

INSIGHTS INTO OCULAR HYPERTENSION



Laser treatment efficacy and central corneal thickness in patients with ocular hypertension.

BY JUNRU YAN, BA, AND LAUREN S. BLIEDEN, MD

SALT TRIAL: STEROIDS AFTER LASER TRABECULOPLASTY: IMPACT OF SHORT-TERM ANTI-INFLAMMATORY TREATMENT ON SELECTIVE LASER TRABECULOPLASTY EFFICACY

Groth SL, Albeiruti E, Nunez M, et al¹

Industry support: No

ABSTRACT SUMMARY

The double-masked, randomized, placebo-controlled, dual-center, multisurgeon Steroids After Laser Trabeculoplasty (SALT) trial examined whether the administration of steroids or NSAIDs after selective laser trabeculoplasty (SLT) had a beneficial or detrimental effect on IOP at 12 weeks. The study enrolled patients with ocular

hypertension (OHT) who were 18 years of age or older and had open angles and an IOP greater than 18 mm Hg. A total of 96 eyes of 85 patients were randomly and evenly divided into three cohorts: saline tears, prednisolone 1%, and ketorolac 0.5%. SLT treatment was 180° to 360° at the surgeon's discretion. Laser energy was 0.8 mJ initially and was then titrated to form champagne bubbles. Postoperatively, patients received unmarked bottles of drops and were instructed to administer the medication four times daily for 4 days starting on the day of the procedure. The primary outcome was IOP at 12 weeks. Secondary outcome measures included IOP at 1 and 6 weeks,

patient-reported pain, and detectable anterior chamber inflammation.

Twelve weeks after SLT, the IOP reduction was significantly greater in eyes that had been treated with steroid or NSAID drops ($P = .02$ and $P = .002$, respectively) than in the saline group. The mean reductions in IOP in OHT patients were as follows: NSAID treatment, -6.2 ± 3.1 mm Hg; steroid treatment, -5.2 ± 2.7 mm Hg; and placebo, -3 ± 4.3 mm Hg. No statistically significant differences were found at the 1- and 6-week marks.

DISCUSSION

► Why do steroids and NSAIDs lower IOP after SLT?

SLT was identified as an alternative to argon laser trabeculoplasty for lowering IOP in patients with open-angle glaucoma.³ In SLT, an Nd:YAG laser is used to target pigmented trabecular meshwork cells. Studies have shown topical NSAIDs and steroids to be useful for controlling inflammation after argon laser trabeculoplasty.^{4,5} Although some studies showing the efficacy of SLT incorporated the use of these medications, it has been unclear whether treating postoperative inflammation with topical steroids or NSAIDs ultimately affects IOP outcomes after this procedure.⁶⁻¹⁵

The presumed theory for how SLT works is that energy from the laser increases cellular recruitment and extracellular matrix remodeling,

STUDY IN BRIEF

- A double-masked, randomized, placebo-controlled trial found that the short-term postoperative use of topical steroids and NSAIDs significantly reduced IOP at 12 weeks after selective laser trabeculoplasty (SLT) in patients with ocular hypertension.

WHY IT MATTERS

It is unclear whether treatment with steroids and NSAIDs after SLT is beneficial. Some have hypothesized that the inflammatory response after SLT promotes the efficacy of the procedure and that administering an antiinflammatory medication could therefore lessen the effect of SLT.¹⁶ Other studies evaluating the ability of either a topical steroid or a topical NSAID to control inflammation after laser trabeculoplasty are limited by a retrospective design or small sample size.^{2,4,5} The Steroids After Laser Trabeculoplasty (SALT) trial is the first prospective, randomized study to compare the effects of postoperative treatment with a topical steroid, topical NSAID, and saline.

possibly via activation of inflammatory pathways, which facilitates aqueous outflow across the trabecular meshwork and thereby lowers IOP.¹⁶⁻¹⁸

It has been hypothesized that the inflammatory signaling response after SLT promotes the procedure's efficacy, in which case the administration of antiinflammatory agents such as steroids and NSAIDs would be counterproductive.¹⁶ An alternative theory, suggested by the SALT investigators, is that some inflammatory pathways trigger fibrosis and scarring and that the administration of antiinflammatory agents may improve the effect of SLT, at least at the 12-week mark. Parsing out the intricacies of specific inflammatory signaling cascades and their effects on SLT outcomes is beyond the scope of this article.

► **What are the advantages and limitations of this study?**

The main advantages of the SALT trial are its large sample size, study

design, and inclusion of three treatment arms. Although other studies have not found administering antiinflammatory medications after SLT to be beneficial, none of those study designs is comparable to that of the SALT trial.^{8,19-23} The SALT investigators acknowledge the existing literature, which failed to show a difference between treatment and control. They explain that the baseline IOP of the patients enrolled in those studies was lower than average, with values ranging from 13 to 18 mm Hg, whereas the baseline IOP in the SALT trial was 23 mm Hg. Because a higher baseline IOP is associated with a more significant absolute decrease in postoperative IOP, the SALT investigators say that they were better able to detect changes after treatment.²⁴ Given the similar baseline IOP range in each treatment arm of the SALT trial, the statistically significant effect of antiinflammatory treatment versus saline was borne out in this population, at least at 12 weeks.

