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Effect of Hydroxychloroquine Therapy Duration on Retinal Pigment Epithelium in Rheumatological Diseases by Optical Coherence Tomography. A Systematic Review and Meta-Analysis

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Abstract

Background: Hydroxychloroquine is used increasingly in the management of a variety of autoimmune disorders, However, Hydroxychloroquine has been associated with irreversible visual loss due to retinal toxicity. Cessation of the use of hydroxychloroquine at an early stage of damage might prevent functional loss; however, after maculopathy has developed, cessation of the drug does not show clinical recovery. Because discontinuation of therapy may reverse retinal toxicity, early detection of toxicity changes is important.

Aim of Study: To find a relationship between duration of hydroxychloroquine therapy in rheumatological diseases and retinal pigment epithelium changes by optical coherence tomography.

Material and Methods: Medical data bases and Cochrane Library were searched for studies from 2011 until 2021. The primary outcome was Retinal Pigment Epithelium thickness ,the secondary outcome was Outer Retinal Thickness and the third outcome was full retinal thickness but unfortunately we didn't find enough papers for the first two outcomes so, our outcome will be the full retinal thicknessat central macula in its four quadrants: Superior, inferior, nasal and temporal difference between hydroxychloroquine drug users of rheumatological patient in different duration of therapy and healthy controls using optical coherence tomography.

Results: Five trials (cross-sectional studies) involved studies and they show in superior quadrant of central macular thickness difference between HCQ users and controls as: Cohran Q = 8.577135 (df = 4) p = 0.0726 and Moment-based estimate of between studies variance = 16.257044, I^2 (inconsistency) = 53.4% (95% CI = 0% to 80.9%), the inferior quadrant of central macular thickness difference as: Cohran Q = 7.759158 (df = 4) p = 0.1008 and Moment-based estimate of between studies variance = 15.932414, I^2 (inconsistency) = 48.4% (95% CI = 0% to 79.4%),while nasal quadrant of central macular thickness difference was: Cohran Q = 14.113529 (df = 4) p = 0.0069 and Moment-based estimate of between studies variance = 37.768684, I^2 (inconsistency) = 71.7% (95% CI = 0% to 86.8%) and the temporal quadrant of central macular thickness difference between HCQ users and controls was: Cohran Q = 29.001671 (df = 4) p<0.0001, Moment-based estimate of between studies variance = 86.284155, I^2 (inconsistency) = 86.2% (95% CI = 65.5% to 92.3%).

Conclusion: OCT enables quantitative evaluation of the central macular thickness in rheumatological eyes under treatment of hydroxychloroquine and it has demonstrated the ability of OCT to detect early changes in hydroxychloroquine users group as compared to control group by finding significant thinning between themas found in three studies and decrease inner retinal layers thickness and no changes in outer retinal layers thickness as in one study and no difference in central macular thickness between cases and controls in another study.

No relation between retinopathy and neither duration of treatment nore cumulative dose.

Key Words: *OCT – Optical coherence tomography – Rheumatological diseases – Hydroxychloroquine – Hydroxychloroquineretinotoxicity – Rheumatoid arthritis – Systemic lupus erythematosus – Retinal pigment epithelium.*

Introduction

HYDROXYCHLOROQUINE (HCQ) is antimalarial drug which have been used since 1950 to treat auto-inflammatory diseases such as rheumatoid arthritis (RA), and connective tissue diseases (CTDs) including systemic lupus erythematosus (SLE) **[1]**.

Hydroxychloroquine can cause pathologic ocular damage include corneal deposits, posterior subcapsular lens opacity, ciliary body dysfunction, macular pigment loss, peripheral bone spicules formation, vascular attenuation and optic disc pallor. Ocular symptoms of retinopathy associated with this medication include blurred vision, partial loss of central and peripheral vision and in the later stage, loss of night vision **[2]**.

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Hydroxychloroquine retinal toxicity appears as a result of an affinity to bind to melanin in the retinal pigment epithelium (RPE) and cause damage to the macular cones outside of the fovea. The drug inhibits RPE lysosome activity, reduces phagocytosis of shed photoreceptor outer segments causing an accumulation of outer receptor segments [3].

The risk of toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years. High dose and long duration of use are the most significant risks. The risk of toxicity depends on the daily dose (5mg/kg of HCQ), duration of treatment exceeding 5 years [4].

In response, pigment-containing RPE cells migrate into the outer nuclear and outer plexiform layers of the retina resulting in irreversible photoreceptor loss and RPE atrophy. The development of retinopathy is thought to be completely reversible on discontinuation of the drug at the preclinical stage. The patients with early retinopathy can be asymptomatic, and the fundus may remain normal before any signs of maculopathy appear; hence, screening for early detection in the premaculopathy stage is recommended [5].

When retinopathy is recognized early, before the retinal pigmented epithelium is damaged, there is only a limited progression after discontinuing medication and visual loss can be avoided; hence, screening for early detection of retinal toxicity is very important. The American Academy of Ophthalmology recommendations on screening for hydroxychloroquine retinopathy suggest that after a baseline fundus examination to rule out any preexisting maculopathy, patients should undergo both an automated visual field examination and an optical coherence tomography (OCT) which are considered the primary screening tests because they are widely available and shows the damage functionally, while multifocal electroretinogram (mfERG) and fundus autofluorescence (FAF) are considered useful additional screening tests and shows the damage topographically. OCT was shown to be less sensitive than visual field and multifocal ERG but, it gives higher specificity of structural changes, noninvasive nature and wide availability in many clinics [6].

