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# Uveitis and Oral Fluoroquinolone Use

Recent studies have linked oral fluoroquinolones, the most frequently prescribed class of antibiotic in the outpatient setting, to uveitis. The precise mechanism by which this class of drugs may lead to uveitis remains unclear, but studies have shown that fluoroquinolones can sensitize the skin to phototoxic effects, and one particular fluoroquinolone—moxifloxacin—concentrates in melanin-containing structures, including the iris. Sandhu et al from the University of Pennsylvania conducted a retrospective cohort study using 13 years of data from a U.S. managed care network to evaluate the risk of uveitis in patients taking oral fluoroquinolones.

The researchers created 2 cohorts based on patients without prior diagnoses of uveitis or any of 18 uveitis-associated systemic diseases who had been prescribed 1 of 2 families of antibiotics:

- fluoroquinolones ($n$ = 843,854)
- β-lactams ($n$ = 3,543,797)

For comparison, the authors used β-lactams (a class of antibiotics that shares similar indications for prescribing but has not been associated with uveitis) with the hope of reducing the indication bias inherent in the study. Patient records were analyzed for subsequent diagnoses of uveitis.

The fluoroquinolone cohort was older than the β-lactam cohort and included women and black patients. Uveitis diagnoses among the fluoroquinolone cohort rose from 0.03% at 30 days to 0.22% at 365 days; a similar increase, from 0.02% to 0.15%, was seen in the β-lactam cohort. In the multivariate analysis, no significant difference at 30, 60 or 90 days was found between patients taking fluoroquinolones and patients taking

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β-lactams ($p > .38$ for all comparisons). However, a small but significant increase in the hazard ratio (HR) for fluoroquinolones was seen at 365 days. Similar results were seen when only cases of anterior uveitis were analyzed (Table 1).

Fluoroquinolones reach a high concentration in the blood shortly after use followed by a quick decay after use ends. Adverse effects of fluoroquinolones begin within a short time after initiating treatment. The results of this study—that oral fluoroquinolones are associated with uveitis only at 365 days—appear to be counterintuitive. The authors hypothesized that those patients who developed uveitis may have an underlying undiagnosed inflammatory uveitis-associated condition that mimics infection, leading the treating physician to prescribe a fluoroquinolone. The difference in outcomes for moxifloxacin and levofloxacin may be explained by indication bias; indications for moxifloxacin, which are more limited than those for levofloxacin, include infections that may have a higher propensity to be related to an underlying uveitis-associated systemic disease.

Oral fluoroquinolones did not demonstrate a greater risk associated with uveitis than did β-lactams during the period of time that one would expect to see adverse effects. Oral fluoroquinolone use more likely identifies patients at greater risk of developing a disease associated with uveitis rather than causing uveitis.

*Sandhu HS, Brucker AJ, Ma L, VanderBeek BL. Oral fluoroquinolones and the risk of uveitis.* JAMA Ophthalmol *2016;134:38-43.*

## Effect of Postoperative Endophthalmitis

Cataract surgery is the most common eye surgery performed worldwide, and the rate of this procedure is likely to rise even higher in the near future, especially among the aging population. While postoperative endophthalmitis is an extremely rare complication, occurring in between 0.04% and 0.41% of procedures, its visual outcomes are poor, with half the individuals not regaining vision better than 20/40. The more recent use of injectable lenses and topical anesthesia, microincisions, and sutureless surgical wounds has improved technique and reduced the rates of postoperative endophthalmitis.

To evaluate the effect of epidemiologic and surgical factors on postoperative endophthalmitis, Jabbarvand et al from Tehran University of Medical Sciences, Iran, conducted a retrospective analysis of 480,104 eyes of patients (mean age, 79 ± 9.5 years) who had undergone senile cataract surgery at a single tertiary care referral hospital in Iran from 2006 through 2014. All patients received 5% povidone–iodine for 5 minutes before surgery and were prescribed a topical antibiotic–corticosteroid solution at the time of discharge. If endophthalmitis was suspected, a vitreous biopsy was performed.

