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Rubeosis iridis after vitrectomy for diabetic retinopathy

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Abstract ● Background: Iris rubeosis and neovascular glaucoma (NVG) are serious complications of vitrectomy for proliferative diabetic retinopathy. The present study analyzes incidence and risk factors of these complications. ● Methods: Preoperative and postoperative iris rubeosis were compared in 389 diabetic eyes after vitrectomy. Minimum follow-up was 6 months (median 26 months). Risk factors were studied using multivariate logistic regression analysis. ● Results: Following vitrectomy, in 8.5% of the eyes stromal iris rubeosis developed de novo; NVG occurred in 5%. Significant risk factors for postoperative rubeosis were preexisting iris neovascularizations and postoperative retinal detachment. Six months after surgery, regression of preexisting iris rubeosis was observed in 57% of the eyes. In eyes without preoperative iris rubeosis, progression was found in 13% of cases 6 months postoperatively. ● Conclusion: With current surgical techniques iris rubeosis is more commonly regressive than progressive after vitreous surgery in diabetic eyes.

Introduction

Rubeosis of the iris and neovascular glaucoma (NVG) are serious complications of diabetic eye disease. Vitreous surgery is believed to increase the risk for the development of rubeosis and NVG. The incidence of iris neovascularizations after diabetic vitrectomy in published series was 23–42% and of NVG 10–23% [1, 4, 6, 12, 15, 18, 20–22]. These publications mainly studied patients treated in the early years of vitreous surgery. Since that time several strategies to reduce the risk for the development of NVG and iris rubeosis have been developed [3, 13, 16, 19].

In the present study a large number of eyes that underwent vitreous surgery for complications of diabetic retinopathy were analyzed. Pre- and postoperative iris rubeosis were compared to assess incidence and risk factors for these serious complications with current surgical techniques.

Methods

Between 1990 and 1994, a total of 337 patients (420 eyes) were operated on by the authors for complications of diabetic retinopathy. For 389 eyes (311 patients) a follow-up of at least 6 months was available; the others were excluded. Median follow-up was 26 months. Indications for surgery were vitreous hemorrhage in 151 cases, tractional-rhegmatogenous detachment in 47 eyes, tractional detachment of the macula in 50 eyes and severe progressive proliferative retinopathy in 141 eyes. Intraoperatively, endolaser coagulation was performed in 198 eyes, cryotherapy of the peripheral retina in 147 eyes. Liquid silicone was used at the first vitrectomy in 60 eyes and during reoperations in 48 additional eyes. Extracapsular lens extraction was performed during vitreous surgery in 20 eyes, intracapsular extraction in 36 eyes. In 18 eyes intracapsular lens removal was combined with silicone tamponade. During the postoperative course cataract surgery was performed in 103 eyes: extracapsularly in 70 eyes and intracapsularly in 33 eyes. Postoperative retinal detachment developed in 70 eyes after vitrectomy and in 8 additional eyes after reoperations. In 68 of the 78 eyes with postoper-

Table 1 Demographic data of the 311 patients

Age	56±14 (range 24–91) years
Sex	M: 145, F: 166
Diabetes type	Type I: 109, type II: 202
Follow-up	27±14 (range 6–89) months
Laser preoperatively	372/389 eyes (96%)
Retinal cryotherapy preoperatively	62/389 eyes (16%)

Table 2 Risk factors for the development of a stromal rubeosis "de novo" after vitreous surgery

	Significance (P)[a]	Risk ratio
Postoperative retinal detachment	<0.0001	9
Preoperative rubeosis	0.0005	5
Intracapsular cataract extraction	n.s.	
Extracapsular cataract extraction	n.s.	
Preoperative retinal detachment	n.s.	
Endolaser	n.s.	
Retinal cryotherapy	n.s.	
Silicone	n.s.	

