Comparative study of two different techniques of diode laser transscleral cyclophotocoagulation in management of refractory glaucoma
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Purpose
The aim was to compare between two techniques of diode laser transscleral cyclophotocoagulation in treatment of refractory glaucoma, that is, standard titratable (audible pops’ technique) versus slow coagulation technique, regarding safety and efficacy.

Patients and methods
In this prospective randomized study, 40 patients with refractory glaucoma were divided into two study groups: group A underwent standard technique of diode laser transscleral cyclophotocoagulation (audible pops technique), and group B underwent slow coagulation technique of diode laser transscleral cyclophotocoagulation. Patients were followed up at 1 week, 1 month, 3 month, and 6 month duration postoperatively, and changes in visual acuity, intraocular pressure (IOP), as well as postoperative complications were documented.

Results
The mean IOP was reduced significantly from 46.3±8.9 to 18.9±5.45 mmHg in patient of group A and from 42.8±8.53 to 20.05±8.28 mmHg in patient of group B at the end of 6-month follow-up (P<0.0001). The mean number of postoperative antiglaucoma drugs needed to control IOP was also reduced significantly in both groups. No serious complications such as hypotony were reported in the two study groups.

Conclusion
Both techniques of diode transscleral cyclophotocoagulation were of near equal safety and efficacy in treatment of refractory glaucoma with different underlying etiologies. Both had good efficacy in IOP lowering, reduced number of antiglaucoma medications used by patients, and relieved pain, with near equal incidence of postoperative complications.

Keywords:
cyclophotocoagulation, diode laser, intraocular pressure, refractory glaucoma

Introduction
Refractory glaucoma has been managed using different modalities that include shunt procedures, for example, Ahmed glaucoma valve and cyclodestructive procedures [1]. High treatment energy used by diode laser cyclophotocoagulation was argued to be associated with increased frequency of serious complications such as vision loss, hypotony, and phthisis [2,3]. These concerns necessitate modulation of the parameters of laser treatment used [4].

The aim of the present study was to compare between two techniques of diode laser transscleral cyclophotocoagulation in treatment of refractory glaucoma: standard titratable (audible pops’ technique) versus slow coagulation technique regarding safety and efficacy.
less than or equal to 3/60 (≥1.3 LogMAR) in the treated eyes.

Patients with visual acuity greater than or equal to 1.3 LogMAR in the treated eye, patients with visual acuity 3/60 (1.3 LogMAR) or less in other eye, and patients with previous cyclodestructive procedure in same eye were excluded.

Explanation of the procedure and its expected outcomes was done, and informed consents were provided by all patients. Confidentiality of all study data was ensured, and study procedures were committed to the declaration of Helsinki and were approved by the Institutional Review Board.

Complete medical and ocular history, including patients’ age, race, sex, type of glaucoma, underlying ocular disease, antiglaucoma medications, previous glaucoma surgeries, and other ocular surgeries, was obtained from all the patients. Thorough ophthalmological examination then followed, including visual acuity, intraocular pressure (IOP) measuring by Goldman applanation tonometer, slit lamp biomicroscopic examination of anterior segment, and optic nerve head evaluation when possible.

Patients were divided into two groups: group A was treated using standard technique (audible pops-titrated technique of diode laser transscleral cyclophotocoagulation). Group B was treated using the alternative slow coagulation technique of diode laser transscleral cyclophotocoagulation.

The procedure was done under peribulbar anesthesia using 1:1 mixture of xylocaine 2% and bupivacaine 0.5%. Eyes were treated using G-probe of 810 nm diode laser (Iris Medical OcuLightSLx, Iridex Co, Mountain View, California, USA). Laser was applied to group A using power of 1750 mW for 2000 ms with increment and decrement by 150 mW till prominent audible pops are heard and then the power was decreased just below the level at which prominent pops are heard. However, for group B, power applied was 1200 mW for 4000 ms. Both study groups were treated with 18–24 shots at 360° around the limbus with sparing of 3 and 9 o’clock positions to avoid harming long ciliary nerves. Treated were patched for 6 h after laser set to avoid corneal exposure.

