# Long Term Evaluation of the Efficacy And And Safety of Nd:Yag Laser Vitreolysis for Symptomatic Vitreous Floaters

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# Abstract

**PURPOSE:** this study evaluates the long-term safety and efficacy of Nd:YAG vitreolysis for symptomatic vitreous floaters, as it remains a controversial procedure due to the lack of robust evidence in the literature for its maintenance of the results and absence of adverse effects.

**METHODS:** this is an observational extension to the previously presented prospective, randomized, double-blind clinical trial study. Eight of thirteen subjects who underwent vitreolysis with YAG laser returned for a late reevaluation, 18 months after the procedure, to evaluate the efficacy and safety of the procedure.

**RESULTS:** all patients maintained the improvement in symptomatology noted after the procedure, with 25% showing complete improvement, and a similar proportion (37.5%) reporting significant or partial improvement. Objective improvement in opacity was similar to that found at 6 months follow-up. The NEI-VFQ 25 quality of life questionnaire showed no statistically significant difference in responses between the sixth and eighteenth month. No adverse effects were noted on clinical examination or reported by patients.

**CONCLUSION:** vitreolysis efficacy observed at 6 months of follow-up was maintained until the eighteenth month, with all patients reporting improvement from the pre-procedure state. No late adverse effects were noted. A larger randomized clinical trial is needed to confirm the safety of the procedure.


# 1. Introduction

Vitreous floaters represent a consequence of posterior vitreous detachment (PVD), and is clinically perceived as vitreous opacities that present as moving dark spots in the vision [1, 2].

This is one of the most frequent complaints to ophthalmologists. In the great majority of patients, this condition is not very symptomatic, mainly when related to opacities outside the visual axis or after a certain period of neuroadaptation. However, for a portion of individuals, mainly detailers, myopic or pseudophakic people, vitreous floaters can be very annoying, interfering with perception and daily visual comfort, becoming psychically and physically exhausting [3-5].

Some management options in the face of symptomatic vitreous floaters are: patient observation and orientation, pars plana vitrectomy and laser vitreolysis.

To avoid the complications of a vitrectomy, such as retinal breaks, cataract development, retinal detachment, choroidal hemorrhage and vitreoretinal proliferation, the possibility of performing vitreolysis with Nd:YAG (neodymium-doped yttrium aluminium garnet) laser has emerged as an alternative treatment. The mechanism of laser vitreolysis is photodisruption of vitreous aggregates, causing reduction of opacity and displacement off the visual axis [6-10].

Vitreolysis with Nd:YAG laser would represent an option with lower financial cost to the patient and to the health system, a lower demand of time for not requiring hospital admission and a lower emotional distress of the patient by the shorter and less invasive process.

In our previous study, a randomized clinical trial published by Ludwig et al. in 2020, the Nd:YAG laser was applied in symptomatic patients for vitreolysis, and showed a good safety profile and improvement in the symptomatology of vitreous opacities. We demonstrated complete or significant improvement of vitreous floaters-related symptomatology in 75% of patients. No patients who underwent the laser had significant adverse effects, such as retinal ruptures, macular edema, or macular hole [11].

Other studies such as Shah *et* al. have obtained compatible results. In this study, a series of 36 eyes submitted to vitreolysis with Nd:YAG laser was analyzed. It showed an improvement of 54% in the symptoms of patients undergoing the procedure without the occurrence of significant side effects [12]. This result is corroborated by Souza et al. who reported an objective improvement of 93.7% and subjective improvement of 46.1% after a single laser session [13].

However, vitreolysis with YAG laser is still a controversial treatment due to the lack of robust evidence in the literature regarding its safety and the lack of long-term follow-up [12].

There are several complications related to the method described in the literature, including prolonged increase in intraocular pressure, development of cataract, intraocular lens damage, posterior capsule defects, retinal ruptures, retinal hemorrhages, and retinal detachment [14, 15]. However, the vast majority of studies are reports of isolated cases, so the real risk and complication rate of the procedure is not known [16].

The aim of this study is to follow up the patients from the original clinical trial who underwent vitreolysis with YAG laser, evaluating the efficacy of the procedure by measuring the maintenance of long-term benefit, as well as assessing the risk of late complications of the procedure.

## 2. Methodology

# Population:

This study evaluated the efficacy and long-term safety of another previously presented study: a randomized, controlled, masked, double-blind clinical trial conducted at a single hospital center in São Paulo, Brazil. The initial clinical trial included a total of 24 patients at the Hospital do Servidor Público Estadual de São Paulo. They were randomized and divided into two groups: YAG laser intervention (13 patients) or control, and a simulated procedure was performed (11 patients). The Ethics Committee of the São Paulo State Public Servant Hospital approved the off-label use of the YAG laser for vitreolysis in this study (reference number: 2.755.274). The study was performed in accordance with the principles of the Declaration of Helsinki and registered in the Brazilian Registry of Clinical Trials under code RBR-2jq3v. The initial planned and submitted follow-up was six months.

