Graefes Arch Clin Exp Ophthalmol (2012) 250:981–987
DOI 10.1007/s00417-011-1919-y

RETINAL DISORDERS

Systemic corticosteroids reduce the risk of cellophane membranes after retinal detachment surgery: a prospective randomized placebo-controlled double-blind clinical trial

Fritz Koerner · Ursula Koerner-Stiefbold · Justus G. Garweg

Received: 27 October 2011 / Revised: 21 December 2011 / Accepted: 23 December 2011 / Published online: 21 January 2012

Abstract
Background Cellophane membranes are an early stage of proliferative vitreoretinopathy (PVR) complicating retinal detachment surgery. Our aim was to assess whether a prolonged administration of systemic corticosteroids would attenuate early stages of PVR such as cellophane membranes.
Design Prospective randomized placebo-controlled double-blind clinical trial.
Patients and methods A total of 220 consecutive eyes (220 patients) were operated for primary rhegmatogenous retinal detachment (RD), mainly by scleral buckling procedures. Patients were randomized into two groups: 110 patients (steroid group) received prednisone for 15 days starting with 100 mg at the day of surgery and being tapered to 12.5 mg. The control group of 110 patients received placebo in a comparable manner. Follow-up examinations were performed at 1, 3 and 6 months postoperatively, and included visual acuity and assessment of retinal findings.
Results Cellophane membranes occurred in 41.8%, 46.9%, and 39.1% in the placebo group and 26.7%, 23.6%, and 19.8% in the steroid group at 1, 3 and 6 months postoperatively ($p<0.05$, = 0.0005, and <0.005 respectively). The application of five or more cryocoagulation spots was associated with more cases developing cellophane membranes in the placebo than the steroid group ($p<0.05$). A complete reattachment of the retina was achieved in 95% steroid and 89% placebo group eyes, and a reattachment of the macula in 98% of both groups. There was no significant difference of the final visual outcome in both groups.
Conclusion Early stages of PVR such as cellophane membranes after retinal detachment surgery can be reduced with corticosteroids in oral doses.

Keywords Retinal detachment · Retinal detachment surgery · Proliferative vitreoretinopathy · Corticosteroids · Cellophane membranes

Data for this study were collected from patients at the Department of Ophthalmology, University of Bern, Switzerland; former Director F. Koerner.

The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments, Good Clinical Practice, and applicable regulatory requirements. The study was approved by the local institutional ethics committee, and all participants gave written informed consent prior to entry into the study.

No proprietary interest of any author.

F. Koerner (✉) · U. Koerner-Stiefbold
Klinik Siloah,
CH-3073 Guemligen Bern, Switzerland
e-mail: fritz.koerner@bbox.ch

J. G. Garweg
Berner Augenklinik am Lindenhofspital,
CH-3012, Bern, Switzerland

Introduction

Proliferative vitreoretinopathy (PVR) is a cicatrizing process complicating retinal detachment surgery [1]. Cellophane membranes are usually understood as presenting idiopathic or secondary epiretinal fibrosis, i.e., as an early stage of PVR [2, 3]. Glial material, pigment epithelial elements, and laminocytes are found in membranes removed from eyes with cellophane retinopathy [4]. Cellophane retinopathy or macular pucker (Fig. 1) occurs in 4% to 8% after retinal detachment surgery [5–7]. Surgical removal of epimacular membranes is only indicated in cases where macular pucker causes persisting metamorphopsia and reduced visual acuity. Mild stages of cellophane retinopathy are usually observed.

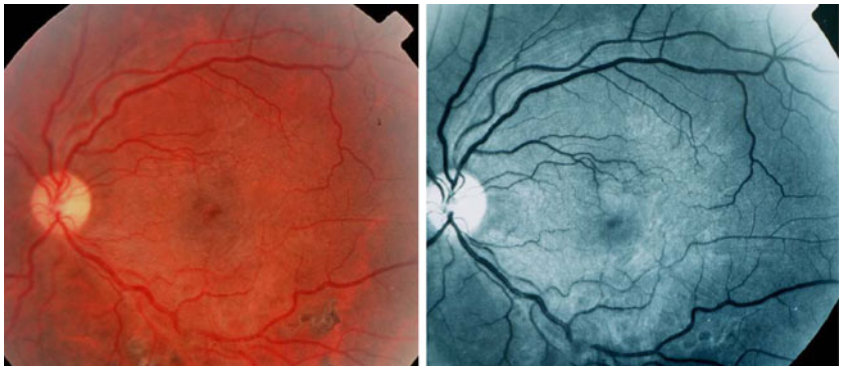

Fig. 1 Cellophane appearance after retinal detachment surgery. Epimacular membrane is easily recognized on black and white photo

While surgical interventions are the gold standard in the treatment of PVR, various preventive pharmacological approaches have been investigated in recent years (see review [8]).

