ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LXI, N1, 40 SECTIO D 2006

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Evaluation of blood–aqueous barrier after vitrectomy in patients with proliferative diabetic retinopathy

The blood–aqueous humour barrier represents a complex system for exchange processes between blood and avascular tissue. Breakdown of the blood–aqueous barrier is caused by inflammation, chronic ocular and systemic diseases such as diabetes mellitus, hypertension or the surgical trauma, which is clinically apparent as flare and cells in the anterior chamber of the eye. (1, 3, 6-8). Assessment of these parameters is of fundamental clinical importance in ophthalmic surgery, laser therapy and inflammatory ocular diseases (9, 14). It has been shown that surgical trauma to the eye directly induces the disruption of the blood–aqueous barrier (1, 11). Protein leakage and cellular reaction in the aqueous humour has been noticed not only after surgery in the anterior segment of the eye but also after posterior segment procedures such as vitrectomy (12, 15).

The degree of inflammation (flare and cells) can be evaluated by slit-lamp biomiscroscopy, however, this is primarily a qualitative and subjective method. The laser flare and cell meter (LFCM) provides a precise, objective, and non-invasive measurements of aqueous flare (10, 11).

The aim of this study was to evaluate changes of blood–aqueous barrier permeability in eyes with proliferative diabetic retinopathy treated with pars plana vitrectomy. Furthemore, the influence of silicone oil administered into the eyeball to the barrier permeability was investigated.

METHODS

Clinical examination of 39 patients with proliferative diabetic retinopathy included in this study was performed before surgery, the preoperative diagnose included non-clearing vitreous haemorrhage, progressive fibrovascular proliferations, tractional retinal detachment, and combined traction/rhegmatogenous retinal detachment. Only patients treated by primary procedure were included in this study. One surgeon performed all operations. The type of surgical procedure (simple vitrectomy, vitrectomy with membrane peeling, advanced vitrectomy with segmentation and/or delamination of the membranes and retinal reattachment) and the duration of surgery were noticed in each case. Panretinal photocoagulation was routinely applied during vitrectomy. The final decision of using silicone oil tamponade was made during the surgical procedure. After the surgery patients were divided into two groups depending on the application of silicone oil: group I (25 eyes) – patients treated by vitrectomy without silicone oil, group II (14 eyes) – patients treated by vitrectomy with silicone oil tamponade. The patients in both groups received the same routine postoperative medications including topical 1% tropicamide twice a day for 2 weeks and neomycin/dexamethason drops 4 times a day for one month. The mean age in the groups was 54 and 48.5 years, respectively. The control group consisted of 50 eyes out of 39 healthy individuals, mean age 50.5 years.

The blood aqueous–barrier permeability was measured quantitatively with the use of KOWA SM-500 laser flare and cell meter before, 24 hours, 5 days and 30 days after surgery. The apparatus and technique have been previously described by Sawa (10). All measurements were performed by one investigator in the morning. Patients' pupils were dilated before examination using 1% tropicamide. Tyndallometric values were expressed in photons per millisec. The flare and cell measurements were not normally distributed, but were the log-values, transformed to base 10 values, (Kolgomorov-Smirnov test). A two-tailed t-test on the log-transformed values was used to check the significance of in-group and between-group differences in the measurements (9).

RESULTS

In group I (vitrectomy without silicone oil) 18 out of 25 patients suffered from non-clearing vitreous haemorrhage, 5 had fibrovascular proliferations and 2 tractional retinal detachment. In this group most of the cases were treated by simple vitrectomy or vitrectomy with membrane peeling. In group II (vitrectomy with silicone oil) diabetic retinopathy was far more advanced. Five out of 14 cases suffered from severe fibrovascular proliferations, 7 had tractional retinal detachment and in 2 cases combined traction/rhegmatogenous retinal detachment was found. In this group in most of cases advanced vitrectomy with segmentation and/or delamination of the membranes and retinal reattachment was performed. The mean duration of surgical procedure was 52 minutes and 74 minutes in group I and group II respectively.