Topical steroids, cycloplegics, systemic analgesics and antiglaucoma medications were adjusted in accordance with the response to treatment. Follow-up of visual acuity, IOP, optic disc appearance, pain monitoring, and postoperative complications was done 1 day, 1 week, 1 month, 3 months, and 6 months, postoperatively. Postoperative inflammation was defined as mild (1–15 cells), moderate (15–30 cells), and severe (>30 cells, fibrinous exudates or synechia) using 1 mm slit beam.

Data were statistically described in terms of mean, SD, and range when appropriate. Study groups’ comparisons were done using Student’s t-test for independent normally distributed samples data. Comparisons between the preoperative and postoperative data were done using Student’s t-test. P values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

Results
A total of 40 patients with refractory glaucoma were included in this study. They were divided randomly into two groups, with 20 patients in each group. Patients in group A underwent standard technique of diode laser transscleral cyclophotocoagulation (TSCPC), that is, (Titratable) audible pops technique, and group B patients underwent slow coagulation technique of diode laser TSCPC.

The mean age of patients in group A was 51.5±18.9 years (12 males and eight females) and that of patients in group B was 49.8±19.1 years (seven males and 13 females), with no clinical differences. Causes of refractory glaucoma and their distribution are summarized in Table 1.

Preoperative visual acuity ranged from no perception of light (NPL) to 1/60 (1.77 LogMAR) in group A and from NPL to 2/60 (1.47 LogMAR) in group B. No differences were found in mean postoperative visual acuity compared with that of preoperative values in the two studied groups (1.94±0.05–1.98±0.04 LogMAR in

| Table 1 Etiology of refractory glaucoma in treated groups |
|------------------------------------------------------------|
| **Aetiology** | **Group A [n (%)]** | **Group B [n (%)]** |
|----------------|---------------------|---------------------|
| Neovascular glaucoma | 7 (35) | 6 (30) |
| Aphakic/pseudophakic | 4 (20) | 4 (20) |
| Silicon oil induced | 3 (15) | 4 (20) |
| Primary open angle | 2 (10) | 3 (15) |
| Chronic angle closure | 2 (10) | 2 (10) |
| Congenital | 2 (10) | 1 (5) |
| **Total** | **20 (100)** | **20 (100)** |
group A and 1.89±0.02 to 1.92±0.06 in group B, with \( P \) values 0.49 and 0.51, respectively). Moreover, there was no reported loss of vision in the treated eyes in any patient in both study groups.

Moreover, no change was noticed in visible C/D ratios between preoperative and 6 months postoperatively in the studied groups which ranged from 0.9 to total cupping. Optic disc could not be seen in five (25%) patients in group A and in four (20%) patients in group B.

The mean IOP was reduced significantly from 46.3±8.9 to 18.9±5.45 mmHg in patient of group A, treated with standard method, and from 42.8±8.53 to 20.05±8.28 mmHg in patient of group B, treated with slow coagulation technique, at the end of 6-month follow-up (\( P<0.0001 \)) (Table 2).

Regarding group A, the mean IOP reduction ranged from 22.6 mmHg after 1 week to 27.4 mmHg after 6 months after treatment, whereas it ranged from 18.75 mmHg after 1 week to 22.75 mmHg after 6 months of treatment for group B (Table 2, Fig. 1).

In group A, the mean number of postoperative antiglaucoma drugs needed to achieve IOP control was reduced significantly from 3±0.65 (range: 1–5) to 1.35±0.59. One (5%) patient was controlled without any medications and 11 (55%) patients achieve this goal with the use of one medication, whereas eight (40%) patients were controlled only with the use of two drugs. In group B, the mean number of postoperative antiglaucoma drugs needed to control IOP was also reduced significantly from 2.95±0.67 (range: 1–5) to 1.11±0.66. No medications was needed to control IOP.

| Table 2 Mean intraocular pressure and reduction of intraocular pressure at different instances in both study groups |
|---------------------------------------------------------------|
|                  | Preoperative | 1 Week | 1 Month | 3 Months | 6 Months | \( P \) value |
|-------------------|--------------|--------|---------|----------|----------|--------------|
| **Group A**       |              |        |         |          |          | <0.0001      |
| Mean IOP (mmHg)   | 46.3±8.9     | 23.7±6.06 | 20.1±5.43 | 18.1±4.1 | 18.9±5.45 |              |
| IOP reduction     | 22.6         | 26.2   | 28       | 27.4     |          |              |
| **Group B**       |              |        |         |          |          | <0.0001      |
| Mean IOP (mmHg)   | 42.8±8.53    | 24.05±9.53 | 19.35±5.94 | 19.1±5.79 | 20.05±8.28 |              |
| IOP reduction     | 18.75        | 23.45  | 23.7     | 22.75    |          |              |