There are several limitations to the SALT trial. First, the patient data were obtained and analyzed using the intention-to-treat model, which did not involve extensive checks on patients' use of eye drops other than patient-reported compliance. Second, the follow-up period was relatively short, so the long-term effects of administering these medications at the time of SLT remains unknown. Third, the size of the trial limited the investigators' ability to look at subtypes of glaucoma and draw definitive conclusions about particular forms of the disease, such as pigment dispersion and pseudoexfoliation. Finally, this study allowed variation in the degree of SLT treatment based on surgeon preference. Although surgeons were masked to postoperative treatment in this study, and although the variation in treatment parameters across the treatment groups was comparable, this factor might confound the results of a larger study or in the longer term and should be a consideration for future research.

CENTRAL CORNEAL THICKNESS IN THE OCULAR HYPERTENSION TREATMENT STUDY (OHTS)

Brandt JD, Beiser JA, Kass MA, Gordon MO; Ocular Hypertension Treatment Study (OHTS) Group²⁵

Industry support: No

ABSTRACT SUMMARY

This cross-sectional study analyzed central corneal thickness (CCT) in a subgroup of patients in the Ocular Hypertension Treatment Study (OHTS) to determine variation with respect to self-identified race. Data from living OHTS participants enrolled across 23 clinical centers from 1998 until 2001 were included. All data were collected using ultrasonic pachymeters, with five individual measurements per eye taken at the time of an annual visit. Patients with more than a 40- μ m difference between eyes upon confirmatory repeat testing were excluded from this study.

Because of the small sample sizes in other self-identified racial and ethnic cohorts, only patients who identified themselves as White or Black were

included. A total of 1,233 patients were analyzed, 318 (25%) of whom identified themselves as Black. Sex, age at testing, patient-reported medical

STUDY IN BRIEF

- A cross-sectional study examining patients enrolled in the Ocular Hypertension Treatment Study (OHTS) found that average central corneal thickness (CCT) was thinner in the Black cohort compared to the White cohort. Younger age, female sex, and diabetes were correlated with a greater mean CCT in all OHTS patients, regardless of race.

WHY IT MATTERS

Corneal thickness can significantly influence applanation readings and has been shown to have a positive correlation with IOP. A significant finding in OHTS was that thinner CCT may indicate an increased risk of developing glaucoma independent of IOP level. Most of the published information on CCT comes from studies of homogeneous White or Scandinavian populations. To date, there is limited information about CCT in Black populations, whether they are healthy or have ocular hypertension or glaucoma. A better understanding of the potential contribution of CCT to glaucoma risk and how IOP is determined in certain populations could help clinicians determine glaucoma risk. This study compared CCT in Black and White patients enrolled in OHTS.

history, baseline refraction, and baseline IOP were also considered.

Mean CCT was determined to be $573 \pm 39 \mu\text{m}$, greater than the mean CCT of $534 \mu\text{m}$ reported in a recent meta-analysis of the literature on corneal thickness.²⁶ In the OHTS, mean CCT was $23 \mu\text{m}$ thinner in Black patients than in White patients ($555.7 \pm 40 \mu\text{m}$ vs $579.0 \pm 37 \mu\text{m}$, $P < .0001$). The distribution curves of CCT across each cohort were almost identical, with that of the Black cohort shifted toward thinner measurements. Statistically significant positive correlations with thicker CCT measurements were found in patients who were younger ($P < .0001$), who were female ($P = .01$), and who reported that they had diabetes ($P = .006$). These correlations did not differ by race. No correlation was found between baseline IOP and CCT in this OHTS population.

The observed propensity to thinner corneas in this cohort of Black patients with OHT may be an important clinical consideration. Although the use of factors to correct for the influence of CCT on IOP measurements is controversial, Brandt et al point out that, if a conservative cutoff of $600 \mu\text{m}$ were used in this study, the racial cohorts would include 27% of White patients but only 14% of Black patients. Further investigation is required to assess whether the relationships observed in this OHT cohort hold in a healthy population.

DISCUSSION

► What factors affect CCT variation?

Although a strong positive correlation between CCT and IOP exists, what that means clinically is controversial. Existing data and data gathered in this study show that factors such as race, sex, and age contribute to existing variations observed in healthy individuals and those with OHT and glaucoma.

Factors correlated with CCT in this study were consistent with the published literature and were consistent in both racial cohorts. Increasing age correlated with thinning of the central

cornea ($6.3 \mu\text{m}$ per decade), consistent with prior studies.^{27,28} Men's corneas were $5 \mu\text{m}$ thinner on average than women's. Interestingly, although diabetes correlated with increased CCT in both racial cohorts, systemic hypertension was correlated with thinner corneas only in the Black cohort.

► What are the clinical implications of this study?

To date, most corneal thickness studies have involved racially homogeneous patient populations. In this study, Black patients had thinner corneas than White patients. Given that the incidence and prevalence of glaucoma are high among people of African descent, these new data may explain, in part, why population screening via tonometry alone has performed so poorly in this population.

Brandt et al did not attempt to solve the question of how CCT affects glaucoma risk. Rather, they sought to bring attention to the complexity of this issue and, in line with the goal of OHTS, to ensure that corneal thickness is taken into consideration when developing a risk model for the development of glaucoma in this high-risk population. ■

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