· Original article ·

Suprachoroidal drainage of aqueous humour with a novel implant: Suprajet

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Received: 2016-05-20 Accepted: 2017-07-31

新型经脉络膜上腔引流房水植入装置 Suprajet 的疗效观察

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摘要

目的:评估一种由睫状体前和脉络膜上腔引流房水的新型植入装置 Suprajet 的有效性和安全性。

方法:该项研究使用 5 只兔子。每只兔子的一眼植入 Suprajet。引流器通过位于上方的透明角膜切口,经由前房置入脉络膜上腔。引流器近端位于睫状体根部,远端位于脉络膜上腔。兔子饲养、观察 4wk。使用 Tonopen AVIA 测量术前和术后的眼压。最后一次随访观察时,兔子被牺牲处死,眼球摘除,进行大体上和组织学的观察评估。

结果:术前眼压为 18.6±6.1mmHg。术后 1wk 眼压为 8.4±1.1mmHg。术后 2wk 1 只兔子死亡。因此,仅有 4 只兔子进行了后续观察。术后 2wk 眼压为 11.0±2.8mmHg,术后 3wk 为 9.50±3.1mmHg,术后 4wk 为 11.3±3.3mmHg。与术前平均眼压相比,仅第 1 周的平均眼压显著降低(P=0.042),术后 2wk、3wk 和术后 4wk 的平均眼压无明显变化(P=0.66, P=0.66, P=0.102)。术中并发症包括 3 眼少量出血。术后 2d 出血已经完全吸收。对摘除眼球的大体观察发现,1 眼中引流器的远端位于玻璃体内,而不是位于脉络膜上腔;其它 3 眼引流器的远端位于脉络膜上腔。所有眼中,近端都位于前房角。对摘除眼的组织学检查发现:不规则的胶原蛋白束和纤维沉积,包括引流器周围大量的成纤维细胞和组织细胞。

结论:这一项初始动物研究显示,青光眼中 Suprajet 植入是一项有前景的术式。需要进行更进一步的研究以评估其有效性和安全性。

关键词:青光眼;引流器;脉络膜上腔

引用:Gunenc U, Arikan G, Gunenc F, Lebe B, Eren S, Ocmen E, Ozturk AT. 新型经脉络膜上腔引流房水植入装置 Suprajet 的疗效观察. 国际眼科杂志 2017;17(10):1807-1811

Abstract

• AIM: To evaluate the efficacy and safety of a new implant, Suprajet (VSY Biotechnology, Istanbul, Turkey), which is developed for supraciliary and suprachoroidal drainage of aqueous humour.

• METHODS: Five rabbits were included in the study. One Suprajet shunt was implanted in one eye of each rabbit. Implantation was performed by a superior clear corneal incision through the anterior chamber into the suprachoroidal space. Proximal end of the implant was placed in the iris root resting against the scleral spur, distal end was placed in the suprachoroidal space. Rabbits were followed for 4wk. Preoperative and postoperative intraocular pressure (IOP) levels were measured with Tonopen AVIA. At last follow-up visit animals were sacrificed and eyes were enucleated. Macroscopic and histopathologic evaluation of the eyes were made.

• RESULTS: Mean preoperative IOP was 18.6±6.1 mmHg. Mean postoperative IOP was 8.4±1.1 mmHg, at one week. At the 2nd week of the follow-up period one rabbit died. Thereafter, only 4 rabbits were followed. Mean postoperative IOP was 11.0±2.8 mmHg at the 2nd week, 9.50±3.1 mmHg at the 3rd week and 11.3±3.3 mmHg at 4th week after the operation. When mean preoperative IOP was compared with the postoperative IOP values, only the IOP at the first week was found as significantly lower (P=0.042). There was no statistically significant difference between mean preoperative IOP level and mean IOP level at 2, 3 and 4wk postoperatively (P=0.66, P=0.66 and P=0.102, respectively). As an intraoperative complication, minimal hyphema was noted in three eyes during the surgery. However, the next day hyphema cleared completely. Macroscopic evaluation of the enucleated material showed that in one eye the distal end of the implant was in the vitreous instead of suprachoroidal space, in the other 3 eyes the distal end of the implant was noted in the suprachoroidal space. In all eyes, proximal end of the implant was localized in the anterior

chamber angle. Histopathologic evaluation of the enucleated eyes showed deposition of irregular collagen bundles and fibroplasia including numerous fibroblastic and histiocytic cells around the implant.