IOP, intraocular pressure. \( P<0.06 \) significant (paired t-test).
in three (15%) patients, whereas 11 (55%) patients achieve this goal with the use of one medication only and six (30%) patients were controlled with the use of two drugs (Table 3).

In group A, postoperative pain was reported in 14 (70%) patients at first day, and this number was reduced to eight (40%) patients by the end of first week and three (15%) patients after one month, with only one (5%) patient complaining of discomfort by the end of 6 months. On the contrary, in group B, postoperative pain was present in 12 (60%) patients at first day and this number was reduced to seven (35%) patients by the end of first week and two (10%) patients only after 1 month with no discomfort reported later on (Table 4).

Hyphema was reported in three (15%) patients of group A postoperatively, one was cleared after 1 month and the other two faded before 3 months with medical treatment, whereas only one (5%) case was reported in group B that resolved completely before 1 month (Table 4).

At first postoperative day, inflammation was observed in all patients treated by standard technique. Moderate uveitis was seen in seven (35%) of them and severe inflammation was seen only in 1 (5%) case, all of them resolved completely after 3 months of follow-up. The remaining 12 patients presented only with mild uveitis that resolved with treatment by the first postoperative week. Regarding group B, 12 patients were presented in the first day postoperative with uveitis, nine (45%) of them had mild one, and two (10%) had moderate inflammation, whereas one (5%) was severe at first day postoperative. All of the cases resolved completely after one month except one that resolved before 3 months of follow-up. In both study groups, no cases of hypotony (IOP <5 mmHg) was found (Table 4).

Table 3 Mean number of antiglaucoma medications needed to control intraocular pressure postoperatively in both study groups

|                          | Group A (20 patients) | Group B (20 patients) | P value |
|--------------------------|-----------------------|-----------------------|---------|
| Preoperative             | 3 ± 0.65              | 2.95 ± 0.67           | 0.33    |
| Postoperative            | 1.35 ± 0.59           | 1.11 ± 0.66           | 0.31    |
| P value                  | <0.0001*              | <0.0001*              |         |

Table 4 Pain and postoperative complications in both study groups during follow-up period

| Postoperative complications | (n=20) in each group |
|-----------------------------|----------------------|
| Pain                        | Group A 14           | Group B 12           |
| Hyphema                     | Group A 3            | Group B 1            |
| Uveitis                     | Group A Mild 12      | Group B Mild 9       |
|                             | Moderate 7           | Moderate 2           |
|                             | Severe 1             | Severe 1             |

Group A, (Titratable) audible pops’ technique; group B, slow coagulation technique.

Discussion

Improvement of the quality of life of patients with refractory glaucoma could be achieved with the use of transscleral diode laser (TS-CPC) through diminution of the number of antiglaucoma drugs, maintained IOP reduction, as well as alleviation of pain [5].

Multiple studies suggested that high energy used in treatment with diode laser TS-CPC can be associated with occurrence of severe complications [6]. Murphy et al. [7] postulated that hypotony may be associated with high treatment energy levels in neovascular glaucomas.

The most common cause of refractory glaucoma in a recent study sample in both study groups was neovascular glaucoma. Many investigators also reported the same finding, probably as diabetic retinopathy is common in the population of study with late diagnosis and poor control [5,8,9].

On the contrary, pseudophakic and aphakic glaucomas [10] as well as primary open angle glaucoma [11] were reported to be the most common cause of refractory glaucoma.

Most eyes of recent study sample had darkly pigmented uveal tissues; this was similar to the study population in Abdull et al. [12].

No significant fall in visual acuity was reported after 6 months of follow-up in both groups which may be owing to poor baseline visual acuity in the study sample.
(range from NPL to 1.77 LogMAR in group A and to 1.47 LogMAR in group B) and short follow-up duration. In other recent studies with good pretreatment visual acuity, no significant loss in visual acuity was found also [13].