Long-term follow-up included a total of 13 patients treated with vitreolysis with YAG laser in a single hospital center in São Paulo - Brazil, who were seen between July 2018 and September 2020. Five patients missed follow-up for the following reasons: two did not answer repeated phone calls, and three refused to participate due to the COVID-19 pandemic.

All of these patients were followed up for 18 months, with clinical examinations performed at the following post-procedure periods: week 1, month 1, month 3, month 6, and month 18. The primary outcomes, measured at month 6 and month 18, were: 10-point visual disturbance score as described by Singh [17], 4-level qualitative scale as described by Delaney *et al*. [8], contrast sensitivity measured with the Pelli-Robson table, and the National Eye Institute Visual Functioning Questionnaire 25 (NEI VFQ-25) adapted to Portuguese [18]. Of these, the NEI VFQ-25 is the only validated method. Secondary endpoints included objective change in vitreous opacities based on masked retinography grading, visual acuity with best correction, intraocular pressure (IOP) change, and adverse event assessment.

# Statistical analysis:

The data were organized and recorded in a database in Microsoft Office Excel 2007® program with double entry. Statistical analysis was performed in the statistical program STATA® 11 SE.

The normality of the variables was tested by the Shapiro Wilk test. The evaluated variables were presented in tables with absolute and relative frequency distribution. Associations were tested by Pearson's chi-square test or Fisher's exact test, when necessary.

Statistical significance of the differences in means between the quantitative variables was verified using the paired and unpaired Student's t-test. The differences in variances were verified by means of analysis of variance (ANOVA) with repeated measures, used to evaluate the different times within a group. All analyses were performed at a 5% significance level, and the results were considered statistically significant when the p value was less than 0.05, always considering two-tailed alternative hypotheses.

## 3. Results

# Patient data:

13 eyes of 13 patients were included, 5 patients were lost to follow-up and were excluded from the study. The mean age of the patients was 60 years, with a standard deviation of 7.7, ranging from 48 to 72 years. Most of the patients analyzed were female (75.0%) and had the right eye as the most symptomatic (75.0%). All patients were phakic, had a mean complaint time of 29 months, and bothered 6.2 on the 0-10 symptom scale.

# Subjective and objective improvement:

All patients who underwent the procedure reported symptom improvement. Most patients at the sixth month of follow-up showed, in subjective improvement, a significant improvement (50.0%), followed by complete improvement (25.0%) and partial improvement (25.0%). At the eighteenth month, they showed a similar proportion of partial and significant improvement (37.5%)

In the objective assessment by the blinded evaluator, at the sixth month of follow-up, a similar proportion of patients showed significant improvement (50.0%) and partial improvement (50.0%). This proportion was maintained at the eighteenth month.

# Intraocular pressure:

The study patients started treatment with a mean IOP of 13.0±3.7. At the sixth month they had a mean IOP of 14.4±3.5. There was no statistically significant difference between IOP measurements (p=0.841). The last IOP measurement (15.1±2.7), taken at 18 months, also showed no statistically significant difference (p=0.963).

# NEI-VFQ 25:

The intervention group reported a significantly better general vision (75.8 versus 59.2; p=0.037) and a significant difference in mental health (p=0.048) was observed when comparing the sixth month values of the intervention group (84.3) and the control group (70.3).

The answer given to the questionnaire from the initial time point, at the sixth month, and at the eighteenth month of follow-up was compared, with no statistically significant difference observed.

# Subjective perception 0-10 scale:

The patients in the study started with a subjective perception of symptomatology of 6.2±1.0. At the sixth month they presented a mean perception of 2.5±2.4, representing a statistically significant difference (p = 0.001). At 18 months, they had a subjective perception of 2.4±2.3, maintaining the difference with statistical significance in relation to the initial evaluation.

# Adverse effects:

No retinal detachment, retinal tear, uveitis, cystoid macular edema, macular hole or other significant adverse effects were identified in the study. Three patients (37.5%) reported temporary blurring of vision after the procedure, with spontaneous resolution within the first day.

# Additional YAG laser treatment:

Only one patient required and desired a further session for retreatment with YAG laser vitreolysis. The patient is still being followed up for evaluation of symptomatology improvement and for the retreatment safety profile.