The results of tyndallometric measurements before and after operation in both groups are depicted in Table 1.

Tab. 1. Mean laser flare values before and after TPP vitrectomy without (group I) and with the use of silicone oil (group II); tyndallometric values in photons/ms

Measure	Group I TPP vitrectomy without silicone oil	Group II TPP vitrectomy with silicone oil
Before	32.84	86.21
24 h after	88.36*	132.95
5 days after	71.33*	115.5*
1 month after	42.02	86.84

*p<0.05

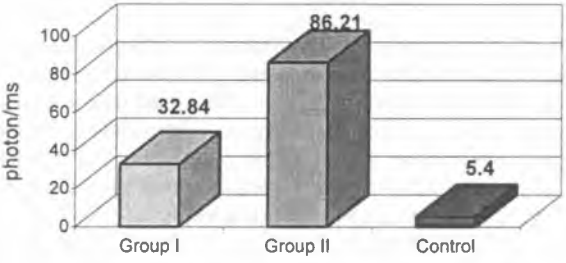

Fig. 1. Mean laser flare values before operation

In all patients aqueous flare values taken before surgery were significantly higher compared to the control ($p<0.05$); (Fig. 1). The surgical procedure resulted in a significant increase of the values compared to the preoperative measurements in both groups ($p<0.05$). The highest values were noticed 24 hours after surgery ($p<0.05$) and diminished promptly within the first five days after surgery. Aqueous flare values reached the preoperative level by 30 days postoperatively ($p>0.05$); (Fig. 2).

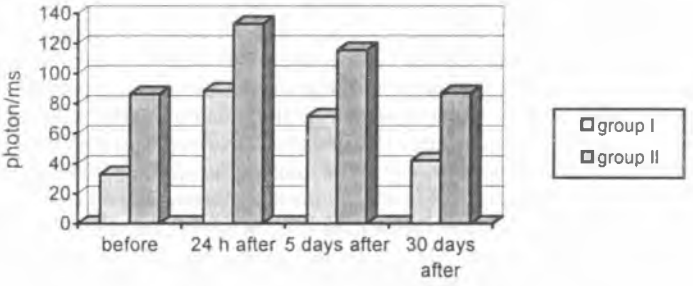

Fig. 2. Mean laser flare values in both groups before and after operation

This was observed regardless of the use of the silicone oil. Patients treated with vitrectomy and silicone oil had significantly higher tyndalometric values before and after the operation when compared to those operated without oil ($p<0.05$). But the course of tyndalometric curve was similar in both groups (Fig. 3.).

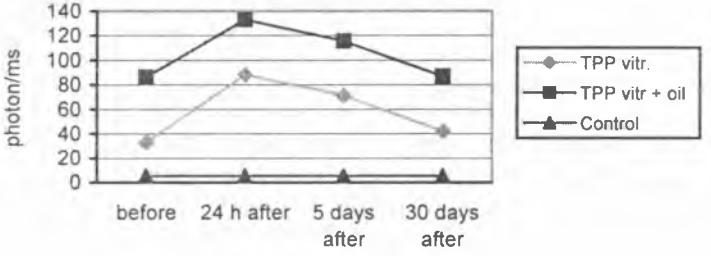

Fig. 3. The course of the laser flare values change curve in both groups

DISCUSSION

It has been demonstrated previously that surgical trauma to the anterior segment of the eye directly induces the disruption of the blood–aqueous barrier, however, little data exists in the literature about the influence of vitrectomy on the blood aqueous barrier breakdown (12, 15).

