IJMA

International Journal of Medical Arts

Volume 3, Issue 2 [Spring (April-June) 2021]

http://ijma.journals.ekb.eg/

Print ISSN: 2636-4174

Online ISSN: 2682-3780

About IJMA [last updated March, 1st, 2021]

- ✓ International Journal of Medical Arts is the Official Journal of the Damietta Faculty of Medicine, Al-Azhar University, Egypt
- ✓ It is an International, Open Access, Double-blind, Peer-reviewed Journal
- ✓ Published four times a year
- ✓ The First Issue was published in July 2019
- ✓ Published under the following license: Creative Commons Attribution-ShareAlike 4.0 International Public License (CC BY-SA 4.0). It had updated from the Creative Commons license [CC BY] in volume 2, Issue 4, October 2020 About IJMA
- ✓ The Egyptian Knowledge Bank hosts the web site of IJMA
- ✓ The Egyptian Knowledge Bank supports IJMA
- ✓ IJMA follows the regulations of the International Committee of Medical Journal Editors
- ✓ IJMA is indexed in the "Directory of Open Access Journals" [Indexed on 15 January 2021].
- ✓ IJMA is a member of the International Society of Managing and Technical Editors
- ✓ Listed in "Index Copernicus", "Publons", "Academic resource index [ResearchBib]", "Electronics journal library", "Eurasian Scientific Journal Index", and "Citefactor"
- ✓ IJMA introduced to the search engine [BASE] through DOAJ

Click image to reach the page

International Journal of Medical Arts 2021; 3 [2] April -June: 1384-1389

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main subject [Ophthalmology] *

Original article

Assessment of Suprachoroidal Injection of Triamcinolone Acetonide in Cases of Diabetic Macular Edema

Mahmoud Samy Yousef [1], Yonis Alsaeid Abd Elhafez [1], Mohamed Hassanein Farag [2].

Department of Ophthalmology, Damietta Faculty of Medicine, Al-Azhar University, Egypt [1]
Department of Ophthalmology, Faculty of Medicine, Al-Azhar University, Egypt [2]

Corresponding author: Mahmoud Samy Yousef
Email: mahmoudsamy217@gmail.com
Submission date: December 26, 2020; Revision date: March 20, 2021; Acceptance date: March 22, 2021

DOI: 10.21608/ijma.2021.55079.1230

ABSTRACT

Background: Diabetic retinopathy [DR] remains one of the main causes of visual reduction in the world. The visual reduction in patients with DR is usually due to diabetic macular edema [DME]. Suprachoroidal triamcinolone acetonide injection is a new effective modality used for the management of diabetic macular edema.

The aim of the work: To assess the visual acuity [VA], central macular thickness [CMT] by optical coherence tomography [OCT] and intraocular pressure [IOP] measurement in patients with DME injected with Triamcinolone Acetonide through suprachoroidal space.

Patients and Methods: Forty eyes of 37 patients [18 males and 19 females]] with DME were included and followed-up for 6 months to assess VA, CMT and IOP. Patients were included if they were diagnosed as DME.

Results: Baseline measurements were logMAR best corrected visual acuity [VA] which was 0.83 ± 0.09, [OCT] which was 422.42 ± 64.1 µm and [IOP] which was 15.25 ± 1.46 mmHg. Post injection measurements of VA during the four points of the follow-up period showed statistically significant improvement. At one-week post-injection, logMAR VA was 0.82 ± 0.09, at one-month follow-up was 0.72 ± 0.09, at three months was 0.68 ± 0.1, at six months, was 0.62 ± 0.1,. OCT follow-up measurements showed highly significant improvements, which started from the first week post-injection till the end of the follow-up period at six months point. At one week, it measured 391.7 ± 60.6 µm, at one month the measurement was 337.1 ± 54.5 µm, at three months was 302.7 ± 46.5, at six months, was 267.9 ± 40.7.

Conclusion: Injection of TA to the suprachoroidal space in DME, was well tolerated without any serious ocular adverse events and produced significant resolution in CST and significant improvement in BCVA.

Keywords: Diabetic; Macular edema; Triamcinolone acetonide; Suprachoroidal space; Optical coherence tomography.

Citation: Yousef MS, Abd Elhafez YA, Farag MH. Assessment of Suprachoroidal Injection of Triamcinolone Acetonide in Cases of Diabetic Macular Edema. IJMA 2021; 3[2] April -June: 1384 – 1389. [DOI: 10.21608/ijma.2021.55079.1230].

* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Diabetic macular edema [DME] is one of the main causes of visual deterioration in patients with diabetes mellitus [DM] [1]. The visual deterioration in patients with diabetic retinopathy [DR] is usually related to diabetic macular edema [DME] [2].

Laser photocoagulation one of the modality for treatment of patients with DME can keep or enhance visual acuity; however, it may lead to a reduction in the field of vision, color vision or contrast sensitivity impairment [3].

It has been shown that the intravitreal injection of steroids can decrease macular edema related to different ocular diseases [4]. Also, due to multiple and repeated injections, compliance with treatment and follow up is usually low with increased risk of ocular or systemic adverse effects [5]. The supra-choroidal space [SCS] provides a new route for drug administration to the posterior segment because it crosses the internal limiting membrane and may theoretically provide higher concentration within the choroid, retinal pigment epithelium [RPE], and ciliary body while decreasing drug levels in the anterior segment, so decreasing the risk of cataract and intraocular pressure [IOP[elevation. However, this flow in restricted and sectionalized by the scleral spur anteriorly and optic nerve posteriorly, so anterior segment component is spared [6].

The SCS is a new modality for intraocular drug administration which can pass the sclera without the risk of IO penetration [7]. SCS drug administration can be done using microneedles, small-gauge needles only 0.7–1.0 mm in length, that are long enough to pierce the sclera and access the SCS [8]. Micro-needles have also been developed which allow for injection into the SCS using procedure like that used for intravitreal injections [9].

Triamcinolone acetonide [TAAc] is a synthetic corticosteroid formulated as an injectable suspension and has a 7.5 –fold higher in anti –inflammatory potency than cortisone [10]. The clinical efficacy and safety of intravitreal TAAc injections have been evaluated in a number of trials. TAAc increases the levels of tight-junctions in between endothelial cells and thus lessens vessel leakage. It also has an angiostatic action through vascular endothelial growth factor [VEGF] inhibition and therefore may have a useful effect on DME. The dose of TAAc administered by this root is 4 mg/100 µL which was administrated in our study [11].

AIM OF THE WORK

This work aims to assess the visual acuity [VA] and central macular thickness [CMT] by [OCT] in patients with DME injected with Triamcinolone Acetonide through suprachoroidal space.

PATIENTS AND METHODS

This prospective study included 40 eyes in patients with evident diabetic macular edema in Faculty of medicine [Damietta] Al Azhar University from March 2020 to December 2020. The study was approved by the Medical Ethics Committee of Al-Azhar University Faculty of Medicine. Calculation of sample size was done using EPI-INFO 2002 software package designed by WHO and centers of disease control and prevention revealed that, at least 38 eyes were required to find a significant difference in visual acuity and central macular thickness at α value of 0.05 and power of study 95%. This calculation was based on results of a previous study [12].

Forty eyes of 37 patients [18 males and 19 females] with [DME] were included and followed-up for 6 months to assess VA, CMT and IOP. Patients were included with diabetic macular edema and patients with evident DME by OCT [Topcon 3D OCT 2000]. Mean patient age was 57.4 years [range 44–67 years].

Inclusion criteria: Written informed consent will be obtained from all patients included in the study after the nature and possible consequences of the procedure have been explained, Patients with diabetic macular edema and patients with evident DME by OCT [Topcon 3D OCT 2000].

Exclusion criteria: Patients who refuse to participate in the study, if there is media opacity interferes with preoperative evaluation [e.g. dense cataract & dense vitreous hemorrhage], macular edema that results from non-diabetic causes [e.g. CRVO, BRVO, Vitro-macular traction, Uveitis or any collagen and vascular disease] and intraoperative complications [choroidal hemorrhage & vitreous hemorrhage].

Surgical procedure: Before the injection, topical

anesthesia was administered at the injection site: either benoxinate or subconjunctival lidocaine 1%. The administration of 2–3 drops of 5% Betadine topically in the lower fornix was performed. The eyelids were scrubbed with cotton-tipped applicators soaked in 5% Betadine. TA vial was drawn up into a sterile syringe using a non-filtered 28 gauge needle. Needles were changed to sterile SCS injection needle, and then air bubbles and excess volume were expelled to 0.1 ml preserved TA. A sterile lid speculum was placed. The patients were asked to look down and the injection site was marked 3.5–4.0 mm posterior to the limbus in the superotempotal quadrant with calipers. Small-gauge needles only 0.7–1.0 mm in length that are long enough to pierce the sclera and access the SCS. This technique was done in several clinical trials. The dose of triamcinolone acetonide administered by this root is 4 mg/100 µL. The eye was rinsed with eye wash or saline.

