

Clinical & Refractive Optometry is pleased to present this continuing education (CE) article by Dr. Leonid Skorin, Jr. et al entitled **Short-Term Intraocular Pressure Trends Following Intravitreal Ranibizumab (Lucentis) Injection**. In order to obtain a 1-hour Council of Optometric Practitioner Education (COPE) approved CE credit, please refer to page 106 for complete instructions.

Short-Term Intraocular Pressure Trends Following Intravitreal Ranibizumab (Lucentis) Injection

Leonid Skorin, Jr., DO, OD, FAAO, FAOCO;
Alicia Yantes, BS; Shea Holman, BS

ABSTRACT

Purpose: To report the trends in intraocular pressures (IOP) following intravitreal injection of ranibizumab (Lucentis) for the treatment of exudative age-related macular degeneration. **Methods:** Study of 33 patients who underwent 33 consecutive ranibizumab injections. Analysis of the short-term effect of ranibizumab injections on IOP and correlation with age, gender, pseudophakia, history of glaucoma, refractive error, and previous intravitreal injections was performed. **Results:** Baseline IOP was 16.03 ± 3.396 mm Hg (mean \pm standard deviation) with a median of 16 mm Hg and a range of 10 to 23 mm Hg. Immediate post-injection IOP was 34.787 ± 9.08 mm Hg with a median of 34 mm Hg and a range of 10 to 56 mm Hg. All IOP measurements were below 25 mm Hg within 45 minutes of intravitreal injection. Baseline IOP, age, gender, history of glaucoma, refractive error, and previous intravitreal injections were of no predictive value in determining post-injection IOP. Patients who were phakic versus pseudophakic may have a slight correlation of having a higher IOP after injection. **Conclusions:** IOP returned to below 25 mm Hg in all patients within 45 minutes after ranibizumab injection. Post-injection IOP cannot be predicted by age, gender, baseline IOP, history of glaucoma, number of previous intravitreal injections, or refractive error. Phakia may have some correlation to increased post-injection IOP but more research is needed.

L. Skorin, Jr. — Staff Ophthalmic Surgeon, Albert Lea Eye Clinic, Mayo Health System, Albert Lea, MN; A. Yantes; S. Holman — Pacific University College of Optometry, Forest Grove, OR

Correspondence to: Dr. Leonid Skorin, Jr., Albert Lea Medical Center, Mayo Health System, 404 West Fountain Street, Albert Lea, MN 56007; E-mail: skorin.leonid@mayo.edu

TRANSIENT POST-INJECTION ELEVATION OF IOP

Multiple studies have reported no sustained increase in intraocular pressure (IOP) following long-term ranibizumab (Lucentis) injection therapy for the treatment of exudative age-related macular degeneration; however, transient increase in IOP has been shown to occur.^{1,2,3} One study by Heier et al reported transient increase in IOP more than 10 mm Hg above baseline IOP in 22.6% of treated eyes.¹ Elevated IOPs were found to be mild and resolved without treatment.¹

In the MARINA study, Rosenfeld et al reported that post-injection IOP increased 1.9 to 3.5 mm Hg after intravitreal injection of 0.3 mg ranibizumab and 2.1 to 3.4 mm Hg after 0.5 mg injection.² This is compared to an IOP increase of 0.8 to 1.5 mm Hg in the sham-injection group.² He also reported that IOP more than 30 mm Hg occurred in 13% of patients in the 0.3 mg group and in 17.6% of patients in the 0.5 mg group, as compared to 3.4% of patients in the sham-injection group. Intraocular pressures of 40 mm Hg or more were found in 2.3% of patients in both 0.3 mg and 0.5 mg injection groups and none in the sham-injection group.² A post-injection IOP of 50 mm Hg or more occurred in 0.6% of patients in each ranibizumab group and none in the sham-injection group.² All increases in IOP were transient and had no long-term effect.²

