Journal of Glaucoma Publish Ahead of Print
DOI:10.1097/IJG.0000000000002051

Efficacy and Safety of micropulse transscleral laser therapy in silicone oil-induced glaucoma

Authors:

Walid ZBIBA (1), Sana SAYADI (1), Malek KHARRAT (1), Maroua DAOUED (1)

(1) Ophthalmology department, Mohamed Taher Maamouri hospital, Faculty of Medicine Tunis El Manar, Tunisia

E-mails:

Walid Zbiba: walidzbiba@hotmail.com

Sana Sayadi: Drsanasayadi@gmail.com

Malek Kharrat: kharrat.malek.abn@gmail.com

Maroua Daoued: daoudmaroua2013@gmail.com

Corresponding author:

Sana Sayadi

Address: Rue Mohamed Salah Sayadi 5000 Monastir, Tunisia

Phone number: 0021652252791

E-mail: Drsanasayadi@gmail.com

Abstract

Purpose: To assess the efficiency and safety of MicroPulse® Transscleral Laser Therapy (TLT) in the management of silicone oil-induced glaucoma.

Methods:

A prospective case series of 33 eyes with uncontrolled silicone oil-induced glaucoma was enrolled at the department of ophthalmology of Mohamed Taher Maamouri Hospital, Nabeul, Tunisia. Patients were treated with MicroPulse TLT using the IRIDEX Cyclo G6® Glaucoma Laser System with the MicroPulse P3® fiberoptic handheld probe. Patients underwent complete ophthalmologic examination during the 12-month follow-up period.

Results:

The study included 33 eyes of 33 patients. The mean age was 50.39 years old. We included patients with silicone oil-induced glaucoma. Silicone oil tamponade was indicated for complicated rhegmatogenous retinal detachment in 22 cases, diabetic tractional retinal detachment in 10 cases, and post-traumatic retinal detachment in one case. Silicone oil was already removed before the procedure in 23 eyes. Silicone oil tamponade duration varied between 3 to 26 months. IOP measurements at enrolment, day 1, day 7, day 15, 1 month, 3 months, 6 months and 12 months was respectively 37.94 ±13.61, 19.03 ±10.98, 16.5 ±6.17, 19.45 ±9.73, 19.27 ±8.33, 19.39 ±9.52, 19.97 ±10.03 and 19.7 ±9.58 mmHg. The percentage of IOP lowering was 45.38% at 6 months and 45% at 12 months. The success rate was 93.93% at 6 months remaining stable at 12 months. No major side effects were observed, in particular, no phthisis bulbi nor prolonged inflammation. There was no difference in IOP lowering between patients with silicone oil or those after silicone oil removal (p= 0.99).

Conclusion:

MP-TLT was safe and effectively lowered intraocular pressure in uncontrolled silicone-oil induced glaucoma.

Keywords: Glaucoma; ocular hypertension; silicone oils; lasers; therapeutics

Introduction:

Micropulse laser technology is a novel technique dividing laser beams in short bursts [1–4]. It was developed to reduce side effects caused by continuous laser in treating retinal diseases and glaucoma. It was first introduced for the management of open-angle glaucoma (OAG). Studies were interested especially in primary open-angle glaucoma (POAG) [2,3,5–10]. In current practice, secondary glaucoma such as silicone oil-induced glaucoma (SOG) are frequent and their management may be very challenging. SOG is a main complication of intraocular tamponade. Inflammation and silicone oil emulsification may lead to trabecular meshwork damage and to chronic ocular hypertension even after silicone oil removal[11–13]. Micropulse laser transscleral treatment (MP-TLT) has proven its efficiency and safety in treating POAG. Comparatively, it may be interesting to find out more about the place of MP-TLT in treating SOG.

Methods:

This was a prospective, non-comparative study. Thirty-three eyes with a previous diagnosis of silicone oil-induced glaucoma were enrolled at the ophthalmology department of Mohamed Taher Maamouri Hospital (MTMH) Nabeul, Tunisia. The MTMH ethics committee approved this study. All patients provided informed consent for the use of their data. The study adhered to all tenets of the declaration of Helsinki.

Inclusion criteria were patients over 18 years old with uncontrolled silicone oil-induced glaucoma. All patients underwent complete ocular examination including visual acuity, intraocular pressure (IOP) measurement, and fundus examination. IOP measurements were taken by the same ophthalmologist using the Goldmann applanation tonometer. Follow-up visits were always scheduled between 9 to 10 am to avoid nycthemeral IOP fluctuation.

