneficial in reducing the pain and decreasing the risk of deformity. (Merck & Co., 2005)

Joint Aspiration

Some gout attacks are treated with the aspiration of affected joints after which corticosteroid esters are instilled. Depending on the size of the joint, prednisolone tebutate from 10 mg to 50 mg is used. (Merck & Co., 2005)

Exercise and Rest

During the acute phase of a gout attack, the joint should be rested. After that, normal exercise and rest is recommended. (Merck & Co., 2005)

SUMMARY

The implications of arthritis involve the entire health care team. The treatment of arthritis often involves multiple interventions such as medications, pain relief, physical and/or occupational therapy, applications of heat or cold and patient/family education. A team approach involving a number of professional disciplines and a thorough knowledge of arthritis are the keys to success in the management of this widespread and often chronic disease.

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