Material and Methods

Design:

We searched the electronic medical databases, including PubMed, EMBASE, Scopus, Web of scince and Cochrane Library with a combination with key words as "OCT", "optical coherence tomography", "rheumatological diseases", "hydroxychloroquine", "hydroxychloroquine retinotoxicity", "rheumatoid arthritis", "systemic lupus erythematosus", "retinal pigment epithelium" databases were searched for articles from 2011 until 2021 following the PRISMA guidelines.

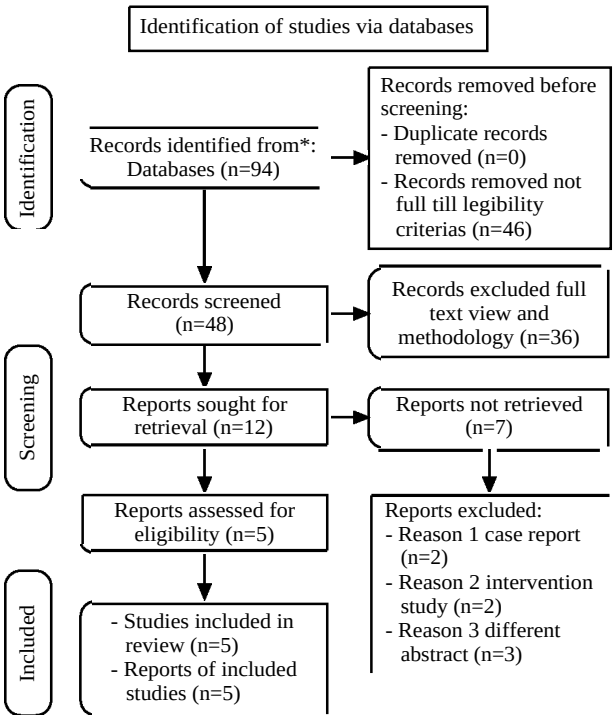

Fig. (1): PRISMA flow diagram showing process of studies selection.

Inclusion/exclusion criteria:

To be included in the meta-analysis, the articles had to meet the following criteria:

- Population: Rheumatological patients aged from 20 to 50 of both sex on hydroxychloroquine therapy with different durations.
- Intervention: OCT in rheumatological patients.
- Comparator: OCT in healthy controls.
- Outcome parameters: Detecting early changes of retinal pigment epithelium thickness or outer retinal thickness or full retinal thickness using OCT.
- Study design: Clinical trials, whether randomized or nonrandomized, prospective and retrospective comparative case-control studies.

The excluded articles:

Exclusion of animal studies, reviews, book chapters, thesis, editorial letters and papers with overlapped dataset.

Table (1): Included studies characteristics.

Study ID	Study design	Sample size (n)	Female/male (n)	Age (y) mean±SD	Duration of use (y) mean±SD
A.H. El Habbak et al., 2021	Cross-sectional	HCQ20 (20 eyes) Control 20 (20 eyes)	HCQ 19/ 1 Control 19/ 1	HCQ 43.55±15.4 Control 41.30±13.4	>2ys.
Marwa et al., 2021	Cross-sectional	HCQ 100 (100 eyes) Control 50 (50 eyes)	HCQ 100/0 Control 50/0	HCQ 40.8±10.0 Control 38.7±8.4	5.9±4.6
Zeynep D and Orhan A., 2018	Cross-sectional	HCQ 31 (31 eyes) Control 21 (21 eyes)	HCQ 29/2 Control 19/2	HCQ 46.3±12.5 Control 45.5±8.3	–
Riham et al., 2015	Cross-sectional	HCQ40 (40 eyes) Control 40 (40 eyes)	HCQ 40/0 Control 40/0	HCQ 49.95±7.78 Control 50±7.38	3.8±2.79
Yigit et al., 2013	Case-control	HCQ15 (15 eyes) Control 15 (15 eyes)	HCQ 13/2 Control 12/3	HCQ 49±9.89 Control 48.93±9.51	<5 years

Data collection and extraction:

Eligibility screening studies was conducted in a two step-wise manner (title/abstract screening and full-text screening). Each step was done by two reviewers independently according to the predetermined criteria. The duplicated articles were removed primarily using the Endnote X8 program (Thompson Reuter, USA) and manually using titles and abstracts screening.

The data was extracted by two independent authors and revised by another two independent authors. The characteristics of each study were extracted as following: Hydroxychloroquine using, changes of retinal pigment epithelium thickness or outer retinal thickness or full retinal thickness, these outcomes were reported across the included studies.

Statistical analysis:

Statistical analysis was done using an R-based software (Openmeta) and StatsDirect statistical software version 2.8.0 (StatsDirect Ltd. StatsDirect statistical software. http://www.statsdirect.com . England: StatsDirect Ltd. 2013.).

Testing for heterogenety:

Studies included in meta-analysis were tested for heterogeneity of the estimates using the following tests:

1- Cochran Q chi square test: A statistically significant test (p-value <0.1) denoted heterogeneity among the studies.

2- I-square (I^2) index which is interpreted as follows:

- I^2 = 0% to 40%: Unimportant heterogeneity.
- I^2 = 30% to 60%: Moderate heterogeneity.
- I^2 = 50% to 90%: Substantial heterogeneity.
- I^2 = 75% to 100%: Considerable heterogeneity.