In the ANCHOR study, Brown et al reported that transient increase in IOP after ranibizumab injection was common.³ Intraocular pressure of 30 mm Hg or greater occurred in 8.8% of patients in the 0.3 mg group and 8.6% in the 0.5 mg group.³ Intraocular pressure measurements of 40 mm Hg or more occurred in 2.9% of patients in each ranibizumab group.³

CLINICAL TRIAL RESULTS

Short-term IOP trends following intravitreal pegaptanib (Macugen) and triamcinolone injections have also been reported.^{4,5} However, to our knowledge, the trends of who may experience increased IOP following intravitreal ranibizumab injections have not been investigated. We analyzed the IOP of 33 eyes following intravitreal injection of ranibizumab and compared these measurements

Table I Summary of the average, median, and range of IOP taken before ranibizumab injection and at the first, second, and third post-injection measurements.

| | Number of Patients | Average IOP (mm Hg) | Median IOP (mm Hg) | Range of IOP (mm Hg) |
|------------------------|--------------------|---------------------|--------------------|----------------------|
| Baseline IOP | 33 | 16.03 ± 3.396 | 16 | 10-23 |
| 1st post-injection IOP | 33 | 34.787 ± 9.08 | 34 | 10-56 |
| 2nd post-injection IOP | 30 | 25.83 ± 5.75 | 24 | 17-37 |
| 3rd post-injection IOP | 12 | 25.16 ± 3.64 | 25 | 18-31 |

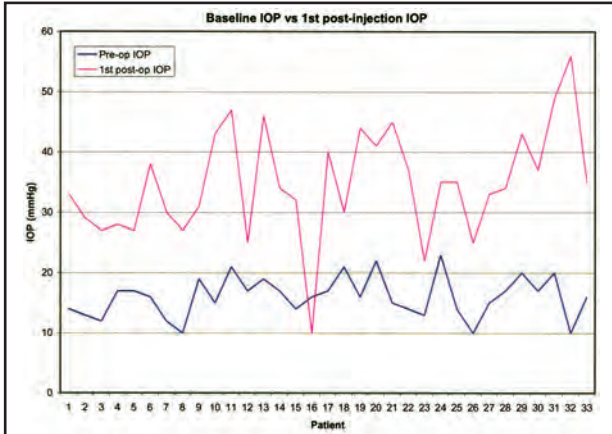


Fig. 1 Comparison of IOP before ranibizumab injection and IOP measured within five minutes after injection.

Table II Comparing the first post-injection IOP ranges with age, number of males versus females, history of glaucoma and no glaucoma, and number of hyperopes versus myopes versus emmetropes.

| Demographic | Total Number of Patients | 1st Post-Injection IOP Ranges |
|-------------------|--------------------------|-------------------------------|
| Age (71-92 years) | 33 | <20-56 mm Hg |
| Gender | | |
| Males | 10 | <20-50 mm Hg |
| Females | 23 | 21-56 mm Hg |
| Glaucoma Hx | | |
| Glaucoma | 6 | 36-40 mm Hg |
| No glaucoma | 27 | <20-56 mm Hg |
| Refractive Error | | |
| Hyperopes | 20 | <20-56 mm Hg |
| Myopes | 10 | 21-50 mm Hg |
| Emmetropes | 1 | 31-35 mm Hg |
| Unavailable | 2 | 31-40 mm Hg |

to patients' age, gender, phakia versus pseudophakia, glaucoma history versus no glaucoma, refractive error (hyperopia versus myopia versus emmetropia), and number of intravitreal injections (first versus second injection).

All patients in this study received ranibizumab injections according to the package insert (injection volume 0.05 milliliters). All IOP measurements were taken using the Tono-Pen XL applanation tonometer. On the day of injection, baseline IOP was 16.03 ± 3.396 mm Hg (mean ± standard deviation) with a median of 16 mm Hg and a range of 10 to 23 mm Hg. Within five minutes after the ranibizumab injection, IOP was 34.787 ± 9.08 mm Hg with a median of 34 mm Hg and a range of 10 to 56 mm Hg. Intraocular pressure was measured again within 10 minutes following ranibizumab injection in those patients with an IOP above 25 mm Hg (30 patients) and was 25.83 ± 5.75 mm Hg with a median of 24 mm Hg and a range of 17 to 37 mm Hg. A third IOP measurement was taken in 12 patients who still had an elevated IOP above 25 mm Hg after the second post-injection measurement. The third IOP measurement was taken within 25 minutes of the ranibizumab injection and was 25.16 ± 3.64 mm Hg with a median of 25 mm Hg and a range of 18 to 31 mm Hg (Table I).