Local injections of triamcinolone acetonide and systemic administration of steroids against PVR reactions have been tested experimentally and in humans [9–13]. The combination of systemic methylprednisolone, sodium diclofenac and colchicine reduced significantly the rate of PVR-induced retinal detachment in rabbits [14]. In a pilot study of 20 patients with retinal and choroidal detachment oral steroids given for 1 week resulted in better reattachment rates compared to no steroids [15].

Assuming inflammatory reactions and a breakdown of the blood–retinal barrier following retinal detachment surgery as relevant factors for the development of PVR, we were interested whether systemic corticosteroids would modify this risk and reduce the incidence of cellophane membranes. Therefore, we designed a randomized prospective placebo-controlled clinical trial to study the effect of systemic corticosteroids on the development of membrane formation after retinal detachment surgery. After taking note of an increasing number of scientific reports appearing between 2000 and 2010 showing that autoimmune mechanisms and inflammatory processes are involved in the development of PVR, we finally decided to submit our results for publication, as they are clearly compatible with actual cellular and clinical research.

Patients and methods

In this placebo-controlled double-blind randomized clinical trial, 220 consecutive patients with rhegmatogenous retinal detachment (RD) were included who were hospitalised for surgery between January 1994 and April 1999. Exclusion criteria were preoperative advanced stages of PVR C, previous vitreoretinal surgery, age younger than 18 or older than 75 years, uveitis, glaucoma, pregnancy, and systemic diseases such as diabetes, arterial hypertension, peptic ulcer, and immune deficiency.

Patients were divided at random into two groups, i.e, a steroid group (n=110) and a placebo group (n=110). The grouping code of the individual patient was kept in a sealed envelope that was not opened before termination of the study, i.e., 6 months after the last detachment surgery (last patient, last visit).

The majority of cases (87%) were operated by two vitreoretinal surgeons (FK 62%, JG 25%), and the remaining cases by surgically trained senior residents. All surgeries were performed at earliest possible convenience, at the latest within 24 hours of referral.

All patients presented with rhegmatogenous RD of one eye. The extent of RD, as well as the number and the cumulative size of retinal tears, was comparable in both study groups (see Table 1). The macula was detached in 41.8% of the steroid group and 50% of the placebo group.

A 2-mm encircling band was applied in the majority of cases. In some eyes, it was combined with radial or circumferential buckles. An external drainage of subretinal fluid was usually done (see Table 1). Air or SF6 gas was injected in 53.6% eyes of the steroid group and 47.3% eyes of the placebo group. A primary vitrectomy was necessary in 14.6% and 12.7% respectively, and was always combined with buckling procedures. The number of cryocoagulation spots was slightly higher in the placebo group. The total area of cryopexy was comparable in both study groups.

Surgery was generally done under local anesthesia with a retrobulbar injection of 4 ml mepivacaine.

Classification of PVR was adopted from Machemer et al. [16] and is shown in Table 2.

In the steroid group, the initial dosage of prednisone was 100 mg for 6 days, thereafter being tapered to 50 mg for 5 days, and 12.5 mg for another 4 days. Placebo was administered in the control group in a way that was indistinguishable from the dispense of prednisone in the steroid group.

In the steroid group, 85 eyes (77.3 %) were phakic, 22 pseudophakic, and three aphakic. In the placebo group there were 90 phakic (80.2 %), 18 pseudophakic, and two aphakic eyes. Posterior Nd:Yag capsulotomy was performed in nine eyes of the steroid and 11 eyes of the placebo group.