Results

We obtained 57 articles from PubMed, 11 articles from Scopus and 12 from the Web of Science. Then, 48 articles manually underwent title and abstract screening and 12 articles underwent full-text review. Five studies finally met our inclusion criteria that evaluated central macular thickness at its four quadrants: Superior, inferior, nasal and temporal change in rheumatological patients under treatment with hydroxychloroquine in different durations of therapy using OCT, with a total of 206 cases with 206 eyes compared to 146 healthy controls with 146 healthy eyes. The mean age of patients across the studies ranged between 20 and 50 years.

The statistical analysis for superior quadrant:

Table (2): Study weights of central macular thickness - superior quadrant difference between cases and controls.

Study	Weights
Yigit Ulviey et al. (2013)	14.562%
Riham et al. (2015)	19.928%
Zeynep D and Orhan A. (2018)	19.016%
Marwa et al. (2021)	29.029%
A.H. ELHabbak et al. (2021)	17.466%

Non-combinability of studies:

Cohran Q=8.577135 (df=4) p=0.0726, Moment-based estimate of between studies variance= 16.257044, I^2 (inconsistency)=53.4% (95% CI= 0% to 80.9%).

Random effects (DerSimonian-Laird):

- Pooled wmd+=–7.051828 (95% CI=–11.968361 to –2.135294).
- Z (test wmd+differs from 0)=–2.811194 p=0.0049.

Bias indicators:

- Begg-Mazumdar: Kendall's tau=0.2 p=0.8167 (low power).
- Egger: bias=0.753482 (95% CI=–10.172579 to 11.679542) p=0.8404.

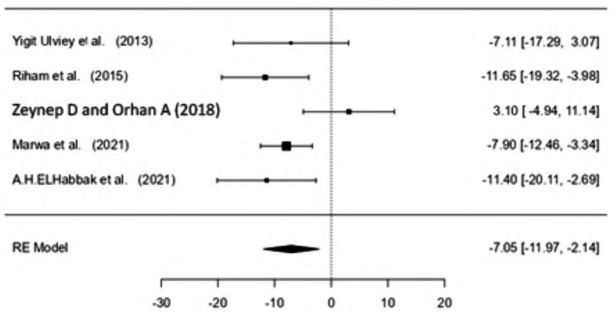

Fig. (2): Forest plot of central macular thickness - superior quadrant difference between cases and controls.

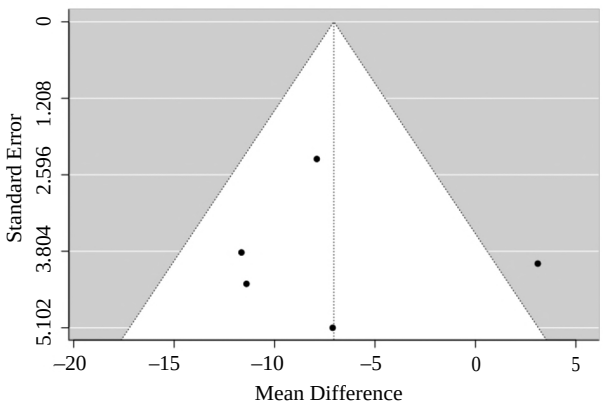

Fig. (3): Forest plot of central macular thickness - superior quadrant difference between cases and controls.

The inferior quadrant:

Table (3): Study weights of central macular thickness - inferior quadrant difference between cases and controls.

Study names	Weights
Yigit Ulviey et al. (2013)	4.989%
Riham et al. (2015)	22.825%
Zeynep D and Orhan A. (2018)	13.974%
Marwa et al. (2021)	52.685%
A.H. ELHabbak et al. (2021)	5.526%

Non-combinability of studies:

- Cohran Q=7.759158 (df=4) p=0.1008.
- Moment-based estimate of between studies variance=15.932414.
- I^2 (inconsistency)=48.4% (95% CI=0% to 79.4%).

Fixed effects (Mulrow-Oxman):

- Pooled effect size wmd+=6.823956 (95% CI =10.065184 to 3.582728).
- Z (test wmd+differs from 0)=–4.126432 p<0.0001.

Bias indicators:

- Begg-Mazumdar: Kendall's tau=0.2 p=0.4833 (low power).
- Egger: bias=–1.489918 (95% CI=–6.885896 to 3.90606) p=0.4442.

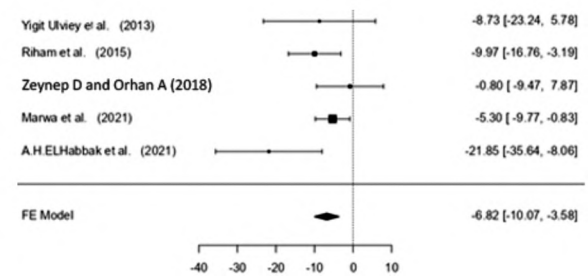

Fig. (4): Forest plot of central macular thickness - inferior quadrant difference between cases and controls.

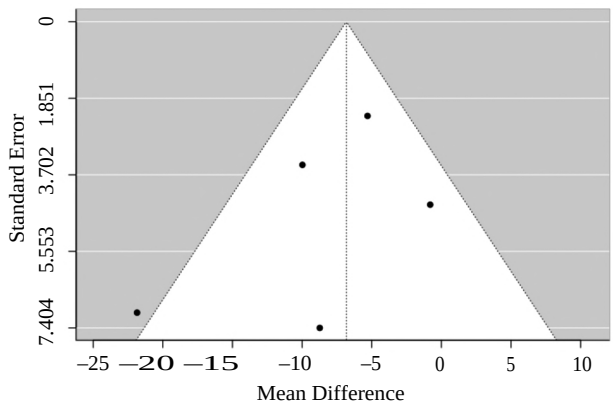

Fig. (5): Funnel plot of central macular thickness - inferior quadrant difference between cases and controls.

