Practical Classification for the Use of Nonsteroidal Anti-inflammatory Drugs

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The podiatric physician is faced with a multitude of nonsteroidal anti-inflammatory drugs from which to choose. Podiatric physicians are overwhelmed with advertisements in the literature, outlining the safety and efficacy of one or another of these medications. This article will categorize the nonsteroidal anti-inflammatory drugs to aid in their selection.

History

The term "nonsteroidal anti-inflammatory" drug was first applied to phenylbutazone in 1949. All currently marketed nonsteroidal anti-inflammatory drugs were initially identified by their *in vivo* effects against inflammation induced in the rat paw by injection of carrageenan. The first known nonsteroidal anti-inflammatory drug was salicin, a precursor to aspirin. Salicin is an extract of willow and poplar bark that has been used since ancient times to treat pain, gout, and fever. Colchicine is an extract of the autumn crocus that has been used since the 6th century to treat acute gout.

Classification of Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs are generally classified by their chemical structure; however, this classification does little to aid the practitioner in choosing the proper medication for the condition. A more useful classification of the nonsteroidal anti-inflammatory drugs may be made by their half-lives. The half-life of a medication is the amount of time necessary for the body to eliminate half of the drug from the system. Drugs with long half-lives are generally given once or twice daily, and since five half-lives are required to reach steady state, they will take longer to reach their therapeutic effect. Drugs with short half-lives are generally given every 4 to 6 hr; they reach therapeutic effect in less time than drugs with long half-lives.

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Nonsteroidal Anti-inflammatory Drugs With Long Half-lives

Naprosyn (naproxen)

Naprosyn reaches peak plasma levels in 2 to 4 hr, and has a half-life of 12 to 15 hr. It reaches steady state in 2 to 3 days and is given in doses of 250 to 500 mg every 12 hr. The administration of probenecid increases half-life by 50%. This drug has been approved for nonprescription use.

Clinoril (sulindac)

Clinoril reaches steady state in 2 to 3 days, and has a half-life of 16 to 18 hr. The maximum dosage is 20 mg twice daily. It is reported to have a low incidence of gastrointestinal upset.

Dolobid (diflunisal)

Dolobid is a salicylic acid derivative, but is not metabolized to salicylate. It reaches steady state in 3 to 9 days and has a half-life of 7 to 8 hr. The dosage is 125 to 500 mg twice daily.

Feldene (piroxicam)

Peak plasma levels are reached in 2 to 5 hr with steady state achieved in 1 to 3 weeks. The half-life is 38 hr, and the dosage is 20 mg once a day. This drug may potentiate the effects of coumarin, and peptic ulceration is common in doses higher than 20 mg a day.

Relafen (nabumetone)

Relafen reaches steady state in 1 to 2 days and has a half-life of 24 hr. This is the only nonacidic nonsteroidal anti-inflammatory drug and has a decreased incidence of peptic ulcers. The dosage is 1,000 mg a day.

Daypro (oxaprozin)

Daypro reaches steady state in 4 to 7 days, and peak plasma levels are reached in 3 to 5 hr. It has a half-life of 25 hr. The dosage is 1,200 mg once daily.

Nonsteroidal Anti-inflammatory Drugs With Short Half-lives

Indocin (indomethacin)

This is the prototype of the short half-life nonsteroidal anti-inflammatory drugs, and was first marketed in 1965. The peak plasma concentration is reached in 45 min, the half-life is 1 to 2 hr, and the drug reaches steady state in 5 to 10 hr. The dosage is 25 to 50 mg three times a day. Aspirin decreases the absorption, and there is a high incidence of gastrointestinal symptoms and headaches. A 75-mg sustained release capsule is available.

Motrin (ibuprofen)

Motrin reaches peak plasma concentration in 1 to 2 hr and the half-life is 1.7 hr. The drug reaches steady state in 8.5 hr. The dosage is 400 to 1,200 mg daily in divided doses for analgesia and 2,400 to 3,600 mg daily in divided doses for anti-inflammatory effect. The doses are generally given every 6 to 8 hr. This drug is approved for nonprescription sale.

Nalfon (fenoprofen)

This drug has a half-life of 2.7 hr and reaches steady state in 13.5 hr. The dosage is 300 to 600 mg, 3 to 4 times daily. The absorption is reduced 30% by food.

Orudis (ketoprofen)

The drug has a half-life of 1.6 hr, and reaches steady state in 8 hr. The dosage is 100 to 300 mg daily in divided doses every 6 to 8 hr. The peak plasma levels may be delayed by food, and lithium levels may be increased in patients on lithium therapy. This drug has been approved for nonprescription use.

Tolectin (tolmetin)

The peak plasma concentration is reached in 20 to 60 min and the half-life is 2 to 6 hr, and the drug reaches steady state in 10 to 30 hr. The dosage is 600 to 2,000 mg daily in three to four divided doses. This drug is approved by the Federal Drug Administration for use in children at a dosage of 20 mg/kg/day, age 2 years or older.