On the contrary, loss of two or more Snellen’s line was reported in Scholte et al. [14] and Rotchford et al. [15] who reported visual acuity loss in 30% of cases in 5-year follow-up but was unrelated to treatment power. Visual loss of more than two Snellen’s lines was also reported in 32–33% of patients when investigating efficacy and safety of transcleral diode laser cyclophotocoagulation in eyes having good vision [16,17].

Both techniques of treatment with different settings resulted in significant reduction in IOP along different follow-up visits, with no significant difference in mean IOP reduction at 6 months postoperatively between the two techniques. Reduction in mean IOP was 27.4 and 22.75 mmHg in group A and group B, respectively, and both were comparable with the results of other investigators who reported mean IOP reduction of 23 mmHg [7], 19.75 mmHg [5], and 20 mmHg [12] respectively [5,7,12]. Ness et al. [11] in 2012 reported mean IOP reduction of 11.8 mmHg only; however, the mean baseline IOP was lower than mean baseline IOP in the recent study.

Significant reduction in mean number of antiglaucoma medications was achieved in group A and B (1.65 and 1.84, respectively), without statistically significant difference between both the groups. These results were slightly greater than other investigators who reported reduction in mean antiglaucoma medications number, which ranged from 0.9 to 1.2 [5,7,9,11].

Regarding postoperative complications, pain, uveitis, as well as hyphema were reported less frequently and found in fewer number of patients in the group treated with the slow technique compared with that of group treated with standard technique. Although these differences were statistically not significant, they still point to the slow coagulation technique as an alternative to standard technique of diode cyclophotocoagulation. In both study groups, no serious complications such as hypotony and phthisis bulbi were found. Alzuhairey et al. [9] reported persistent hyphema in 1.4% of patients treated with short duration and high energy compared with slow coagulation treatment after 1 year of postoperative follow-up. In this study, the rate and severity of complications were recognized to be relatively less compared with other previous studies. This finding could be owing to the considerably low mean energy power per treatment sessions used (76 J). These findings also agreed with that previously disclosed by other studies such as that of Scholte and colleagues, who used average power of 40–60 J per session, and Bloom and colleagues, who used an average power of 60–80 J per session [14,19]. Moreover, Stevenson-Fernandez et al. [4] and Frezzotti et al. [18] reported no serious complications in their series, as they used mean power of 79 and 72 J, respectively.

On the contrary, persistent hypotony was variably reported to follow standard treatment transscleral diode laser cyclophotocoagulation ranging from 1.4 to 10%. This was associated with the use of mean energy power ranging from 92 J in the study of Han and colleagues to 165 J in that of Chang and colleagues, who used 135–165 J [2,3,7,20–22].

The number of eyes in each diagnostic subgroup was too small to analyze the data separately and to make significant comparisons. Further studies are recommended with larger study groups and categorized subgroups with longer follow-up duration to investigate safety and efficacy in different refractory glaucoma underlying etiologies and with better baseline visual acuity.

## Conclusion
Both techniques of diode transscleral cyclophotocoagulation were of near equal safety and efficacy in treatment of refractory glaucoma with different underlying etiologies. Both had good efficacy in lowering IOP, reducing the number of antiglaucoma medications used by patients, and relieving pain, with near equal incidence of postoperative complications.

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Conflicts of interest
There are no conflicts of interest.

