

Clinical significance of tunica vasculosa lentis in the outcome of threshold ROP

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Background: Many intraocular vessels are transitory and disappear by birth. In this report we analyse the importance of tunica vasculosa lentis (TVL) in treatment outcome of threshold ROP.

Materials and methods: The study was performed at Vilnius University Children's Hospital (VUCH) between July 1, 1997 and May 1, 2006. All consecutive and otherwise unselected infants who reached threshold ROP and underwent treatment were included into the study cohort, comprising 261 babies. Tunica vasculosa lentis of various grades (1–4) was found bilaterally in 94 infants (188 eyes). This group was labeled TVL(+) group. The rest of investigated infants (167) formed the TVL(–) group (331 eyes).

Results: Cryo or laser / cryotherapy was applied on 518 eyes (261 infants) with threshold ROP. Treatment was applied once in 449 eyes. 160/187 eyes of the TVL(+) group and 289/331 eyes of the TVL(–) group underwent one treatment session. Treatment was carried out twice in 27 eyes with TVL and in 38 eyes without TVL. Three times were treated 4 eyes, all in the TVL(–) group.

Tunica vasculosa lentis disappeared in 151 eyes after the first session of therapy. Treatment was successful in all these eyes.

The total number of failures – 30 eyes: 19 / 187 eyes (10 children) in the TVL(+) group and 11/331 eyes (8 children) in the TVL(–) group. All failed eyes belonged to Zone I disease.

Conclusions: Eyes with persistent tunica vasculosa lentis at threshold have a greater likelihood of unfavourable outcome after therapy for threshold ROP. Cryotherapy can be used safely in eyes with tunica vasculosa lentis. Dissolution of tunica vasculosa lentis after threshold ROP treatment was directly proportional to favourable fundus outcome.

Key words: tunica vasculosa lentis (TVL), retinopathy of prematurity (ROP), threshold ROP, cryotherapy, laser-cryo therapy

INTRODUCTION

Many intraocular vessels are transitory during ontogenesis and have disappeared by birth. As described by Isenberg (1), at the 17-mm stage of embryogenesis, small buds from the annual vessel form vascular loops carrying mesodermal tissue onto the anterior surface of the lens even before development of the anterior chamber. By the 22-mm stage, the lamina iridopupillaris is a richly vascularized layer of mesodermal cells closely opposed to the anterior surface of the lens. The peripheral part thickens to form the embryonic iris. The central portion is much thinner, composed almost entirely of blood vessels. It is this plexus of blood vessels that constitutes

the tunica vasculosa lentis (TVL), also known as the anterior vascular capsule of the lens. With time, this plexus further thins, only to eventually disappear.

In 1977, Hittner and colleagues (2) reported that the degree of dissolution of tunica vasculosa lentis could be closely correlated to gestational age. According to their grading system, the lens surface can be entirely covered by vessels (grade 4), corresponding to 27–28 weeks of gestational age (GA). In grade 3 (29–30 weeks of GA), central vessels begin to atrophy, in grade 2 (31–32 weeks) the central lens area is more visible, peripheral vessels are thin. Grade 1 (33–34 weeks of GA) is characterised by only a few vessels remaining at the lens periphery.

In 1999, we published the data that showed a correlation between TVL dissolution and a positive outcome after cryotherapy for ROP (3). This small retrospective study of 8 infants (16 eyes) was in service as a pilot

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study which encouraged us to perform a prospective study and to extend our knowledge on TVL value for ROP outcome. In this report, we analyse the importance of TVL in threshold ROP treatment outcome. Such or similar data were not reported in the literature available to us.

MATERIALS AND METHODS

The study was performed since July 1, 1997 till May 1, 2006 at the Vilnius University Children's Hospital (VUCH). All consecutive and otherwise unselected infants who reached threshold ROP and underwent treatment were included into the study cohort which comprised 261 babies. Tunica vasculosa lentis of various grades (1–4) was found bilaterally in 94 infants (188 eyes). This group was named TVL(+) group. One eye was excluded from the further study: retinal detachment was diagnosed in this eye before treatment (because of delayed transportation to VUCH). The remaining infants (167) formed the TVL(–) group. The number of investigated eyes was 331 in this particular subgroup (three eyes were excluded from the study: persistent primary hyperplastic posterior vitreous was diagnosed in one eye, and ROP less than threshold in one eye of two infants).