• CONCLUSION: This preliminary animal study showed that implantation of Suprajet in glaucoma is a promising procedure. Further studies are needed to evaluate its efficacy and safety profile.

• KEYWORDS: glaucoma; shunt; suprachoroidal surgery
DOI: 10.3980/j.issn.1672-5123.2017.10.02

Citation: Gunenc U, Arikan G, Gunenc F, Lebe B, Eren S, Ocmen E, Ozturk AT. Suprachoroidal drainage of aqueous humour with a novel implant: Suprajet. *Guoji Yanke Zazhi* (*Int Eye Sci*) 2017;17(10):1807-1811

INTRODUCTION

In traditional glaucoma filtration surgery (trabeculectomy or tube shunt surgery) it is aimed to drain the aqueous humour from the anterior chamber to the subconjunctival space. Failure occurs mainly due to the subconjunctival or episcleral fibrosis. Besides this, there is a bleb formation and this causes patient to be in a lifetime risk for severe bleb related complications such as leakage, blebitis and endophthalmitis[1-4].

Suprachoroidal space lies betweeen the choroid and the sclera. There is a pressure gradient between the anterior chamber and the suprachoroidal space and this difference in pressure is the driving force for uveoscleral outflow. Suprachoroidal space may be used as an alternative outflow pathway in glaucoma surgery[5-6]. Draining of aqueous humour to the suprachoroidal space instead of subconjunctival space may have some advantages. Firstly, in suprachoroidal drainage surgery no bleb formation occurs, thus bleb related complications are avoided. Secondly, there is no subconjunctival fibrosis. Recently, numerous clinical trials evaluating the efficacy and safety of this approach were published with good success rates[7-13]. In all these studies, an implant was used for draining aqueous humour. Suprajet (VSY Biotechnology, Istanbul, Turkey) is a novel implant that developed for supraciliary and suprachoroidal drainage of the aqueous humour. In this study we aimed to evaluate the efficacy and safety of this new implant in rabbit eyes.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of the Research of Laboratory Animals at Dokuz Eylul University. Five healthy adult New Zealand albino rabbits (three female, two male) weighing between 2.4 kg and 3.2 kg were included in the study. Under general anaesthesia one Suprajet shunt was implanted in the randomly selected one eye of each rabbit by one surgeon (Gunenc U).

The Suprajet implant (Figure 1) is a tube made of polyvinylidene difluoride. The length of the implant is 7.35 mm. Inner diameter is 0.30 mm, outer diameter is 0.50 mm. The Suprajet shunt insertion device (Figure 2) houses an implant delivery guide wire assembly measuring 0.28 mm in diameter. The guide wire assembly delivers the implant to the desired location within the eye. Implant is pre-loaded on to the guide wire assembly by the operator before insertion (Figure 3). Shunt implantation was performed by a superior clear corneal incision through the anterior chamber into the suprachoroidal space using a goniolens. The anterior chamber was entered at the limbus at superior position with a 20 gauge MVR knife. Anterior chamber was filled with a viscoelastic agent to maintain the chamber and deepen the angle. With the aid of goniolens the angle was visualized and guidewire tip inserted bluntly between the iris and scleral spur into the suprachoroidal space (Figure 4). Proximal end of the implant was placed in the iris root resting against the scleral spur, distal end was placed in the suprachoroidal space. Once the microstent was placed in the appropriate position, the guidewire was retracted. Viscoelastic agent was removed. The cornea was closed with 10-0 nylon suture. All eyes were treated with eye-drops 6 times daily postoperatively for 2wk; treatment was then tapered in 4wk based on follow-up examinations. Preoperative and postoperative intraocular pressure levels were measured with Tonopen AVIA (Reichert, Depew, NewYork, USA) intraocular pressure (IOP) value was the mean of three consecutive readings. Rabbits were followed for 4wk. Follow-up visits were performed on day 1, week 1, 2, 3 and 4. At last follow-up visit eyes implanted with Suprajet were enucleated. Macroscopic and histopathologic evaluation of the eyes were made.

Statistical analysis was performed using the Wilcoxon signed-rank test in SPSS version 15.0 (SPSS, Chicago, IL, USA). P-value <0.05 was considered statistically significant.

