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ORIGINAL ARTICLE

Comparative Study between the Efficacy and Safety of Subthreshold Laser and Conventional Grid Laser for Diabetic Macular Edema

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Abstract

Background: ***One of the most prevalent and potentially devastating eye consequences of diabetes mellitus is diabetic retinopathy (DR). Damage to the retina's microvascular system causes diabetic macular edema (DME). Retinal laser photocoagulation has been the gold standard for treating numerous retinal diseases, including DME.***

Objective: ***To compare the efficacy and safety of conventional grid laser photocoagulation and Subthreshold laser treatment (STLT) in cases of DME.***

Patients and methods: ***A Total of 40 eyes of patients diagnosed with DME were divided into two groups, each group containing 20 eyes. Group (A) received subthreshold laser treatment sessions, and group(B) received conventional grid laser photocoagulation treatment. Before treatment, all patients in both groups underwent best corrected visual acuity (BCVA) measurement, ophthalmological Examination including slit lamp biomicroscopy examination, fundus color photos and optical coherent tomography (OCT) imaging. All cases were selected from the outpatient clinic of the Ophthalmology Department at Al-Azhar University Hospitals (AL-Hussein and Sayed Galal) from November 2022 to January 2024.***

Results: ***The mean of BCVA After Three months for patients of STLT group was 0.80±0.16 and it was 0.57±0.16 for patients of conventional laser photocoagulation (CLP) group. The mean of central macular thickness (CMT) After Three months for patients of SLT group was 277.90μm±27.28μm and it was 332.10μm±43.63μm for patients of CLP group, and these was highly statistically significant.***

Conclusion: ***Subthreshold laser treatment is a more effective and safer treatment option for diabetic macular edema than conventional laser photocoagulation in the form of grid laser treatment.***

Keywords: Subthreshold laser; Diabetic macular edema; Grid laser

1. Introduction

A section of the retina called the macula lutea is located in the back of the eye, just beyond the optic disc. It has two sections, the fovea and the foveola, as well as a ring of structures called parafoveal and perifoveal surrounding the fovea. From a clinical perspective, the macular area is a roughly 5.5 mm wide horizontally elliptical region bordered by the temporal and upper arcuate retinal veins. As a whole, the macula represents about fifteen degrees of the visual field.[1]

A buildup of intraretinal fluid (IRF) or subretinal fluid (SRF) can happen as a result of DME, which is caused by an imbalance between the retina's hydraulic conductivity, fluid entrance, and fluid escape. Retinal fluid accumulates in the extracellular spaces of the Inner Nuclear Layer (INL), Outer Plexiform Layer (OPL), and Outer Nuclear Layer (ONL) as IRF, and subretinal fluid accumulates just beneath the neurosensory retina and above the retinal pigment epithelium (RPE) as SRF. According to the Starling equation, in a healthy retina, the active drainage function of Müller glia and RPE, as well as the integrity of the blood-retinal barrier (BRB), keep the retina's fluid balance in check. The active drainage function of the retinal pigment epithelium (RPE) and Müller glial cells keeps the retina relatively dry and functionally normal.[2]

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By controlling protein, ion, and water levels, the BRB protects the retinal neural functioning. Inner and outer BRB are the building blocks of BRB. Retinal fluid accumulates abnormally due to BRB breakdown. Damage to the BRB disrupts the balance between the oncotic and hydrostatic pressure gradients across the BRB, which in turn causes macular edema to worsen.[3]

In order to keep a cell healthy, it is essential to keep its proteins intact. Different kinds of ocular cells have their own unique systems for helping proteins fold correctly, refold partially folded or misfolded proteins, and get rid of irreparably damaged proteins. Heat shock proteins (Hsps) are molecular chaperones that protect retinal cells from damage; some authors claim that they play a pivotal role in these critical cellular protein activities.[4]

One of the first prospective, multi-centre, randomized clinical trials to show that focal (direct/grid) laser therapy was effective in treating clinically significant macular oedema (CSME) caused by diabetes was the Early Treatment Diabetic Retinopathy Study (ETDRS).[5]