Voltaren (diclofenac sodium)

The peak plasma concentration is reached in 1.5 to 2 hr and the half-life is 75 min. The drug reaches steady state in 6 hr. The dosage is 75 to 200 mg a day in divided doses. This drug has an enteric coating that delays release.

Cataflam (diclofenac potassium)

The peak plasma concentration is reached in 1 hr, the half-life is 75 min, and the drug reaches steady state in 6 hr. The dosage is 75 to 200 mg a day in divided doses. This drug is not enteric coated.

Ansaid (flurbiprofen)

This drug has a half-life of 4 to 6 hr and reaches steady state in 20 to 30 hr. The dosage is 100 to 300 mg a day in two to four divided doses.

Lodine (etodolac)

This drug has a half-life of 6 to 7 hr and reaches steady state in 30 to 35 hr. The dosage is 100 to 300 mg twice daily. This drug has an analgesic effect 1 to 2 hr after administration.

Toradol (ketorolac tromethamine)

The peak plasma concentration is reached in 50 min, and the half-life is 4 to 6 hr. The dosage is 10 mg every 6 hr. This drug is indicated for short-term pain management.

Short-Term Pain Management and Inflammation

Indocin

Indocin is fast and effective, but has a high potential for gastrointestinal upset, headaches, and dizziness. The dosage is 25 mg three times a day for 5 to 7 days for acute pain and inflammation, and 50 mg three times a day for 5 to 7 days for acute gout. A 75-mg timed release capsule is available, but this dosage is not effective for acute gout.

Motrin

Motrin is fast and effective and is available over the counter. Various strengths are available, providing easy adjustability of doses. The dosage is

2,400 to 3,600 mg a day in divided doses, generally every 6 to 8 hr.

Lodine

Lodine has a fast analgesic effect (1 to 2 hr after administration) and convenient twice-per-day dosage at 100 to 300 mg.

Long-Term Pain Management and Inflammation

Relafen

This is the only nonacidic nonsteroidal anti-inflammatory drug and reduces initial gastrointestinal upset. This is important in long-term management. It is a convenient dosage of 1,000 mg a day.

Daypro

This drug has a fast steady state (4 to 7 days), and a convenient 1,200 mg once-a-day dosage. A one-time 1,800-mg initial dose provides faster onset.

Clinoril

This drug has a decreased incidence of gastrointestinal upset because of the low 20-mg dosage. The dosage is 20 mg twice a day.

Nonsteroidal Anti-inflammatory Drugs for Children

Tolectin

Tolectin is approved by the Federal Drug Administration for children at a dosage of 20 mg/kg a day, age 2 years or older.

Children's Motrin

This drug is a liquid 100 mg/5 ml. The dosage is 5 mg/kg to a maximum of 40 mg/kg every 8 hr.

Nonsteroidal Anti-inflammatory Drugs for Pain Management

Toradol

This drug is by prescription only and is reported to be as effective as Tylenol 3. Dosage is 10 mg every 6 hr for pain. This drug is for short-term usage only, and it is recommended that this drug be prescribed orally for a maximum of 5 days.

Motrin

This drug may be purchased over the counter in various brand names.

Aleve (naproxen)

This drug may be purchased over the counter.

Summary

The nonsteroidal anti-inflammatory drugs are an asset to the podiatric medical practice. It is important to remember that these drugs reduce inflammation, but they do not cure the condition. The etiology of the condition must be treated.

The number of nonsteroidal anti-inflammatory drugs has increased during the last 5 years, with competition among the drug manufacturers increasing. Learning the half-lives of nonsteroidal anti-inflammatory drugs, and applying that factor along with the amount of time necessary to achieve steady state in the bloodstream, will aid in determining which drug to use in a given situation.

Trade Names

Aleve, Procter & Gamble, Cincinnati.
Ansaid, The Upjohn Co, Kalamazoo, MI.
Cataflam, Geigy Pharmaceutical, Summit, NJ.
Clinoril, Merck & Co, Inc, West Point, PA.
Daypro, G.D. Searle & Co, Chicago.
Dolobid, Merck & Co, Inc, West Point, PA.
Feldene, Pratt Pharmaceuticals, New York.
Indocin, Merck & Co, Inc, West Point, PA.
Lodine, Wyeth-Ayerst Laboratories, Philadelphia.
Motrin, The Upjohn Co, Kalamazoo, MI.
Nalfon, Dista Products Co, Indianapolis.
Naprosyn, Syntex Laboratories, Inc, Palo Alto, CA.
Orudis, Wyeth-Ayerst Laboratories, Philadelphia.
Relafen, SmithKline Beecham Pharmaceuticals, Philadelphia.
Tolectin, McNeil Pharmaceutical, Raritan, NJ.
Toradol, Syntex Laboratories, Inc, Palo Alto, CA.
Tylenol 3, McNeil Pharmaceutical, Raritan, NJ.
Voltaren, Geigy Pharmaceutical, Summit, NJ.