Patients lost to follow-up within 6 months were omitted from the study. MicroPulse TLT was performed under peribulbar anesthesia using 4-6 ml of lidocaine chlorhydrate 2%. The same surgeon (WZ) performed the procedure using the Cyclo G6® Glaucoma Laser System with the MicroPulse P3® fiberoptic handheld probe (IRIDEX Corporation, Mountain View, CA, USA) delivering 810 nm wavelength laser energy. A lid speculum was used, and the MicroPulse P3 probe was positioned perpendicularly to the surface of the globe, the probe's notch was adjacent to the limbal margin. Using a 2000 mW power setting and a 31.3% duty cycle, the probe was applied with firm pressure and moved in a continuous back and forth sweeping motion during 80 seconds in each hemisphere from 9:30 to 2:30 and from 3:30 to 8:30 clock hours; the 9:00

and 3:00 meridians were spared. During each 80-second duration, we performed 5 continuous sweeps, each sweep duration was 16 seconds. The total energy used for each treatment session was approximately 100 joules.

Topical non-steroidal anti-inflammatory diclofenac 0.1% (DICLOABAK®, THEA, France) 2 times daily was prescribed for mild post-operative inflammation and topical dexamethasone 0.1% (Frakidex®, Bausch and Lomb, US) 4 times daily in moderate and severe cases. Anti-glaucoma medication was continued during the first post-operative month. Follow-up examinations were scheduled at days 1, 7, 15, and months 1, 3, 6, and 12 months. Best-corrected visual acuity (BCVA), IOP, detailed anterior segment examination including conjunctiva injection, anterior chamber inflammation, and fundus examination were assessed. Post-operative pain was evaluated according to the verbal analogic pain scale. Anterior chamber inflammation was assessed according to slit-lamp examination.

Patients were initially kept under their anti-glaucoma medications that were tapered during follow-up while maintaining the IOP ≤21 mmHg. Oral acetazolamide was the first to be eliminated. Additionally, further tapering was accomplished in the following order: alpha-adrenergic agonists, topical acetazolamide, beta-blockers, and prostaglandin were reduced systematically depending on the IOP.

Success criteria were defined as a decrease in IOP of more than 20%, or an IOP under 21 mmHg with a decrease in medications without visual acuity decline at the final follow-up [14,15]. Visual acuity decline was defined as a loss of 2 lines of vision.

Statistical analysis:

All statistical analysis was performed using Statistical Package for Social Sciences (version 21.0; SPSS, Inc., Chicago, IL, USA). BCVA data was converted to the logarithm of the minimal angle of resolution (log MAR) for statistical analyses. Categorical variables are presented as frequencies and percentages. Continuous variables are presented as means and standard deviations (SD). To compare IOP values during follow-ups to the baseline IOP and the BCVA at the final follow-up to the initial BCVA, we used a paired t-test. We used an independent t-test to compare the results of the two groups (before SO removal and after SO removal). A p-value < 0.05 was accepted as statistically significant.

Results:

The study included 33 eyes of 33 patients. Six patients were lost to follow-up at 12 months. The mean age of patients was 50.39 ± 12 years old. The sex ratio (ratio of male to female) was 1.75. The mean best-corrected visual acuity (BCVA) was 1.59±0.74 ranging between hand motion and 6/10. We included patients with silicone oil-induced glaucoma. Silicone oil tamponade was indicated for complicated rhegmatogenous retinal detachment in 22 cases, diabetic tractional retinal detachment in 10 cases, and post-traumatic retinal detachment in one case. Silicone oil was already removed before the procedure in 23 eyes. Silicone oil tamponade duration varied between 3 to 26 months. Ten patients (30.30%) underwent Mp-TLT without SO removal (Table 1).

At enrollment, mean anti-glaucoma treatments including drops and oral acetazolamide were 3.88 ±0.96. The mean initial IOP was 37.94 ±13.61 mm Hg. Thirty-one patients were under medical treatment only. One patient previously underwent a trabeculectomy, and one patient underwent an Ahmed valve.

