Chloroquine and Hydroxychloroquine retinopathy in Rheumatologic Patients: Incidence and Risk Factors

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Introductions

- Elderly (> 60)
- Duration > 5 years
- Kidney or liver dysfunction
- Cumulative dose
  - CQ > 460 g, HCQ > 1000 g
  - Daily dose
  - CQ > 250 mg/d or 3 MKD
  - HCQ > 400 mg/d or 6.5 MKD


Objective

- To determine the incidence and risk factors of CQ and HCQ retinopathy in Thai patients.

Methods
Retrospective cohort study.

<table>
<thead>
<tr>
<th>Inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>started receiving CQ or HCQ from 2004 - 2014</td>
</tr>
<tr>
<td>Rheumatologic patients, aged &gt; 15 years old</td>
</tr>
<tr>
<td>Underwent routine eye screening examination</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete medical records</td>
</tr>
<tr>
<td>switched between CQ and HCQ</td>
</tr>
<tr>
<td>retinal or macular disease or optic neuropathy</td>
</tr>
</tbody>
</table>

Methods

- Basic data: Age, Sex, Body weight, Underlying disease
- Rheumatologic disease
- Duration of receiving medication
- Dosage: cumulative dose, daily dose
- Presence of signs of CQ or HCQ retinopathy
- AAO criteria for diagnosis

Results

234 patients

CQ: 173 pts

HCQ: 61 pts

Disease: 14

Non disease: 159

Incidence 8.09%

Incidence 3.28%
### Results: CQ

#### Risk factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Retinopathy Median (min, max)</th>
<th>No retinopathy Median (min, max)</th>
<th>Hazard ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>53(27,65)</td>
<td>44(15,78)</td>
<td>1.06 (1.00-1.12)</td>
<td>0.04</td>
</tr>
<tr>
<td>Age &gt; 60 years*</td>
<td>3(21)</td>
<td>16(10)</td>
<td>2.98 (0.82-10.73)</td>
<td>0.10</td>
</tr>
<tr>
<td>Sex(Male)*</td>
<td>6(3)</td>
<td>37(23)</td>
<td>1.68 (0.55-5.14)</td>
<td>0.36</td>
</tr>
<tr>
<td>Body weight(kg)</td>
<td>57(48,98)</td>
<td>53(36,80)</td>
<td>1.00 (1.00-1.10)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cumulative dose (g)</td>
<td>101.3(14,325.1)</td>
<td>91.56(111.1)</td>
<td>0.99 (0.98-1.00)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

#### Cumulative dose > 460 g

- Daily dose (mg/day) | 250(46,8,250) | 234(54,3,500) | 1.00 (0.99-1.01) | 0.50
- Daily dose > 250 mg/day | 0 | 3 | - | -
- Daily dose/body weight(mg/kg/day) | 4.20(8,18.5) | 4.20(8,25,64) | 1.00 (0.92-1.16) | 0.58
- Daily dose > 3 mg/kg/day | 9 | 126 | 1.27 (0.42-3.81) | 0.67

*Data was shown in numbers(percentage)

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### Results: CQ

#### Cumulative dose: significant difference but all of retinopathy received ≤ 460 g

- Age > 60 years*        | 3(21) | 16(10) | 2.98 (0.82-10.73) | 0.10
- Sex(Male)*             | 6(3) | 37(23) | 1.68 (0.55-5.14) | 0.36
- Body weight(kg)        | 57(48,98) | 53(36,80) | 1.00 (1.00-1.10) | 0.04
- Cumulative dose (g)    | 101.3(14,325.1) | 91.56(111.1) | 0.99 (0.98-1.00) | 0.03

#### Kaplan-Meier survival estimate

- Duration (days) 72(13,1920) | 30(7,17,200) | - | 0.69
- Duration > 5 years | 1 | 25 | - | 0.39

#### Duration: Incidence were high in the first 3 years.

### Results: HCQ

#### Risk factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Retinopathy Median (min, max)</th>
<th>Non-retinopathy Median (min, max)</th>
<th>Hazard ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>37.5(36,39)</td>
<td>43(18,72)</td>
<td>0.96 (0.89-1.09)</td>
<td>0.80</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>0</td>
<td>6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sex(Male)*</td>
<td>0</td>
<td>13.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Body weight(kg)</td>
<td>56(54,65)</td>
<td>54(33,73)</td>
<td>1.04 (0.90-1.20)</td>
<td>0.62</td>
</tr>
<tr>
<td>Cumulative dose (g)</td>
<td>105(180,130)</td>
<td>77(68,4,375.6)</td>
<td>1.00 (0.98-1.01)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

#### Cumulative dose > 1000 g

- Daily dose (mg/day)    | 164(729,4,200) | 200(40,22,500) | 1.00 (0.98-1.02) | 0.86
- Daily dose > 400 mg/day | 0 | 1 | - | -
- Daily dose/body weight(mg/kg/day) | 3.2(1,9,4.4) | 3.8(0,7,9.8) | 0.93 (0.35-2.53) | 0.89
- Daily dose > 6.5 mg/kg/day | 0 | 6 | - | -

*Data was shown in percentage


**Results**

### Cumulative dose: all of patients received HCQ < 1000 g

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Duration (days)</th>
<th>Risk factor</th>
<th>Hazard ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>744 (60,320)</td>
<td>Median</td>
<td>1.00 (0.98-1.01)</td>
<td>0.62</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>331 (18,3052)</td>
<td>Median</td>
<td>-</td>
<td>0.18</td>
</tr>
</tbody>
</table>

### Daily dose: all of patients received HCQ < 400 mg/day or < 6.5 mg/kg/day

<table>
<thead>
<tr>
<th>Duration (days)</th>
<th>Cumulative dose (g)</th>
<th>Daily dose (mg/day)</th>
<th>Daily dose/body weight (mg/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 5 years</td>
<td>77 (8.4,375.6)</td>
<td>1.64 (12.9,20)</td>
<td>3.2 (0.9,4.4)</td>
</tr>
</tbody>
</table>

*Data was shown in percentage*

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**Discussion**

Previously: prevalence of CQ retinopathy 7.3-26.6%

Our study: incidence of CQ retinopathy 8.09%

Prevalence 14.9%

Previously: the incidence of HCQ retinopathy was 0 - 4%

Our study: incidence of HCQ retinopathy 3.28%

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**Discussion**

Thai patients have less body weight, more dose per kg.
Discussion

- CQ and HCQ bind to melanin pigment.
- Thais have more pigment than Caucasians.

Strength and limitations

- Strength
  - Cohort study: more temporal sequence
  - First study of HCQ retinopathy in Thailand

- Limitations
  - Retrospective
  - Small number in the HCQ group

Conclusions

- Incidence of CQ retinopathy: 8.09%
- Incidence of HCQ retinopathy: 3.28%

- Although, we found no clinical significant risk factors.
- In Thai people, CQ and HCQ retinopathy tend to occur in younger age with less duration and less cumulative dosage.

Conclusions

- Recommended eye screening exam starting at 6 months and then once or twice a year.
- The routine 250 mg CQ tablet should be used cautiously, especially in low-body weight patients.

- Suggest further study in a prospective cohort design in larger series.

Thank you.