Commentary: Subthreshold micropulse yellow laser in diabetic macular edema

Lasers in retina have been long used and proved to be efficacious. However, the conventional continuous-wave laser, used for photocoagulation, is known to cause severe retinal damage, mainly (scotomas and loss of color vision). To minimize the collateral damage and thereby maintaining the efficacy of the laser, the subthreshold micropulse laser has been extensively studied over the last two decades, especially for macular disorders. Using this, now it is possible to deliver laser therapy, which meets threshold biochemical effects while being well below the visible destructive retinal lesion.[1]

Yellow wavelengths are only minimally absorbed by macular xanthophylls while being well absorbed by melanin and hemoglobin. A wavelength of 577 nm has been found to cause least scatter as compared to green 532 nm and yellow 561/568 nm wavelengths, allowing higher energy concentration and low power usage.[2] In addition, 577 nm also has the highest oxyhemoglobin to melanin absorption ratio, making it most effective for vascular structures.[3]

Micropulse, largely implies that the laser energy reaches only a small fraction of time, being interspaced with relaxation or off time. This fraction and on-off period are called the duty cycle. The longer the off time, lesser is the laser energy used, lower is the duty cycle, which has lesser tissue heat and damage. The subthreshold level of laser has been studied to have various therapeutic effects which include vascular endothelial growth factor (VEGF) down-regulation, stimulation of protective cytokines by the RPE, as well as Heat Shock Protein (HSP) activation.[4] The HSP is important for repair of RPE function, retinal auto-regulation, and immunomodulation.

For delivering the micropulse laser, typically, focal test burns are applied, starting at low power until the spots are barely visible. After which, the power is reduced by 50 to 70% to obtain the "subthreshold" power, which has been found to be the balance between therapeutic effect, while avoiding retinal scarring. Confluent spots are applied, guided by the optical coherence tomography (OCT) thickness.[2] One of the limitations, however, is the absence of a visible endpoint, and perceived concern of under treatment.

Optical coherence tomography angiography (OCTA) has been helpful in understanding the mechanism of action of subthreshold micropulse laser in DME. In a study, evaluating changes in the retinal vasculature, using OCTA, following subthreshold micropulse laser, there were more pronounced changes in the DCP, with a decrease in the foveal avascular zone and area of the cysts.[5]

While reviewing the efficacy, specifically for DME, studies indicate that subthreshold micropulse yellow laser does have a statistically significant improvement in best-corrected visual acuity (BCVA), and a reduction in central foveal thickness (CFT), especially in eyes with pretreatment CFT less than 300 μm.[6] In addition, both yellow and infrared diode subthreshold micropulse lasers have been found to be equally efficacious and safe with the lowest duty cycle (5%). When comparing the

5% and 15% duty cycles, the latter achieved better anatomical and functional outcomes. In the United Kingdom, a large scale, multicenter, randomized, double‑masked clinical trial is being conducted in patients with DME, and CFT <400 µm, to determine the effectiveness of subthreshold micropulse laser when compared with the standard laser, called the Diabetic macular oedema and diode subthreshold micropulse laser (DIAMONDS) trial.[7]

The study, "Can Subthreshold Micropulse Yellow Laser Treatment Change The Anti‑VEGF Algorithm In Diabetic Macular Edema? A Randomized Clinical Trial" asks a very relevant question, whether subthreshold micropulse laser can change the frequency of anti‑VEGF therapy in DME, specifically, using aflibercept in their study.[8] Most often, patients with DME require frequent anti‑VEGF injections. Therefore, a need for long‑lasting therapy, avoiding retreatment certainly exists. The need for reinjections in patients receiving a combination of laser and injections was found to be much lower when compared to the injections only group. Similar results have been reported by another group as well.[9] This prolonged efficacy can largely be explained by the above discussed morphological changes caused by the subthreshold micropulse laser.

Thus standard continuous laser has been an effective option over decades, although with known collateral retinal damage. Anti‑VEGF therapy, on the other hand, has been revolutionary, while needing retreatment. Use of steroid therapy is also seeing a resurgence, especially with the use of long‑acting dexamethasone implants. Although slowly gaining use, the potential of subthreshold micropulse laser is also being increasingly recognized. While the debate for the most effective continues, perhaps the most successful option may be a combination of therapies, each consisting a part of the retinal surgeons' armamentarium, and therapy being individualized as per the patients' needs. With a follow‑up of 2 years, studies such as the DIAMONDS trial will increasingly make it clear whether this promising, "subthreshold" therapy is going to make a big difference.

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