Minocycline (Dynacin) Medical Facts

Minocycline (Dynacin) in Brief

Active ingredient: Minocycline hydrochloride

Common brand names: Dynacin, Minocin, Solodyn

Drug class: Tetracycline antibiotic

FDA Approved: June 30, 1971

Legal status: Prescription only

Pregnancy Category: D

Habit forming? No

Originally discovered: 1960s, Lederle Laboratories, USA

Introduction

Minocycline is a semisynthetic second-generation tetracycline antibiotic. Minocycline's antimicrobial spectrum is very similar to that of doxycycline with one important addition: it has much more antistaphylococcal activity.

History

The first tetracycline, chlortetracycline, was discovered in 1948 during systematic screening of soil specimens for antibiotic-producing microorganisms. Chlortetracycline and oxytetracycline come from Streptomyces aureofaciens and Streptomyces rimosus, respectively. Tetracycline is produced semisynthetically from chlortetracycline. Doxycycline and minocycline are both semisynthetic derivatives of tetracycline.

Minocycline was synthesized by Lederle Laboratories in 1967 and became widely available under the brand name Minocin in 1972[16].

Lederle Laboratories, founded in 1902, is a pharmaceutical division of Cyanamid, a large diversified American chemical manufacturer.

FDA approved uses

- Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox and tick fevers
- Respiratory tract infections: laryngotracheitis, tracheobronchitis, bronchitis, bronchiolitis, bronchiectasis, bronchopneumonia, pneumonia (single lobe and multilobe), lung abscess.
- Psittacosis (Ornithosis)
- Trachoma
- Inclusion conjunctivitis
- Nongonococcal urethritis, endocervical, or rectal infections in adults
- Relapsing fever
- Chancroid
- Plague
- Tularemia
- Cholera
- Campylobacter fetus infections
- Brucellosis
- Bartonellosis

Granuloma inguinale

Urinary tract infections: cystitis, pyelonephritis

Skin and skin structure infections: abscess, acne (including cystic and pustular types), cellulitis, infected dermatitis, folliculitis, furunculosis, impetigo, lymphadenitis, suppurative hydradenitis, paronychia, infected wounds.

Gonococcal infections

Syphilis

Yaws

Listeriosis

Anthrax

Vincent’s infection

Actinomycosis

Infections caused by Clostridium species

Intestinal amebiasis: Minocycline may be a useful adjunct to amebicides.

Acne

Minocycline for acne

Minocycline is one of the most effective antibiotics used for acne treatment. This antibiotic has been in use since the 1970's and is usually prescribed for the treatment of moderate to severe acne vulgaris.

Minocycline kills the acne bacteria and has a separate anti-inflammatory effect. It reduces the redness, swelling and tenderness or pimples whether it kills the acne bacteria or not.

Minocycline has been proven to be as effective as tetracycline and doxycycline for the quantitative reduction of inflammatory acne lesions. It is considered to produce a more rapid and sustained improvement in acne symptoms.17-18

Most strains of P. acnes are sensitive to minocycline. It is extremely important becuase of increasing rate of P. acnes resistance to tetracycline, doxycycline and erythromycin.

Currently, minocycline has become an extremely controversial treatment for acne. This is primarily related to the fact that a number of studies have now reported that this drug can lead to the development of many serious side effects.

Off-label & Investigational uses

Rheumatoid arthritis

Minocycline is used as a disease-modifying anti-rheumatic drug (DMARD) in the treatment of rheumatoid arthritis. Rheumatoid arthritis is a chronic inflammatory disease affecting about 1% of the adult population.

Although rheumatoid arthritis is not an infection, minocycline may improve the signs and symptoms of this disease. It may slow the progression of joint damage in arthritis and prevent disability. There is evidence that, besides its antibiotic effects, minocycline can modify some of the body's inflammatory responses. It decreases the production of substances causing inflammation, such as prostaglandins and leukotrienes, while increasing production of interleukin-10, a substance that reduces inflammation.

Results of a 48-week multicenter clinical study20 of 219 adults with rheumatoid arthritis show that minocycline reduces joint pain and swelling and is safe in mild to moderate disease. Minocycline may improve control of disease activity and provide relief from swollen, tender joints.

According to the American College of Rheumatology, "Minocycline is prescribed for patients with symptoms of mild rheumatoid arthritis. It is sometimes combined with other medications to treat patients with persistent symptoms of this form of arthritis."

Osteoporosis

Minocycline has been shown to increase bone mineral density, improve bone strength and

formation, and slow bone resorption in old laboratory animals with surgically-induced menopause[21].

Lyme disease

Lyme disease, or borreliosis, is an emerging infectious disease caused by the bacterium *Borrelia burgdorferi* and is transmitted to humans by the bite of infected blacklegged ticks. Minocycline may be useful for the treatment of Lyme disease[19].

Rosacea

Rosacea is a common inflammatory condition of the skin on the face that causes redness that looks like a flush or blush. It is sometimes called acne rosacea, which is misleading because rosacea and acne are two totally different conditions. Minocycline reduces the redness, papules, pustules and eye symptoms of rosacea. The antibiotic is usually prescribed for 6 to 12 weeks, the duration and dose depend on the severity of the rosacea. Further courses are often needed as the antibiotics don't cure the disorder.

Sarcoidosis

Sarcoidosis is a disease that results from a specific type of inflammation of tissues of the body. Studies[24] indicate that minocycline may be beneficial for the treatment of cutaneous sarcoidosis.

