Pneumatic Vitreolysis With Intravitreal Air for Focal Vitreomacular Traction

Mark E. Seamone, MD, MSc1, Uriel Rubin, MD1, Parampal S. Grewal, MD1, and Mark Greve, MD1

Abstract
Purpose: To determine whether pneumatic vitreolysis with intravitreal air is effective for focal vitreomacular traction (VMT).
Methods: We conducted a retrospective consecutive case series of 20 eyes from 19 individuals with focal VMT who underwent pneumatic vitreolysis with intravitreal air (January 2017 to November 2018). We analyzed patients via spectral-domain optical coherence tomography before intravitreal air injection and at 1 month. The primary outcome measure was release of VMT.
Results: We observed release of VMT in 55% of individuals. An analysis limited to phakic eyes demonstrated release of VMT in 69%, and 65% developed improved best-corrected visual acuity. Individuals with persistent VMT and visual improvement had a significant reduction in angle of vitreoretinal insertion ($P < .01$), area under VMT ($P < .05$), and subfoveal cyst area ($P < .05$).
Conclusions: Intravitreal air is an effective treatment for focal VMT. In individuals with persistent VMT, visual-acuity improvement was associated with a reduction in overall VMT.

Introduction
Vitreomacular traction (VMT) is a disease of the vitreal interface. Vitreous traction on the macula exerts tangential and/or anterior-posterior traction on the foveal retina, distorting the normal foveal architecture. This leads to symptoms of metamorphopsia and decreased vision. VMT adhesion is classified as focal (<1500 μm) or broad (>1500 μm). It can be isolated or associated with other ocular conditions. Tractonal forces can resolve spontaneously, be persistent with reduction in visual acuity (VA), or lead to the development of full-thickness macular hole (FTMH). Spontaneous release of VMT is variable, occurring at a rate of 11% to 32%.

Treatment of VMT aims to improve vision and reduce distortion by releasing tractional forces on the fovea. Release of VMT can be accomplished via pars plana vitrectomy (PPV) in combination with surgical release of the VMT. However, this carries the risks inherent to intraocular surgery. Nonsurgical treatment options include enzymatic or pneumatic vitreolysis. Enzymatic vitreolysis with intravitreal ocirplasmin has been met with mixed success, having a rate of VMT release ranging from 26% to 42%. In addition, ocirplasmin has been associated with complications such as formation of retinal breaks, retinal detachment, electroretinogram changes, alterations of the ellipsoid zone, and lens subluxation. There is emerging evidence supporting pneumatic vitreolysis with expansile gas. In a retrospective analysis, Chan et al reported release of VMT in 86% of eyes following intravitreal injection of perfluoropropane gas. Successful resolution of VMT has also been reported using sulfur hexafluoride gas, with a rate of 56%. Recent studies assessing the utility of pneumatic vitreolysis with intravitreal air have demonstrated mixed success.

Intravitreal injection of air instead of expansile gas has the theoretical benefits of shorter intraocular half-life, avoiding altitude-related limitations, minimizing intraocular pressure spikes, decreased cost, and improving access. We report a retrospective analysis of 20 eyes from 19 patients who received intravitreal air injection for focal VMT. In addition, we provide a quantitative analysis of the vitreoretinal interface in individuals receiving intraocular air injection using spectral-domain optical coherence tomography (SD-OCT).
Methods

Patient Selection

Twenty eyes from 19 individuals who received intravitreal air injection for symptomatic, focal VMT were identified retrospectively using our electronic medical record software (HealthQuest) as a consecutive case series from January 2017 to November 2018. One individual (patient 17, Table 1) underwent consecutive intravitreal air injections for bilateral, symptomatic, focal VMT. Patients with FTMH, preexisting epiretinal membrane, and glaucoma were excluded from the study analysis. Additional exclusion criteria included a diagnosis of diabetes or macular edema from any cause other than the tractional forces of the VMT. All individuals were analyzed via SD-OCT (Heidelberg Engineering) immediately prior to intravitreal air injection and 1 month after injection. Dilated fundus examination with scleral depression was conducted immediately prior to treatment and at all follow-up examinations. After the 1-month time point, the follow-up interval was left to the discretion of the attending vitreoretinal surgeon.