The nasal quadrant:

Table (4): Study weights of central macular thickness - nasal quadrant difference between cases and controls.

Study names	Weights
Yigit Ulviey et al. (2013)	16.914%
Riham et al. (2015)	24.712%
Zeynep D and Orhan A. (2018)	18.817%
Marwa et al. (2021)	26.751 %
A.H. ELHabbak et al. (2021)	12.806%

Non-combinability of studies:

- Cohran Q=14.113529 (df=4) p=0.0069.
- Moment-based estimate of between studies variance=37.768684.
- I^2 (inconsistency)=71.7% (95% CI=0% to 86.8%).

Random effects (DerSimonian-Laird):

- Pooled wmd+=–7.71348 (95% CI=–14.361895 to -1.065066).
- Z (test wmd+differs from 0)=–2.273947 p= 0.023.

Bias indicators:

- Begg-Mazumdar: Kendall's tau=–0.2 p= 0.4833 (low power).
- Egger: bias=–0.905793 (95% CI=–10.097157 to 8.285572) p=0.7743.

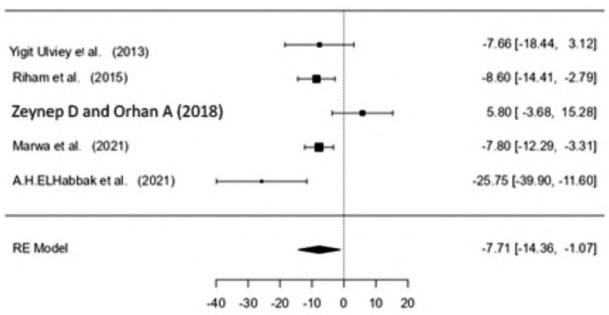

Fig. (6): Forest plot of central macular thickness - nasal quadrant difference between cases and controls.

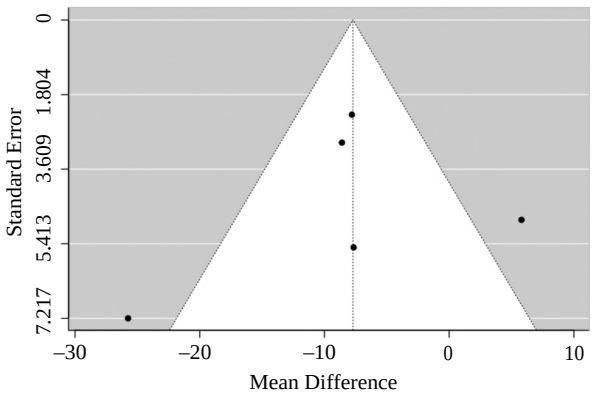

Fig. (7): Funnel plot of central macular thickness - nasal quadrant difference between cases and controls.

The temporal quadrant:

Table (5): Study weights of central macular thickness - temporal quadrant difference between cases and controls.

Study names	Weights
Yigit Ulviey et al. (2013)	17.391%
Riham et al. (2015)	20.467%
Zeynep D and Orhan A. (2018)	21.071%
Marwa et al. (2021)	22.720%
A.H. ELHabbak et al. (2021)	18.351%

Non-combinability of studies:

- Cohran Q=29.001671 (df=4) p<0.0001.
- Moment-based estimate of between studies variance=86.284155.
- I^2 (inconsistency)=86.2% (95% CI=65.5% to 92.3%).

Random effects (DerSimonian-Laird):

- Pooled wmd+=–9.516158 (95% CI=–18.43914 to -0.593177).
- Z (test wmd+differs from 0)=–2.090257 p=0.0366.

Bias indicators:

- Begg-Mazumdar: Kendall's tau=0 p=0.8167 (low power).
- Egger: bias=–2.211866 (95% CI=–18.119682 to 13.69595) p=0.6881

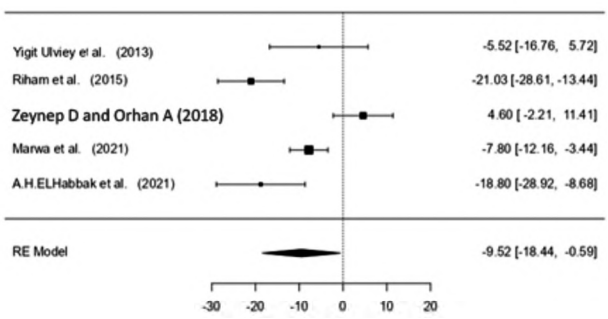

Fig. (8): Forest plot of central macular thickness - temporal quadrant difference between cases and controls.

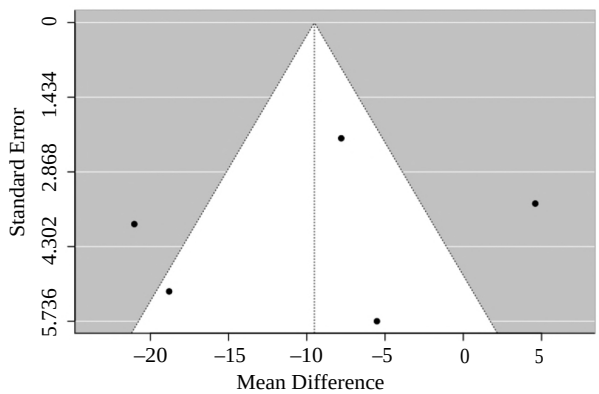

Fig. (9): Funnel plot of central macular thickness - temporal quadrant difference between cases and controls.