References
1. Schimiti RB, Abe RY, Tavares CM, Vasconcellos JP, Costa VP. Intraocular pressure control after implantation of an Ahmed glaucoma valve in eyes with a failed trabeculectomy. J Curr Glaucoma Pract 2016; 10:97–103.
2. Chang SH, Chen YC, Li CY, Wu SC. Contact diode laser transclearal cyclophotocoagulation for refractory glaucoma: comparison of two treatment protocols. Can J Ophthalmol 2004; 39:511–516.
3. Noureddin BN, ZEin W, Haddad C, Ma'luf R, Bashshur Z. Diode laser cyclophotocoagulation for refractory glaucoma: a 1 year follow-up of patients using an aggressive protocol. Eye 2006; 20:329–335.
4. Stevenson-Fernandez MO, Rodriguez-Garcia A, Espino-Barros Palau A, Gonzalez-Madrigal PM. Efficacy and safety of pop-litiated versus fixed-energy trans-scleral diode laser cyclophotocoagulation for refractory glaucoma. Int Ophthalmology 2019; 39:513–519.
5. Cruz S, Cabral D, Brazy F, Escada AV, Ferreira JG, Fernandes J, et al. Diode laser cyclophotocoagulation in the management of pain and intraocular pressure control in patients with terminal glaucoma – six years experience. Open J Ophthalmol 2017; 7:88–94.
6. Ishida K. Update on results and complications of cyclophotocoagulation. Curr Opin Ophthalmol 2013; 24:102–110.
7. Murphy CC, Burnett CAM, Spyr PGD, Broadway DC, Diamond JP. A two centre study of the dose-response relation for transscleral diode laser cyclophotocoagulation in refractory glaucoma. Br J Ophthalmol 2003; 87:1252–1257.
8. Kaushik S, Pandav SS, Jain R, Bansal S, Gupta A. Lower energy levels adequate for effective transcleral diode laser cyclophotocoagulation in Asian eyes with refractory glaucoma. Eye 2008; 22:398–405.
9. Alzuhairy S, Albahalal A, Aljaadaan I, Owaithah O, Al Shahwan S, Craven ER, et al. Intraocular pressure outcomes following transcleral diode cyclophotocoagulation using long and short duration burns. J Glaucoma 2016; 25:e782–e786.
10. Singh K, Dangda S, Ahir N, Mutreja A, Bhattacharyya M. Diode laser cyclophotocoagulation paves way to a safer trabeculectomy in eyes with medically uncontrollable intraocular pressure. Int Ophthalmol 2017; 37:365–370.
11. Ness PJ, Khairi MA, Feldman RM, Tabet R, Sarkisian Jr SR, Skuta GL, et al. Intermediate term safety and efficacy of transcleral cyclophotocoagulation after tube shunt failure. J Glaucoma 2012; 21:83–88.
12. Abdullah MM, Broadway DC, Evans J, Kyari F, Muazu F, Gilbert C. Safety and effectiveness of primary transcleral diode laser cyclophotoblation for glaucoma in Nigeria. Clin Exp Ophthalmol 2018; 46: 1041–1047.
13. Ansari E, Gandhewar J. Long-term efficacy and visual acuity following transscleral diode laser photoacoagulation in cases of refractory and non-refractory glaucoma. Eye 2007; 21:936–940.
14. Scholle T, Derse M, Zierhut M. Transscleral diode laser cyclophotocoagulation for the treatment of refractory glaucoma secondary to inflammatory eye diseases. Br J Ophthalmol 2000; 84:999–1003.
15. Rotchford AP, Jayasawal R, Madhusudhan S, Ho S, King AJ, Vernon SA. Transscleral diode laser cycloablation in patients with good vision. Br J Ophthalmol 2010; 94:1180–1183.
16. Spencer AF, Vernon SA. ‘Cyclodiode’: results of a standard protocol. Br J Ophthalmol 1999; 83:311–316.
17. Shah P, Bhakta A, Vanner EA, Kishor KS, Greenfield DS, Maharaj ASR. Safety and efficacy of diode laser transscleral cyclophotocoagulation in eyes with good visual acuity. J Glaucoma 2018; 27:874–879.
18. Frezzotti P, Mittica V, Martone G, Motolese I, Lomurmo L, Peruzzi S, et al. Longterm follow-up of diode laser transscleral cyclophotocoagulation in the treatment of refractory glaucoma. Acta Ophthalmol 2010; 88:150–155.
19. Bloom PA, Tsai JC, Sharma K, Miller MH, Rice NS, Hitchings RA, Khaw PT. Cyclodiode: trans-scleral diode laser cyclophotocoagulation in the treatment of advanced refractory glaucoma. Ophthalmology 1997; 104:1508–1519.
20. 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; 83:713–717.
21. Iliev ME, Gerber S. Long-term outcome of trans-scleral diode laser cyclophotocoagulation in refractory glaucoma. Br J Ophthalmol 2007; 91:1631–1635.
22. Martin KR, Broadway DC. Cyclodiode laser therapy for painful, blind glaucomatous eyes. Br J Ophthalmol 2001; 85:474–476.