In this study we evaluated changes of blood–aqueous barrier permeability in eyes with proliferative diabetic retinopathy after pars plana vitrectomy. To avoid a diurnal variation of flare intensity all measurements were taken in the morning (8). Mean preoperative tyndalometric values (32.84 photons/ms in the group treated without silicone oil and 86.21 in the group treated with silicone oil) were significantly higher compared to the control eyes of healthy patients (5.4 photons/ms) ($p<0.05$). Similar results were reported by Yamazaki et al., who found that the protein value measured by laser flare-cell meter before vitrectomy in eyes with diabetic retinopathy was 5 times higher compared to normal control eyes (15). The extremely high preoperative flare values found in the silicone oil treated group in our series were related to a far more advanced proliferative diabetic retinopathy in this group. Most of the patients had severe fibrovascular proliferations or traction retinal detachment, compared to the group treated without silicone oil tamponade.

Previous studies with LFCM measurements in diabetic patients have also demonstrated increased flare values in eyes with diabetic retinopathy, rising with an increase in severity of a retinopathy (4. 6, 13). Additionally Nguyen et al. found a correlation existing between aqueous flare and the type of angiographic retinal capillary changes with higher flare values in eyes with retinal capillary dilatation and exudation (6). Although vitrectomy is a procedure in a posterior segment of the eye, our study confirmed, that surgical trauma to the eye induces blood–aqueous barrier

breakdown leading to augmented protein leakage and cellular reaction in the anterior chamber, expressed as increase of tyndallometric values. In both analyzed groups of patients, receiving surgery either with or without silicone oil, the surgical procedure resulted in a significant increase of the tyndallometric values compared to the preoperative measurements ($p<0.05$). The highest values were noticed 24 hours after operation ($p<0.05$) and diminished promptly within the first five days after surgery. Aqueous flare values reached the preoperative level by 30 days postoperatively ($p> 0.05$). This is in accordance to Yamazaki et al. who found the highest flare values on day 3 after surgery with a gradual decrease to the preoperative value 1 month after surgery. They also observed that increase of laser flare values in diabetic eyes treated with vitrectomy was higher in more complicated procedures (15). Ariki and Ogino have shown that postoperative anterior chamber inflammation of triple procedure, diabetic pars plana vitrectomy, lensectomy with anterior capsulae left intact and posterior chamber intraocular lens implantation anterior to anterior capsulae, were more intense than those after the following 3 surgeries; phacoemulsification and in the bag intraocular lens implantation, extracapsular extraction with lens implanantion, and vitrectomy in diabetic retinopathy eyes alone. The inflammation, however, was less intense compared with another method of triple procedure; pars plana vitrectomy, phacoemulsification and lens implantation.

The integrity of the blood–aqueous barrier after experimental vitrectomy and placement of silicone oil into the rabbits eyes was evaluated by Sparrow et al. They found temporary breakdown in blood–aqueous barrier after surgery, with recovery of normal function approximately one week after vitrectomy. They concluded that placement of silicone oil in the vitreous cavity after vitrectomy does not, in itself, prolong or exacerbate disruption in the blood–aqueous barrier (12).

In our study the patients treated with vitrectomy and silicone oil had significantly higher tyndallometric values before and after surgery, when compared to those operated without silicone oil ($p< 0.05$). Higher values in group treated with silicone oil are rather a result of more advanced diabetic retinopathy than the effect of the surgical trauma and silicone oil tamponade. This was confirmed by the course of tyndallometric curve, which was similar in both treated groups. A slightly higher mean final flare value compared to the preoperative one in the group treated without silicone (42.02 versus 32.84 photons/ms) and equal final and preoperative mean value in the group with silicone oil (86.84 versus 86.21 photons/ms) could suggest the better recovery of blood–aqueous barrier integrity in eyes with silicone oil tamponade. It is possible that silicone oil acts via a decompartimentalization between posterior and anterior segment of the eye, and prevents a transfer of cells and proteins from vitreous cavity to anterior chamber. However, the difference is not significant, the observation time should have probably lasted longer. From the clinical point of view, several authors have pointed out the positive effect of silicone oil in the reduction of preexisting or postoperatively new iris neovascularisation and preventing postoperative rebleeding or retinal detachment (2, 3). Stabilization of the above listed clinical situations may be the factor contributing to decrease of the blood–aqueous barrier breakdown. (5)

In conclusion, our study confirms that in proliferative diabetic retinopathy blood–aqueous barrier breakdown corresponds to the severity of pathological changes in the eye. Blood–aqueous barrier permeability increases significantly shortly after pars plana vitrectomy and operation had a significant influence on blood retinal barrier function up to the 5th day. Silicone oil tamponade had no significant influence on the blood–aqueous barrier breakdown related to the surgical procedure during short-term observation, however, our preliminary results encouraged us to include into the future studies patients with different indications for vitrectomy and silicone oil tamponade and to prolong the follow-up time.