All infants were outborn. They were followed by the same two ophthalmologists (RB and RS) using an indirect binocular ophthalmoscope, lid speculum and strabismus hook for rotation and indentation (if necessary) of the eyeball. The pupil was dilated with Phenylephrine 2.5% and Tropicamide 0.5% eyedrops. The ophthalmic examinations were started at the age of three–four weeks and continued weekly or more often thereafter until therapy for threshold ROP was indicated.

We investigated the anterior vascular capsule of the lens with a binocular indirect ophthalmoscope and +20 dioptres Nikon ophthalmic lense (as a magnifier) being kept in a close proximity to the cornea.

Retinal changes were recorded according to the international classification (4, 5), indications for therapy – as defined by CRYO ROP CG (5, 6).

Threshold ROP was estimated as a minimum of five contiguous or eight non-contiguous clock hours of stage 3 disease (extraretinal fibrovascular proliferation) in Zone 1 or Zone 2 with vascular dilation and tortuosity at the posterior pole (4).

Cryo or laser-cryo therapy was performed under general anaesthesia by the same surgeons (R B and R S.).

All babies were followed at least two months after the treatment. Retreatment (if necessary) was performed on 8–14 days after the first therapy session. The third treatment session (if necessary) was carried out 14 to 21 days after the second therapy session.

An unfavourable outcome (as described by the CRYO ROP CG) was defined as a retinal fold involving macula, posterior retinal detachment or retrolental tissue obscuring the view of the posterior pole (7, 8).

All photographs were taken with a hand-held Kowa RC-2 fundus camera by the authors.

RESULTS

In total, 518 eyes were treated during the study period. Threshold ROP was treated in 187 eyes of 94 preterm infants (46 girls and 48 boys) with tunica vasculosa lentis. In all cases TVL was detected in both eyes, but the grade of TVL (see Fig. 1–4) was not always equal bilaterally (Table 1).

Table 1. The grade of TVL at threshold ROP

Grade of TVL	Children, n	Right eye, n	Left eye, n	Total eyes, n
4	4	4	3	7
3	25	24	25	49
2	51	51	44	95
1	14	15	21	36

The data on postconceptional age (PA) at which the highest grade of TVL was present on the first treatment session are shown in Table 2.

Table 2. Postconceptional age at different grades of TVL

	PA, weeks			
	grade 4 TVL	grade 3 TVL	grade 2 TVL	grade 1 TVL
Mean	35.4	34.3	35.0	35.0
Median	35.5	34.0	35.0	35.0
Mode	36.0	34.0	36.0	35.0
Standard Deviation	0.8	2.4	1.5	1.4
Minimum	34.5	31.0	32.0	33.0
Maximum	36.0	41.0	38.0	37.0
Confidence level (95.0%)	1.2	1.0	0.4	0.6

As mentioned above, in one infant only one eye was treated.

In the TVL(–) group, threshold ROP was treated in 331 eyes of 167 prematures (83 girls and 84 boys).

Birth weight (BW) of TVL(+) infants ranged from 630 to 1685 g, (mean $\pm$ SD = 1025.6 $\pm$ 240.8 g), BW of TVL(–) infants ranged from 450 to 2240 g, (mean $\pm$ SD = 1211.1 $\pm$ 346.0 g), the difference of mean BW was statistically significant ($p < 0.0001$ using Student's *t* test).

The gestational age (GA) of TVL(+) infants varied from 24 to 32 weeks (mean $\pm$ SD = 27.2 $\pm$ 1.9 weeks). GA of TVL(–) infants ranged from 23 to 35 weeks (mean $\pm$ SD = 28.3 $\pm$ 2.3 weeks). The difference of mean GA was also statistically significant ($p < 0.0001$).