Analysis found 112 cases of postoperative endophthalmitis, for a rate of 0.023%. The mean

**Table 1.** Multivariate HRs for fluoroquinolones vs β-lactams by diagnosis

| | Diagnosis | | | | | |
|---|---|---|---|---|---|---|
| | All uveitis | | Anterior uveitis | | Systemic illness | |
| | Adjusted HR (95% CI)[a] | *p* value | Adjusted HR (95% CI)[a] | *p* value | Adjusted HR (95% CI)[a] | *p* value |
| ≤30 days | 0.96 (0.82–1.13) | .61 | 1.05 (0.84–1.30) | .69 | 1.96 (1.87–2.07) | <.001 |
| 60 days | 0.99 (0.88–1.12) | .93 | 1.10 (0.92–1.30) | .30 | 1.81 (1.74–1.89) | <.001 |
| 90 days | 1.05 (0.95–1.16) | .38 | 1.10 (0.95–1.28) | .19 | 1.72 (1.67–1.79) | <.001 |
| 365 days | 1.11 (1.05–1.17) | <.001 | 1.11 (1.03–1.21) | .01 | 1.46 (1.42–1.48) | <.001 |

*CI, confidence interval.*
[a]*Adjusted for age, sex and race.*

age of patients who developed endophthalmitis was 81 ± 7.8 years. Mean duration between surgery and diagnosis was 8 days; 100 of the cases were acute-onset endophthalmitis (≤6 weeks after surgery); the remaining 12 cases were late-onset (>6 weeks after surgery).

Multivariate logistic regression and single-variable analyses found the following:

- Diabetes was an independent risk factor for endophthalmitis (odds ratio [OR] 2.92; $p = .018$).
- Vitreous loss was also an independent risk factor for endophthalmitis (OR 7.83; $p < .001$).
- Endophthalmitis did not develop in any of the patients for whom intracameral cefuroxime was used at the end of surgery ($p = .001$).
- Endophthalmitis had significantly higher occurrence among patients from rural areas vs those from urban areas ($p = .001$).
- Older patient age was also associated with a higher risk of endophthalmitis.

This study was one of the largest of its kind. The 0.023% endophthalmitis rate was similar to rates reported in Sweden (0.029% and 0.048%) and lower than rates reported in China (0.06%), the United Kingdom (0.09%), and Ontario (0.14%) and Quebec (0.15%), Canada. Differences in incidence among countries may be attributed to differing prophylactic regimens, sensitivity of the definition of the condition, and racial and socioeconomic populations.

While the role of antibiotics in surgical prophylaxis continues to be controversial, the authors found intracameral cefuroxime to be far more effective than traditional topical or subconjunctival approaches. This finding is consistent with previous studies.

*Jabbarvand M, Hashemian H, Khodaparast M, et al. Endophthalmitis occurring after cataract surgery: outcomes of more than 480 000 cataract surgeries, epidemiologic features, and risk factors.* Ophthalmology *2016;123:295-301.*

# Geographic Atrophy Progression

A progressive form of dry age-related macular degeneration (AMD), geographic atrophy (GA) is characterized by irreversible loss of macular retinal tissue, retinal pigment epithelium and choriocapillaris. GA can cause irreversible, bilateral central vision loss and is responsible for severe vision loss in nearly 20% of AMD patients.

Schmitz-Valckenberg et al from the University of Bonn, Germany, reported on lesion progression using 2 different imaging modalities—color fundus photography (CFP) and fundus autofluorescence (FAF)—and on the relationship between changes in progression rate and changes in best-corrected visual acuity (BCVA). Data from the Natural History of Geographic Atrophy Progression (GAP) study, a prospective, multicenter, 18-month, noninterventional natural history study, was used to identify risk factors and quantify atrophic lesion progression in 603 participants (mean age, 76.9 ± 7.7 years) with GA secondary to AMD in ≥1 eye and without evidence of choroidal neovascularization in either eye.