Table 1 Baseline data. Chi square statistics (Student's *t*-test and Fisher's exact test)

Item	Steroid	Placebo	*P*
No. of patients	110	110	
Eye R/L	59 / 51	42 / 68	n.s.
Gender F/M	42 / 68	34 / 76	n.s.
Age mean/SD	54.5 ±13.8	54.1 ±14.4	n.s.
Lens			
Phakic	85 (77.3%)	90 (80.2%)	n.s.
Pseudophakic	22 (20.0%)	18 (16.4%)	n.s.
Aphakic	3 (2.7%)	2 (1.8%)	n.s.
Dropout 1 month	4 (3.6%)	11 (10%)	n.s.
Dropout 3 months	3 (2.7%)	11 (10%)	<0.05
Dropout 6 months	8 (7.3%)	16 (14.6%)	n.s.
RD extension (clock hours)	4.74 ± 1.96	5.21 ± 2.7	n.s.
Number of tears			
None	12	6	n.s.
1	56	52	n.s.
2–5	35	41	n.s.
>5	7	11	n.s.
Cumulative size of retinal breaks	1.17 ± 1.0	1.29 ± 1.2	n.s.
Macula detached	46 (41.8%)	55 (50.0%)	n.s.
Duration of symptoms			
1–3 days	31 (28.2%)	31 (28.2%)	n.s.
4– 6 days	42 (38.2%)	41 (37.2%)	
1–2 weeks	16 (14.5%)	20 (18.2%)	
3–4 weeks	14 (12.7%)	7 (6.4%)	
> 4 weeks	7 (6.4%)	11 (10%)	
1st operation / buckling procedures			
0 none	2 (1.8%)	3 (2.7%)	n.s.
1 radial buckle	21 (19.1%)	24 (21.8%)	
2 circumferential buckle	5 (4.5%)	10 (9.1%)	
3 encircling band	66 (60.0%)	60 (54.5%)	
1+3	11 (10.0%)	9 (8.2%)	
2+3	5 (4.5%)	3 (2.7%)	
1+2+3	0	1 (0.9%)	
Intrascleral implant	1 (0.9%)	3 (2.7%)	
External drainage	87 (79.1%)	83 (75.7%)	n.s.
Primary vitrectomy	16 (14.5%)	14 (12.7%)	n.s.
Air ± SF6 tamponade	59 (53.6%)	52 (47.3)	n.s.
Cryopexy/no. of applications	5.7 ± 2.9	6.5 ± 3.0	<0.05
Cryopexy extension (clock hours)	3.1 ± 2.0	3.5 ± 2.6	n.s.

Preoperative and follow-up examinations after 1, 3, and 6 months that were done by one senior resident (UK) included best-corrected Snellen decimal visual acuity measurement at a distance of 5 meters, slit-lamp biomicroscopy, tonometry, direct and indirect ophthalmoscopy, and fundus examination with a Goldmann 3-mirror contact glass. OCT for an assessment of the macular situation was not available at the time of our study.

Table 2 Classification of proliferative vitreoretinopathy (PVR)

Stage A:	Pigment clusters
	Pigment cells
	Vitreous flare
Stage B:	Wrinkling of inner retinal surface
	Cellophane appearance
	Retinal rigidity
	Tortuosity of retinal vessels
	Epiretinal membranes
Stage C:	Single or multiple retinal star folds
	Confluent star folds
	Subretinal proliferation
	Funnel detachment
	Circumferential contraction
	Anterior displacement

Data from preoperative and postoperative examinations were recorded prospectively and entered into an electronic database. Baseline data are listed in Table 1. After confirmation of a normal distribution, data of both groups were compared with chi square statistics and, in the case of small numbers of eyes, with two-tailed Fisher's exact test.

The number of dropouts at given follow-up intervals are shown in Table 1. Reasons for dropout were patient's wish, loss of patients to follow-up, or unplanned discontinuation or change of medication.

Results

A total retinal attachment was achieved in 95% of eyes of the steroid group and 89% of the placebo group eyes. The macula was finally attached in 98% of both groups. More than one reoperation was needed in 14 steroid and 22 placebo group eyes (Table 3). Postoperative PVR stage B was present in 21% of 29 reoperated steroid group eyes, as compared to 54% of 39 reoperated placebo group eyes ($p < 0.01$).

Any PVR stages according to the classification of Machemer et al. [16] were found in 121 of the total of 220 eyes of both groups, i.e., in 55%. The postoperative rates at 1, 3 and 6 months were comparable between placebo- and steroid-treated eyes.