Postconceptional age (PA = gestational age + chronological age) at the first treatment session in TVL(+) group was 31 to 41 weeks (mean $\pm$ SD = 34.9 $\pm$ 1.7 weeks). PA of TVL(–) infants ranged from 32 to 43 weeks

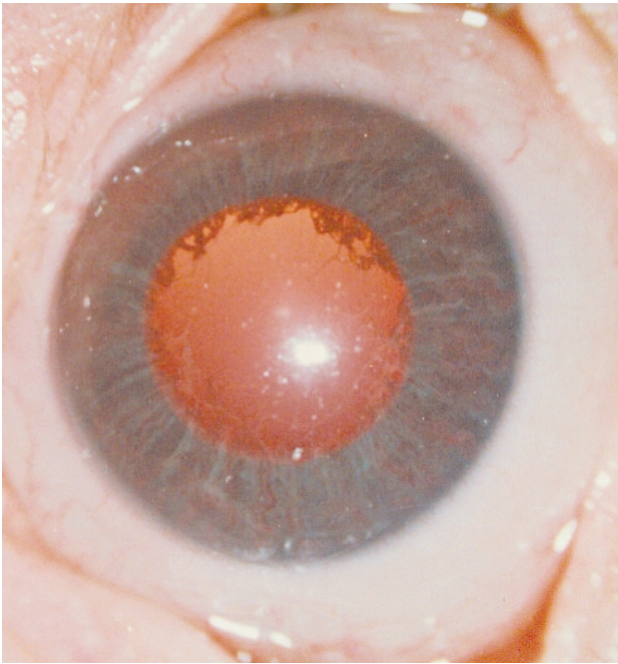


Fig. 1. Stage 1 of tunica vasculosa lentis.



Fig. 2. Stage 2 of tunica vasculosa lentis.

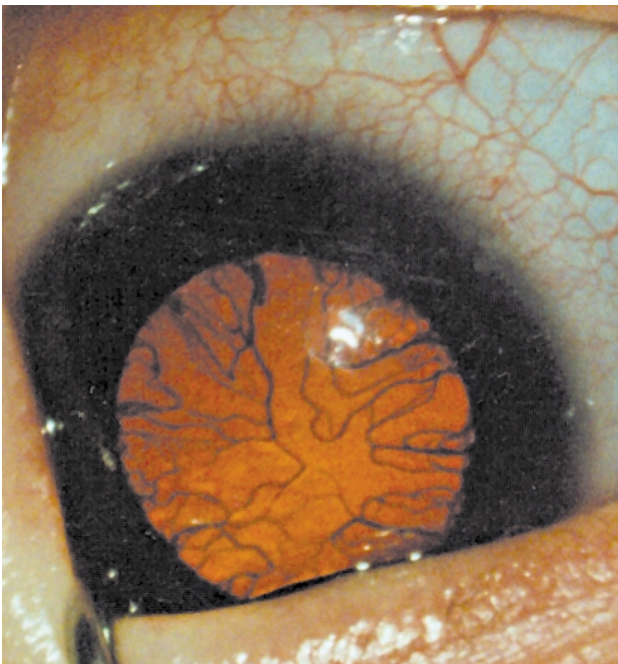


Fig. 3. Stage 3 of tunica vasculosa lentis.

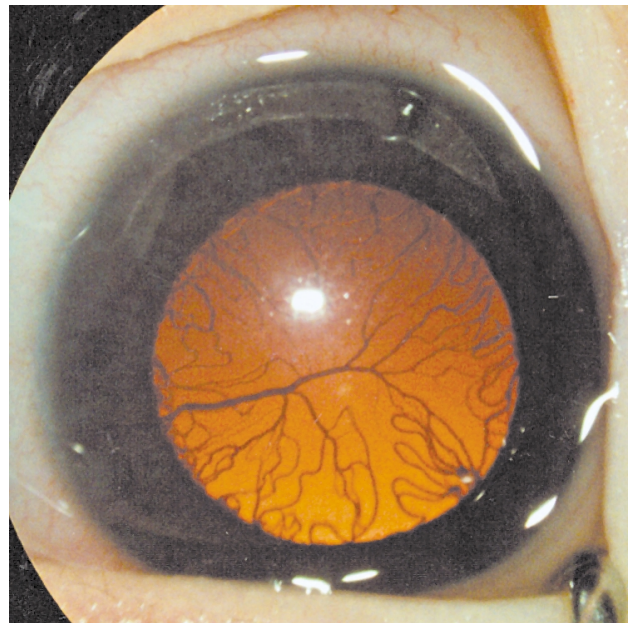


Fig. 4. Stage 4 of tunica vasculosa lentis.