Discussion

Despite various advances in the treatment of systemic lupus erythematosus (SLE) and rheumatoid artheritis, hydroxychloroquine is still almost universally recommended for patients with these diseases. Ruiz-Irastorza et al., [7].

Hydroxychloroquine treatment is associated with wide ranging benefits, including improve quality of life and reduction in disease activity. Thomas J et al., [2].

Long term use of hydroxychloroquine can cause pathologic ocular damage include corneal deposits, posterior subcapsular lens opacity, ciliary body dysfunction, macular pigment loss, peripheral bone spicules formation, vascular attenuation and optic disc pallor. Ocular symptoms of retinopathy associated with this medication include blurred vision, partial loss of central and peripheral vision and in the later stage, loss of nightvision. Marmor et al., [8].

Hydroxychloroquine retinopathy is most influenced by daily dose and duration of use and the risk for toxicity is less with <5.0mg/kg real weight/day. Rodriguez-Padilla et al., [9].

The earliest clinical changes in HCQ retinopathy are subtle changes at the macula, with pigmentary stippling and loss of the foveal reflex (the typical light reflection seen on fundoscopy). Patients are usually asymptomatic, because the earliest functional changes occurparacentrally in a ring around central fixation. Rodriguez-Padilla et al., [9].

Since central visual acuity is preserved, the patient may not complain until much later in the disease process. So, the standard visual acuity tests (such as Snellen distance acuity) are similarly unlikely to detect early changes, although formal central visual field testing (such as the use of a 10-2 Humphrey visual field) may detect the paracentral reduction in sensitivity at an early stage. Rodriguez-Padilla et al., [9].

Newer imaging modalities have revealed some of the structural changes that occur at these early stages. Spectral Domain Optical Coherence Tomography (SD-OCT) shows that there is early thinning of outer retinal layers. Omri et al., [10].

Typically with loss of the parafoveal photoreceptor inner segment/outer segment (IS/OS) junction (Moth-eaten photoreceptor) and central foveal sparing. Riham et al., [11]. As in the Fig. (10).

There is preservation of the RPE and external limiting membrane. These perifoveal changes also later on include perifoveal thinning of outer nuclear layer, apparent posterior displacement of inner retinal structures towards RPE, creating a flying saucer sign. Chen et al., [12]. As shown in the Fig. (11).

The next stage shows by fundus examination a subtle "Bull's eye" macular lesion characterized by central foveolar island of pigment surrounded by a depigmented zone of RPE atrophy which is itself encircled by a hyperpigmented ring Pandya et al., [13]. As shown in this Fig. (12).

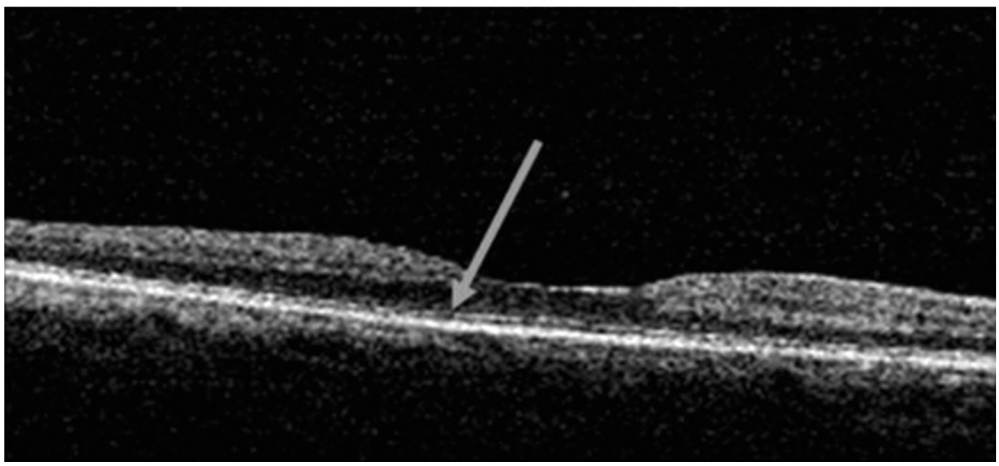

Fig. (10): Interrupted IS/OS junction (Moth-Eaten photoreceptor). Riham et al. [11].