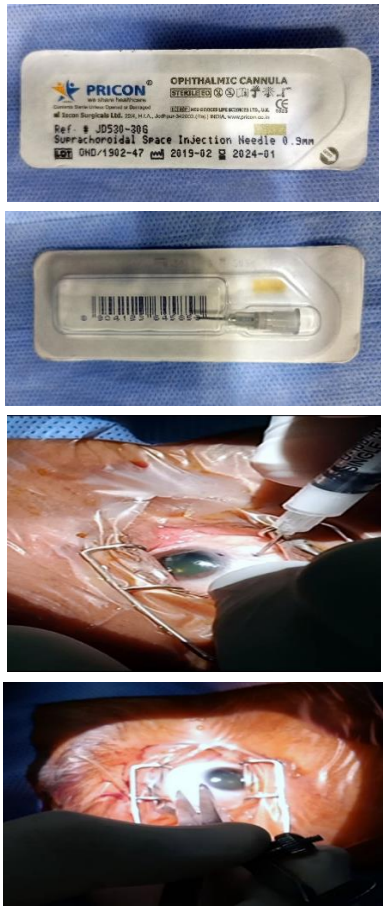

Figure [1]: Instruments and surgical technique

Follow-up: All patients underwent an ophthalmic examination on days one and seven post injections, to assess injection-related complications such as anterior chamber reaction or IOP rise, etc. Follow-up was performed regularly by determining BCVA, IOP measurement, fundus biomicroscopy and CMT using spectral-domain OCT one week, one month, three months and six months post injection**.** Anterior segment OCT and UBM were done for some cases immediately after injection and reported that TA located in SCS in these cases. Not done for all cases as this this work aims to assess [VA] and central macular thickness by [OCT] in patients with [DME] not to assess anatomical site of the injection as this technique of imaging is cost-effective on patients and medical authorities.

Statistical Analysis: All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows [SPSS Inc., Chicago, IL, USA] & MedCalc 13 for windows [MedCalc Software bvba, Ostend, Belgium]. Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD [Standard deviation] for parametric and median and range for non-parametric data. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates a highly significant difference while, P> 0.05 indicates non-significant difference.

RESULTS

We included forty eyes [20 right eyes and 20 left eyes] of 37 patients, out of them, there were 18 males [48.6%] and 19 females [51.4%]. The mean age of the study patients was 57.4±5.1 years. Baseline [pre-injection] measurements were logMAR visual acuity [VA] which was 0.83±0.09, optical coherence tomography [OCT] which was 422.42 ± 64.1 µm, and intraocular pressure [IOP] which was 15.25 ± 1.46 mmHg measured by applanation tonometer [Table 1]. Post injection measurements of VA during the four points of the follow-up period showed statistically significant improvement. One-week post-injection, logMAR VA was 0.82±0.09, [P = 0.02]; at one-month follow-up was 0.72±0.09, [P < 0.001]; at three months was 0.68±0.1, [P < 0.001]; at six months, was 0.62±0.1, [P < 0.001] [Table 2].

OCT follow-up measurements showed highly significant improvements, which started from the first

week post-injection till the end of the follow-up period at six months point. At one week, it measured 391.7± 60.6µm, [P < 0.001]; at one month, the measurement was 337.1±54.5 µm, [P< 0.001]; at three months was 302.7± 46.5, [P < 0.001]; at six months, was 267.9± 40.7, [P < 0.001] [Table 3]. IOP showed a transient rise during the follow-up period at one-week [15.7±1.52mmHg, P-value < 0.001] and one-month points [15.55±1.33 mmHg, P-value = 0.006]. However, at three and six-months point, the IOP nearly returned to baseline and there was no identified significant change from baseline. At three months, the IOP was 15.35±1.38 mmHg, [P = 0.3]; at six months it was 15.3±1.4 mmHg, [P = 0.5] [Table 4].

Table [1] shows the demographics and baseline characteristics of the study patients

Variable		Result
Age		57.4 ± 5.1
Gender	Male	18 [48.6%]
	Female	19 [51.4%]
Eye	Right	20 [50%]
	Left	20 [50%]

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months' post injection; P4: comparison between baseline values and values at six months' post injection.