(mean $\pm$ SD = 37, 0 ± 2.2 weeks). The difference of mean PA at the first treatment session was also statistically significant ($p < 0.0001$).

Zone I ROP was present in 101 / 187 (54%) eyes of the TVL(+) and 61 / 331 (18,4%) eyes in TVL(-) group. Zone II ROP was diagnosed in 86 / 187 (46%) eyes of TVL(+) and in 270 / 331 (81,6%) eyes of TVL(-) groups (Fig. 5).

Retinal haemorrhages were present in 48 eyes before treatment. None of the eyes showed preoperative vitreous haemorrhage.

Cryo or laser / cryotherapy was applied on 518 eyes with threshold ROP. Treatment was applied once in 449 eyes. 160 / 187 eyes of TVL(+) group and 289 / 331

eyes of TVL(-) group underwent one treatment session. Treatment was carried out twice in 27 eyes with TVL and in 38 eyes without TVL. Four eyes, all in TVL(-) group, were treated three times.

Tunica vasculosa lentis disappeared in 151 eyes after the first session of therapy. Treatment was successful in all these eyes (no one eye progressed to stages IV or V ROP). In 36 eyes tunica vasculosa lentis was still present during the first examination after therapy (6–8 days after treatment). The proliferation was still present in all those eyes. In 9 eyes ROP progressed to stages IV–V. Cryotherapy and / or lasertherapy procedure was repeated within 8–14 days in 27 eyes. Complete extinction of tunica vasculosa lentis was found in 17 eyes after the second session of treatment. No proliferation in

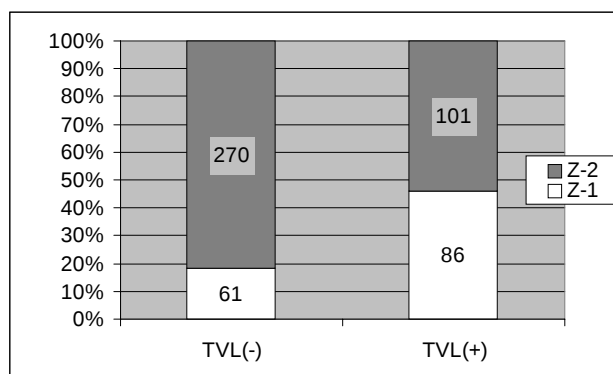


Fig. 5. Proportion of Z-1 and Z-2 eyes in TVL(-) and TVL(+) groups

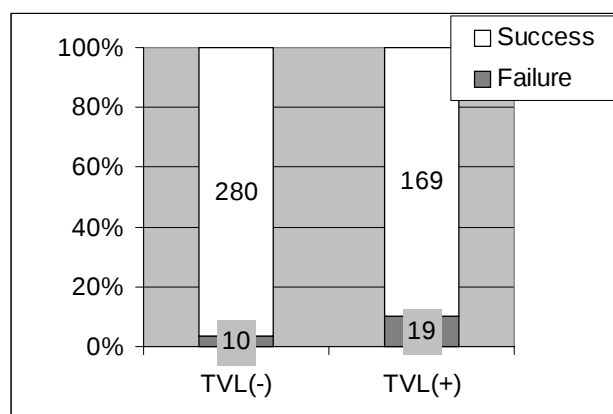


Fig. 6. Percentage of failure and success in TVL(-) and TVL(+) groups

the fundus was observed after the second treatment procedure in those 17 eyes. In spite of two treatment sessions, 10 eyes with TVL progressed to end stages. All the 19 failed eyes from TVL(+) subgroup had remnants of the anterior vascular capsule of the lens after the final treatment.

No complications in connection with tunica vasculosa lentis were observed in the anterior segment of the eye during and after therapy.

