EDITORIAL

Analyzing the Shortcomings of Trabecular Micro-bypass Stents for Surgical Management of Glaucoma

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"Our lives begin to end the day we become silent about things that matter."

—Martin Luther King Jr

Trabecular meshwork (TM) is the site of main resistance (75%) to aqueous outflow by the conventional aqueous outflow pathway.[1] Hence, minimally invasive glaucoma surgeries (MIGS) target the TM either by bypassing it using stents (e.g., iStent inject), ripping it [gonioscopy-assisted transluminal trabeculotomy (GATT)] or by excisional procedures [e.g., bent ab interno needle goniectomy (BANG), Kahook dual blade (KDB)].

Clinical studies have shown that the surgical removal of TM (e.g., BANG, KDB, and microhook) can reduce intraocular pressure (IOP).[2,3] MIGS stenting procedures like iStent can bypass the TM at 2 or 3 points while the hydrus microstent can dilate the Schlemm's canal (SC), stretch the TM across 3 o'clock hours, which causes a decrease in resistance of juxtacanalicular TM and in turn reduction in IOP.[4,5] There is no doubt that MIGS is rapidly evolving with continuous improvements in the device; and we have good 2–5-year study outcomes available that demonstrate MIGS's safety and efficacy in reducing medication burden and the need for filtration surgery. While techniques for incising the TM are generally economical, the concern arises from the widespread adoption of expensive trabecular bypass stents, which can overwhelm healthcare systems. These devices have inherent shortcomings that need to be discussed, and innovations should be made to improve their designs, reduce costs, and, finally, provide better long-term outcomes.

Mild Intraocular Pressure Lowering and Minimal Medication Reduction

Surgical procedures to bypass the TM with the help of implants include iStent inject and hydrus microstent. Ahmed et al.[6] compared the efficacy of standalone MIGS between 1 hydrus microstent (n = 75) or 2 iStent (n = 77) devices in open-angle glaucoma eyes and at 12 months, IOP reduction of ≥20% was seen in 39.7% of eyes in the hydrus group and 13.3% of eyes in iStent group.[6] Only 30.1% of the eyes in the hydrus group and 9.3% of the eyes in the iStent group achieved IOP ≤ 18 mm Hg without additional medications/interventions. There are two important takeaway messages from the study—IOP lowering with devices that dilate the SC over 3 o'clock hours may be superior to implanting trabecular bypass devices at 2 pinpoint locations, and medication-free target IOP is unlikely to be achieved by these devices even for early glaucoma. In a recent report by the American Academy of Ophthalmology by Richter et al.,[7] which reviewed 10, level 1 randomized control trials to determine IOP reduction by trabecular procedures like iStent, iStent inject or hydrus combined with cataract surgery versus cataract surgery alone, it was found that trabecular MIGS procedures led to a decrease in IOP by only 1.6–2.3 mm Hg (3.8–8.9%) over cataract surgery which alone provided 21–28% IOP reduction at 2 years postsurgery.[7] The decrease in medication attributed to these devices alone was 0.4 at 2 years. This report clearly shows that trabecular stents have very minimal additional benefit in terms of IOP lowering, and the impressive IOP drops being used to convince both patients/surgeons to undergo/adopt these procedures are mainly due to the effect of cataract surgery on the anterior chamber angle and improving the facility of outflow. Even this mild IOP reduction may be exaggerated due to industry sponsorship bias as all trials discussed in the above report were industry-sponsored, and nearly all had first or corresponding authors with a financial interest in the specific companies whose device they were evaluating.

In addition, many of these studies wash out the medications and then report outcomes. In patients who are on long-term medications, there may be drug tachyphylaxis, and this may reverse after a drug holiday due to an increase in drug-receptor sensitivity. So, even a single drug may be very effective when introduced after a drug holiday and lead to a significant reduction in IOP. This may lead to the trial showing a reduction in the number of medications, which may not be an accurate depiction of the actual outcomes.

Incorrect Implantation

Gillmann et al.[8] assessed the structural position of iStent inject after implantation in 25 eyes using anterior segment optical coherence tomography and found that 72% of the device's heads were not positioned in the SC. This, in turn, was associated with decreased SC dilation and higher postoperative IOP.[8] Nearly half of the devices (46%) were completely buried within the TM and thus not draining. In a subsequent follow-up study, Gillmann et al.[9]

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found that at 1 year, 44.9% of devices were completely buried within the trabeculum, and in most cases, the device positions were unchanged, highlighting the importance of the initial implantation location. Even though the implantation of iStent looks to be a simple procedure, the above studies highlight high rates of incorrect implant placement, which leads to poor outcomes and is also a waste of precious resources. However, with improvements in stents, educational tools and injector design, the proportion of correctly placed stents is increasing. Furthermore, surgeons can evaluate stent drainage on the table by injecting trypan blue and also develop skills to correct malpositioned stents.