Postoperative advanced PVR signs (stage C, see Table 2) were too rare to allow statistical calculations. Significant differences were found especially for various appearances of stage B. In the placebo group, the postoperative prevalence of cellophane membrane at the posterior pole and elsewhere was twice that of the steroid group (Table 4, Fig. 2).

Table 3 Retina reattachment. Number of eyes and percentage of total group

Item	Steroid	Placebo	*P*
Reattachment after 1st operation	95/110 (86.4%)	94/110 (85.5%)	
None	15	15	n.s.
End of 1st operation	81	72	
After 24 hrs.	3	10	
After 2–4 days	7	4	
After 4–8 days	0	2	
After >8 days	4	6	
Re-operations			
Total number	29	39	n.s.
PVR stage B	6/29 (20.7%)	21/39 (53.8%)	<.0.01
Reattachment at 6 months *			
Total reattachment	97/102 (95.1%)	84/94 (89.4%)	n.s.
Macular reattachment	100/102 (98.0%)	92/94 (97.9%)	n.s.

* Dropouts excluded

The number of cryocoagulation spots correlated with the incidence of cellophane membrane in the placebo group: about 16% of eyes showed cellophane membrane in eyes with less than five cryo spots, but nearly 30% in eyes with more extensive cryocoagulation (Fig. 3). In eyes of the steroid group, there was a slight non-significant tendency of higher rates of cellophane membrane from 14 to 16% with five or more cryocoagulation spots.

The preoperative as well as postoperative visual acuity did not differ significantly between steroid and placebo group eyes (Table 5, Fig. 4). Cellophane membranes did not seem to cause additional vision loss in eyes with retinal detachment.

We did not observe any unwanted side-effects due to the administration of systemic corticosteroids.

Discussion

This is the first trial to assess the effect of oral prednisone on the development of cellophane membranes as an early sign of PVR in a placebo-controlled randomized double-blind clinical study, in a population of 220 patients with primary rhegmatogenous retinal detachment. In accordance with published experimental and laboratory studies, oral anti-inflammatory doses of prednisone, starting at the day of surgery and continued for 15 days, had clearly a therapeutic effect.

PVR is a pathological process complicating retinal detachment, trauma, inflammatory diseases and retinal surgery. Cellophane reflexes are an early clinical sign of the formation of epiretinal membranes. These membranes consist of glial cells, retinal pigmentary cells, myofibroblasts,

Table 4 Pre- and postoperative PVR signs

Item	Steroid	Placebo	*P*
Cellophane appearance (total)			
Preop	17/110 (15.5%)	21/109 (19.3%)	n.s.
1 month	28/105 (26.7%)	41/98 (41.8%)	<0.05
3 months	25/106 (23.6%)	46/98 (46.9%)	=0.0005
6 months	20/101 (19.8%)	36/92 (39.1%)	<0.005
Cellophane including posterior pole			
Preop	10/110 (9.1%)	15/109 (13.8%)	n.s.
1 month	23/105 (21.9%)	36/98 (36.7%)	<0.05
3 months	23/106 (21.7%)	41/98 (41.8%)	<0.005
6 months	17/102 (16.8%)	32/92 (34.8%)	<0.005
Cellophane *only* posterior pole			
preop	4/110 (3.6%)	6/109 (5.5%)	n.s.
1 month	15/105 (14.3%)	26/98 (26.5%)	<0.05
3 months	19/106 (17.9%)	32/98 (32.7%)	<0.02
6 months	15/102 (14.9%)	24/92 (26.1%)	=0.05
Retina rigidity			
preop	28/110 (25.5%)	40/110 (36.4%)	n.s.
1 month	14/105 (13.3%)	17/98 (17.3%)	n.s.
3 months	9/107 (8.4%)	15/99 (15.2%)	n.s.
6 months	6/102 (5.9%)	13/94 (13.8%)	n.s.
Wrinkling inner retinal surface			
preop	10/110 (9.1%)	14/110 (12.7%)	n.s.
1 month	11/105 (10.5%)	12/98 (12.2%)	n.s.
3 months	11/107 (10.3%)	13/99 (13.1%)	n.s.
6 months	7/102 (6.9%)	14/94 (14.9%)	=0.07
Epiretinal membranes			
Preop	1/109 (0.9%)	1/110 (0.9%)	n.s.
1 month	7/106 (6.6%)	3/98 (3.1%)	n.s.
3 months	7/106 (6.6%)	6/99 (6.1%)	n.s.
6 months	5/101 (5.0%)	12/94 (12.8%)	=.05
PVR stage A			
Preop	16/110 (14.5%)	18/110 (16.4%)	n.s.
1 month	5/106 (4.7%)	7/99 (7.1%)	n.s.
3 months	6/107 (5.6%)	4/99 (4.0%)	n.s.
6 months	1/102 (1.0%)	4/94 (4.3%)	n.s.
PVR stage B *			
Preop	38/110 (34.5%)	46/110 (41.8%)	n.s.
1 month	28/106 (26.4%)	40/99 (40.4%)	<0.05
3 months	27/107 (25.2%)	45/99 (45.5%)	<0.005
6 months	23/102 (22.5%)	43/94 (45.7%)	<0.0005
PVR stage C			
Preop	1/110 (0.9%)	2/110 (3.0%)	n.s.
1 month	5/106 (4.7%)	3/99 (3.0%)	n.s.
3 months	3/107 (2.8%)	2/99 (2.0%)	n.s.
6 months	2/102 (2.0%)	3/94 (3.2%)	n.s.
PVR any stage (A,B,C)			
Preop	55/110 (50.0%)	66/110 (60.0%)	n.s.
1 month	38/106 (35.8%)	50/99 (50.5%)	<0.05
3 months	36/107 (33.6%)	51/99 (51.5%)	<0.02
6 months	26/102 (25.5%)	50/94 (53.2%)	<0.0002