Mild whitening of the retinal pigment epithelium is the intended result of grid therapy, which employs spots with sizes ranging from 50 to 200 µm for durations of 0.05 to 0.5 seconds, avoiding locations within 500 µm of the disc edge or the macula's centre. At the end of the third year of follow-up, individuals with mild to moderate non-proliferative diabetic retinopathy and macular edema who underwent grid laser photocoagulation had a 50% lower risk of vision loss compared to the control group that did not receive treatment.[5]

Another innovative laser photocoagulation method, STLT, aims to treat the macula with little collateral tissue damage.[6]

There is no discernible intra-retinal damage or scarring during or after the application of "subthreshold" laser energy, as the name suggests. While the specific way STLT triggers a therapeutic response remains a mystery, one possible explanation is that it changes the RPE's metabolic activity, which in turn releases cytokines that control angiogenesis and vascular leakage—all without causing any harm to the retina.[6]

Although STLT has demonstrated short-term improvements in visual acuity and macular oedema resolution, its most common use is in the treatment of DME.[7]

In instances of diabetic macular edema, this study aimed to evaluate the safety and effectiveness of STLT with traditional grid laser treatment.

2. Patients and methods

Individuals with type 1 or type 2 diabetes mellitus, ranging in age from 30 to 60 years old, who exhibit non-proliferative diabetic retinopathy and diabetic macular edema on optical coherence tomography (OCT), and whose central retinal thickness is less than 400 micrometers.

Exclusion criteria:

The following conditions are considered: age less than 30 and greater than 60, ocular diseases (such as pre-existing glaucoma, high myopia, media opacity, vitreous hemorrhage, dense cataract), systemic medications (such as chloroquine or tamoxifen) linked to retinopathy, prior ocular surgery (such as retinal surgery or laser treatment), and diabetic macular edema (DME) with a central macular thickness greater than 400µm.

Before treatment:

History taking and Examination:

Age, gender, Duration, onset and type of diabetes mellitus, History of medications, systemic diseases, previous operation or laser therapy. Unaided visual acuity and BCVA, Intraocular pressure by Goldman applanation tonometer. The cornea, lens, and rubeosis iridis are examined by slit lamp biomicroscopy during the Examination of the anterior segment. A non-contact fundus lens is used to examine the dilated fundus by slit lamp biomicroscopy.

Investigations:

OCT performed by Topcon DRI OCT PLUS Retina scans for assessment of: Central macular thickness, presence of Intraretinal Diabetic changes as hard exudates, presence of macular oedema. Colored fundus photography: to document the picture of the diabetic retinopathy changes in the fundus and to provide a baseline for follow-up.

Fluorescein angiography is used for several purposes: documenting any leakage in the macular area, detecting macular microaneurysms (hypofluorescent spots on the angiogram that leak later), assessing the foveal avascular zone, and identifying dot and blot haemorrhages (hypofluorescent spots on the angiogram that don't leak).

Treatment:

Group (A) received subthreshold 532 nm laser treatment using a titrating method for determining the power and duty cycle. 15% was used to apply laser in the macular area with confluent laser spots covering the whole macular area, spot size 50um, duration 100ms and interval 50ms. The area for using the IRIDEX IQ 532 machine.

Group (B) received conventional grid laser treatment with spot size 50um, power 400 mw,

duration 100ms, interval 50ms sparing the papillo-macular bundle using IRIDEX IQ 532 machine.

After treatment, the following was assessed every month for 3 months: BCVA, OCT.

Statistical analysis:

The data was input into the Statistical Package for the Social Sciences (IBM SPSS) version 26 after it had been edited, coded, and gathered. Numbers and percentages were used to represent the qualitative data, whereas means, standard deviations, and ranges were used to represent the quantitative data when their distribution was found to be parametric. When comparing two groups utilizing qualitative data, the Chi-square test was employed. However, if any cell's predicted count was less than 5, the Fisher exact test was used instead. The independent t-test was used to compare two groups with quantitative data and a parametric distribution. We allowed a 5% margin of error and put the confidence interval at 95%. This led to the conclusion that the p-value was statistically significant: The significance level is denoted as NS when P>0.05, S when P<0.05, and HS when P<0.001.