[a] *n.s.* not significant, $P \geq 0.05$

ative retinal detachment the retina had already been detached preoperatively. During the postoperative course additional laser treatment was carried out in 67 eyes and cryotherapy to the retina in 12 eyes. Tabulated demographic data are presented in Table 1. Other patient data have been published previously [9–11].

Rubeosis iridis was assessed by slit-lamp biomicroscopy and chamber angle neovascularizations using gonioscopy. Iris neovascularizations were divided into four groups: no rubeosis; neovascularizations at the pupillary margin; additional neovascularization of the iris stroma and/or the chamber angle; easily visible neovascularizations of all four quadrants of the iris stroma and the chamber angle (massive rubeosis). NVG was defined as at least stromal and/or chamber angle neovascularizations and an intraocular pressure (IOP) of 25 mmHg or higher.

Multivariate analysis of risk factors for the development of postoperative rubeosis (Table 2) was performed using logistic regression analysis with the statistical program JMP. The level of significance was P=0.05 using the Wald test. The risk ratio is the relative risk of developing a postoperative stromal rubeosis for eyes with and eyes without the risk factor.

Results

Preoperatively there were 376 eyes without rubeosis or with rubeosis limited to the pupillary margin. At some time during the postoperative course 32 eyes (8.5%) developed at stromal rubeosis. Nineteen of these eyes (5%) had an increased IOP (NVG). A risk factor analysis for the development of a "de novo" rubeosis of the iris stroma using multivariate logistic regression analysis is shown in Table 2. Of the eight factors tested, postoperative retinal detachment and the presence of preoperative rubeosis of the pupillary margin were identified as significant risk factors. Twenty-one (28%) of 74 eyes with postoperative retinal detachment but only 11 (3.5%) of 302 eyes without postoperative retinal detachment developed stromal iris rubeosis. Seventeen (18%) of 94 eyes with preoperative rubeosis of the pupillary margin but only 15 (5%) of 282 without preoperative rubeosis developed stromal rubeosis after vitreous surgery.

Table 3 Incidence of de novo stromal rubeosis and neovascular glaucoma (*NVG*) after vitrectomy

Indicating for vitrectomy	n	De novo stromal rubeosis (%)	NVG (%)
Vitreous hemorrhage	148	6 (4%)	5 (3%)
Tractional detachment of macula	44	9 (20%)	5 (11%)
Tractional-rhegmatogenous detachment	45	5 (811%)	3 (7%)
Severe progressive proliferative retinopathy	139	12 (9%)	6 (4%)

Table 4 Rubeosis before and 6 months after surgery

		Preoperative rubeosis			
		None	Pupillary margin	Stroma	"Massive"
Rubeosis 6 months postoperatively	None	246	49	0	0
	Pupillary margin	29	40	9	1
	Stroma	6	3	1	2
	"Massive"	1	2	0	0

The incidence of de novo stromal rubeosis and NVG in patients with different indications for vitrectomy is shown in Table 3. While only 4% of the eyes with vitreous hemorrhage developed stromal rubeosis during the postoperative course, in 20% of the eyes with tractional detachment of the macula as indication for surgery neovascularizations of the iris stroma were observed. Of the 32 eyes that developed de novo stromal rubeosis only 5 (16%) had visual acuity of ≥5/200 at the last follow-up. Only 1 eye of 19 with NVG had vision of ≥5/200 at the last follow-up.

Table 4 shows the rate of pre- and postoperative rubeosis. Altogether, preoperatively 107 (27.5%) of 389 eyes had some degree of iris neovascularization. Six months postoperatively, 94 (24.2%) of 389 eyes had iris rubeosis. Six months after surgery, regression of the iris neovascularizations was observed in 61 of 107 eyes (57%) with preoperative rubeosis. In 36 out of 282 eyes (13%) without preoperative rubeosis, iris neovascularizations were found 6 months after surgery (Table 4).

In 19 eyes with rubeosis and attached retinae, liquid silicone was used to prevent recurrent hemorrhage and NVG. In 12 of these eyes, the iris neovascularization had regressed after 6 months, while in 7 eyes it remained stable. No increase of the neovascularizations was observed in this situation.

