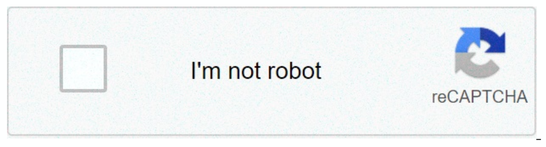

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Plaquenil maculopathy guidelines

Issue: September 10, 2018 ADD SUBJECT TO EMAIL ALERTS We were unable to process your request. Please try again later. If you continue to have this question please contact customerservice@slackinc.com. The American Academy of Ophthalmology has published several dosing and screening recommendations for hydroxychloropathy to avoid potential retinal toxicity, but some patients still experience permanent vision loss as a result of hydroxychloroquine retinopathy due to improper dose of the drug and improper screening. A cookie-cutter method to make Plaquenil (hydroxychloroquine, Sanofi-Aventis), a antimalarial drug that has been used as a treatment for systemic lupus erythematosus and rheumatoid arthritis, by rheumatologists and physician medicine may lead to an increased risk of hydroxychloroquine (HCQ) retinopathy, according to OSN Retina/Vitreous Section Andrew A. Moshfeghi, MD, MBA. Plaquenil comes in 200 mg tablets, and many doctors just off-handedly put everyone at 200 mg twice a day. And they feel they provide good care if they remember to send the patient to an ophthalmologist every year or even more often, not knowing what screening is needed or whether that ophthalmologist knows what to do. Screening is good, but they can significantly reduce the likelihood of morbidity or the actual need for these patients to stop using the drug if they had done these patients appropriately in the first place, he said. A variety of tests are needed to detect the earliest possible signs of hydroxychloroquine toxicity, according to Andrew A. Moshfeghi, MD, MBA. Image: USC Roski Eye Institute AAO revised guidelines AAO published dosage and screening recommendations for chloroquine and hydroxychloroquine in 2016, revising previous recommendations published in 2011. The current maximum daily HCQ dose recommended by AAO is 5 mg/kg real weight. The 2011 Guidelines proposed a maximum dose of 6.5 mg/kg of ideal weight. The main difference between 2011 and current recommendations is the need for patients to be made of their real weight instead of their ideal weight. The guidelines for dosing the ideal weight were based on a set of articles written about scientific experiments done on rats and some skinny monkeys nearly half a century ago, according to Michael Marmor, M.D., professor of ophthalmology at Stanford University and chairman of the committee that revised the AAO guidelines in 2016. Michael Marble These articles concluded that HCQ does not bind to adipose tissue. So therefore you would like to measure its effective weight in the body from non-adipose tissue, which is what ideal weight is, more or less, Marmor said. But other evidence clearly shows that the pattern of toxicity in monkeys takes long-term chloroquine, a similar drug to HCQ, causing damage to their cells that is completely different from the human disease, he said. IN OTHER WORDS, animal testing can be powerful and useful, but they are not evidence human diseases, he said. If you read the old HCQ studies carefully, what they really show is that HCQ binds mainly to pigmented (melanotic) tissues and glandular tissues and liver, and that's about it. It doesn't bind much to muscles, brains or anything else, including fat. It's not that it's not just binding in fat, it's that it's not binding on much of anything. These experiments are not very convincing for using ideal weight, Marble said. And now we have a large human demographic study that compares the predictive value of real- and ideal-weight-dosing. Conclusion: Real weight is better. Until 2011, there were essentially no good demographic studies on this drug due to the number of years it takes to accumulate toxicity and the lack of sensitive tests such as OCT to recognize early retinal lesions. Until then, the only way toxicity was demonstrated was by looking in the fundus for a bull's-eye, which is now considered irreversible damage, Marble said. But the situation has now changed. Real Body Weight Based on new scientific evidence, like Marble and Ronald B. Melles, Md., published in JAMA Ophthalmology, it was clear that new dosage guidelines were needed, Marmor said. We had nearly 2,500 patients using the drug for more than 5 years in whom we were able to document toxicity with OCT as well as field of vision and autofluorescence in various patients. We could really document it, he says. The study showed real body weight predicted risk of toxicity better than ideal body weight for all patients. In addition, co-authors found that the presence of toxicity relative to actual body