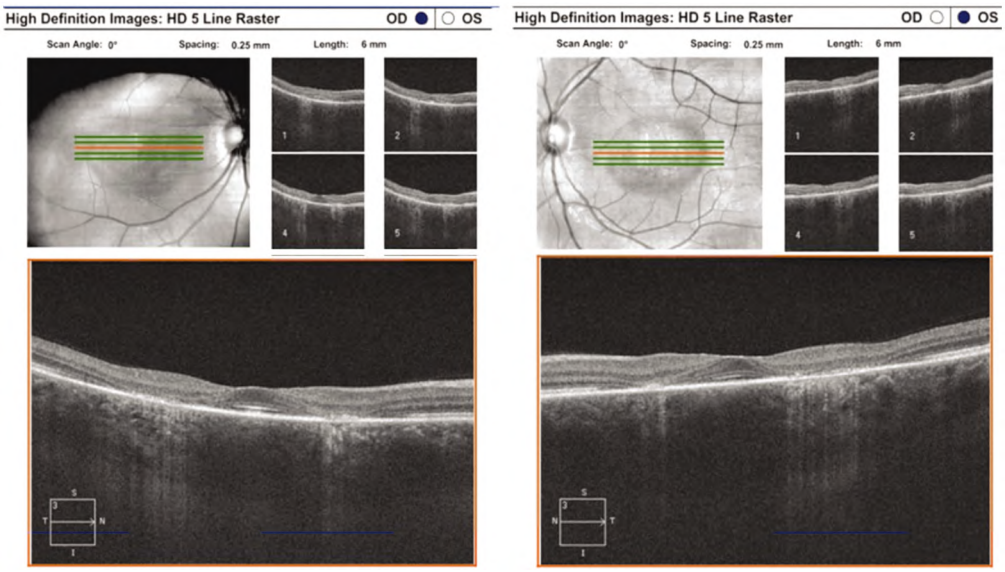

Fig. (11): Spectral-domain optical coherence tomography: Bilateral parafoveal outer retinal and retinal pigment epithelium atrophy with central sparing "flying saucer sign". Pandya et al. **[13]**.

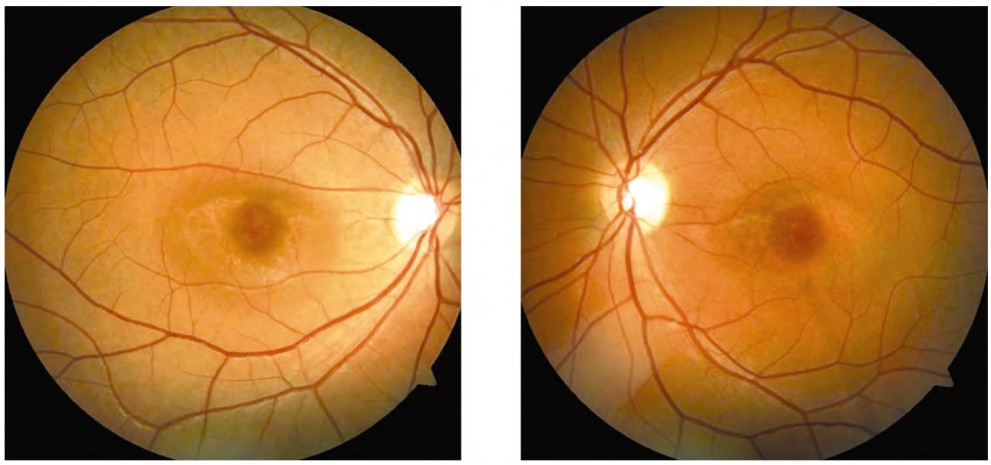

Fig. (12): Color fundus photography: Bilateral parafoveal retinal pigment atrophy "Bull's eye maculopathy". Pandya et al. **[13]**.

Hence, the current meta-analysis was conducted to review the literature to determine if OCT can detect early retinal changes in rheumatological diseases patients with hydroxychloroquine therapy.

One of the main outcomes of this meta-analysis is the assessment of retinal pigment epithelium thickness or outer retinal thickness but unfortunately, we didn't find enough papers for meta-analysis.

So, our outcome in this meta-analysis is full central macular thickness in its four quadrants: Superior, inferior, nasal and temporal.

Therefore, in this meta-analysis we evaluated the ability of OCT to observe the changes of macular thickness parameters.

However, we have found a significant difference in central macular thickness in its four quadrants specifically at central fovea which indicates decrease thickness of ganglion cell layer, photoreceptor layer and retinal pigment epithelium layer between the cases and the controls involved in El Habbak et al., **[14]**, Marwa et al., **[15]** and Riham et al., **[11]** studies reflecting atrophic changes along these layers with HCQ therapy among rheumatological patients.

In Yigit et al., **[16]** study, there was decrease in inner retinal layers thickness and no changes in outer retinal layers thickness between cases and controls involved in this study as same as find in Pasadhika and Fishman **[17]**, study implying that the outer retinal changes seen with optical coherence tomography are unlikely to be the earliest sign of toxicity.

In Zeynep et al., **[18]** study, there was no difference in central macular thickness between cases and controls involved in this study. This situation can be explained by the prevention of recurrent vasculitis attacks by treatment and control of immune complex deposits in patients enrolled in this study and due to the fact that all of patients were under the treatment of hydroxychloroquine, it can be concluded that the use of hydroxychloroquine did not cause a change in the thickness of the macula **[18]**.

In our meta-analysis all studies involved were revealed that there was no relation between toxicity and cumulative dose in grams or grams per kilogram, as the same as find in Marmor et al., **[19]** study.

In Worme et al., **[20]**, meta-analysis 6 studies were included that have published in the period between 1997 to 2018, and have data for quantitative analysis by OCT, 2 were cohort and 4 were case control study included 4112 evaluated patients. The pooled prevalence of HCQ retinopathy was 6% (95% CI 2-10). We found no statistical association (p>0.05) between the prevalence of retinopathy and the well-known risk factors associated with development of retinopathy, including duration of HCQ use, cumulative dose and daily dose.