IOP measurements at enrolment, day 1, day 7, day 15, 1 month, 3 months, 6 months and 12 months was respectively 37.94 ±13.61, 19.03 ±10.98, 16.5 ±6.17, 19.45 ±9.73, 19.27 ±8.33, 19.39 ±9.52, 19.97 ±10.03 and 19.7 ±9.58 mmHg (figure 1). The percentage of IOP lowering was 45.38% at 6 months and 45 % at 12 months. The number of medications decreased to 3.18±1.55 at 6 months and 3.15±1.14 at 12 months (figure2). Mean BCVA at last follow-up was 1.56 ±0.76 (p=0.08). The success rate was 93.93% at 6 months and remained stable at 12 months. Treatment failed in two multi-operated eyes for a recurrent retinal detachment.

Post-operative complications are presented in table 2. Ten patients (30.3%) manifested moderate pain. No patients manifested severe pain. Hyperemia occurred in 24 eyes (73%), chemosis occurred in 2 eyes (6%) and severe anterior chamber inflammation (ACI) occurred in only 1 eye (3%). ACI and chemosis were controlled within 1 week using steroid drops. No major side effects were observed in particular, no phthisis bulbi, prolonged inflammation, or corneal decompensation.

Table 3 resumes a comparison between patients operated before SO removal and those operated after SO removal at 6 and 12 months. There was no significant difference between the two groups (p=0.51).

Discussion:

Transscleral micropulse laser therapy was lately introduced as a non-invasive technique for treating glaucoma. Its efficiency has been proven in treating OAG

[3,5,8,16,17]. Published studies included particularly patients with POAG. As far as we know, only a few studies included patients with SOG [5,8] and no authors studied particularly SOG patients. The IOP control in these cases may be challenging.

Glaucoma is a main complication of prolonged silicone oil tamponade [11–13,17–20]. Silicone oil-induced ocular hypertension may be caused by different acute or chronic mechanisms. In this study, we got interested in chronic ocular hypertension. Currently, it is usually related to the emulsification of silicone oil and the migration of silicone droplets to the anterior chamber and the iridocorneal angle. It may obstruct trabecular meshwork or cause trabecular inflammation altering aqueous humor drainage. It may be responsible for a synechial angle-closure glaucoma and/or OAG [11–13,18–22]. Intraocular hypertension is often persistent even after silicone oil removal for different reasons. Indeed, a trabecular irreversible damage is usually constituted [11,12], and while silicone oil removal, silicone splits into small droplets and emulsifications which may potentiate intraocular inflammation and trabecular damages[11].

Silicone oil-induced glaucoma management is challenging. It may respond poorly to medical treatment. Silicone oil removal may be suggested. However, as explained before it is usually insufficient in chronic ocular hypertension, and also it exposes to a high risk of retinal detachment in some instances[11]. Invasive techniques are often needed [2,18,19]. Trabeculectomy in SOG has poor outcomes due to high inflammation related to silicone oil emulsification in the subconjunctival space and the absence of naïve conjunctiva due to scarring resulting from previous vitreoretinal surgery [2,12,13,23]. Drainage devices were suggested as a better solution. However, complications rate remains remarkable such tubes exposure, endophthalmitis, and failure due to silicone oil migration into tubes [2,12,18,23]. Finally, transscleral cyclodestructive techniques such as cyclocryotherapy and conventional laser cyclophotocoagulation were suggested as a final efficient technique but exposing to a high risk of complications[4,24]. Cyclocryotherapy is not any more commonly used nowadays due to the high risk of complications particularly inflammation, hypotony, and globe phthisis. Laser cyclocoagulation was performed using Nd-Yag laser and currently, it is replaced by diode laser cyclophotocoagulation. These techniques may expose to fewer risks than cyclocryotherapy, however, it remains a last resort solution suggested for refractory glaucoma with poor visual prognosis[2,4,24–27]. Recent studies tried to prove the efficiency and safety of slow cyclophotocoagulation in SOG performing diode laser transscleral cyclophotocoagulation under low parameters compared to conventional ones[28]. This leads ophthalmologists to

seek more efficient and safe techniques such as MP-TLT that have already proven its efficiency and safety profile in other glaucoma types[1,3,5–10,14,15,17,29,30].

In our study, after MP-TLT, IOP dropping started since day 1 after treatment with a maximal efficiency during the first month. The mean IOP percentage drop at 6 months was over 45% and remained remarkably stable at 12 months. IOP was steady during the 12-month follow-up.