weight dosage was independent of body habitus, while thin individuals dosed by ideal body weight had a much higher risk of developing toxicity. When using real weight to calculate the dosage, the risk is exactly the same whether you weigh 90 pounds or 250 pounds. For me, that's how drug prediction should work, Marble said. Giving less to heavy patients by calculating their dose by height makes no sense even if 'safer' — we give drugs to have an effective dose on board, no matter what the patient weighs. Dosing based on ideal weight should be dismissed completely because it was based on ancient science that was misinterpreted and propagated in literature, according to Marble. Ophthalmology now has good human evidence showing a better prediction comes from real weight, and we should all practice evidence-based medicine. When someone comes up with a new comparable series that shows the ideal weight or another formula is better, well, I'll change. But we have to use the best evidence we have, he said. PAGE BREAK Many of our patients overdose. A 2018 study published in Arthritis Research & Therapy found that already about a third of patients with normal BMI overdosed with dose based on ideal body weight. However, when calculated using the updated dosing guidelines using actual body weight, more than half of the were excessively dosed. Therefore, more patients will have to reduce the dosage under the new guideline, Judy E. Kim, MD, OSN Retina/Vitreous board member, said. This means that we should make a practice of asking our patients about their body weight at each visit for HCQ screening and calculating the safe dosage based on actual body weight, even in those who were previously thought to be in the safe range based on ideal body weight. The change from using ideal body weight to real body weight actually makes this calculation easier to do. It also requires further research to find ways to give doctors consistent reminders that exact dose, such as through electronic health records, as well as research to determine safe and effective dosage, she said. Judy E. Kim In addition to dosing, long duration of HCQ use may put patients at higher risk of developing retinal toxicity. Other risk factors, such as underlying maculopathy, kidney disease and the use of tamoxifen, also increase the risk of toxicity, Kim said. However, previous risk factors such as age, liver disease and obesity were not included in the revised recommendations, she said. Giving a patient a higher dose than necessary for a long time is the most significant risk factor for developing HCQ retinal toxicity, according to AAO guidelines. Calculating a correct dosage using real weight is not difficult, but HCQ pills come in only 200 mg tablets. If a patient needs 265 mg of HCQ, how can the drug be carefully prescribed for a patient? Marble asked. In fact, it is very easy because the drug is slow to stabilize in the body, so it does not need to be taken in the exact same dose every day. All you do is calculate the weekly dose; in other words, if you want 265 mg per day, you multiply by seven to get the weekly dose. You then divide by 200, and it will tell you how many pills you have to take for the week (in this case nine) — it's easy to count what days to take two pills and what days to take one. If it comes off as an uneven number, round off one day or the other. In our example, 5 days a week the patient would take one tablet and 2 days a week they would take two, he said. PAGE BREAK An ophthalmologist only has to establish a relatively stable HCQ level in the blood, so it's very easy to give people the right and correct dose, Marmor said. Risks of toxicity According to AAO, patients taking an appropriate dose based on actual weight have a less than 1% risk of developing HCQ retinal toxicity during the first 5 years of use and less than 2% during the first 10 years of use. The risk increases to almost 20% after 20 years of use, but a patient who screens as usual after 20 years has only a 4% risk of converting to toxicity in the following year. HCQ retinopathy is usually asymptomatic in patients who are in the early stages of the disease, according to a 2015 study published in the Indian Journal of Ophthalmology of Hemang K. md, and colleagues, so continued of patients to monitor for signs is important. But when the disease advances, it can result in a worsening of visual acuity, peripheral vision and night vision. When patients are present with a classic bull's-eye maculopathy, the disease is usually advanced and has caused irreversible damage, according to the study. When you take this drug and you take it wrong or too long or too high a