



## ADVERSE EFFECTS OF HYDROXYCHLOROQUINE (PLAQUENIL) IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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**Abstract:** *Hydroxychloroquine (Plaquenil) is an antimalarial drug commonly used in the management of autoimmune diseases such as rheumatoid arthritis (RA). While generally considered safe and well-tolerated, hydroxychloroquine is associated with a range of adverse effects, some of which can be serious. This article reviews the common and rare side effects of hydroxychloroquine when used in the treatment of RA, along with mechanisms, risk factors, and clinical implications.*

### **Introduction:**

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized by persistent synovial inflammation, progressive joint destruction, and significant functional disability. It affects approximately 0.5–1% of the global population and poses a major burden on patients' quality of life and healthcare systems. The management of RA has evolved substantially over recent decades, with the goal of achieving remission or low disease activity through early initiation of disease-modifying antirheumatic drugs (DMARDs).

**Hydroxychloroquine (HCQ)**, a derivative of chloroquine originally developed as an antimalarial agent, has been widely used as a conventional synthetic DMARD in the treatment of mild to moderate RA. It is particularly favored due to its immunomodulatory properties, relatively low toxicity compared to other DMARDs, and its beneficial effects in comorbid conditions such as systemic lupus erythematosus and Sjögren's syndrome. HCQ functions by



interfering with lysosomal activity and antigen presentation in immune cells, thereby reducing the inflammatory response.

Despite its established efficacy and safety profile, hydroxychloroquine is not devoid of adverse effects. While most side effects are mild and reversible, some can be serious and potentially irreversible, especially with prolonged use or in predisposed individuals. The most concerning adverse effect is **retinopathy**, which may lead to irreversible visual impairment if not detected early. Other reported side effects include gastrointestinal disturbances, cutaneous reactions, neuromuscular complications, and cardiotoxicity.

Given the widespread and long-term use of hydroxychloroquine in RA management, a clear understanding of its potential adverse effects is crucial for clinicians to ensure optimal therapeutic outcomes while minimizing risks. This article aims to provide a comprehensive overview of the adverse effects associated with hydroxychloroquine therapy in RA patients, highlight risk factors, and underscore the importance of appropriate screening and monitoring strategies.

### **Mechanism of Action and Pharmacokinetics**

Hydroxychloroquine modulates the immune system by inhibiting lysosomal activity and antigen presentation, reducing pro-inflammatory cytokines such as TNF-alpha and IL-1. It also interferes with toll-like receptor signaling. Its long half-life (40-50 days) and tissue accumulation contribute to both its efficacy and potential toxicity.

### **Common Adverse Effects**

Common side effects include gastrointestinal disturbances (nausea, diarrhea, abdominal pain), skin reactions (rashes, pigmentation changes), and central nervous system symptoms (headache, dizziness). These effects are typically mild and reversible upon drug discontinuation.

### **Serious and Rare Adverse Effects**



Serious adverse effects include retinal toxicity, cardiomyopathy, and myopathy. Retinopathy is the most notable complication and can lead to irreversible vision loss. Risk factors include long duration of therapy, high cumulative dose, renal impairment, and pre-existing retinal disease. Cardiotoxicity, although rare, can manifest as conduction disorders and heart failure.

### **Monitoring and Risk Mitigation**

Regular ophthalmologic screening is recommended to detect early signs of retinal damage. Baseline and periodic ECG monitoring may be advised for patients with cardiovascular risk factors. Dose adjustment in renal or hepatic impairment is crucial to minimize toxicity.

### **Conclusion**

Hydroxychloroquine remains a cornerstone in the treatment of RA due to its efficacy and relatively safe profile. However, clinicians must be vigilant in monitoring for adverse effects, particularly those affecting the eyes and heart. Patient education and individualized risk assessment play a key role in optimizing treatment outcomes.

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