Demographic information including age, sex, eye (right or left), and lens status (phakic or pseudophakic) was collected for each patient. For pseudophakic eyes, intravitreal air injection was not conducted until at least 90 days postoperatively to avoid confounding effects of cataract surgery. Patients who had had previous posterior capsulotomy were not excluded from the study. The primary outcome was release of VMT at 1 month. Release of VMT was determined via SD-OCT and clinical examination. Secondary outcomes included improvement in best-corrected VA (BCVA) at 1 month. Individuals with persistent VMT (n = 7) at 1 month underwent analysis of the vitreoretinal interface (see Analysis of Vitreoretinal Interface).

Injection Technique

The affected eye of patients with symptomatic, focal VMT was prepared using 5% povidone. A lid speculum was placed into the patient’s fornix for optimum ocular exposure. Filtered air (0.4 mL) was injected through the pars plana using a 30-gauge short needle on a tuberculin syringe (BD Technology). Following the injection of intravitreal air, an anterior chamber paracentesis was performed using a 30-gauge short needle on a tuberculin syringe (BD Technology). Following intravitreal injection, patients were instructed to position using a “steamroller technique.” Patients were positioned upright for 15 minutes, face down for 15 minutes, on their right side for 15 minutes, and on their left side for 15 minutes for a total of 1 hour of positioning.

Analysis of the Vitreoretinal Interface

Individuals with persistent VMT (n = 7) at 2 months were analyzed using SD-OCT. Parameters analyzed included angle of vitreous insertion, area under VMT, horizontal length of vitreomacular adhesion, subfoveal cyst area, and retinal thickness (Figure 1). The angle of vitreous insertion was defined as the immediate angle of intersection of the posterior vitreous face to the retina, referenced to a line drawn perpendicular to the retinal pigment epithelium. The angle was measured using ImageJ software (National Institutes of Health and The Laboratory for Optical and Computational Instrumentation, University of

| Patient | Sex, M/F | Age, y | Pseudophakic, Y/N | BCVA*, pre-air | Release of VMT, 1 mo | BCVA, 1 mo | Complications, 1 mo |
|---------|----------|--------|-------------------|----------------|----------------------|------------|---------------------|
| 1       | F        | 74     | N                 | 20/60          | N                    | 20/40      | None                |
| 2       | F        | 70     | N                 | 20/150         | Y                    | 20/60      | None                |
| 3       | F        | 81     | Y                 | 20/70          | N                    | 20/60      | None                |
| 4       | F        | 72     | N                 | 20/40          | Y                    | 20/50      | FTMH                |
| 5       | F        | 93     | Y                 | 20/100         | N                    | 20/80      | None                |
| 6       | F        | 46     | N                 | 20/50          | Y                    | 20/50      | None                |
| 7       | F        | 66     | N                 | 20/150         | Y                    | 20/150     | None                |
| 8       | F        | 62     | N                 | 20/50          | Y                    | 20/30      | None                |
| 9       | M        | 68     | N                 | 20/80          | Y                    | 20/100     | None                |
| 10      | M        | 82     | Y                 | 20/40          | N                    | 20/30      | None                |
| 11      | F        | 65     | N                 | 20/70          | Y                    | 20/70      | FTMH                |
| 12      | F        | 82     | Y                 | 20/70          | N                    | 20/70      | None                |
| 13      | M        | 77     | Y                 | 20/50          | Y                    | 20/40      | None                |
| 14      | M        | 86     | Y                 | 20/200         | N                    | 20/200     | None                |
| 15      | F        | 79     | Y                 | 20/80          | Y                    | 20/50      | None                |
| 16      | F        | 64     | N                 | 20/40          | N                    | 20/40      | None                |
| 17      | F        | 72     | N                 | 20/50          | Y                    | 20/50      | None                |
| 18      | F        | 63     | N                 | 20/50          | Y                    | 20/25      | None                |
| 19      | M        | 63     | N                 | 20/60          | Y                    | 20/40      | None                |

Abbreviations: BCVA, best-corrected visual acuity; F, female; FTMH, full-thickness macular hole; M, male; N, no; VMT, vitreomacular traction; Y, yes.

*Snellen.
The angle of insertion on both the nasal and temporal sides of the fovea were measured and averaged, generating an average angle of vitreous insertion.

