gives us a chance to elaborate on different aspects of our article. The results of our study showed that corneal resistance factor was significantly reduced in eyes with macular corneal dystrophy (MCD) compared with normal corneas.[1] This parameter did not return to the normal value after penetrating keratoplasty (PK), which may suggest a decrease in the rigidity of the sclera, in addition to the cornea, in patients with MCD.[1] Reduced corneal rigidity can lead to underestimating intraocular pressure (IOP) in eyes with MCD and those undergoing corneal transplantation for this condition.[1] Furthermore, decreased corneal and scleral rigidity explains why corneal transplantation is more challenging technically in MCD compared with other stromal dystrophies (eg, lattice and granular). It is a common observation by corneal transplant surgeons that the anterior chamber collapses easily and that the lens–iris diaphragm displaces forward during PK for MCD, increasing the incidence of iris prolapse and iridocorneal adhesions. The following are answers to questions raised by Nair and associates.

As mentioned in our article, all PK eyes had clear grafts at the time of enrollment, and the presence of any graft opacities, including recurrence of dystrophy in the graft, led to patient exclusion.

Evaluation of the accuracy of different tonometers for measuring IOP in patients with MCD was not in the scope of our study, which aimed to evaluate corneal biomechanics in this stromal dystrophy. It can be a subject for future investigations to compare IOP measurements by different tonometers in MCD. Per the recommendation of Nair and associates, we opted to compare IOP measured by the ocular response analyzer, including Goldmann-related IOP (IOPg) and cornea-compensated IOP (IOPcc), with that measured by the Goldmann applanation tonometer (GAT). IOP_{GAT}, IOPg, and IOPcc were 11.25 ± 1.69 mm Hg, 12.06 ± 4.03 mm Hg, and 14.37 ± 3.41 mmHg in the MCD group, respectively ($P < .001$). These measurements were 12.0 ± 2.67 mm Hg, 11.44 ± 3.04 mm Hg, and 13.90 ± 2.90 mm Hg in the PK group ($P = .01$) and 13.46 ± 2.17 mm Hg, 14.02 ± 2.01 mm Hg, and 13.63 ± 2.70 mm Hg in the control group ($P = .42$), respectively. Intragroup analyses revealed that IOP_{GAT} and IOPg were significantly lower than IOPcc in the MCD and PK groups, whereas these 3 IOP measurements were comparable in control subjects. Intergroup comparisons showed that IOP_{GAT} and IOPg were significantly lower in the MCD and PK groups than the corresponding measurements in the control group. IOPcc, however, was comparable among the 3 groups.

Mean keratometry and keratometric astigmatism were 46.35 ± 2.91 diopters (D) and 6.28 ± 2.80 D after PK, respectively. These readings were 42.81 ± 1.19 D and 1.74 ± 0.61 D in the control group, respectively. Keratometry readings had no significant correlation with corneal hysteresis, corneal resistance factor, IOP_{GAT}, IOPg, or IOPcc in PK or control group. Nonsignificant association of astigmatism with IOP_{GAT} readings in the PK group is attributable to the method we used to reduce the effect of corneal astigmatism on readings by GAT, which was rotation of the tonometer prism 43° to the least-curved meridian.

SEPEHR FEIZI
ZAHRA KARJOU
HAMED ABBASI
MOHAMMAD ALI JAVADI
AMIR A. AZARI
Tehran, Iran

FUNDING/SUPPORT: NO FUNDING OR GRANT SUPPORT. Financial disclosures: The following authors have no financial disclosures: Sepehr Feizi, Zahra Karjou, Hamed Abbasi, Mohammad Ali Javadi, and Amir A. Azari. The authors attest that they meet the current ICMJE criteria for authorship.

REFERENCE

1. Feizi S, Karjou Z, Abbasi H, Javadi MA, Azari AA. Characterization of in vivo biomechanical properties in macular corneal dystrophy. *Am J Ophthalmol* 2020;215:8–13.

Comment on: Long-term Results of Trimethoprim Sulfamethoxazole Versus Placebo to Reduce the Risk of Recurrent *Toxoplasma gondii* Retinochoroiditis

EDITOR:

WE READ WITH GREAT INTEREST THE ARTICLE TITLED "Long-term results of trimethoprim sulfamethoxazole versus placebo to reduce the risk of recurrent *Toxoplasma gondii* retinochoroiditis" by Fernandes Felix and associates.[1] This prospective double-masked clinical trial found superior effects of 1 year of treatment with trimethoprim-sulfamethoxazole (TMP-SMZ) vs placebo in reducing the risk of recurrence during a 6-year follow-up period. The authors concluded that TMP-SMZ may be used safely for prophylaxis of recurrent toxoplasmic retinochoroiditis.[1]

Visual acuity loss in toxoplasma retinochoroiditis occurs because of the involvement of the macula or optic nerve head. In healthy individuals, toxoplasmic retinochoroiditis is a self-limited disease. Small peripheral lesions may be observed for spontaneous resolution. The majority of lesions in this study were peripheral (around 70% in the TMP-SMZ arm and 65% in the placebo arm).[1] There was no benefit in terms of visual acuity improvement with drug therapy over placebo treatment. Even with multiple recurrences, the visual acuity improvement and final visual acuity were not inferior as compared to cases with no/single recurrence. Perhaps such cases with peripheral lesions could have been observed.