* Definition PVR stage B: cellophane membrane, retinal rigidity, vascular tortuosity, wrinkling of inner retinal surface, epiretinal membranes

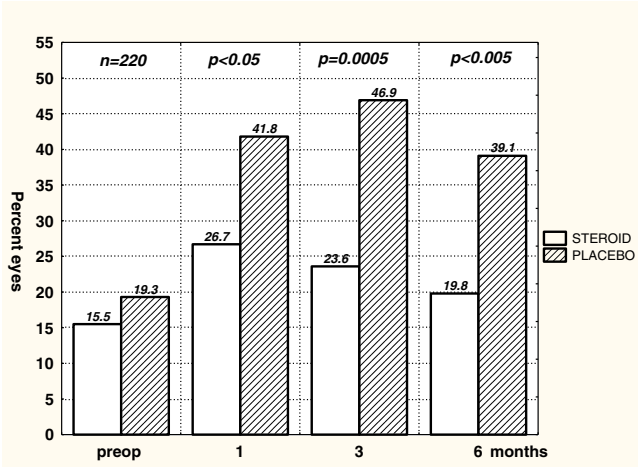

Fig. 2 Cellophane membrane pre- and postoperatively

hyalocytes, laminocytes and Müller cells [4]. Multiple studies indicate that inflammatory mechanisms are involved in the development of periretinal membranes [17]. Immediately with

