CHAPTER 7

ANTIMALARIAL TREATMENT IN DERMATOLOGY

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INTRODUCTION

Antimalarial drugs have been known since long time. Firstly quinine is founded as natural antimalarial.[1] It extracted from South American cinchona bark tree.[1] It was used for protect healty persons against to malaria. In 1894, Payne showed beneficial effects of antimalarials on the lupus erythematosus patients.[2] Later, synthetic antimalarials are produced such as quinacrine(in 1930), chloroquine (in 1934), hydroxychloroquine (in 1955).[3] Page succesfully treated 18 cutaneus lupus patiens with quinacrine (QC) although this patients were unresponsible to quinine treatment.[4] But then chloroquine (CQ) and hydroxychloroquine (HCQ) became most appropriate drugs for the cutaneus lupus treatment.[5] Because they are well-tolerated and more effective than other antimalarials on lupus patients.[5] Usage of antimalarial drugs in dermatology is not limited only lupus; they are alse used various skin disease.

PHARMACOKINETICS

CQ and HCQ are absorbed in gastrointestinal system about %90 to %100.[6-7] They reach stable plasma levels after 4-6 weeks.[6-7] CQ binds plasma proteins and this proteins accumulate tissues such as liver, kidneys, spleen,lungs,blood cells.[6-7] On the other hand, it is also accumulate some tissues which include melanin.[8] So it's concentrations can be high in skin and retinal cells.[8] CQ has a long half-life. It can stay in skin about 6-7 months after discontinuance of treatment.[8] CQ and HCQ can pass to placenta and can join to milk as little amount.[9]

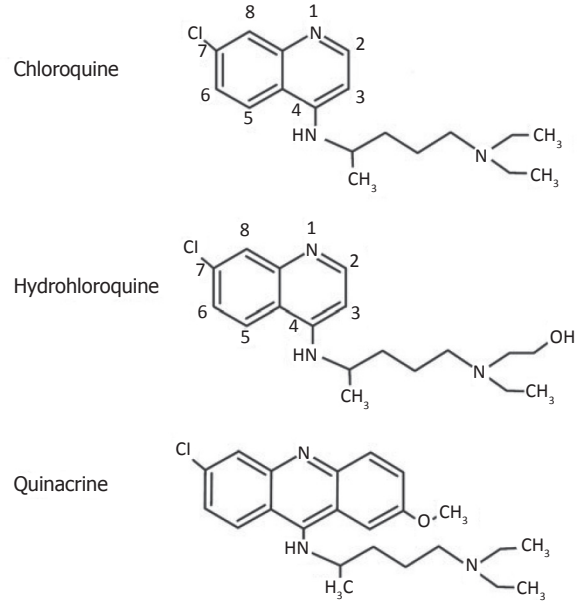


Figure 1. Antimalarial's Chemical Strustures.

MECHANISM OF ACTION

Antimalarial drugs have many different mechanisms. So they have very various effects on metabolism of patients. Some of them are antiinflamatory, immunomodulatory, antiproliferative and photoprotective effects.[10] Antimalarials can cross to plasma membran easily and enter the asidic vesiculs, then start to accumulate in there(especially lisosoms).[10] PH of the lisosom increases; thus, presentation of antigens to T-lymphocytes disrupts.[31-12] Releasing of cytokines is blocked on this pathway and an anantiinflammatory effect occurs.[31-12]

On the other side, on a similar mechanism; when PH increases in lisosoms, exogen peptides show more affinity to MHC molecules than autoantigen peptides.[13-14] For this reason, antimalarials can play a role as a immunomodulators without causing any immunosupression.[13-14] Other mechanism of antimalarials explained on table 1-2.

TABLE 1. MECHANISMS OF ANTIMALARIAL DRUGS29-30-31
1.Inhibition of cytokine release: interleukin (IL) 1, IL-2, IL-6,IL-18, tumor necrosis factor α , interferon γ
2.Inhibition of antigen presentation
3.Inhibition of the activity of cytotoxic CD8+ T lymphocytes and self-reactive CD4+ lymphocytes
4.Regulation of apoptosis
5.Inhibition of stimulation of TLR (toll-like receptors) 9 that join in immune response
6.Decreasing activity of natural killer cells
7.Inhibition of lysosome protease activity
8.Reduce in membrane receptor concentrations: reduced response to mitogenic stimuli
9.Inhibition of polymorphonuclear chemotaxis
10.Superoxide radical block

PREGNANCY

Antimalarials can cross the placenta.[79] However according to a few studies about safety of these drugs in pregnancy, it wasn't detected increasing risk for congenital anomalies.[80-83,9,85,70] According to some studies with pregnant patient who have SLE, continuing treatment is usually reasonable because when stopping drug, activity or complications of disease can more damage than usage of drug in fetus.[31]

CONCLUSION

Antimalarials have important for every dermatologists. When comparing to other immunomodulatory drugs,antimalarials have quite safety profils. Most important subject in this therapy is arrangement of dosage. Various disease can be treated with antimalarials as safety with correct doses.

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