RESULTS

Mean preoperative and postoperative intraocular pressure (IOP) values are shown in the Table 1. The mean preoperative IOP was 18.6 ± 6.1 mmHg (range: 12-26 mmHg). At the second week of the follow-up period, one rabbit (rabbit 3) died. Thereafter, only 4 rabbits were followed. When mean preoperative IOP was compared with the postoperative IOP values, only the IOP at the first week was found significantly lower (P = 0.042). There was no statistically significant difference between mean preoperative IOP level and mean IOP level at 2, 3 and 4wk postoperatively (P=0.66, P=0.66 and P=0.102, respectively).

Minimal hyphema was noted in three eyes during the surgery (rabbit 1, rabbit 2 and rabbit 5). However, the next day hyphema cleared completely. Macroscopic evaluation of the enucleated material showed that in one eye (rabbit 1) the distal end of the implant was in the vitreous instead of suprachoroidal space (Figure 5). In the other 3 eyes the distal end of the implant was noted in the suprachoroidal space. In all eyes, proximal end of the implant was localized in the anterior chamber angle. Histopathologic evaluation of the enucleated eyes showed deposition of irregular collagen bundles and fibroplasia including numerous fibroblastic and histiocytic cells around the implant (Figure 6). The formation of an encapsulating fibrous tissue was not detected in any eyes.

Table 1 Preoperative and postoperative intraocular pressure levels (mmHg)

Time	Rabbit 1	Rabbit 2	Rabbit 3	Rabbit 4	Rabbit 5	Mean
Preoperatively	16	15	12	24	26	18.6±6.1
Postoperatively (1wk)	9	8	7	10	8	8.4±1.1[a]
Postoperatively (2wk)	15	9	–	9	11	11±2.8
Postoperatively (3wk)	14	8	–	7	9	9.5± 3.1
Postoperatively (4wk)	16	9	–	9	11	11.3±3.3

[a]At the first week after the implantation, intraocular pressure was significantly lower when compared to preoperative intraocular pressure level (P<0.05).

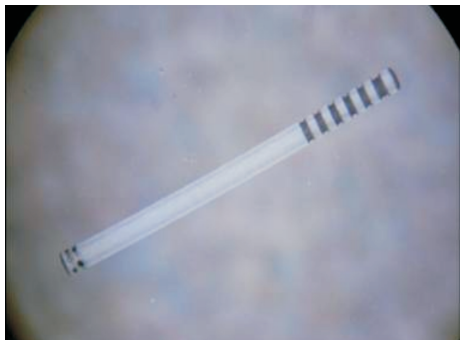

Figure 1 Suprajet implant.

Figure 2 Suprajet shunt insertion device.

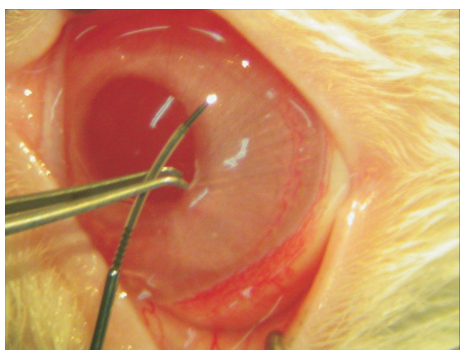

Figure 3 Before insertion, implant is pre-loaded on to the guide wire assembly by the operator.

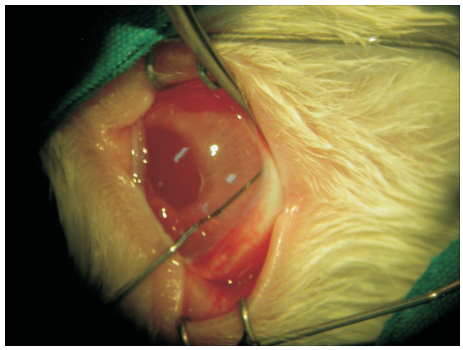

Figure 4 Implantation of the shunt.

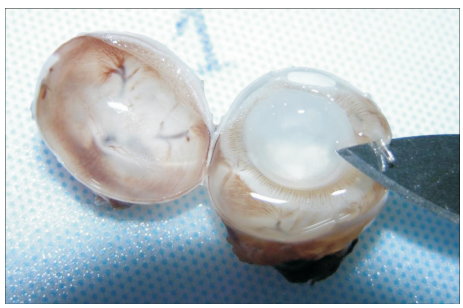

Figure 5 In macroscopic evaluation of the enucleated material, in one eye distal end of the implant was in the vitreous instead of suprachoroidal space.