3. Results

This is 3 months, prospective interventional study that was carried on 40 eyes in patients with DME.

Demography of the study shows that the number of males to females in STLT group was 11:9, while it was 11:9 in CLP) group, and this was statistically insignificant (Fig. 2) (Table 1).

The ages ranged from 31 to 60 years (mean 50.95 years) in STLT Group, while the ranged from 33 to 60years (mean 47.00 years) in CLP Group, and this was statistically insignificant (Fig. 1) (table 1).

The Disease duration ranged from 11 to 24 years (mean 17.76 years) in STLT Group, while the ranged from 15 to 26 years (mean 18.83 years) in CLP Group, and this was statistically insignificant (Table 1).

Comparison between studied groups regarding BCVA reveals that; the mean of BCVA before intervention for patients of STLT group was 0.49±0.10 and 0.50±0.11 for patients of CLP group, and this was statistically insignificant (Table 2).

The mean of BCVA after one month for patients of STLT group was 0.64±0.12 and 0.55±0.12 for patients of CLP group, and this was statistically significant (Table 2).

The mean of BCVA after two months for patients of STLT group was 0.72±0.15 and 0.56±0.13 for patients of CLP group, and this was highly statistically significant (Table 2).

The mean of BCVA after three months for patients of STLT group was 0.80±0.16 and 0.57±0.16 for patients of CLP group, and this was highly statistically significant (Table 2). There was highly statistically significance between before intervention, after one month, after two month and after three months regarding BCVA in both groups, (Fig. 3).

Comparison between studied groups regarding CMT in microns (u): reveals that; the mean of CMT before intervention for patients of STLT group was 358.45 µm±31.05 µm and 355.50 µm±35.34 µm for patients of CLP group, and this was statistically insignificant (Table 3).

The mean of CMT after one month for patients of STLT group was 312.60 µm±37.24 µm and 333.20 µm±41.02 µm for patients of CLP group, and this was statistically insignificant (Table 3).

The mean of CMT after three months for patients of STLT group was 277.90 µm±27.28 µm and it was 332.10 µm±43.63 µm for patients of CLP group, and this was highly statistically significant (Table 3).

There was highly statistically significance between before intervention, after one month, after two month and after three months regarding CMT in both groups (Fig. 4)

Table 1. Comparison between studied groups regarding sex, age and disease duration (years).

	STLT Group	CLP Group	Test value	P-value	Sig.	
	No.=20	No.=20				
Sex	Female	9(45.0%)	9(45.0%)	0.000	1.000	NS
	Male	11(55.0%)	11(55.0%)			
Age	Mean±SD	50.95±8.36	47.00±8.35	1.494	0.143	NS
	Range	31-60	33-60			
Disease duration (years)	Mean±SD	17.76±3.75	18.83±2.99	-1.002	0.323	NS
	Range	11-24	15-26			

