PLAQUENIL MACULOPATHY
Anthony DeWilde, OD

Goals

Understand Diagnostic Tests
Understand AAO Recommendations
Develop Strategy for Diagnosis

Chloroquine

Malaria
Peruvian Bark (Quinine)
WWII
Not used in US
Hydroxychloroquine

Plaquinil
Safer Anti-Malarial
Used for
  Lupus
  Rheumatoid Arthritis
  Sjogren’s
  Lyme Arthritis

Side Effects

Headache
Anxiety / Depression
GI (Nausea, Cramps, Diarrhea)
Skin
Tinnitus
Vision Changes

Side Effects

Headache
Anxiety / Depression
GI (Nausea, Cramps, Diarrhea)
Skin
Tinnitus
Vision Changes
Plaenil Retinopathy

- Ganglion, Photoreceptor, RPE
- Atrophy
- Scotoma
- Irreversible Damage

Ophthalmology 2015;122:110-116

Risk Factors

- Age > 60
- Retinal Disease?
- Renal and/or Liver Disease
- Daily Dose
- Cumulative Dosage

Daily Dose

- Typically 400 mg/day
- Used to worry about weight
- Does not store in fatty tissue
- Concern now with height/ideal weight
## Cumulative Dosage

| HCQ | 1000 g | 400 mg/day | >5-7 years |

## Quantifying Risk

| 1-5 years | 1/1000 |
| >5 years | 1/100 |

## Quantifying Risk

Retrospective Review of 3500 patients
Taking Plaquenil ≥ 5 years

JAMA Ophthalmol. 2014 Dec;132(12):1453-60
Quantifying Risk

Found up to 7.5% had toxicity

Quantifying Risk

Risk factors
Dosage
Duration
Kidney disease
Tamoxifen use

Plaquinil

Quantify risk
Under 5 years = 1%
10 years = 2%
20 years = 4%
Testing

Find HCQ toxicity before it is visible on fundus
Prevent irreversible vision loss

Testing

Testing should be/have:
Noninvasive
Good Sensitivity/Specificity
Practical
Cost/Benefit
Common Diagnostics

Amsler Grid
Color Vision
Visual Fields (10-2)
mfERG
Fundus Autofluorescence (FAF)
OCT
Fundus Examination

Amsler Grid

Very poor sensitivity
Other macular disease

Color Vision

Not specific to HCQ toxicity
Other macular disease
Optic nerve disease
Not Recommended

- Fundus Photography
- Time Domain OCT
- Fluorescein Angiography
- Full-Field ERG
- Amsler Grid/Color Vision
- Electro-oculogram

mfERG

Measures bioelectrical potential
Gold standard

mfERG

Pro:
Objective
Reliable
Targets macula
mfERG

Con:
Interpretation
Expense
Hassle
Accessibility

FAF

Pro:
Objective
View changes over time
Con: Interpretation Available
Not as reliable as 10-2, SD-OCT, ERG

Visual Fields
24-2 and 30-2 not sufficient
Need 10-2 white-on-white
## Visual Fields

**False Positives**

*What is Sensitivity/Specificity?*

*Consider risk of developing toxicity*

<table>
<thead>
<tr>
<th>Risk before 7 years</th>
<th>Risk after 7 years</th>
<th>Specificity</th>
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</thead>
<tbody>
<tr>
<td>1/1000</td>
<td>1/100</td>
<td>90%</td>
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</table>

10-100 times more FALSE positives than TRUE
Visual Fields

Pro:
- Available
- Inexpensive
- Interpretation

Visual Fields

Con:
- Subjective
- Patients dislike
- False Positives

SD-OCT
“Flying Saucer”


25 people studied

9 abnormal fundus
16 normal fundus
SD-OCT
Correctly found abnormal 50%
Incorrectly abnormal 6%