Mean medication per patient decreased from 3.88 to 3.15. This slow decrease is due to the high mean IOP at enrollment. Most patients had a high initial IOP, MP-TLT permitted to control IOP while keeping the same anti-glaucoma medication.

After treatment, no major side effects were registered. Particularly, no phthisis bulbi nor prolonged inflammation. Some rare instances of phthisis were reported in published series concerning other glaucoma types [8,31] as well as corneal edema, prolonged ocular inflammation, vision loss, scleral thinning, and neurotrophic keratitis [3,16,31].

The success rate in our serie was 93.93% which is superior to other studies. In literature, success rates range between 66.6% and 89.5% [3,5,6,8–10,14,17,32,33]. We can speculate that micropulse TLT is more efficient in the case of silicone oil-induced glaucoma due to anatomical susceptibility.

In fact, in a histological study, Johnstone found that micropulse laser causes the ciliary muscle to shorten, the ciliary muscle face and the scleral spur to move posteriorly, the trabecular meshwork to move inwards and Schlemm's canal to enlarge which enhances trabecular and uveoscleral outflow [34]. We can emit the hypothesis that the absence of vitreous gel may facilitate the posterior and inward movement of the ciliary body when constricting under the effect of micropulse laser and that MicroPulse TLT could be an effective mean to treat silicone oil-induced glaucoma and to decrease anti-glaucoma medications use in those eyes. This hypothesis needs to be confirmed in further studies comparing anatomical changes in vitrectomised and non-vitrectomised eyes.

Conclusion:

MP-TLT is an interesting alternative for the management of medically uncontrolled silicone oil-induced glaucoma in patients with silicone oil or after its removal. The study showed a high success rate with a good safety profile.

Acknowledgments:

The authors declare that there is no conflict of interest in this study.

All authors participated in different steps of the study as well as the writing of the article.

Statistical analyses were performed by Mr. Chouikha Firas a statistician in the department of epidemiology and medical statistics of the University of Sousse (Tunisia).

References:

1. Brader HS, Young LHY. Subthreshold Diode Micropulse Laser: A Review. *Semin Ophthalmol*. 2016;31(1-2):30-39.

2. Abdelrahman A. Refractory Glaucomas. Types and Management. *Journal of Ophthalmology and Related Sciences*. 2017;1(1):1-14.

3. Aquino MCD, Barton K, Tan AMW, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study: Micropulse cyclophotocoagulation. *Clin Experiment Ophthalmol*. 2015;43(1):40-6.

4. Dastiridou AI, Katsanos A, Denis P, et al. Cyclodestructive Procedures in Glaucoma: A Review of Current and Emerging Options. *Adv Ther*. 2018;35(12):2103-27.

5. Jammal AA, Costa DC, Vasconcellos JPC, Costa VP. Prospective evaluation of micropulse transscleral diode cyclophotocoagulation in refractory glaucoma: 1 year results. *Arq Bras Oftalmol*. 2019;82(5):381-8.

6. Zaarour K, Abdelmassih Y, Arej N, Cherfan G, Tomey KF, Khoueir Z. Outcomes of Micropulse Transscleral Cyclophotocoagulation in Uncontrolled Glaucoma Patients: *J Glaucoma*. 2019;28(3):270-5.

7. Yelenskiy A, Gillette TB, Arosemena A, et al. Patient Outcomes Following Micropulse Transscleral Cyclophotocoagulation: Intermediate-term Results. *J Glaucoma*. 2018;27(10):920-5.

8. Tan AM, Chockalingam M, Aquino MC, Lim ZI, See JL, Chew PT. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. *Clin Exp Ophthalmol*. 2010Apr;38(3):266-72.

9. Souissi S, Baudouin C, Labbé A, Hamard P. Micropulse transscleral cyclophotocoagulation using a standard protocol in patients with refractory glaucoma naive of cyclodestruction. *EurJ Ophthal*. 2021 Jan;31(1):112-9.

10. Emanuel ME, Grover DS, Fellman RL, et al. Micropulse Cyclophotocoagulation: Initial Results in Refractory Glaucoma. *J Glaucoma*. 2017;26(8):726-9.

11. Ichhpujani P, Jindal A, Katz LJ. Silicone oil induced glaucoma: A review. *Graefes Arch Clin Exp Ophthalmol*.2009 Dec;247(12):1585-93.