# 4. Discussion

The present study demonstrated expressive and consistent improvement in the symptoms of vitreous floaters after a single laser session, with 62.5% of treated patients reporting significant or complete improvement, even after 18 months of the procedure. This finding was slightly lower, however, without statistical significance compared to that found at the sixth month of follow-up, when 75% reported this improvement [11]. These data are in agreement with the findings by Shah *et al*. who obtained 50% significant or complete improvement in a similar study with 34 patients at the end of 2,3-year follow-up [19].

Other comparative data were consistent with the findings at the sixth month of follow-up, such as the 0-10 point symptomatology scale, the objective assessment of improvement of the appearance of opacity, and the responses to the NEI-VFQ 25 quality of life questionnaire. In none of the parameters evaluated was there a statistically significant difference between the sixth and eighteenth month. This suggests the durability of the long-term effects of vitreolysis with YAG laser, and is corroborated by other long-term studies [19].

The improvement in mental health found in the original study is interesting, especially considering that some patients who are bothered by floaters tend to have a higher anxiety psychological profile. This finding is supported by the study by Shah *et al*. in their long-term follow-up [19].

In this study, follow-up was performed referring to only a single laser session. In the long-term study conducted by Shah, a second vitreolysis session was performed in the sixth month of follow-up, which showed an additional improvement of 17.8% in the symptomatology related to floaters, but without statistical relevance [19]. In our case series, two patients wished to undergo a new vitreolysis session: one in the same eye as the complaint because he reported a slight worsening of the perception of opacity, and the other patient in the contralateral eye, which also presented floaters. A standardized follow-up of these patients has not yet been performed, and it is not possible to evaluate any further improvement or the safety of a new procedure. Thus, the benefit of multiple sessions for this purpose should be reevaluated in future studies, with a larger number of patients and with more accurate criteria for retreatment.

There were no clinically significant adverse effects such as retinal breaks, retinal detachment, cystoid macular edema, macular hole, uveitis, glaucoma or cataract during the entire follow-up of these patients. This is in agreement with some other studies [8, 13, 17].

Meanwhile, in the study by Shah *et al*., three late retinal tears were noted, presented between 1.4 and 2.8 years after the procedure. All ruptures were asymptomatic and detected during clinical examination. This highlights the need for long-term follow-up of these patients and a thorough clinical examination to

confirm the safety of the procedure, as well as the importance of educating the patient about alarm symptoms. However, since there was no follow-up of a control group, it is not possible to say if these late retinal ruptures are related to the treatment performed or if it would already be a risk inherent to these eyes [19].

Given a still uncertain safety profile due to the lack of robust evidence and well-designed studies, the selection of patients to undergo vitreolysis is extremely important to reduce the risk of complications and maximize individual satisfaction with the procedure. Priority should be given to patients with single opacities that are a reasonable distance from the lens and retina. If the patient is experiencing photopsias or a change in the floaters pattern, suggestive of recent PVD, observation remains as the best option [21]. It is also important to guide the patient well and inform them that multiple laser sessions may be required and that there is a chance that the treatment may not resolve the symptoms completely. All these aspects maximize the patient's satisfaction with the procedure performed.

Some limitations are inherent to this study, among them the small number of patients and the still limited follow-up. The low number of patients prevents the identification of potential rarer complications. The loss to follow-up of a considerable percentage of the initial participants may have created a selection bias. This evaluation was performed from only 1 laser session; however, in a real-life scenario more sessions may be required for complete resolution of the opacities, which would theoretically further increase its effectiveness.

Another limitation is that only vitreous opacities associated with PVD and Weiss ring were treated, making it impossible to infer that these results would be replicable to other types of vitreous opacities.

Therefore, a large, randomized, controlled study with a long follow-up is needed to determine the real risks and benefits of vitreolysis with YAG laser, comparing this procedure with vitrectomy alone and with only observation and follow-up of cases [21].

# 5. Conclusion

This study suggests that vitreolysis with Nd:YAG laser is effective and improves visual outcomes subjectively and objectively, with no adverse effects considered clinically relevant in an 18-month follow-up period. It is proposed that this procedure may be indicated for patients presenting with visual disturbances secondary to clinically confirmed vitreous opacity and with complete posterior vitreous detachment confirmed by ultrasonography (B-scan).

# Declarations

The authors report no conflicts of interest or fund source.

The authors have not presented this article in a meeting or conference.

The authors have registered this clinical trial at the Brazilian Registry of Clinical Trial under the code: RBR-2jq3v.

This research adhered to the guidelines set by the Declaration of Helsinki and was approved by the Ethics Committee of Hospital do Servidor Público Estadual under the number: 2.755.274

# DATA AVAILABILITY

The data of the current study are available from the corresponding author on reasonable request.

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