The study reports only mild epigastric burning pain in 2 subjects (2.8%) in the TMP-SMZ group.[1] The common side effects of TMP-SMZ include mild gastrointestinal symptoms and mild maculopapular rash.[2,3] Although the combination is generally well tolerated, it can be associated with several serious adverse reactions. The serious complications, which may occur immediately or months after starting therapy, include skin eruptions (Stevens-Johnson syndrome, toxic epidermal necrolysis), hematologic abnormalities (thrombocytopenia, agranulocytosis, anemia), neurotoxicity, nephrotoxicity, and potential drug interactions (warfarin, phenytoin, oral hypoglycemics, etc).[2,3] Therefore, ophthalmologists must preferably take clinician's opinion during therapy for blood counts, renal functions, and serum electrolytes. In addition, given the preponderance in young female patients, extended use as blanket coverage in women of childbearing age must be weighed against harmful effects of trimethoprim in pregnancy (category D drug).[3]

Keeping in mind the possible benefits and the rare, yet possible fatal adverse effects, the indications and regimen of treatment (type, dose, frequency, and duration) needs to be defined. The role of steroids as adjunct to antiparasitic therapy in active disease is not clear.[4] Whether steroid given during the active phase to reduce the retinal inflammation and prevent further blood-retinal barrier breakdown will affect the distribution of tissue cysts to the margin of lesion and late recurrences has not been studied. The minimum dose and frequency of antiparasitic therapy needs to be chosen based on pharmacokinetics. The duration of treatment has been variable in previous studies (6-20 months[5,6] vs 10 months in the present study), and it is unclear if shorter or longer duration will be appropriate.

Instead of recommending the prophylaxis in all cases, it may be considered only for lesions involving the macula or close to the optic disc, where reactivation may lead to profound visual loss/field defect. It would be interesting to know if drug therapy prevents recurrences adjacent to previous scars or in the normal retina or at both locations. If recurrences, remote from the pre-existing scars, had occurred at the macula in the placebo group, then the indication for treatment may be extended to even peripheral lesions.

DEVESH KUMAWAT
RAMANUJ SAMANTA
Rishikesh, India
PRANITA SAHAY
New Delhi, India

FUNDING/SUPPORT: THIS RESEARCH DID NOT RECEIVE ANY specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Financial Disclosures: The authors have no financial disclosures. All authors attest that they meet the current ICMJE criteria for authorship.

REFERENCES

1. Fernandes Felix JP, Cavalcanti Lira RP, Grupenmacher AT, et al. Long-term results of trimethoprim-sulfamethoxazole versus placebo to reduce the risk of recurrent Toxoplasma gondii retinochoroiditis. *Am J Ophthalmol* 2020;213:195–202.
2. Wormser GP, Keusch GT. Trimethoprim-sulfamethoxazole in the United States. *Ann Intern Med* 1979;91(3):420–429.
3. Ho JM-W, Juurlink DN. Considerations when prescribing trimethoprim–sulfamethoxazole. *CMAJ Can Med Assoc J* 2011;183(16):1851–1858.
4. Jasper S, Vedula SS, John SS, Horo S, Sepah YJ, Nguyen QD. Corticosteroids as adjuvant therapy for ocular toxoplasmosis. *Cochrane Database Syst Rev* 2017;1(1):CD007417.
5. Borkowski PK, Brydak-Godowska J, Basiak W, et al. The impact of short-term, intensive antifolate treatment (with pyrimethamine and sulfadoxine) and antibiotics followed by long-term, secondary antifolate prophylaxis on the rate of toxoplasmic retinochoroiditis recurrence. *PLoS Negl Trop Dis* 2016;10(8):e0004892.
6. Silveira C, Belfort R, Muccioli C, et al. The effect of long-term intermittent trimethoprim/sulfamethoxazole treatment on recurrences of toxoplasmic retinochoroiditis. *Am J Ophthalmol* 2002;134(1):41–46.

Reply to Comment on: Long-term Results of Trimethoprim Sulfamethoxazole Versus Placebo to Reduce the Risk of Recurrent *Toxoplasma gondii* Retinochoroiditis

FIRST, WE WOULD LIKE TO THANK KUMAWAT AND ASSOCIates for their interest and critical reading of our article entitled "Long-term results of trimethoprim sulfamethoxazole versus placebo to reduce the risk of recurrent *Toxoplasma gondii* retinochoroiditis."

Regarding the indication for prophylaxis of recurrent disease, we agree that prophylaxis should be considered only for lesions involving the macula or close to the optic disc, where reactivation may lead to profound visual loss/field defect. In our study, the recurrences were adjacent to previous scars, and recurrences from the peripheral pre-existing scars had not occurred at the macula.

JOÃO PAULO FERNANDES FELIX
Campinas, Brazil
RODRIGO PESSOA CAVALCANTI LIRA
Campinas, Recife, Brazil
ALEX TREIGER GRUPENMACHER
HERMANO LUCIO GOMES DE ASSIS FILHO
ALEXANDRE BRITO COSIMO
MAURICIO ABUJAMRA NASCIMENTO
CARLOS EDUARDO LEITE ARIETA
Campinas, Brazil