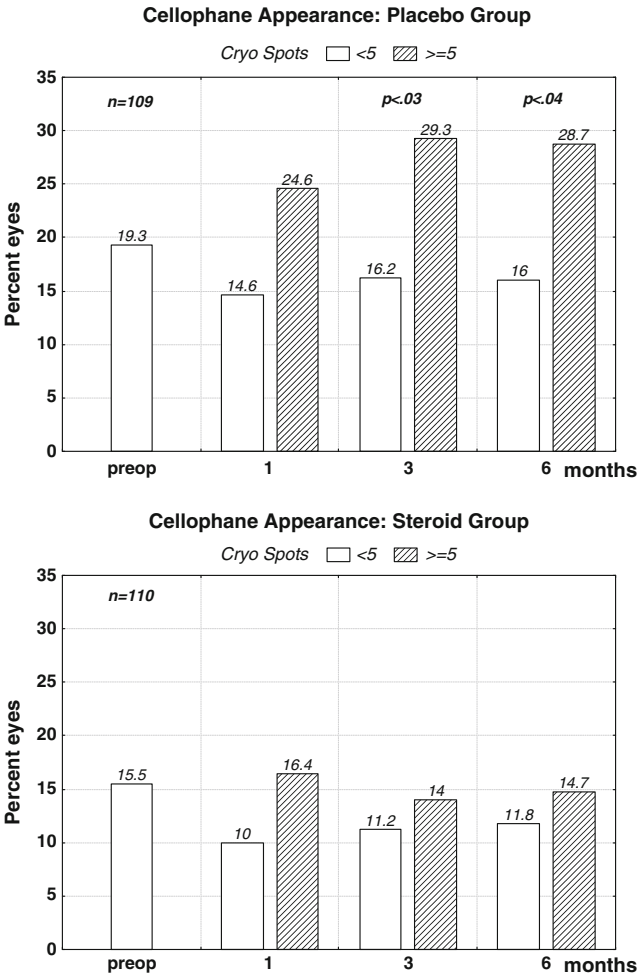

Fig. 3 Rates of eyes with cellophane appearance depending on number of cryocoagulation spots

Table 5 Pre- and postoperative visual acuity. No significant difference between study and control group at any interval. Missing values due to dropouts

	Steroid			Placebo		
	N	VA	LogMar	*N*	VA	LogMar
Preop	110	0.44	0.36	110	0.37	0.43
Month 1	106	0.56	0.25	99	0.54	0.27
Month 3	107	0.61	0.21	99	0.58	0.24
Month 6	102	0.63	0.20	94	0.61	0.21

VA = decimal; logMAR = log10(1/VA)

the onset of RD, Müller cells start to proliferate, migrate onto the inner and outer surface of the retina and cause periretinal fibrosis [18]. Increased levels of IL-8 and VEGF indicate an inflammatory process associated with a breakdown of the blood–retina barrier [19]. Müller cells were shown to express IL-8 (CXCL8), a proinflammatory chemokine that adheres to CXCL1 receptors. An upregulation of CXCL8 and CXCL1/CXCL2 receptors in Müller cells and microglial cells has been found in retinas and vitreous of human and rabbit PVR eyes [20, 21]. Other cytokines were found to be elevated in PVR eyes in a more recent study indicating an inflammatory mechanism in the development of PVR [23].

Postoperative autoimmune reactions against retina antigens have been found to be much stronger in the presence of vitreoretinal proliferation, and more frequent in eyes with excessive cryocoagulation [22]. Autoimmune mechanisms and inflammatory reactions are discussed in context with a presumed breakdown of the blood–retina barrier in eyes with RD [24]. Therefore, the effect of corticosteroids as an adjuvant of retinal detachment surgery has been investigated in several trials. In an experimental model of PVR in rabbits, PVR-associated RD was induced by injection of macrophages. In this experiment, a single injection of 1 mg triamcinolone acetonide together with macrophages into the vitreous reduced markedly the development of PVR from

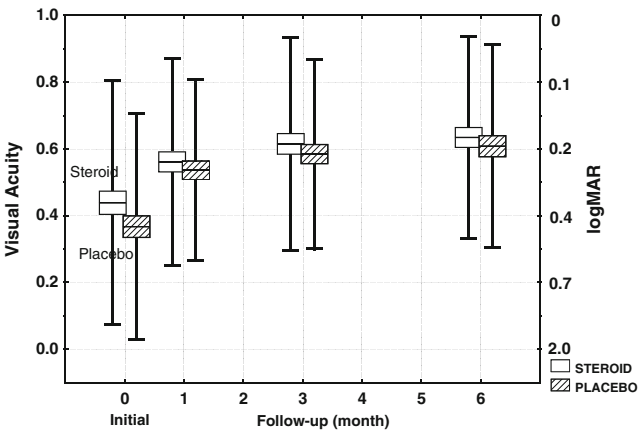

Fig. 4 Pre- and postoperative visual acuity (*n*=220 eyes)

77% in controls to 14% [11]. In humans, systemic steroids starting at the day after scleral buckling surgery did not reduce postoperative complications in a randomized placebo-controlled study, but the study was not powered to allow conclusions with regard to a steroid effect on the development of PVR [12]. PVR rates of 4 % in the steroid group and 11 % in the control group in this study are apparently too small for reliable statistical evidence. Subconjunctival injection of dexamethasone immediately before retinal detachment surgery was claimed to reduce the leakage of the blood–retinal barrier and was discussed as a potential means of reducing the incidence of PVR in a study of Bali et al. [13]. Laser flare photometry of the anterior segment was used in this study. Park [25] argued that this method detected a blood–aqueous rather than a blood–retinal barrier breakdown, but would in any event substantiate an inflammatory process.