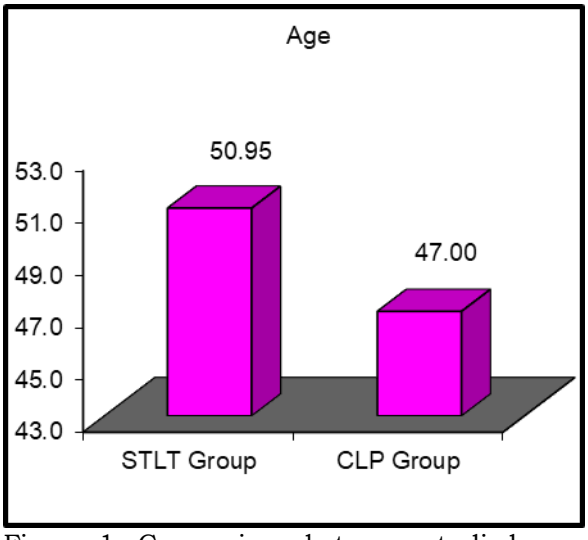

Figure 1. Comparison between studied groups regarding Age

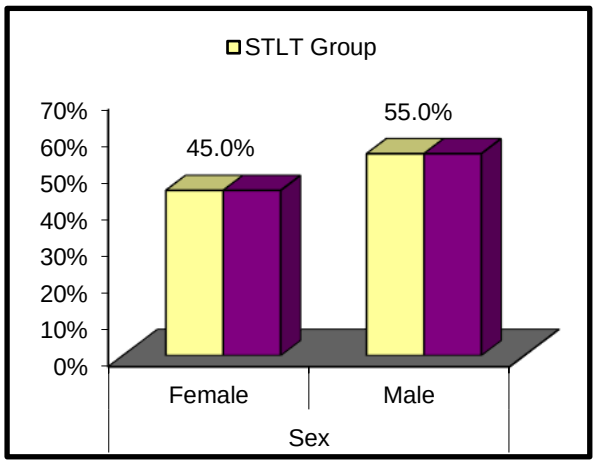

Figure 2. Comparison between studied groups regarding sex

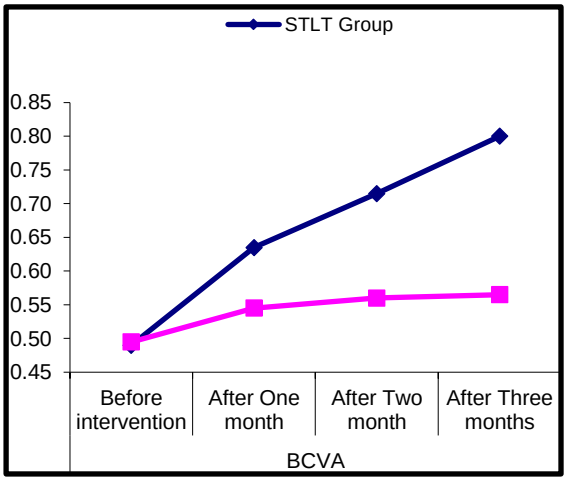

Figure 3. Comparison between studied groups regarding BCVA

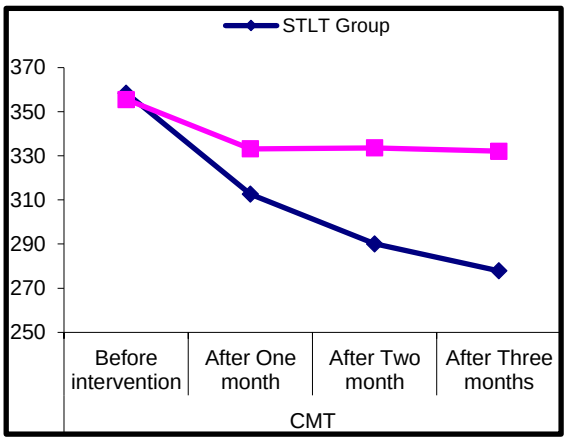

Figure 4. Comparison between studied groups regarding CMT.

Table 2. Evaluation of the research groups in relation to BCVA.

BCVA		STLT Group No.=20	CLP Group No.=20	Test value•	P-value	Sig.
Before intervention	Mean±SD	0.49±0.10	0.50±0.11	-0.149	0.882	NS
	Range	0.3-0.7	0.3-0.7			
After One month	Mean±SD	0.64±0.12	0.55±0.12	2.355	0.024	S
	Range	0.4-0.8	0.4-0.8			
After Two month	Mean±SD	0.72±0.15	0.56±0.13	3.436	0.001	HS
	Range	0.4-1	0.4-0.8			
After Three months	Mean±SD	0.80±0.16	0.57±0.16	4.662	0.000	HS
	Range	0.5-1	0.3-0.9			
Test value€		750.694	381.769	–	–	–
P-value		0.000	0.000	–	–	–
Sig.		HS	HS	–	–	–

Table 3. Comparison between studied groups regarding CMT in microns (µm)