Area under VMT was defined as the average area (in square micrometer) between the posterior vitreous face and the internal limiting membrane (ILM) within 750 μm nasally and temporal of the foveal center. The horizontal length of vitreomacular adhesion was defined as the length (in micrometer) of contact between the posterior hyaloid and the ILM. Subfoveal cyst area was defined as the area (in square micrometer) of the subfoveal cystic change induced by the VMT. Finally, retinal thickness (in micrometer) was measured directly under the foveal center and defined by the boundaries of the ILM and the retinal pigment epithelium.

*Figure 1.* Analysis of the vitreoretinal interface. (A) Angle of vitreous insertion was measured using a line perpendicular to the retinal pigment epithelium. (B) Area under vitreomacular traction measured 750 μm on either side of the foveal center. (C) Subfoveal cyst area. (D) Horizontal length of vitreomacular adhesion. (E) Retinal thickness defined by the boundaries of the internal limiting membrane and the retinal pigment epithelium.

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**Statistics**

Statistical analysis was conducted using GraphPad Prism 8 software. *T* test, 1-way analysis of variance, and χ² statistic were used when appropriate.

**Results**

**Population Characteristics**

Eyes from individuals with symptomatic focal VMT were analyzed retrospectively (n = 20 eyes from 19 individuals). The mean age of the study population was 72 years (range, 46-93 years). Fifteen individuals were women, and 4 were men. Thirty-five percent of eyes (7 of 20) were pseudophakic (Table 1).

**Intraocular Air Injection Is an Effective Treatment of Focal VMT**

Intravitreal air injection resulted in release of VMT in 55% (11 of 20) of eyes at 1 month (see Table 1). When adjusted for lens status, release of VMT was noted in 69% (9 of 13) of phakic and 29% (2 of 7) of pseudophakic eyes. The difference in VMT release between phakic and pseudophakic eyes did not reach statistical significance (Table 2). Interestingly, 65% of individuals (13 of 20) experienced visual improvement after intravitreal air injection. Average visual improvement was 2.8 Snellen lines. At the 1-month time point, 35% of eyes had persistent VMT (7 of 20). Unexpectedly, 20% (4 of 20) of eyes had persistent VMT but experienced improvement in BCVA. Two eyes proceeded to develop FTMH (see Table 1). The average follow-up period was 448 days (range, 43-837 days). After the 1-month time point, 1 individual who underwent PPV for FTMH developed a rhegmatogenous retinal detachment that required further surgery.

No additional complications related to intravitreal air injection were documented. Five individuals underwent PPV, including the 2 who developed FTMH, 2 with persistent VMT without visual improvement, and 1 with persistent VMT and visual improvement who wished to pursue further intervention. One individual with persistent VMT without visual improvement had spontaneous release of the VMT 8 months after intravitreal air injection.

**Individuals With Persistent VMT and Visual Improvement Demonstrate Compression of the Vitreoretinal Interface**

To determine why individuals with persistent VMT would demonstrate improvement in VA, an analysis of the vitreoretinal interface was conducted. Parameters analyzed included angle of vitreous insertion, area under VMT, subfoveal cyst area, horizontal length of vitreous adhesion, and retinal thickness (see Analysis of the Vitreoretinal Interface for definitions).

**Table 2. Analysis of Intravitreal Air Injection for Focal Vitreomacular Traction in Phakic and Pseudophakic Eyes.**

| Lens status  | No. of patients | Release of VMT, % |
|--------------|-----------------|-------------------|
| Phakic       | 13              | 69.2              |
| Pseudophakic | 7               | 28.6              |

Abbreviation: VMT, vitreomacular traction.
Analysis of the vitreoretinal interface was conducted 1 month following intravitreal air injection.