Also, recent statistics showed that introduction of OCT technology has more advantage in early detection of HCQ retinotoxicity because of the ease, speed, and safety of the optical coherence tomography procedure in everyday clinical practice compared to mf ERG and VF in recent years as found in Eliwa et al., **[21]** study.

The data obtained from this study also suggests that OCT is a valid tool in the detection of early retinopathy in rheumatological patients with different durations with HCQ therapy and no correlation with treatment duration and the cumulative dose of the drug.

Acknowledgement:

First and foremost, thanks to ALLAH, the Most Merciful.

I wish to express my deep appreciation and sincere gratitude to Prof. Dr. Rafik M. El Ghazzawy, Professor of ophthalmology at Ain Shams, Assis. Prof. Dr. Walid M. El Zwahry, Assistant Professor of ophthalmology, Ain Shams University, Dr. Ali M. El Sawy, Lecturer of Ophthalmology, Ain Shams University, and to Prof. Dr. Moustafa El Husseine-Moustafa, Professor of Community, Environmental and Occupational Medicine, Ain Shams University, for thier kind supervision, indispensable advice and great help in this work.

Recommendations:

Additional studies of a larger sample size are needed to validate our findings.

OCT is recommended for screening and regular follow-up for early detection of retinopathy in rheumatological patients under treatment with hydroxychloroquine.

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دراسة تحليلية عن تأثير المدة العلاجية بدواء الهيدروكسيكلوروكين فى الأمراض الروماتيزمية على الخلايا الصبغية الطلائية بالشبكية بالتصوير المقطعى البصرى

دواء الهيدروكسيكلوروكين الذى يستخدم لعلاج مرض الملاريا يستخدم أيضاً لعلاج أمراض أخرى روماتيزمية منذ عام ١٩٥٠م كمرض إلتهاب المفصل الروماتويدى وأمراض الأنسجة الضامة كالذائبة الحمراء، يمكنه أن يسبب أضرار بصرية مرضية بالعين كترسبات بالقرنية، عتامة تحت المحفظة الخلفية بعدسة العين، إختلال وظيفى بالجسم الهدبى بالعين، فقدان الصباغ البقعى بمركز الابصار، تشكيل عظمى محيطى، وهن بالعصب البصرى وشحوب بقرص العصب البصرى. أعراض إعتلال الشبكية المصاحبة لهذا الدواء تشمل عدم وضوح الرؤية وفقدان جزئى للرؤية المر كزية ومحيط الرؤية، وفى المراحل المتلاحقة يحدث فقدان للرؤية الليلية. سمية الشبكية بدواء الهيدروكسيكلوروكين تحدث نتيجة قابلية هذا الدواء للإرتباط بصبغة الميلانين فى الخلايا الصبغية الطلائية بالشبكية، إحداث دمار فى المخاريط البقعية بمركز الإبصار. حيث أن الدواء يقوم بمنع نشاط الليزوزوم فى الخلايا الصبغية الطلائية بالشبكية وتقليل إبتلاع الأجزاء الخارجية فى المستقبلات الضوئية مما يؤدى إلى تراكم هذه الأجزاء. خطر السمية من هذا الدواء يعتمد على الجرعة اليومية (٥ مجم/كغم) ومدة إستخدامه، وفى الجرعات الموصى بها فإن خطر السمية إلى ٥ سنوات يصل إلى أقل من ١٪ وإلى ١٠ سنوات يصل إلى أقل من ٢٪ لكن ترتفع إلى ما يقرب من ٢٠٪ بعد ٢٠ سنة. فالجرعات العالية والمدة الطويلة من الإستخدام الذى يتخطى الخمس سنوات هما أهم عوامل الخطورة للسمية الشبكية. وكرد فعل تقوم الخلايا الصبغية الطلائية بالشبكية التى تحتوى على صبغة الميلانين بالإنتقال إلى الطبقات النووية الخارجية والضفيرة الخارجية بالشبكية مما يؤدى إلى فقدان غير رجعى للمستقبلات الضوئية وضمور فى الخلايا الصبغية الطلائية بالشبكية، ويعتقد أن تطور إعتلال الشبكية يمكن عكسه تماماً عند التوقف من تناول الدواء فى المرحلة قبل السريرية، فالمرضى الذين يعانون من إعتلال الشبكية المبكر بدون أعراض قد يظل قاع العين طبيعى قبل ظهور أى علامات على إعتلال الشبكية لذلك، يتم التوصية بإجراء فحص للكشف المبكر فى مرحلة ما قبل الإعتلال. حيث أنه عندما يتم الكشف مبكراً قبل تدمر الخلايا الصبغية الطلائية بالشبكية فإنه يحدث تقدم محدود فقط وبعد إيقاف الدواء يكون من الممكن تجنب حدوث فقدان البصر. لذلك فإن توصيات الاكاديمية الأمريكية لطب العيون للكشف المبكر عن الإعتلال الشبكى تقتضى أن يتم عمل فحص آلى للمجال البصرى وتصوير مقطعى بصرى بعد فحص مبدأى لقاع العين لإستبعاد أى إعتلال شبكى سابق الوجود واللذان يستخدمان كفحوصات أولية لأنهما واسعى الإنتشار ويظهران الدمار الخلوى وظيفياً على عكس فحص مخطط كهربية الشبكية متعدد البؤر وفحص التألق الذاتى لقاع العين اللذان يستخدمان كفحوصات إضافية لكشف الإعتلال الشبكى ويظهران الدمار الخلوى شكلياً. التصوير المقطعى البصرى تبين أنه أقل حساسية من مجال الإبصار ومخطط كهربية الشبكية متعدد البؤر ولكنه يمتاز بخصوصية أعلى فى التغيرات الهيكلية، وطبيعته الغير جراحية، وتوفره بشكل كبير فى الكثير من العيادات. الصبغية الطلائية بالشبكية مبكراً فى مرضى الأمراض الروماتيزمية تحت العلاج بدواء الهيدروكسيكلوروكين بفترات علاجية مختلفة.