HVF
Correctly found abnormal 50%
Incorrectly abnormal 50%

SD-OCT
Pro:
Available
Objective
Interpretation?
Con:
Early detection
Cost
<table>
<thead>
<tr>
<th>American Academy of Ophthalmology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2002 Recommendations</strong></td>
</tr>
<tr>
<td>High risk if &gt; 6.5 mg/kg/day</td>
</tr>
<tr>
<td>Color vision</td>
</tr>
<tr>
<td>10-2 or Amsler</td>
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</tbody>
</table>

| **2011 Recommendations**         |
| High risk if 1000g cumulative dose |
| Consider height                   |

| NO Color vision or Amsler Grid   |
| 10-2 combined with               |
| OCT, FAF, mfERG                  |
2016 Recommendations

High risk if >5 mg/kg/day REAL weight
or 6.5 mg/kg/day IDEAL weight

2016 Recommendations

Continues testing recommendations from 2011

Low risk drug if correct dosage
If proper dosage, should never see “bull’s eye maculopathy”
Consider modifying risk by modifying dosage
Only come in 200 mg tablets
Patient may want to take fewer than 14 tablets/week

Study of 500 patients started on Plaquenil
50% were on too high dose for ocular safety

Ophthalmology 2017;124:604-608

Height to take med safely based on IDEAL weight
Men - 5'5"
Women - 5'7"
For every 2" below ideal, subtract 1 tablet per week

Safe weight for 400 mg/day - based on REAL weight
180 lbs
For every 13 lbs less than this subtract 1 tablet/week

Recommendations

Baseline Examination
If low risk, then test after 5 years
If high risk, test yearly
Recommendations

High Risk
Kidney Disease
Liver Disease
Cumulative Dose
Tamoxifen Use

Recommendations

Fundus Exam
Subjective 10-2
Objective SD-OCT

Outcomes

(+) HVF, (+) SD-OCT
(+) HVF, (-) SD-OCT
(-) HVF, (+) SD-OCT
(-) HVF, (-) SD-OCT
Case 1

60 Year Old White Female
Blur at distance
Photophobia
Dry eye

Plaquenil x 20 years
400 mg/day
Lupus
5'4"
105 lbs - safe dosage is 200 mg

Case 1 - OD OCT
Case 1

Plaquenil toxicity
Should have been on lower dose
Need to discontinue medicine

Case 2

86 Year Old White Male
Blur at distance
Ocular History: Early AMD

Case 2

Medical History
Psoriatic Arthritis
HTN
CAD
Hyperlipidemia
Case 2

Medications
Plaquenil
Fluocinonide
Coreg
ASA 325 mg

Case 2

5'7" tall
130 lbs - would need 10 tablets/week

Case 2

Patient at VA since 1999
Every exam: RPE changes OS>OD
Called AMD
20/20- OD and OS
Case 2

September 2010
Ring shaped atrophy OS
Fundus Photos/OCT

Fundus OS

SD-OCT - OS
Management

Discontinue Plaquenil
See Rheumatologist -- Patient refused initially
Management

Patient eventually discontinued meds
Asymptomatic
Good outcome?

Case 3

71 Year Old White Male
Evaluation for Plaquenil Maculopathy
No vision complaints

On Plaquenil for 7 years
200 mg BID
RA/Lupus
Normal kidney, liver
Normal BMI
Case 3

5'11" tall
155 lbs - should be on 12 tablets/week

Case 3

BCVA 20/20 OD/OS
Anterior Segment Unremarkable
Posterior Segment - Mild ERM OD

OD
Case 3

Normal macula
Normal OCT
> HVF
Case 3

Do we continue medication?
Do we discontinue medication?

Plan
Continue medication
RTC 6 months - retest

Case 4

64 Y/O White Male
10 years on Plaquenil for RA
+AMD
Case 4

5'11"
182 lbs

Case 4 - HVF OD

Case 4 - HVF OS
Case 4

Informed Rheumatologist
They discontinued Plaquenil
Was this the right call?
Could we have done better?

Frustrations

False positives
No gold standard
We are the authority
Benefits of Plaquenil

Goals

Understand Diagnostic Tests
Understand AAO Recommendations
Develop Strategy for Diagnosis
Thank you!

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