Patients with persistent VMT and visual improvement demonstrated a significant reduction in the angle of vitreous insertion after injection of intravitreal air ($P < .01$, 95% CI, 4.5-12.6; Figures 2 and 3). This change was not observed in individuals with persistent VMT who did not demonstrate improvement in BCVA (see Figure 3). Individuals with improvement in BCVA and persistent VMT also demonstrated a significant decrease in area under VMT ($P < .05$, 95% CI, 9.1-40.9; Figure 4) and subfoveal cyst area ($P < .05$, 95% CI, 2.3-32.0; Figure 5). No change was noted in area under VMT or subfoveal cyst area in individuals with persistent VMT who did not demonstrate improvement in BCVA. Interestingly, no change was noted in retinal thickness or horizontal length of vitreomacular adhesion at 1 month (data not shown). Taken together, these results...
improving visual symptoms. However, this treatment option relieves tractional forces, restores foveal anatomy, and prevents breaks, cataract, elevated intraocular pressure, and altitude-related complications. Moreover, the use of expansile gas may be limited by accessibility.

The central hypothesis of this manuscript is that pneumatic vitreolysis using a single injection of intravitreal air represents an effective treatment of focal VMT. Moreover, the use of intravitreal air for pneumatic vitreolysis would theoretically place the patient at lower risk for the complications associated with injection of expansible gas. Primavera et al assessed the effectiveness of intravitreal air injection in 4 individuals with VMT. Release of VMT was observed in 100% of the patients.12 In contrast, Gruchociak and colleagues demonstrated release of VMT in 23% of individuals (3 of 13) using intravitreal air.11 We retrospectively reviewed the effectiveness of intravitreal air injection in 20 eyes from 19 individuals with focal VMT in a retrospective, consecutive cases series. In this series, release of VMT was observed in 55% of individuals. This is similar to results reported when using sulfur hexafluoride gas (56%) and superior to ocirplasmin.5,6,10

Moreover, an analysis limited to phakic eyes demonstrated release of VMT in 69% of individuals. Although the difference in VMT release between phakic and pseudophakic eyes was not statistically significant, the observation that intravitreal air injection may be more effective in phakic eyes is supported by previous series of pneumatic and enzymatic vitreolysis.13-15 Importantly, release of VMT using intravitreal air was not associated with significant adverse effects throughout the entire follow-up period. Taken together, the results of this study demonstrate that intravitreal air represents a safe and effective treatment of focal VMT.

Thirty-five percent of eyes in our study were observed to have persistent VMT after intravitreal air injection. Interestingly, a cohort of these eyes (4 of 7) demonstrated visual improvement in spite of persistent VMT. Injection of expansile gas destabilizes the vitreoretinal interface by inducing liquefaction during expansion followed by vitreous collapse as the bubble resorbs.16,17 Our results suggest that injection of intravitreal air may lead to destabilization of the vitreoretinal interface and reduction in traction via a similar mechanism. Although air is nonexpansile, we believe that our positioning protocol (requiring the patient to position upright, face down, and on either side for 15 minutes each) creates compression of the vitreous and expansion of the central vitreous cavity. This in turn results in a reduction of vitreous traction on the fovea. Our hypothesis is supported by a compression of the vitreoretinal interface as measured by reduction of the angle of vitreoretinal insertion, area under VMT, and subfoveal cyst size in those individuals with persistent VMT and visual improvement.

Limitations to this study include its retrospective design and lack of a comparison group. To our knowledge this study represents the largest case series using intravitreal air for the treatment of focal VMT. However, sample size remains a limitation of this study. This is particularly true when analyzing the vitreoretinal interface in individuals with persistent VMT (7 of 20 eyes). Nonetheless, we believe these results provide valuable information regarding the efficacy of intravitreal air for the treatment of focal VMT and sheds light onto its mechanism of action.

In summary, this study provides evidence for the use of intravitreal air for the treatment of VMT. In addition, we are the first to our knowledge to provide quantitative evidence of the mechanism by which intravitreal air leads to VMT release. These results are of clinical significance as pneumatic vitreolysis with intravitreal air may represent a safe, effective, and accessible in-office treatment of focal VMT with fewer theoretical adverse effects than intravitreal injection of expansible gas.

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**Ethical Approval**

Ethical approval was obtained from the Health Research Ethics Board Health Panel at the University of Alberta (Pro00077075). The study adhered to the tenets of the Declaration of Helsinki.

**Statement of Informed Consent**

Informed consent was not sought for this study because this was a retrospective series and no identifying information was included.

**Declaration of Conflicting Interests**

The author(s) declare no conflict of interest with respect to the research, authorship, and/or publication of this article.

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