dose, you develop an atrophy of the macula in a ring-like pattern that surrounds the center of the macula initially. If you continue to take it and do not stop, it will continue to cause progressive damage that will involve the very center of the macula, similar to the type of atrophy that one gets with dry age-related macular degeneration with the advanced form of geographic atrophy. Like dry AMD, whatever damage you get at this point is irreversible, Moshfeghi said. In addition, serious injuries will continue to develop and worsen even if the medicine is stopped. Proper screening practice Due to the extensive and irreversible lesions that may stem from HCQ retinal toxicity, proper screening practices take at an elevated level of importance. Ophthalmologists should use Humphrey visual field tests and OCT — and fundus autofluorescence if there is can help, too — to detect signs of HCQ toxicity, Moshfeghi said. The bottom line is, we use a variety of tests at every visit. The reason we do this is because we want to try to pick up the earliest possible signs of toxicity. If you only did one test, an OCT for example, which is very specific on picking up toxicity, it could be that you see age-related issues that only look like HCQ toxicity. Or a field test, which is very sensitive, may not have been conducted reliably. You do not want to stop the drug unnecessarily because it may be the only drug that is helpful to the patient's rheumatological condition, such as lupus or rheumatoid arthritis. And of greater importance, Plaquenil has less systemic side effects than other drugs used for lupus, so there is a real benefit in using it as long as one can. You want a high threshold to say you're going to stop this medication, he said. PAGE BREAK Additionally, knowing the differences between toxicity symptoms in different ethnicities can help validate HCQ toxicity and find signs of it before it causes irreversible damage, Brian Toy, M.D., of the USC Roski Eye Institute, said. For example, wide-angle field imaging must be used in Asian patients in addition to the smaller field imaging used in Caucasian patients. Asian patients tend to have toxicity that starts a little farther from fovea compared to Caucasian patients, often in the arcade region, so a wide field imaging test is needed, Toy said. Brian Toy Widefield fundus autofluorescence and OCT may be helpful in detecting toxicity in Asian patients who may present with a pericentral pattern. Also, a Humphrey field of view 24-2 in addition to a necessary. This can add significantly to testing testing but when patients find out what it's for, they're generally OK with it, he said. The signs can be easily missed in Asian patients if a widefield test is not used, Moshfeghi agreed, and if ophthalmologists are not up to date with the latest AAO guidelines, they may not know the test is necessary. If you only do what was previously recommended, such as what you learned in the resident, 10-2 Humphrey field of view, it will only test the central 10° of a patient's vision. If you do it in an Asian patient who actually has injuries, you will miss it many times. You didn't learn this at your residence or community because this is a recent guideline — you have to do a 24-2 instead of these patients, he said. Field of vision tests take a long time to complete and can be difficult for patients. A traditional 10-2 test takes at least 15 minutes per eye, and if a 24-2 is added, a patient takes the tests for an hour or more, Marble said. When you do this, people fall asleep, they're angry, they're ready to go out. It's not working. However, there is a variant of the field test called SITA Fast. SITA Fast takes half as long, and even most glaucoma people realize it's about as good a test. So, for my Asian patients, I do both a 10-2 and a 24-2 SITA Fast; does not take more time than the standard 10-2, Marble said. Using electronic health records Because of the need for continuous screenings for patients taking HCQ, Toy said it is important for patients not to be lost to referral. An electronic journal can be an interesting tool to track screenings and ensure that proper dose utilizing, he said. PAGE BREAK The [electronic health record] system allows us to make a record of patients taking HCQ to keep track of when they need to come in for their screening. I think it's particularly useful in implementing the AAO recommendation to postpone screening for the first 5 years when there is little risk of toxicity developing, but we don't want patients to be lost to follow-up for 10 to 15 years, Toy said. To improve screening rates, Toy and colleagues work with Cerner to improve their EMRs. Programmers