طريقة الدراسة : أجرينا بحث إلكترونياً من خلال قواعد بيانات مختلفة مثل (PubMed و SCOPUS و Web of Sciene) وستتضمن هذه الدراسة المنهجية تجارب عشوائية وغير عشوائية ذات علاقة بتأثير مدة العلاج بالهيدروكسيكلوروكين على الخلايا الصبغية الطلائية بالشبكية بالتصوير المقطعى البصرى.

تم إجراء فحص العنوان والملخصات بتنسيق الذى تم نشره بين عامى ٢٠١١ و ٢٠٢١ وتمت الدراسة على مرضى الأمراض الروماتيزمية من الجنسين وتتراوح أعمارهم من ٢٠-٥٠ عام تحت العلاج بدواء الهيدروكسيكلوروكين بفترات مختلفة.

نتائج الدراسة التحليلية : من إجمالى ٩٥ دراسة تم فحصها، حققت خمس دراسات معايير التضمين الخاصة بالدراسة بإجمالى ٢٠٦ حالة و ٣٥٢ عيناً.

كانت نتائجنا الرئيسية هى سمك طبقة الخلايا الصبغية الطلائية بالشبكية أو سمك الطبقة الخارجية للشبكية ولكن لسوء الحظ لم يتم توفر عدد كافى من الدراسات لإتمام الدراسة، لذلك استخدمنا سمك الشبكية كاملاً فى مركز الإبصار فى أركانها الأربعة العلوى، السفلى، الأنفى والخارجى.

اقترحت نتائج هذه الدراسة التحليلية مؤشرات حيوية محتملة تكشف الاختلاف فى سماكة البقعة المركزية لمركز الإبصار التى تعكس طبقة الخلايا العقدية وطبقة المستقبلات الضوئية وسماكة طبقة الخلايا الصبغية الطلائية بالشبكية بين مرضى الروماتيزم الذين استخدموا دواء الهيدروكسيكلوركين بفترات مختلفة وعناصر صحية خالية من المرض.

فيما يتعلق بالربع الأعلى من البقعة المركزية :

Cohran Q=8.577135 (df=4) p=0.0726 والتقدير القائم على اللحظة للتباين بين الدراسات = ١٦.٢٥٧٠٤٤، I^2 عدم الاتساق = ٥٣.٤٪ (٩٥٪ CI% = 0 إلى ٨٠.٩٪).

الربع السفلى هو :

Cohran Q=7.759158 (df=4) p=0.1008 والتقدير القائم على اللحظات للتباين بين الدراسات = ١٥.٩٣٢٤١٤، I^2 (عدم الاتساق) = ٤٨.٤٪ (٩٥٪ CI% = 0 إلى ٧٩.٤٪).

بينما الربع الأنفى :

Cohran Q=14.113529 (df=4) p=0.0069 والتقدير القائم على اللحظة للتباين بين الدراسات = ٣٧.٧٦٨٦٨٤، I^2 (عدم الاتساق) = ٧١.٧٪ (٩٥٪ CI% = 0 إلى ٨٦.٨٪).

الربع الخارجى :

Cohran Q=29.001671 (df=4) p<0.0001 والتقدير القائم على اللحظة للتباين بين الدراسات = ٨٦.٢٨٤١٥٥، I^2 (عدم الاتساق) = ٨٦.٢٪ (٩٥٪ CI% = 65.5 إلى ٩٢.٣٪).

تكشف معظم الدراسات المشاركة فى هذه الدراسة التحليلية أن هناك تغيراً فى مقاييس سمك الشبكية الكاملة فى البقعة المركزية كما فى (A.H. ElHabbak et al., 2021) و (Marwa et al., 2021) و (Riham et al., 2015) هذه الدراسات تعكس ضمور الشبكية مع علاج الهيدروكسيكلوروكين بين مرضى الروماتيزم، بينما فى دراسة (Yigit et al., 2013) وجدت أن هناك انخفاضاً فى سمك طبقات الشبكية الداخلية ولم تحدث تغييرات فى سمك طبقات الشبكية الخارجية بين الحالات والأصحاء المشاركين فى هذا فى الدراسة، وفى دراسة (Zeynep et al., 2018) لم يكن هناك اختلاف فى سمك البقعة المركزية بين الحالات والأصحاء المشاركين فى هذه الدراسة.

بشكل عام، تخلص هذه الدراسة التحليلية إلى أن التصوير المقطعى البصرى أداة جيدة من الممكن استخدامها فى الكشف المبكر عن اعتلال الشبكية فى المرضى الذين يستخدمون دواء الهيدروكسيكلوركين لأنها تتيح التقييم الكمى لسمك الشبكية الكامل فى المنطقة البقعية المركزية لمركز الإبصار مما يعكس تغيرات الخلايا الصبغية الطلائية بالشبكية مع علاج الهيدروكسيكلوروكين فى مرضى الأمراض الروماتيزمية من أجل جودة إبصار أفضل لهؤلاء المرضى.