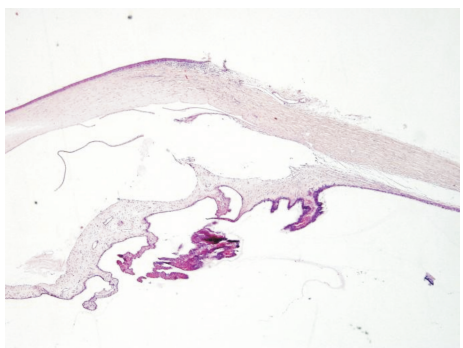

Figure 6 Histopathologic evaluation showed deposition of irregular collagen bundles and fibroplasia including numerous fibroblastic and histiocytic cells.

DISCUSSION

Inconventional filtration surgery subconjunctival space is the main site for draining of the aqueous humour. In suprachoroidal drainage surgery it is aimed to enhance uveoscleral outflow by draining aqueous humour from the anterior chamber to the suprachoroidal space. Suprachoroidal space is a potential space providing a pathway for uveoscleral outflow. In uveoscleral outflow, aqueous humour passes through the ciliary muscle bundles into the suprachoroidal space, from which it is drained by choroidal blood vessels and sclera. Uveoscleral outflow route was described more than 40 years ago and in non-human primates 40-50% of the aqueous leaves the eye by this way. Direct measurements in human eyes showed that less than 15% of aqueous humour is drained by uveoscleral outflow. In indirect calculations, it was found as 35% in young adults and 3% in the eldery persons. Uveoscleral outflow is minimally affected by increments in intraocular pressure (IOP), however, in cyclodialysis or uveitis it rises with an IOP dependent manner.

Besides, it is well known that drugs such as prostaglandin analogs and atropine increase the uveoscleral outflow[14].

The idea of draining aqueous humour into the suprachoroidal space as a glaucoma surgery is not a new concept, actually. Several surgical techniques have been described in this context. The oldest one is surgical cyclodialysis. Some modifications of the primary surgical approach have been introduced[15]. Although good success results were achieved, unpredictability of the postoperative surgical results prevented the procedure to be popular among the ophthalmologists.

In suprachoroidal drainage surgery, a stent is necessary for maintaining the communication between the anterior chamber and the suprachoroidal space. Several implants have been used for this purpose[11].

Gold microshunt (SOLX Ltd, Boston, Massachusets, USA) is a flat-plate drainage device made from gold that designed for implantation into the supraciliary place to drain aqueous humour from the anterior chamber to the suprachoroidal space. Melamed *et al*[10] evaluated the efficacy and safety of this shunt in 38 patients with uncontrolled glaucoma. Mean follow-up time was 11.7 mo. Surgical success (IOP between 5-22 mmHg, with or without antiglaucoma medication) was achieved in 79% of the patients. Complete success (IOP between 5-22 mmHg without antiglaucoma medication) rate was only 13.2%. Postoperative complications were shunt exposure (one patient), exudative retinal detachment (one patient), transient hyphema (8 patients). Figus *et al*[16] evaluated the efficacy and safety of Gold microshunt in 55 eyes of 55 patients with refractory glaucoma. At 2y after the surgery qualified success rate was 67.3% (37 eyes) with a mean IOP decrease of 13.9 mmHg. Complete success was achieved in only 3 eyes (5%). Postoperative complications were mild to moderate hyphema (12 eyes), bullous choroidal detachment (6 eyes), corneal oedema due to endothelial contact (2 eyes) and exudative retinal detachment (one eye). In these last three cases authors removed the implant.

Jordan *et al*[9] used a silicone tube to communicate the anterior chamber and suprachoroidal space. In their surgical technique a limbus based scleral flap was prepared and the suprachoroidal space was accessed *via* a deep posterior scleral flap. The silicone tube was inserted as an intrascleral connection from the anterior chamber to the suprachoroidal space. Thirty one eyes of 31 patients with intractable glaucoma were included in the study. The success rate was 70% at 30wk, 60% at 1y, and 40% at 76wk after the surgery. Postoperative hypotony or suprachoroidal bleeding was not observed in any of the eyes. Anterior chamber lavage was required in two patients because of bleeding. In two patients the tube had to be removed because of corneal endothelial touch. Palamar *et al*[12] also used the same technique in 15 eyes with intractable glaucoma and functional success (IOP≤ 21 mmHg with or without antiglaucomatous medication) was achieved in 93.3% of the eyes. Unal *et al*[13] applied the similar technique in 24 glaucomatous eyes and reported a success rate of 63.3% at 12mo after the surgery.