Table [2] shows the BCVA outcomes during the follow-up period and their comparison to the baseline

VA [logMAR]	Result	P-value
VA at baseline [logMAR]	0.83 ± 0.09	-----
VA at 1-week post-injection	0.82 ± 0.09	P1= 0.02*
VA at 1-month post-injection	0.72 ± 0.09	P2 < 0.001*
VA at 3 months post-injection	0.68 ± 0.1	P3 < 0.001*
VA at 6 months post-injection	0.62 ± 0.1	P4 < 0.001*

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months' post injection; P4: comparison between baseline values and values at six months' post injection.

Table [3] shows the OCT outcomes during the follow-up period and their comparison to the baseline

OCT [µm]	Result	P-value
OCT at baseline [µm]	422.42 ± 64.1	-----
OCT at 1-week post-injection	391.7 ± 60.6	P1 < 0.001*
OCT at 1-month post-injection	337.1 ± 54.5	P2 < 0.001*
OCT at 3 months post-injection	302.7 ± 46.5	P3 < 0.001*
OCT at 6 months post-injection	267.9 ± 40.7	P4 < 0.001*

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months' post injection; P4: comparison between baseline values and values at six months' post injection.

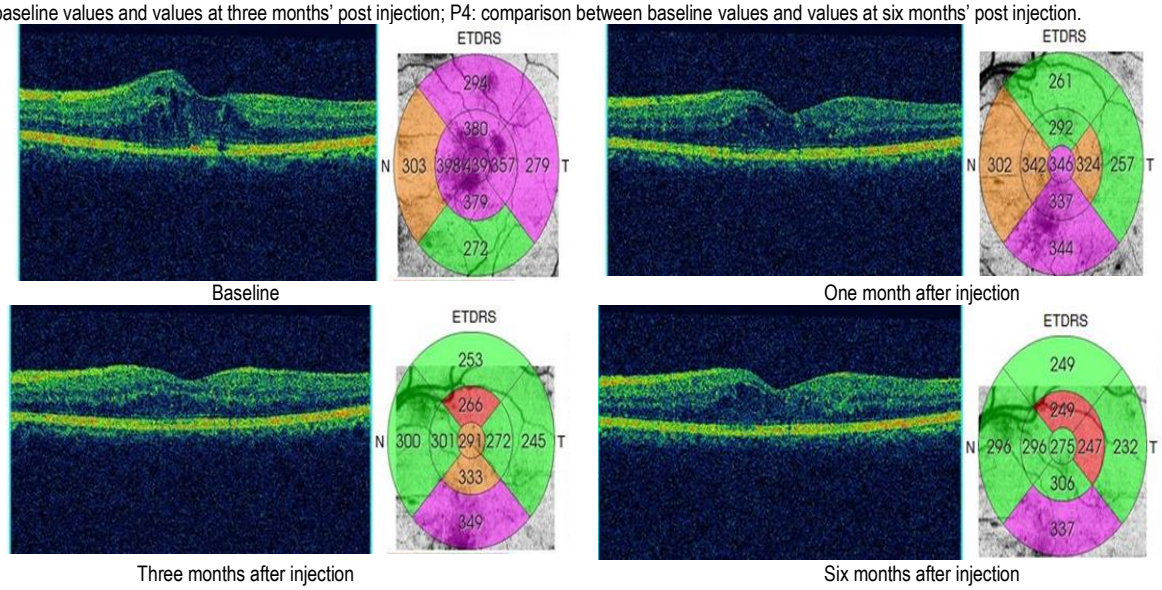

Figure [2] shows OCT changes after injection compared to basal values

Table [4] shows the IOP outcomes during the follow-up period and their comparison to the baseline

IOP [mmHg]	Result	P-value
IOP at baseline [mmHg]	15.25 ±1.46	-----
IOP at 1-week post-injection	15.7 ± 1.52	P1< 0.001*
IOP at 1-month post-injection	15.55 ± 1.33	P2=0.006*
IOP at 3 months post-injection	15.35 ± 1.38	P3=0.3
IOP at 6 months post-injection	15.3 ± 1.4	P4=0.5

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months' post injection; P4: comparison between baseline values and values at six months' post injection.

DISCUSSION

The injection of corticosteroid to the supra-choroidal space has the same efficacy to that of intravitreal injection. One difference, however, is that suprachoroidal imjection is associated with longer half-life [no washout, more absorption time] and low incidence of IOP rise [13].

