OASIS DERMATOLOGY GROUP

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Hydroxychloroquine

Hydroxychloroquine (brand name: Plaquenil), a derivative of chloroquine, was approved by the U.S. Food and Drug Administration (FDA) in 1955 for the treatment of malaria. While hydroxychloroquine shares structural similarities with chloroquine, it is particularly distinguished by its widespread use in systemic autoimmune and dermatologic disorders. Hydroxychloroquine is an oral medication that is rapidly absorbed and metabolized in the liver, with high tissue binding, particularly in melanin-rich tissues such as the retina. Its long half-life, approximately 45 days, presents both therapeutic advantages and challenges in terms of monitoring and side effect management.

Mechanism of Action

Hydroxychloroquine's therapeutic effects stem from its anti-inflammatory and immunomodulatory properties. In diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus, hydroxychloroquine suppresses T-lymphocyte activation and reduces the inflammatory response. This is thought to occur through the inhibition of lysosomal acidification, which reduces leukocyte chemotaxis and their subsequent migration to sites of inflammation . Furthermore, hydroxychloroquine diminishes the activation of toll-like receptors, which are pivotal in the immune response, and reduces the production of rheumatoid factor and acute-phase reactants in RA patients.

In malaria treatment, hydroxychloroquine exerts its antiprotozoal effects by preventing the parasitic *Plasmodium* species from utilizing hemoglobin in red blood cells, impairing the parasite's ability to survive and replicate. It is effective against multiple *Plasmodium* species, including *P. vivax*, *P. malariae*, *P. ovale*, and some strains of *P. falciparum*.

Clinical Uses

Hydroxychloroquine is utilized in the management of various systemic and dermatologic conditions:

- ***Systemic and Discoid Lupus Erythematosus (SLE):*** Hydroxychloroquine is foundational in the management of SLE, helping to prevent disease flares, reduce organ damage, and improve survival. Additionally, it plays a role in reducing the risk of bone mass loss, thrombosis, and alopecia in SLE patients.
- ***Rheumatoid Arthritis (RA):*** As a disease-modifying antirheumatic drug, hydroxychloroquine improves joint mobility, reduces swelling, and alleviates tenderness, although symptomatic relief may take up to six months.

- ***Sjögren's Syndrome:*** Hydroxychloroquine alleviates symptoms such as arthralgia, myalgia, lymphadenopathy, and dermatologic manifestations in Sjögren's syndrome, thereby enhancing patients' quality of life.
- ***Idiopathic Vasculitis and Post-Lyme Disease Arthritis:*** Hydroxychloroquine may serve as an adjunct in managing autoimmune diseases like idiopathic vasculitis and inflammatory arthritis following Lyme disease.
- ***Dermatologic Conditions:*** Hydroxychloroquine is effective in treating porphyria cutanea tarda, polymorphous light eruption, and graft-versus-host disease, where it helps control skin lesions and systemic symptoms. Its role in managing discoid lupus erythematosus is also critical, especially in preventing disease progression and reducing scarring.

In malaria prevention, hydroxychloroquine is typically initiated 1-2 weeks before travel and continued for 4–8 weeks post-return to ensure complete parasite eradication.

Side Effects

While hydroxychloroquine is generally well-tolerated, several side effects can occur, including:

- *Gastrointestinal symptoms:* nausea, loss of appetite, diarrhea, and abdominal discomfort
- *Central nervous system effects:* Headaches, dizziness, and visual disturbances
- *Dermatologic reactions:* rashes, and in rare cases, it may exacerbate psoriasis
- *Neuromuscular toxicity:* muscle weakness or myopathy

More severe side effects, though less common, include:

- *Retinal toxicity:* A critical concern with long-term use, where hydroxychloroquine accumulates in the retina, potentially leading to irreversible vision impairment. Regular ophthalmologic monitoring is essential, with baseline retinal exams followed by assessments every 6-12 months.
- *Blood dyscrasias:* Hydroxychloroquine can induce anemia, leukopenia, and thrombocytopenia by affecting bone marrow function.
- *Severe dermatologic reactions:* Rare but serious conditions such as exfoliative dermatitis and Stevens-Johnson syndrome have been linked to hydroxychloroquine use.
- *Cardiovascular complications:* Arrhythmias can occur, particularly in patients with pre-existing heart conditions or those on other drugs interacting with hydroxychloroquine.

Drug Interactions and Precautions

Hydroxychloroquine interacts with several drugs, including those that alter its metabolism. For example, hydroxychloroquine may inhibit the metabolism of penicillamine (used in RA) and propafenone (used for arrhythmias), potentially affecting their efficacy. Care should be taken when prescribing hydroxychloroquine to patients with G6PD deficiency or impaired liver and renal function, as these conditions may exacerbate side effects. In particular, hydroxychloroquine

interacts negatively with digoxin and acetaminophen, necessitating careful monitoring when used together.

Hydroxychloroquine is classified as pregnancy category C, meaning it should be used during pregnancy only if clearly needed. It is generally recommended for SLE patients to continue hydroxychloroquine during pregnancy to prevent disease flares, as studies have not shown teratogenic effects. However, consultation with a healthcare provider is essential before use in pregnancy.

Conclusion

Hydroxychloroquine remains a critical medication in the treatment of systemic autoimmune diseases such as SLE, rheumatoid arthritis, and Sjögren's syndrome, as well as various dermatologic conditions. Its immunomodulatory and anti-inflammatory properties make it invaluable in these chronic diseases. However, the potential for long-term side effects, particularly retinal toxicity, underscores the need for careful monitoring. Ophthalmologic assessments, drug interaction management, and consideration of individual patient factors, including pregnancy and organ function, are essential components of hydroxychloroquine treatment regimens.

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