are working to include an automatic dose check in EMR of a patient who is prescribed HCQ to automatically calculate the appropriate dose of the drug based on the patient's actual weight. The second idea is to develop a registry of patients in the Los Angeles County health system who are currently at HCQ to keep track of them for future screening needs. Like the IRIS registry, this would include a dashboard that ophthalmologists can pick up to automatically schedule patients for future screenings, he said. The third is to standardize our workflow. I think for any clinic, but especially for our county clinic where we have limited resources in terms of techniques and equipment, we need to optimize our use of resources. So we adopted a telemedicine strategy in which a patient's patient oct, visual field testing and photography, without seeing a supplier during that visit. The test results are interpreted by one of our retinal physicians, and we can send recommendations on dosage and follow-up to our medicine colleagues, Toy said. Toy said screenings would be evaluated and appointments made for patients showing signs of developing HCQ toxicity. Improved HCQ retinopathy screenings can be achieved with better training and better communication with rheumatologists and internists, Kim said. We need to get our message across to others at their meetings and magazines. We have to send them letters after evaluating their patients, she said. Educating patients at higher risk of toxicity on the importance of eye examinations and follow-up can also be helpful. While follow-up is usually not necessary in the first 5 years, Kim said she will have higher-risk patients, such as those on tamoxifen or who have maculopathy or kidney disease, evaluated earlier than the recommended 5 years. Progressive Disease New data presented by Marble at this year's Association for Research in Vision and Ophthalmology meeting show that once a patient has retinal pigment epithelium (RPE) lesions from HCQ toxicity, the disease will never stop progressing. For patients with early toxicity, before a bull's-eye is observed, the disease will stabilize and the risk of visual loss is low. The drug can be stopped and everything will be OK, he said. PAGE BREAK However, when there are RPE injuries, when there is some sign of a bull's-eye, these patients never stop getting worse, and it was something we didn't expect. We thought it might take a few years, but it didn't. It's a progressive disease. Something is destabilized, and it never stops getting worse, Marmor said. HCQ toxicity can be avoided by using a proper dose and screening properly, he said. Bull's-eye retinopathy is a scourge that should be eliminated along with leprosy and small pox. If you're going to audit people, you're never going to see it. It's serious injuries, Marmor said. – by Robert Linnehan References: Jorge AM, et al. Arthritis Res Ther. 2018;doi:10.1186/s13075-018-1634-8. Marble MF, et al. Ophthalmology. 2016;doi:10.1016/j.ophtha.2016.01.058. Melles RB, et al. JAMA Ophthalm. 2014;doi:10.1001/jamaophthalmol.2014.3459. Melles RB, et al. Ophthalmology. 2015;doi:10.1016/j.ophtha.2014.07.018. Modi YS, et al. Ophthalmic Sourg Lasers Imaging Retina. 2016;doi:10.3928/23258160-20160229-02. Pandya HK, et al. Indian J Ophthalmophmol. 2015;doi:10.4103/0301-4738.167120. Pham B, et al. Long-term progression of hydroxychloroquine retinopathy of the drug. Presented at: Association for Research in Vision and Ophthalmology Annual Meeting; 29 April -3 May 2018; Honolulu. Saurabh K, et al. Indian J Ophthalmophmol. 2018;doi:10.4103/ijo. IJO_787_17. For more information: Judy E. Kim, M.D., can be reached at the Medical College of Wisconsin, 925 N. 87th St., Milwaukee, WI 53226; E-mail: Michael Marmor, MD, can be reached at Byers Eye Institute, 2452 Watson Court, Palo Alto, CA 94303-3216; e-mail: marmor@stanford.edu. Andrew A. Moshfeghi, MD, MBA, can be reached at USC Roski Eye Institute, Keck School of Medicine, University of Southern California, 1450 San Pablo St., 4th Floor, Los Angeles, CA 90033; e-mail: amoshfeghi@gmail.com. Brian Toy, MD, can be reached at Keck Medicine of USC, Ophthalmology, HC4 4900 1450 San Pablo St., Health Sciences Campus, Los Angeles, CA 90033; e-mail: brian.toy@med.usc.edu. Information: Kim, Marmor, Moshfeghi and Toy do not report any relevant financial information. Click here to read, Should a patient with signs of retinal toxicity be removed hcq completely, or is a reduced dose and further screening more appropriate? ADD SUBJECT TO EMAIL ALERTS We were unable to process your request. Please try again later. 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