Among the participants, 413 had gradable lesion data from FAF or CFP, 380 of whom were evaluable for the per protocol analysis set, and 321 of whom had gradable lesion data from both FAF and CFP. Mean lesion sizes measured by FAF were significantly smaller than those measured by CFP at baseline (7.0 ± 0.3 $mm^2$ vs 8.4 ± 0.3 $mm^2$; $p < .001$) and at 6, 12 and 18 months. This discrepancy was likely due to differences in the image resolution.

The progression rate from baseline to 6, 12 and 18 months, however, was similar for the 2 imaging modalities. Measured by FAF, the mean lesion change from baseline to month 18 was 3.14 ± 0.4 $mm^2$; measured by CFP, the mean lesion change was 3.17 ± 0.5 $mm^2$ ($p = .944$; Table 2).

**Table 2.** Lesion size change from baseline by imaging modality

| | Lesion size change from baseline, $mm^2$ (mean ± SE) | | |
|---|---|---|---|
| | Month 6 | Month 12 | Month 18 |
| Total, by CFP | 0.78 ± 0.1 | 1.57 ± 0.1 | 3.17 ± 0.5 |
| Total, by FAF | 0.88 ± 0.1 | 1.85 ± 0.1 | 3.14 ± 0.4 |

*SE, standard error.*

Atrophy progression was significantly greater in eyes with extrafoveal lesions than in eyes with foveal lesions, and significantly greater in eyes with multifocal lesions than in eyes with unifocal lesions. No correlation between BCVA and lesion localization, size or progression rate was found in the 343 participants for whom visual acuity was measured at baseline and 12 months.

This study's quantification of lesion subtypes by 2 imaging modalities and correlation with BCVA provided new insights into the natural history of GA. The authors recommended that future studies also include spectral-domain optical coherence tomography and other technologies.

*Schmitz-Valckenberg S, Sahel J-A, Danis R, et al. Natural history of geographic atrophy progression secondary to age-related macular degeneration (Geographic Atrophy Progression Study).* Ophthalmology *2016;123:361-368.*

## Ocular Hemorrhage And Antiplatelet or Anticoagulant Drugs

For a better understanding of the association of antiplatelet and anticoagulant drugs with ocular hemorrhage in patients with age-related macular degeneration (AMD), Ying et al from the University of Pennsylvania evaluated data from the Comparison of Age-Related Macular Degeneration Treatments Trials. The study enrolled 1185 participants ≥50 years of age with untreated active choroidal neovascularization (CNV) resulting from AMD and visual acuity between 20/25 and 20/320. Among the 1165 participants who had gradable fundus photographs, 608 (52.2%) used ≥1 antiplatelet or anticoagulant drugs and 724 (62.1%) had retinal or subretinal hemorrhage at baseline.

Statistical analysis found no association at baseline between use of antiplatelet/anticoagulant drugs and retinal or subretinal hemorrhage, even when adjusted for age, gender, smoking status, medical history of cardiovascular disease and CNV in the fellow eye ($p = .21$). Among patients with hypertension, however, the authors did find a significant association between retinal or subretinal hemorrhage and antiplatelet use (adjusted odds ratio [OR] 1.43; $p = .02$) but not anticoagulant use (adjusted OR 1.24; $p = .42$). Specifically, they found associations between retinal or subretinal hemorrhage and aspirin use (adjusted OR 1.50; $p = .01$) and clopidogrel use (adjusted OR 2.38; $p = .01$).

These findings are significant because some ophthalmologists may be tempted to advise AMD patients to avoid antiplatelet or anticoagulant drugs. Nonhypertensive patients who have been prescribed antiplatelet or anticoagulant drugs can continue to take them without fear of increased risk of hemorrhage. For those with hypertension, the 1.5-fold increased risk of retinal or subretinal hemorrhage should be considered by the physician prescribing the drugs.

*Ying G-S, Maguire MG, Daniel E, et al; Comparison of Age-Related Macular Degeneration Treatments Trials Research Group. Association between antiplatelet or anticoagulant drugs and retinal or subretinal hemorrhage in the Comparison of Age-Related Macular Degeneration Treatments Trials.* Ophthalmology *2016;123:352-360.*

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