Assuming inflammatory reactions and a breakdown of the blood–retinal barrier following retinal detachment surgery, we wished to prove whether systemic corticosteroids may help to prevent or reduce the development of early stages of PVR. In a previous study of 141 patients with retinal detachment, we had tested oral prednisone versus placebo, starting the therapy at the 5th day after surgery. Mild grades of PVR were statistically less frequent in the steroid group [26].

Arguing that inflammatory reactions would start very early in the process of retinal detachment according to an experimental study of Chandler et al. [10] and augmented by reattachment surgery, we decided to launch this trial with oral administration of steroid or placebo starting at the day before initiation of surgery. The assumption of an early PVR induction was later supported by showing early proliferation of Müller cells starting immediately at the time of surgery [18].

Cellophane membranes occurred in our study more frequently in the placebo than in the steroid group. Cellophane membranes were more frequently detected in eyes that received more extensive cryocoagulation, indicating surgical trauma as an important risk factor for PVR. Reattachment rates and visual outcomes were comparable in the steroid and placebo groups. Due to the low number of cases developing advanced stages of PVR, we were not able to investigate the steroid effect on advanced PVR.

Weijtens et al. [27] found that dexamethasone concentrations in the subretinal fluid of eyes with RD were much higher after subconjunctival or peribulbar injection of 2.5 mg than with oral administration of 7.5 mg. It is worth mentioning that in our study much higher oral doses of corticosteroids were used over a period of 2 weeks. We did not measure serum steroid levels or concentrations of dexamethasone in the vitreous.

It is conceivable that subconjunctival injections of depot corticosteroids may have a similar or even stronger prophylactic effect against PVR, with less risk of systemic side-effects than oral doses. This hypothesis should be the subject of a large-scale clinical trial.

In conclusion, our study demonstrates a relevant effect of systemic steroids on the development of early stages of PVR. Whether a comparably strong effect on advanced PVR stages can be shown, and how locally applied and systemic steroids compare, remains to be addressed in large-scale clinical trials.

Acknowledgement The authors would like to express their gratitude to the late Professor Robert Machemer, M.D., and Ulrich Steinhorst, M.D., Department of Ophthalmology, Durham NC, for their substantial support in planning, discussing and designing this study during the years 1993 through 1999.

No funding was received to support this study.

References

1. Kirchhof B (2004) Strategies to influence PVR development. Graefes Arch Clin Exp Ophthalmol 242:699–703
2. Koerner F (1989) Clinical diagnosis of proliferative vitreoretinopathy. Klin Monatsbl Augenheilk 194(5):383–388
3. McCarty DJ, Mukesh BN, Chikani V, Wang JJ, Mitchell P, Taylor HR, McCarty CA (2005) Prevalence and associations of epiretinal membranes in the visual impairment project. Am J Ophthalmol 140(2):288–294
4. Snead DR, James S, Snead MO (2008) Pathological changes in the vitreoretinal junction 1: Epiretinal membrane formation. Eye 22:1310–1317
5. Hagler WS, Aturaliya U (1971) Macular pucker after retinal detachment surgery. Br J Ophthalmol 55:451–457
6. Lobes LD Jr, Burton TC (1978) The incidence of macular pucker after retinal detachment surgery. Am J Ophthalmol 85:72–77
7. Margherio RR, Margherio AR (1995) Macular holes and epiretinal macular membranes. Duane's Clin Ophthalmol 6(61):1–18
8. Iandiev I, Bringmann A, Wiedemann P (2010) Proliferative vitreoretinopathy — pathogenesis and therapy. Klin Monatsbl Augenheilk 227:168–174
9. Tano Y, Chandler D, Machemer R (1980) Treatment of intraocular proliferation with intravitreal injection of triamcinolone acetonide. Am J Ophthalmol 90(6):810–816
10. Chandler DB, Hida T, Sheta S, Proia AD, Machemer R (1987) Improvement in efficacy of corticosteroids therapy in an animal model of proliferative vitreoretinopathy by pretreatment. Graefes Arch Clin Exp Ophthalmol 225(4):259–265
11. Hui YN, Liang HC, Cai YS, Kirchhpf B, Heimann K (1993) Corticosteroids and daunomycin in the prevention of experimental proliferative vitreoretinopathy induced by macrophages. Graefes Arch Clin Exp Ophthalmol 231(2):109–114
12. Dehghan MH, Ahmadieh H, Soheilian M, Azarmina M, Moradian S, Ramezani AR, Tavallal A, Naghibozakerin J (2010) Effect of oral prednisolone on visual outcomes and complications after scleral buckling. Eur J Ophthalmol 20:419–423
13. Bali E, Feron EJ, Peperkamp E, Veckeneer M, Mulder PG, van Meurs JC (2010) The effect of preoperative subconjunctival injection of dexamethasone on blood-retinal barrier breakdown following scleral buckling retinal detachment surgery: a prospective randomized placebo-controlled double blind clinical trial. Graefes Arch Clin Exp Ophthalmol 248:957–962
14. Pastor JC, Rodriguez E, Marcos MA, Lopez MI (2000) Combined pharmacologic therapy in a rabbit model of proliferative vitreoretinopathy (PVR). Ophthalmic Res 32(1):25–29