Recent studies have approved the safety and efficacy of needle-based suprachoroidal drug injection. In this minimally invasive technique, a microneedle penetrates transscleral to the appropriate depth during drug delivery [14].

Similar to our study [HULK Trial; N = 20] [15] found the basis of safety and efficacy of SCTA for DME in treatment. The difference in our study and HULK trial was that did not combine the first injection of SCTA with Aflibercept. The mean pre-treatment CST in HULK trial was 473 um whereas in our study it was 422.42 ± 64.10 um. At six months, mean CST in HULK reduced to 369 um whereas in our study, mean CST at six month follow up was 267.90 ± 40.70 um.

In agreement with the study of Ameen Marashi and Benjamin J. [16] study of 50 eyes of 36 patients. Approximately 42% of eyes required an injection within 8 weeks; the mean CMT was 456 µm at baseline and decreased to 309 µm within 6 weeks but the CMT increased to 384 µm in 8 weeks and decreased again to 330 µm after the second injection. On average, BCVA improved from 0.8 to 0.5 at 16 weeks in these eyes. Approximately 58% of eyes required only one injection during 16 weeks; the mean CMT was 421 µm at baseline and decreased to 339 µm within 6 weeks, but the CMT increased to 384 µm at 16 weeks while in our study showed highly significant improvements which started from the first week post-injection till the end of the follow-up period at six months point. At 1 week, it measured 391.7 ± 60.6 µm; at 6 months, was 267.9 ± 40.7 µm, [On average, BCVA improved from 0.6 to 0.4 at 16 weeks in these eyes this goes with our study which showed statistically significant improvement. At 1 week post-injection, logMAR VA was 0.82 ± 0.09,; at 6 months, was 0.62 ± 0.1.

Injecting triamcinolone into the suprachoroidal space may reduce the risk of IOP elevation because drug delivery is directed to the choroid and the retina and is restricted from the trabecular meshwork achieving better improvement in BCVA and reduction of macular edema compared with intravitreal steroid injection.

Also the study of Isaac DL et al. [17] showed that regarding IOP in the group of eyes treated with triamcinolone, no statistical difference was found between the initial visit and the 4-week [p = 0.08] and the 24-week visits [p = 0.25]. However, a statistically significant difference regarding week 12 [p = 0.01] was determined.

Among the eyes treated with triamcinolone, IOP in three eyes [27.3%] increased to more than 21 mmHg, and for this reason, they were treated with antiglaucoma drugs. While our study showed that a transient rise during the follow-up period at one week [15.7 ± 1.52 mmHg, P-value < 0.001] and one month points [15.55 ± 1.33 mmHg, P-value = 0.006]. However, at three and six months point, the IOP nearly returned to the baseline and there was no identified significant change from the baseline. At three months the IOP was 15.35 ± 1.38 mmHg; at six months it was 15.3 ± 1.4 mmHg.

The most common side effects were local hyperemia or subconjunctival hemorrhage at the site of injection which were self-limited. In our study no patient experienced IOP elevation, the progression of cataract, suprachoroidal and vitreous hemorrhage, choroidal or retinal detachment or endophthalmitis during the period of follow up.

Conclusion: Injection of TA to the suprachoroidal space in DME, was well tolerated without any serious ocular adverse events and produced significant resolution in CST and significant improvement in BCVA. Future studies on larger sample size and longer duration, possibly with a different regimen will need to be conducted to establish the safety and efficacy of this technique.