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SUMMARY

The aim of this study was to evaluate the changes of blood–aqueous barrier permeability in eyes with proliferative diabetic retinopathy after pars plana vitrectomy. Furthermore, the influence of silicone oil on the barrier permeability was evaluated. We examined 39 diabetic patients scheduled for pars plana vitrectomy due to proliferative diabetic retinopathy; 25 have been treated by vitrectomy without silicone oil and 14 with silicone oil tamponade. The blood–aqueous barrier permeability was measured quantitatively with the use of a laser flare cell meter (KOWA SM-500) before and 24 h, 5 days, and 1 month after the operation. The control group consisted of 50 eyes out of 39 healthy individuals. In all patients with PDR baseline aqueous flare values were significantly higher compared to the control ($p<0.05$). The surgical procedure resulted in a significant increase of the values compared to the preoperative measurements. The highest values were noticed 24 hours after surgery ($p<0.05$) and diminished promptly within the first 5 days after operation. Aqueous flare values reached the preoperative level by 30 days postoperatively ($p>0.05$). In proliferative diabetic retinopathy blood–aqueous barrier breakdown corresponds to the severity of pathological changes. Pars plana vitrectomy had a significant influence on blood –aqueous barrier function up to the 5th day after surgery. Silicone oil tamponade had no significant influence on the postoperative blood–aqueous barrier breakdown.

Ocena zmian przepuszczalności bariery krew–ciecz wodnista po operacji witrektomii u chorych z retinopatią proliferacyjną

Celem pracy była ocena zmian przepuszczalności bariery krew–ciecz wodnista u chorych poddanych witrektomii z powodu retinopatii cukrzycowej proliferacyjnej. Oceniano także wpływ oleju silikonowego na przepuszczalność bariery krew–ciecz wodnista. Badaniami objęto 39 chorych z retinopatią cukrzycową proliferacyjną, u których wykonano witrektomię. U 25 osób podczas witrektomii nie stosowano tamponady wewnętrznej, a u 14 osób zastosowano olej silikonowy. Pomiary przepuszczalności bariery krew–ciecz wodnista wykonywano przy użyciu tyndalometru laserowego KOWA SM-500 bezpośrednio przed zabiegiem operacyjnym oraz 24h, 5 dni i 1 miesiąc po operacji. Grupę kontrolną stanowiło 50 oczu (39 zdrowych osób). U wszystkich chorych już przed operacją stwierdzono istotnie wyższe wartości tyndalometryczne w porównaniu z grupą kontrolną ($p<0,05$). Zabieg operacyjny powodował znaczny wzrost wartości tyndalometrycznych w porównaniu z badaniem przedoperacyjnym. Największy wzrost zanotowano 24h po zabiegu operacyjnym ($p<0,05$), wraz z szybkim ich obniżaniem się w ciągu pierwszych pięciu dni po operacji. Wartości tyndalometryczne osiągnęły poziom przedoperacyjny w ciągu 30 dni po zabiegu ($p>0,05$). U chorych z retinopatią cukrzycową proliferacyjną uszkodzenie bariery krew–ciecz wodnista jest proporcjonalne do zaawansowania zmian patologicznych. Zabieg operacyjny witrektomii zwiększa przepuszczalność bariery krew–ciecz wodnista do piątego dnia po operacji. Tamponada olejem silikonowym nie wpływa w istotny sposób na zmiany przepuszczalności bariery krew–ciecz wodnista.