15. Sharma T, Gopal L, Reddy RK, Kasinathan N, Shah NA, Sulochana KN, Miriam KC, Arvind K, Ramakrishna S, Sukumar B (2005) Primary vitrectomy for combined rhegmatogenous retinal detachment and choroidal detachment with or without oral corticosteroids: a pilot study. Retina 25:152–157
16. Machemer R, Aaberg TM, Freeman HM, Irvine AR, Lean JS, Michels RM (1991) An updated classification of retinal detachment with proliferative vitreoretinopathy. Am J Ophthalmol 112:159–165
17. Gilbert C, Hiscott P, Unger W, Grierson I, McLeod D (1988) Inflammation and the formation of epiretinal membranes. Eye 2 (Suppl):140–156
18. Bringmann A, Pannicke T, Grosche J, Francke M, Wiedemann P, Skatchkov SN, Osborne NN, Reichenbach A (2006) Müller cells in the healthy and diseased retina. Prog Retin Eye Res 25:397–424
19. Rasier R, Gormus U, Artunay O, Yuzbasioglu E, Oncel M, Bahcecioglu H (2010) Vitreous levels of VEGF, IL-8, and TNF-in retinal detachment. Curr Eye Res 35(6):505–509
20. Goczalik IM, Raap M, Weick M, Milenkovic I, Heidmann J, Enzmann V, Wiedemann P, Reichenbach A, Francke M (2005) The activation of IL-8 receptors in cultured guinea pig Müller glial cells is modified by signals from retinal pigment epithelium. J Neuroimmunol 161:49–60
21. Goczalik IM, Ulbricht E, Hollborn M, Raap M, Uhlmann S, Weick M, Pannicke T, Wiedemann P, Bringmann A, Reichenbach A, Francke M (2008) Expression of CXCL8, CXCL1, and CXCL2 in neurons and glial cells of the human and rabbit retina. Invest Ophthalmol Vis Sci 49:4578–4589
22. Ricker LJAG, Kijlstra A, Kessels AGH, de Jager W, Liem ATA, Hendrikse F, La Heij EC (2011) Interleukin and growth factor levels in subretinal fluid in rhegmatogenous retinal detachment: A case-control study. PlLoS One 6(4):e19141
23. Remy C (1982) Retinal detachment and retraction. Effect of steroidal and nonsteroidal anti-inflammatory agents on the autoimmune reaction against the retina in idiopathic retinal detachment with signs of retraction. J Fr Ophtalmol 5(10):621–632
24. Baudouin C, Fredj-Reygrobellet D, Baudouin F, Lapalus P, Gastaud P (1989) Immunohistologic study of proliferatived vitreoretinopathy. Am J Ophthalmol 108:387–394
25. Park AH (2011) The effect of preoperative subconjunctival injection of dexamethasone on blood-retinal barrier breakdown following scleral buckling retinal detachment surgery. Graefes Arch Clin Exp Ophthalmol 249:151–152
26. Koerner F, Merz A, Gloor B, Wagner E (1982) Postoperative retinal fibrosis — a controlled clinical study of systemic steroid therapy. Graefes Arch Clin Exp Ophthalmol 219:268–271
27. Weijtens O, Schoemaker RC, Lentjes EG, Romijn FP, Cohen AF, Van Meurs JC (2000) Dexamethasone concentration in the subretinal fluid after subconjunctival injection, a peribulbar injection, or an oral dose. Ophthalmology 107(10):1932–1938