Discussion

The incidence of postoperative rubeosis of the iris and NVG after victrectomy for complications of diabetic retinopathy in the present study was considerably lower than in previously published series of NVG, i.e. only 5%, compared to 10–23% [1, 4, 6, 12, 15, 21]. This low incidence is especially noteworthy since in the present study preoperative rubeosis was present in 27% of eyes, compared to 4–16% in previous studies [4, 12, 18, 20–22]. While most other publications describe a 2–10 times higher incidence of rubeosis postoperatively than preoperatively [4, 12, 18, 20–22], we herein report a lower incidence of iris neovascularizations 6 months postoperatively (24%) than preoperatively (27%).

Reasons for the decreasing rate of this complication are most likely to be found in a better understanding of the pathophysiology of intraocular neovascularizations and consequently a changing surgical approach in recent years. Current concepts for the formation of pathological neovascularization start from the fact that the ischemic retina produces vasoproliferative factors such as vascular endothelial growth factor (VEGF) [2]. These growth factors diffuse to the anterior segment and stimulate the growth of new vessels on the iris. Indeed, in animal models, blocking VEGF could inhibit iris neovascularizations [2]. After surgical removal of the vitreous, vasoproliferative factors more easily gain access from the retina to the anterior segment of the eye. Therefore vitrectomy may increase the risk for the development of iris rubeosis.

Based on this theory, several strategies have been developed to reduce the incidence of iris rubeosis after vitreous surgery. The intraoperative use of endolaser [13] and cryo-ablation [3] of the retina eliminates parts of the ischemic retina and thereby reduces the production of growth factors. However, not all studies found a positive effect of retinal laser treatment on anterior segment neovascularizations [7]. In the present study laser treatment or cryotherapy was performed in almost all eyes, so no statistical significance of this procedures can be detected.

Performing a cataract extraction with extracapsular techniques instead of intracapsularly also significantly lowers the risk for iris rubeosis [19]. Intracapsular cataract surgery removes the major barrier for diffusion of growth factors from the posterior to the anterior segment of the eye and greatly increases the risk of rubeosis. After extracapular surgery the lens capsule and an artificial intraocular lens provide an effective barrier between the anterior and the posterior segment of the eye. In the present study intracapsular cataract surgery was performed relatively rarely, combined in a high proportion of cases with a silicone tamponade. Therefore the numbers are too low to show a statistical significance of intracapsular cataract surgery in a risk factor analysis for postoperative rubeosis.

Instillation of liquid silicone into the vitreous cavity can also create a barrier for diffusion of growth factors from the retina to the iris. Several authors have described a stabilizing effect of liquid silicone on iris neovascularizations [8, 16]. In the present study we have also observed stabilization in several high-risk eyes after silicon tamponade.

Statistically significant risk factors in the present analysis were preexisting rubeosis, as previously described [14], and postoperative retinal detachment. The detached retina has lost its supply from the choroid, is more ischemic and may produce greater amounts of vasoproliferative factors. On the other hand, it is known from histological studies that the photoreceptors of the retina rapidly degenerate after detachment from the pigment epithelium [17], and a reduced metabolism can be expected. The strong association between iris neovascularizations and retinal detachment in diabetic eyes suggests that eyes with acute onset of rubeosis should be carefully checked for retinal detachment [5]. If stromal rubeosis or NVG develop, the functional prognosis is still very poor.

An interesting and important finding of the present study is that the iris neovascularizations after vitrectomy were more commonly regressive than progressive. One should remember that iris rubeosis also develops in the natural course of severe diabetic eye disease and commonly progresses without vitreous surgery [6]. Vitrectomy with laser, cryotherapy, reattachment of the retina and silicone tamponade can be used to effectively treat iris rubeosis. Thus, with current techniques, vitreous surgery should not be considered a major risk factor for iris neovascularizations.

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