Canadian Rheumatology Association Position Statement on the Safety of Hydroxychloroquine in the Treatment of Rheumatic Diseases

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The antimalarial drugs, chloroquine and hydroxychloroquine (HCQ), are essential drugs in the treatment of rheumatic diseases. HCQ is currently the only anti-malarial drug available in Canada for the treatment of rheumatic diseases. HCQ is important in the management of systemic lupus erythematosus (SLE) (1,2). It has been shown to improve patient survival (3,4,5) and prevent disease flares (6,7). Other important benefits include lowering cholesterol (8,9,10), improving glucose metabolism (11,12), decreasing thrombovascular (13) and cardiovascular events (14), and decreasing organ damage (15). In addition, it is safe to use during pregnancy (16). HCQ is also important in the treatment of rheumatoid arthritis and is one of the more commonly prescribed disease-modifying antirheumatic drugs (17,18).

As with all medications, the safety of HCQ needs to be monitored. Retinal toxicity is an important potential side effect encountered and monitoring for this is important (19,20). Skin hyperpigmentation (21), myopathy (22,23), including cardiomyopathy (24,25), are other uncommon side effects. Nonetheless, HCQ is considered to be one of the safest drugs used by the rheumatologist. Data from a rheumatic disease registry found that in evaluating the relative toxicity of several drugs used in rheumatology, HCQ was the least toxic of the drugs studied (26).

With the COVID-19 pandemic, significant cardiac toxicity has been reported with the use of antimalarial drugs (27,28). Concerns have been raised about the increased occurrence of QT prolongation leading to serious arrhythmias such as Torsade de Pointes and cardiac arrest (27,28). However, this pandemic resulted in the unconventional use of HCQ (29), frequently at much higher doses than used to treat rheumatic diseases, and often in combination with azithromycin which may further prolong the QT interval (28). In addition, COVID-19 infection itself can cause arrhythmias and cardiomyopathy (28,30). These patients also commonly have hypokalemia, hypomagnesemia, as well as fever, which can potentiate QT prolongation (30). Cardiac toxicity is known to increase with the concomitant use of drugs that may prolong the QT interval and azithromycin is one of the drugs known to do this (28).

With conventional dosing and use, cardiac toxicity has been rarely encountered in rheumatology practice (29). Recently, concerns have been raised about the occurrence of the prolonged QT interval and resultant cardiac arrhythmias with antimalarials. However, in a study in SLE patients on antimalarials, the prevalence of prolonged QT interval was very low, only 0.7% (31). This study also demonstrated that higher cumulative anti-malarial dose decreases the odds of ECG conduction abnormalities in SLE patients, suggesting a protective effect (31). Others showed that the prevalence of conduction abnormalities in SLE patients on HCQ is similar to a comparable healthy population (32). There was a non-statistically significant increase in the odds of ECG structural abnormalities in those having cumulative antimalarial dose above the median (31). Possible risk factors for cardiotoxicity in patients receiving antimalarials include older age, pre-existing cardiac disease and renal insufficiency (31).

The use of HCQ to treat rheumatic diseases is overall felt to be safe when prescribed appropriately and when the patient is monitored and followed by a rheumatologist (29). The significant benefits of HCQ, particularly in SLE, certainly outweigh its risks.

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