12. Gupta S, Chaurasia AK, Chawla R, et al. Long-term outcomes of glaucoma drainage devices for glaucoma post-vitreoretinal surgery with silicone oil

insertion: a prospective evaluation. *Graefes Arch Clin Exp Ophthalmol*. 2016;254(12):2449-54.

13. Miller JB, Papakostas TD, Vavvas DG. Complications of Emulsified Silicone Oil after Retinal Detachment Repair. *Semin Ophthalmol*. 2014;29(5-6):312-8.

14. Abdelrahman AM, El Sayed YM. Micropulse Versus Continuous Wave Transscleral Cyclophotocoagulation in Refractory Pediatric Glaucoma: *J Glaucoma*. 2018;27(10):900-5.

15. de Crom RMPC, Slangen CGMM, Kujovic-Aleksov S, Webers CAB, Berendschot TTJM, Beckers HJM. Micropulse Trans-scleral Cyclophotocoagulation in Patients With Glaucoma: 1- and 2-Year Treatment Outcomes. *J Glaucoma*. 2020;29(9):794-8.

16. Kuchar S, Moster MR, Reamer CB, Waisbourd M. Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. Laser Med Sci.2016 Feb;31(2):393-6.

17. Toyos MM, Toyos R. Clinical Outcomes of MicropulsedTransscleralll Cyclophotocoagulation in Moderate to Severe Glaucoma. *J Clin Exp Ophthalmol*. 2016;07(06).

18. Davo-Cabrera JM, Lanzagorta-Aresti A, Alcocer Yuste P. A Novel Surgical Technique for Ahmed Valves in Refractory Glaucoma With Silicone Oil Endotamponade: *J Glaucoma*. 2017;26(10):e232-5.

19. Creuzot-Garcher C. Chirurgie du glaucome et pathologie rétinienne. *J F Ophtalmol*. 2007Feb;30(2):200-8.

20. Baillif S, Gastaud P. Surveillance d'un tamponnement par huile de silicone. *J Fr Ophtalmol*. 2014;37(3):259-65.

21. Liu Z, Fu G, Liu A. The relationship between inflammatory mediator expression in the aqueous humor and secondary glaucoma incidence after silicone oil tamponade. *Exp Ther Med*. 2016; Exp Ther Med 14(6):5833-6.

22. Madanagopalan VG, Velis G, Devulapally S. Emulsified silicone oil droplets in the canal of Schlemm. *Int Ophthalmol*. 2019;39(4):925-6.

23. Qian Z, Xu K, Kong X, Xu H. Ahmed Glaucoma Valves versus EX-PRESS Devices in Glaucoma Secondary to Silicone Oil Emulsification. *J Ophthalmol*. 2018;2018:1-7.

24. Ndulue J, Rahmatnejad K, Sanvicente C, Wizov S, Moster M. Evolution of cyclophotocoagulation. *J Ophthalmic Vis Res*. 2018;13(1):55.

25. Ramli N, Htoon HM, Ho CL, Aung T, Perera S. Risk Factors for Hypotony After Transscleral Diode Cyclophotocoagulation: *J Glaucoma*. 2012;21(3):169-73.

26. Gangwani R, Liu DTL, Congdon N, et al. Effectiveness of diode laser transscleral cyclophotocoagulation in patients following silicone oil-induced ocular hypertension in Chinese eyes. Indian J Ophthalmol. Jan-Feb 2011;59(1):64-6.

27. Han SK, Park KH, Kim DM, Chang BL. Effect of diode laser trans-scleral cyclophotocoagulation in the management of glaucoma after intravitreal silicone oil injection for complicated retinal detachments. Br J Ophthalmol.1999 Jun;83(6):713-7.

28. Khodeiry MM, Liu X, Sheheitli H, Sayed MS, Lee RK. Slow Coagulation Transscleral Cyclophotocoagulation for Postvitrectomy Patients With Silicone Oil–induced Glaucoma. *J Glaucoma*. 2021;30(9):789-94.

29. Al Habash A, AlAhmadi AS. Outcome Of MicroPulse® Transscleral Photocoagulation In Different Types Of Glaucoma.Clin Ophthalmol.2019 Dec 2;13:2353-60.

30. Kuchar S, Moster MR, Reamer CB, Waisbourd M. Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. *Lasers Med Sci*. 2016;31(2):393-6.

31. Williams AL, Moster MR, Rahmatnejad K, et al. Clinical Efficacy and Safety Profile of Micropulse Transscleral Cyclophotocoagulation in Refractory Glaucoma: *J Glaucoma*. 2018 May;27(5)445-9.