Cystic fibrosis[22-23]

Cystic fibrosis (also known as CF, mucoviscoidosis, or mucoviscidosis) is a hereditary disease that affects mainly the exocrine (mucus) glands of the lungs, liver, pancreas, and intestines, causing progressive disability due to multisystem failure.

Periodontitis

Periodontitis is a dental disorder that results from progression of gingivitis, involving inflammation and infection of the ligaments and bones that support the teeth. Minocycline is used to control bacteria and reduce the size of periodontal pockets. The periodontist puts the minocycline micro-spheres into the pockets after scaling and root planing. The particles release minocycline slowly over time.

Minocycline "pros" and "cons"

Advantages:

Very effective. Minocycline has several advantages over other tetracyclines in the treatment of acne, including more rapid clinical improvement, superior efficacy and effective absorption with or without food.

Less photosensitizing. Photosensitivity is least likely with minocycline than with other tetracyclines[25-26].

High concentrations in the tissues. Minocycline is widely distributed in body tissues[27], with higher concentrations being found in cerebrospinal fluid and sputum than with other tetracycline antibioticss. As in blood, the concentration in tissues is generally 2 to 4 times higher with minocycline than with tetracycline. Equivalent blood and tissue levels achieved whether administered intravenously or orally.

Long half-life (from 11 to 23 hours).

Broader spectrum of antimicrobal activity. Against certain pathogens, minocycline is more potent than the other tetracyclines. Minocycline has excellent in vitro inhibitory activity against both Staphylococcus aureus and coagulase-negative staphylococci, particularly methicillin-resistant S. aureus and methicillin-resistant S. epidermidis strains[3-5].

Can be used in renal impairment. Minocycline, like doxycycline and unlike other tetracyclines, can be used in patients with renal impairment (malfunction of the kidneys). Doxycycline and minocycline are eliminated through the hepatobiliary and gastrointestinal tracts. Most tetracyclines should be avoided in patients with renal insufficiency.

Less likely to cause bacterial resistance. Minocycline produces less antibiotic resistance than tetracycline.[28-29] Bacterial cell membranes contain a lipid layer. One mechanism of building

up a resistance to an antibiotic is to produce a thicker lipid layer. This layer makes it difficult for an antibiotic to penetrate. Minocycline chemical structure makes it the most lipid soluble of all the tetracyclines.

Disadvantages:

Expensive. Minocycline is considerably more expensive than the other generic tetracyclines.

Contraindicated in children. May cause enamel hypoplasia and permanent teeth discoloration.

Lupus-like syndrome. Minocycline is more likely than other tetracyclines to produce a lupus-like syndrome. Minocycline-induced lupus is characterized by the development of non-specific symptoms after long-term consumption of the drug, and the patient usually continues to take minocycline despite their illness as the association is not immediately obvious1. These abnormalities tend to occur after prolonged therapy (often longer than 12 months).

Serum sickness-like reaction. Minocycline induced serum sickness like reaction (SSLR) was first reported in 199030. This is a type of delayed allergic reaction, in which the immune system interprets the antibiotic as a foreign threat. A serum sickness-like reaction (SSLR) to drug usually consists of cutaneous rash, arthralgia/arthritis, and, often, fever.

Photosensitivity. Minocycline may increase sensitivity to sunlight, resulting in more frequent sunburns or the development of rashes following sun exposure.

Intracranial hypertension (pseudotumor cerebri) is an accumulation of fluid around the brain. Minocycline can cause the rare condition of secondary intracranial hypertension31 which has initial symptoms of headache, visual disturbances, and confusion.

Dizziness and other vestibular side effects. Minocycline can cause quite severe dizziness, nausea, vertigo and vomiting32. Vertigo has been reported in as many as 86% of individuals in some series33.

Hyperpigmentation. Unlike other tetracyclines, minocycline can cause a potentially irreversible slate-grey hyperpigmentation of the skin. Blue or blue-black oral pigmentation was seen in 10% of patients taking minocycline for at least 1 year; the rate increased to 20% after 4 years of continuous use2. Large daily doses of ascorbic acid (vitamin C) may prevent this phenomenon34.

Mode of action

Antibacterial

The tetracyclines are primarily bacteriostatic and are thought to exert their antimicrobial effect by the inhibition of protein synthesis.

Minocycline is a semisynthetic derivative of tetracycline and is active against many tetracycline resistant strains of organisms such as staphylococci, streptococci and E. coli. Thus the combined results of many studies show its activity against approximately 87% of tetracycline resistant staphylococci. Minocycline is also active against many strains of staphylococci which are resistant to penicillin G and certain semisynthetic penicillins.

Neuroprotective effect

Minocycline and other tetracycline derivatives have neuroprotective effects unrelated to their antimicrobial properties. Minocycline has the greatest permeability of all tetracyclines through the blood-brain barrier and is well suited for treatment of CNS disorders.

Minocycline can reduce neuronal death after excitotoxicity and ionizing radiation in culture6-7 and in animal models of stroke7-9, Parkinson's disease10-11, Huntington's disease12, and amyotrophic lateral sclerosis13. The neuroprotective effects of minocycline have been attributed both to reduced inflammation and a direct effect on neuronal survival.

Anti-inflammatory effect

Minocycline induces anti-inflammatory and antinociceptive effects unrelated to its antimicrobial activitiy15. Although the exact mechanisms of minocycline anti-inflammatory effects are still poorly

understood, they may include the inhibition of matrix metalloproteinase-2 activity, the inhibition of inducible nitric oxide synthase14, prostaglandin E2, caspase-1, caspase-3, and COX-2 expressions and the impairment of cytokine production.

Time for Minocycline to clear out the system

Minocycline half-life is 16 hours (range: 11-23 hours).

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