TRENDS IN ELEVATED POST-INJECTION IOP

Twenty-four of the 33 eyes experienced an IOP elevation of greater than 30 mm Hg, with 10 eyes above 40 mm Hg and one above 50 mm Hg. Within 45 minutes of the ranibizumab injection, all IOP measurements were below 25 mm Hg. Only one of the 33 eyes needed IOP lowering drops to control IOP immediately following the injection. This one individual was pseudophakic and had a history of uveitic glaucoma. At the time of injection, the prescribed glaucoma drops were to be instilled. The other individuals with glaucoma did not require additional therapy after injection.

Our study found that 72.7% of patients had an IOP over 30 mm Hg, 30.3% had an IOP of 40 mm Hg, and 0.3% had an IOP over 50 mm Hg. This is significantly higher than the results found in previous studies and may be due to the smaller patient population in our study. Other trends cannot be compared due to different time intervals between IOP measurements. One conclusion that remains constant is that elevation in IOP following intravitreal injection of ranibizumab is transient.

According to our data, baseline IOP showed no trend in determining post-injection IOP (Fig. 1). Age, gender, a positive history for glaucoma, and refractive error were also of no predictive value in determining post-injection

Table III Comparing the first post-injection IOP ranges with the number of phakic patients to the number of pseudophakic patients.

| Demographic | Total Number of Patients | 1st Post-Injection IOP Ranges |
|--------------|--------------------------|-------------------------------|
| Phakia | 6 | 31-56 mm Hg |
| Pseudophakia | 27 | <20-50 mm Hg |

IOP (Table II). Patients who were phakic had a slightly higher increase in post-injection IOP compared to the pseudophakic patients (Table III). All these patients had measurements above 34 mm Hg, including three above 40 mm Hg and one above 50 mm Hg. However, only six of the 33 eyes were phakic and more data is needed to prove a true correlation.

Since ranibizumab injections are approved to be given every month for the treatment of exudative age-related macular degeneration, six eyes had more than one injection within the time frame of our study. We compared the number of injections to the post-injection IOP and found that the number of injections showed no trend in determining post-injection IOP.

CONCLUSION

Intravitreal injection of ranibizumab causes only a temporary IOP elevation with IOP returning to below 25 mm Hg within 45 minutes. Also, no trends were found between post-injection IOP and age, gender, baseline IOP, history of glaucoma, number of intravitreal injections, or refractive error. Phakia may have some correlation to increased post-injection IOP, however, more research is needed. □

REFERENCES

1. Heier JS, Antoszyk AN, Pavan PR et al. Ranibizumab for treatment of neovascular age-related macular degeneration: a phase I/II multicenter, controlled, multidose study. *Ophthalmology* 2006; 113: 633-642.
2. Rosenfeld PJ, Brown DM, Heier JS et al, for the MARINA study group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006; 355: 1419-1431.
3. Brown DM, Kaiser PK, Michels M, et al, for the ANCHOR study group. Ranibizumab versus verteporfin for neo-vascular age-related macular degeneration. *N Engl J Med* 2006; 355: 1432.
4. Hariprasad SM, Shah GK, Blinder KJ. Short-term intra-ocular pressure trends following intravitreal pegaptanib (Macugen) injection. *Am J Ophthalmol* 2006; 141: 200-201.
5. Lee EW, Hariprasad SM, Mieler WF et al. Short-term intraocular pressure trends after intravitreal triamcinolone injection. *Am J Ophthalmol* 2007; 143: 365-367.