32. Amoozgar B, Phan EN, Lin SC, Han Y. Update on ciliary body laser procedures. *Curr Opin Ophthalmol*. 2017 Mar;28(2):181-86.

33. Aquino MC, Lim D, Chew PT. Micropulse P3™ (MP3) Laser for Glaucoma: An Innovative Therapy. J Curr Glaucoma Pract.May-Aug 2018;12(2):51-2.

34. Johnstone MA, Song S, Padilla S, Wen K, Xin C, Wen JC, et al. Microscope Real-time video, High-resolution OCT and histopathology to assess how transscleral micropulse laser affects the sclera, ciliary body, muscle, secretory epithelium, suprachoroidal space, and aqueous outflow system. Investigative ophthalmology and visual science vol 60,28251.

Figures:

Tables:

Number of patients at enrollment	**33 patients (33 eyes)**
Mean age (years) ± SD (Range)	50.39 ±12 (27-71)
Follow-up **6 months** **12 months**	 33 patients (33 eyes) 27 patients (27 eyes)
Sex n (%) **Male** **Female**	 21 (63.6) 12 (36.4)
Laterality n (%) **Right**	 18 (54.54)
Indication of the SO tamponade n (%) **RRD** **TRD** **Traumatic RD**	 22 patients (66.66) 10 patients (30.30) 1 patient (3.03)
Duration of SO tamponade (months)±SD (range)	10.96 ±5.88 (3-26 months)
SO removal before treatment n (%)	23 (69)

SO indicates Silicone oil, RRD rhegmatogenous retinal detachment, TRD tractional retinal detachment, RD retinal detachment

Table1: demographic characteristics of study participants

Complications	N (%)
Moderate pain	10 (30.3%)
Hyperemia	24 (73%)
Chemosis	2 (6%)
Severe AC inflammation	1 (3%)

AC indicates anterior chamber

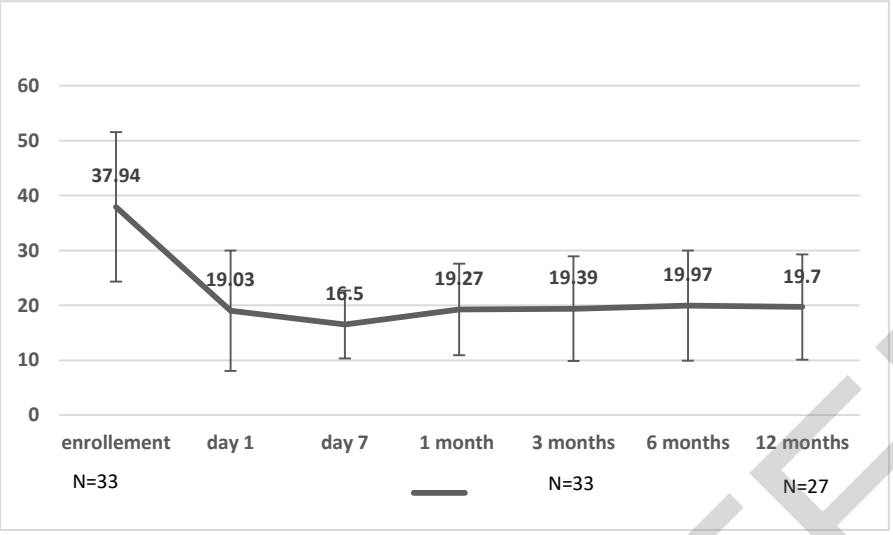
Table2: postoperative complications after Micropulse laser transscleral therapy

	IOP lowering at 6 months Mean percentage ±SD	IOP lowering at 12 months Mean percentage ±SD
Group 1: patients treated after SO removal (23 eyes)	44.40 ±16.57 %	42.51 ±19.30 %
Group 2: patients treated without SO removal (10 eyes)	44.51 ±31.41%	48.82 ± 29.86 %
	P*= 0.99	P*= 0.51

* Student t-test, IOP indicates intraocular pressure, SO silicone oil

Table3: comparative study between patients treated before/after SO removal

Figure1: IOP evolution during 12 months follow-up



IOP indicates intra-ocular pressure, * Indicated paired t-test p value: $p< 10^{-3}$

Figure 2: Number of medications decrease during 12 months follow-up