Financial and Non-financial Relationships and Activities of Interest

None

REFERENCES

1. **Al Rashaed S, Arevalo JF.** Combined therapy for diabetic macular edema. Middle East Afr J Ophthalmol. **2013** Oct-Dec; 20 [4]:315-20. [Doi: 10.4103/0974-9233.120014].
2. **Cheung N, Mitchell P, Wong TY.** Diabetic retinopathy. Lancet. **2010** Jul 10;376 [9735]: 124-36. [DOI: 10.1016/S0140-6736[09]62124-3].
3. **Bhagat N, Grigorian RA, Tutela A, Zarbin MA.** Diabetic macular edema: pathogenesis and treatment. Surv Ophthalmol. **2009** Jan-Feb;54[1]:1-32. [DOI: 10.1016/ j.survophthal.2008.10.001].
4. **Haller JA, Dugel P, Weinberg DV, Chou C, Whitcup SM.** Evaluation of the safety and performance of an applicator for a novel intravitreal dexamethasone drug delivery system for the treatment of macular edema. Retina. **2009** Jan; 29[1]:46-51. [DOI: 10.1097/IAE.0b013e318188c814].
5. **Wang JC, Eliott D.** Accessing the Suprachoroidal Space for Therapeutic Delivery. Int Ophthalmol Clin. **2017** Fall; 57 [4]:179-192. [DOI: 10.1097/IIO.0000000000000195].
6. **Del Amo EM, Rimpelä AK, Heikkinen E, Kari OK, Ramsay E, Lajunen T, et al.** Pharmacokinetic aspects of retinal drug delivery. Prog Retin Eye Res. **2017** Mar; 57: 134-185. [DOI: 10.1016/j.preteyeres.2016.12.001].
7. **Seiler GS, Salmon JH, Mantuo R, Feingold S, Dayton PA, Gilger BC.** Effect and distribution of contrast medium after injection into the anterior suprachoroidal space in ex vivo eyes. Invest Ophthalmol Vis Sci. **2011** Jul 29;52[8]:5730-6. [DOI: 10.1167/iovs.11-7525].
8. **Patel SR, Lin AS, Edelhauser HF, Prausnitz MR.** Suprachoroidal drug delivery to the back of the eye using hollow microneedles. Pharm Res. **2011** Jan;28 [1]:166-76. [DOI: 10.1007/s11095-010-0271-y].
9. **Moisseiev E, Loewenstein A, Yiu G.** The suprachoroidal space: from potential space to a space with potential. Clin Ophthalmol. **2016** Jan 25; 10:173-8. [DOI: 10.2147/OPTH. S89784].
10. **Shamsi HN, Masaud JS, Ghazi NG.** Diabetic macular edema: New promising therapies. World J Diabetes. **2013** Dec 15;4[6]:324-38. [DOI: 10.4239/wjd.v4.i6.324].
11. **Emami-Naeini P, Yiu G.** Medical and Surgical Applications for the Suprachoroidal Space. Int Ophthalmol Clin. **2019** Winter;59[1]:195-207. [DOI: 10.1097/IIO.0000000000000 251].
12. **Yeh S, Kurup SK, Wang RC, Foster CS, Noronha G, Nguyen QD, et al.** Suprachoroidal injection of triamcinolone acetonide, CLS-TA, for macular edema due to noninfectious uveitis: a randomized, phase 2 study [DOGWOOD]. Retina. **2019**; 39[10]. 1880-1888. [DOI: 10.1097/IAE.0000000000002279].
13. **Patel SR, Berezovsky DE, McCarey BE, Zarnitsyn V, Edelhauser HF, Prausnitz MR.** Targeted administration into the suprachoroidal space using a microneedle for drug delivery to the posterior segment of the eye. Invest Ophthalmol Vis Sci. **2012** Jul 1;53 [8]: 4433-41. [DOI: 10.1167/iovs.12-9872].
14. **Olsen TW, Feng X, Wabner K, Conston SR, Sierra DH, Folden DV, Smith ME, Cameron JD.** Cannulation of the suprachoroidal space: a novel drug delivery methodology to the posterior segment. Am J Ophthalmol. **2006** Nov;142[5]:777-87. [DOI: 10.1016/j.ajo.2006.05.045].
15. **Wykoff CC, Khurana RN, Lampen SIR, Noronha G, Brown DM, Ou WC, Sadda SR; HULK Study Group.** Suprachoroidal Triamcinolone Acetonide for Diabetic Macular Edema: The HULK Trial. Ophthalmol Retina. **2018** Aug; 2[8]:874-877. [DOI: 10.1016/ j.oret.2018.03.008].
16. **Marashi A, Benjamin J.** The Mother of Invention: Making Custom Equipment in Syria Developing a custom-made needle for suprachoroidal steroid injections in Syria, **2020**. Available at https://retinatoday.com/articles/2020-may-june/the-mother-of-invention-making-custom-equipment-in-syria. Last accessed December 2020.
17. **Isaac DL, Abud MB, Frantz KA, Rassi AR, Avila M.** Comparing intravitreal triamcinolone acetonide and bevacizumab injections for the treatment of diabetic macular edema: a randomized double-blind study. Acta Ophthalmol. **2012** Feb;90[1]:56-60. [DOI: 10.1111/j.1755-3768.2009.01817.x].

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780