CMT		STLT Group No.=20	CLP Group No.=20	Test value•	P-value	**Sig.**
Before intervention	Mean±SD	358.45 µm± 31.05 µm	355.50 µm± 35.34 u	0.280	0.781	**NS**
	Range	306 µm-400 µm	280 u-400 µm			
After One month	Mean±SD	312.60 µm± 37.24 µm	333.20 µm± 41.02 u	-1.663	0.105	**NS**
	Range	255 µm-392 µm	262 µm-394 µm			
After Two month	Mean±SD	290.10 µm± 31.10 µm	333.60 µm± 39.38 µm	-3.877	0.000	**HS**
	Range	236 µm-373 µm	267 µm-394 µm			
After Three months	Mean±SD	277.90 µm± 27.28 µm	332.10 µm± 43.63 µm	-4.711	0.000	**HS**
	Range	241 µm-353 µm	269 µm-400 µm			
Test value€		3691.825	1607.079	–	–	–
P-value		0.000	0.000	–	–	–
Sig.		HS	HS	–	–	–

4. Discussion

Visual impairment due to abnormal thickening of the macula caused by fluid accumulation in the extracellular space of the neurosensory retina is known as DME.[8]

Continuous wave (CW) laser is utilized in performing CLP, resulting in a visible burn on the region affected by diffuse leakage or targeted non-perfusion. The laser energy is mostly absorbed by the retinal pigment epithelium, one of the layers of the retina, and transformed into thermal energy.[9]

These side effects can be lessened by utilizing a subvisible clinical endpoint for treatment and shortening the time of laser exposure. STLT, where no scar is visible and burns are below the limit of visibility.[10]

Unlike CLP, STLT is a laser emission technique that uses a sequence of repetitive micropulses (short laser pulses) instead of a CW laser. This technique decreases the increasing temperature in the tissue by utilizing comparatively long off-times between each pulse. Pulse spacing allows the tissue to cool between pulses, decreasing heat buildup. However, repetitive micropulses can cause higher peak temperatures and more abrupt increases in tissue temperature compared to CW

laser.[11]

The researchers set out to see how subthreshold laser therapy fared against traditional grid laser treatment for diabetic macular edema, and how safe each method was.

Forty eyes of diabetic macular edema patients participated in this prospective interventional study, which lasted for three months. Clinics at Al-Azhar University saw all of the patients. Two groups were formed from the patients: Twenty eyes in Group A were treated with a subthreshold 532 nm laser. Twenty eyes were treated with the Grid laser in Group B.

In this study, the mean of BCVA after one month for patients of STLT group was 0.64±0.12 and 0.55±0.12 for patients of CLP group, and this was statistically significant. The mean of BCVA after Two month for patients of STLT group was 0.72±0.15 and 0.56±0.13 for patients of CLP group, and this was highly statistically significant. The mean of BCVA after Three months for patients of STLT group was 0.80±0.16 and 0.57±0.16 for patients of CLP group, and this was highly statistically significant.

There were highly statistically significant differences between before intervention, after one month, after two months and after three months regarding BCVA in both groups.

A multicenter clinical trial that was published not long ago by Lois et al.[12] encompassed a sizable sample of 266 eyes exhibiting moderate DMEs (<400 μm). Compared to a traditional laser treatment, STLT was found to be more effective, safer, and cost-efficient in the clinical setting. They found that between baseline and month 24, the average change in best-corrected visual acuity in the eyes of research participants was -2.43 letters (standard deviation 8.20 letters) for the subthreshold micropulse laser group and -0.45 letters (standard deviation 6.72 letters) for the standard threshold macular laser group.

Correspondingly, Fazel et al.[13] determined that moderate DME eyes that had not been treated before saw a considerable improvement in BCVA and CMT measures after STLT. In the extremely brief time frame of four months, the current research demonstrated that STLT was more successful than continuous-wave treatment.

Lavinsky et al.[14] noticed that after a year of follow-up, the anatomical and functional results were better with a high-density, confluent micropulse treatment. None of it changed following the normal-density treatment, which was spaced two burn widths apart.

4. Conclusion

According to this research, STLT, in the form of modified grid laser treatment, is a safer and more effective alternative to CLP for treating DME. Nevertheless, these results require confirmation from other research.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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