Ozdamar *et al*[7] implanted modified Krupin valve into the suprachoroidal space to drain aqueous humour from the anterior chamber to the suprachoroidal space. Four painful-blind eyes of four patients were included in the study. While mean preoperative intraocular pressure was 58.5±9.2 mmHg, it was found as 13.5±4.6 mmHg at 1mo and 15±4.9 mmHg at 3mo after the surgery. None of the eyes developed suprachoroidal hemorrhage, retinal detachment, or phthisis bulbi. Choroidal detachment was developed in one case and regressed spontaneously. They concluded that the drainage of aqueous humor from the anterior chamber to the suprachoroidal space with seton device was effective in lowering intraocular pressure in refractory glaucoma. As some difficulty was encountered while inserting the implant to the suprachoroidal space, authors stated that it was necessary to design a new implant as a suprachoroidal seton device.

The Cypass device (Transcend Medical, Menlo Park, CA, USA) is an implant developed to enhance uveoscleral outflow. It is a fenestrated micro-stent made of polyimide material and designed for implantation into the supraciliary space. Its length is 6.35 mm and its external diameter is 510 nm. Design and surgical implantation technique of this implant is almost similar of our implant used in this current study. Several studies evaluating the efficacy and safety of the Cypass micro-stent were published in the literature with good surgical results. The first clinical study was reported by Hoeh *et al*[8] in 2013. In this prospective study, at 6mo after the surgery 37% IOP reduction was achieved in patients with preoperative IOP ≥ 21 mmHg and in patients with preoperative IOP < 21 mmHg a 71.4% reduction in glaucoma medications was noted. No serious complication was reported. The most common complications were transient early hypotony (13.8%) and transient IOP increase (10.5%). Implantation of both Cypass device and Suprajet is through the clear corneal incision and there is no need for conjunctival or scleral dissection. This makes the procedure easier compared the other methods mentioned before and also suitable for combining the phacoemulsification surgery at the same time, if necessary. In the study of Hoeh *et al*[8] all the surgeries were combined with phacoemulsification. Device repositioning was required in one eye. García-Feijoo *et al*[17] implanted Cypass device in 65 eyes without phacoemulsification. At 12mo, a 34.7% reduction in IOP was achieved. No serious intraoperative or postoperative complication occurred. The most common adverse events were transient IOP increase (11%), transient hyphema (6%), and cataract progression (6%). In this study, in none of the eyes device repositioning was required. Seuthe *et al*[18] described a modified surgery technique of canaloplasty with suprachoroidal drainage. In this surgical approach, in contrast to the conventional canaloplasty, the second scleral fleb consists of the whole remaining sclera thus building an access to the suprachoroidal space. They reported that combining canaloplasty with suprachoroidal drainage yields better results than canaloplasty alone.

STARflo (iSTAR Medical, Isnes, Belgium) is another glaucoma implant that was developed for enhancing uveoscleral outflow. It is made of a silicone microporous material and inserted into the suprachoroidal space through an ab-externo approach under a scleral flap. Pourjavan *et al*[19] evaluated its safety and efficacy in 4 eyes prospectively. Mean preoperative IOP and glaucoma medication was 37.0 mmHg and 3.25, respectively. At 12mo, mean IOP was 14.3 mmHg and mean glaucoma medication was 1.5. No serious intraoperative or postoperative complications were reported. Postoperative complications were transient hypotony, transient choroidal hemorrhage and transient abnormal macula.

Aquashunt (OPKO Health Inc., Miami, FL, USA) is a new suprachoroidal device. It is made of polypropylene. Oatts *et al*[20] compared the fibrosis, aqueous humor dynamics and intraocular pressure in rabbit eyes implanted with gold shunt or aquashunt. They found that both shunts were devoid of foreign body reaction but exhibited fibrosis and besides this gold shunt showed vascularization. Both shunts allowed access of aqueous humour to the suprachoroidal space. The efficacy was found to be better with antifibrotic usage.

As a conclusion, suprachoroidal drainage surgery in surgical management of glaucoma is promising. Suprajet is a novel implant which is designed to drain aqueous humour from the anterior chamber to the suprachoroidal space. Current animal study showed the biocompatibility of this new implant as a suprachoroidal shunt. Further clinical studies are needed to clarify its efficacy and safety profile in human eyes.

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