Non-Drainage Due to Absence of Adjacent Collector Channels

We recently performed a functional assessment of an anatomically well-positioned iStent inject and found nonfunctional (not draining into collector channels) through one of the two iStent injects using the technique of aqueous angiography.[10] The above report highlights that proper placement of the iStent within the TM does not guarantee that aqueous will drain through and exit through the collector channels as there are a lot of variations in the position of these collector channels. Increasing the number of stents implanted in the eye may increase the probability of hitting the collector channel outflow pathway, but this cannot guarantee outflow due to its inherent limitations, as highlighted above. Further studies are required to evaluate anatomical landmarks for guiding stent implantation, signs for correct location (like back flush of blood), and functional assessments at physiological pressures postimplantation. Dye-assisted fluid waves can be used after each implant to evaluate the outflow, although this is done under forced high pressures, which may give a false positive result.

Another point that we would like to highlight is that, on average, the coronal diameter of the SC has been documented to be 44.5 ± 12.6 µm in a normal individual, which decreases to 35.7 ± 8.0 µm in a patient of primary open-angle glaucoma.[11] Furthermore, these implants are implanted with the anterior chamber filled with viscoelastic, which may further compress the canal or collapse it. In this situation, the iStent inject with a length of 360 µm may completely pass through the SC and behave like a skewer (a long, thin, pointed piece of metal or wood that is pushed through pieces of meat, vegetables, etc. to hold them together while they are cooking) with the stem of the implant crossing beyond the outer wall of the SC. The larger flange in the new iStent design (W) is a welcome design change that can potentially decrease the incidence of malpositioned stents.

Can the World Afford Such Expensive Devices, and Can We Globally Impact Glaucoma Blindness?

According to the latest poverty statistics, a huge majority—84% of the world population–live on less than $30 per day. That means there are 6.7 billion people or more who cannot afford these devices, which cost between $1500 and $2000 USD. Thus, on a global scale, these devices are of not much value in decreasing glaucoma morbidity and alleviating blindness. With limited funding available, most countries cannot afford to divert funds for these devices without impacting treatment for other life-threatening diseases.

What should be the Criteria for Adopting a New Technology/Surgical Device?

When we adopt a new technology, it must be more effective than the existing one or equally effective but less costly. We have both stenting and cutting technologies available. Laupacis et al.[12] suggested five grades of recommendation (A–E) for the adoption and appropriate utilization of new technologies, taking the key fundamentals as economic evaluation and net benefit of the application of one technology with that of the others. With the available data, trabecular bypass devices such as iStent may fall into the type E category (do not adopt–reject); that is, new technology is less effective/equally effective as the existing one and is more costly (compared to the trabecular cutting procedures.

Effective and Affordable Alternatives

Surgical techniques (KDB, microhook, GATT, BANG, etc.) that strip a portion of the TM and expose the SC have been shown to be as effective as microstents.[3] Out of these, our favourite is the BANG (excising between 1 and 3 clock hours of the TM), which has the lowest cost, does not need any special instrumentation, has a small learning curve and can be done in any region of the world.[13,14] We have recently introduced a new modification known as visco-BANG, where we introduce a 30 gauge needle into the canal, dilate it with viscoelastic to decrease the risk of injury to the outer wall of SC, cut the TM across 30° and push viscoelastic into the adjacent intact SC to viscodilate and increase outflow.[15]

Scarring, Failure, and Need for Repeat Surgery

While any incisional/excisional procedure on the TM is bound to fail over time due to wound healing,[16] the same is also true for trabecular bypass stents. Histopathologic examination of TM changes after trabecular bypass stent implantation has revealed significant fibrotic changes and membranes over the stent, which can contribute to device failure over time.[17] The need and cost of repeat surgery, preferably using a different surgical technique, is also an important consideration, as target IOP may not be achieved or sustained with canal-based implant surgery.

The Future

There is a need to go back to the drawing board to improve the current stent design (relook at the snorkel design, which accurately goes into the lumen of the SC and covers a larger circumference) and implantation techniques for the best functional fit within the TM. Evaluating the exact location of the collector channels with aqueous angiography, developing high-resolution imaging to confirm the intraoperative location of the device outlets in relation to the canal & reposition them if required, using fibrosis inhibitors around the site of implantation, standardization of the number of implants required to achieve a certain target IOP and developing affordable TM bypass devices to increase access to wider populations is the need of the hour. Low-cost MIGS innovations (like BANG), which can be applied on a global scale, need to be popularized and put through rigorous scientific trials, including head-to-head comparisons with trabecular stents, to establish their safety and effectiveness, especially independent of cataract surgery. The future looks bright as trabecular MIGS becomes the standard of surgical care for early-moderate glaucoma with a well-proven

track record of safety and effectiveness (in reducing visual field progression, medication burden, and need for subsequent filtration surgery) and the continuous development of new technologies for improving it further.

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