In the TVL(-) subgroup we had three eyes with unfavourable outcome after the first treatment session, six eyes progressed to stages IV–V after the second treatment session, and two eyes did not respond even to the third treatment session.

The total number of failures were 30 eyes: 19 / 187 eyes (10 children) in TVL(+) group and 11 / 331 eyes (8 children) in TVL(-) group. The percentage of failure and success is presented in Fig. 6. All failed eyes belonged to Zone I disease.

The mean BW of TVL(+) failed children was 1151.7 g (SD = 328.3 g), the mean BW of TVL(-) failed children being 1293.1 grams (SD = 312.4 g); the difference was not statistically significant ($p = 0.2$).

The mean GA of TVL(+) failed children was 27.3 weeks (SD = 0.9 weeks), the mean GA of TVL(-) failed children being 28.8 weeks (SD = 2.4 weeks); the difference was not statistically significant ($p = 0.07$).

DISCUSSION

Tunica vasculosa lentis occurred rather frequently (36.1%) in the eyes of premature infants who reached threshold ROP (in 187 out of 518 eyes).

The gestational age of our infants did not correspond to the grading system presented by Hittner (1). The error could be due to different time points of observation. None of our infants was examined on the first day of life. Furthermore, the author noticed that “this method of gestational age determination may be invalid in the presence of systemic infection or ocular abnormalities.”

At the 60 mm stage of embryogenesis, corresponding to the 12th week of gestation, tunica vasculosa lentis begins to atrophy. However, it is possible to observe it quite often in very preterm infants. No data concerning dissolution of tunica vasculosa lentis in connection with the outcome of threshold ROP after therapy were found in the literature. For example, Seiberth et al. (9) presented data on laser photocoagulation in 14 eyes with tunica vasculosa lentis. Acute retinopathy of prematurity regressed in all eyes after a single laser session. Elflein et Lorenz in 2005 described twin sisters with TVL and severe ROP, making conclusion that “persistent and dilated TVL is a marker for acute severe ROP that may require treatment” (10). At the very beginning of our work, it was astonishing to discover that tunica vasculosa lentis used to disappear within 6–8 days after therapy, having been unchanged during quite a long time (5–10 weeks) from the infant’s birth till the development of threshold ROP (see Table 2).

BW and GA analysis in both TVL(+) and TVL(-) groups showed that infants with tunica vasculosa lentis were of lower BW and less GA at birth. The difference was statistically significant ($p < 0.0001$), so we could not blame TVL for the poorer outcome in this group. It is possible to assume that smaller infants were more vulnerable. We performed an in-depth study of failed infants. Among the ten infants with failed eyes in the TVL subgroup and eight infants without TVL, neither BW nor GA showed statistical differences. It means that the eyes with tunica vasculosa lentis are at about a threefold greater risk of developing unfavourable structural outcome after treatment. Furthermore, the poorest outcome was observed in those particular cases where tunica vasculosa lentis persisted after therapy.

The results of our study confirm that the risk of developing poor outcome in threshold ROP is inversely proportional to the delayed dissolution of tunica vasculosa lentis after therapy. Thus, the clinicians should anticipate a greater likelihood of serious prognosis when tunica vasculosa lentis is seen on early screening examinations and especially when tunica vasculosa lentis is present after cryo or laser therapy.

We would like to emphasise the importance of delayed dissolution of tunica vasculosa lentis after cryotherapy for threshold ROP as a predictive sign for the

unfavourable outcome of the disease. Attention should be given to infants with tunica vasculosa lentis during screening for ROP.

It is our personal feeling, based on solid experience, that cryotherapy is more effective against tunica vasculosa than laser. We did not observe such a devastating complication as cataract formation in TVL eyes during the whole time of dealing with ROP. On the other hand, there are reports of cataract in infants who were treated with laser for ROP (11). As was emphasized by McNamara, "in children who have earlier stages of disease and are more likely to have a persistent tunica vasculosa lentis, the risk of absorption of the laser energy by haemoglobin in the TVL cases may lead to not only small focal cataracts which may not be important, but also more advanced cataract which could require surgical intervention" (12).

In our opinion, in the presence of severe TVL laser procedures should always be supported by the session of cryoapplications in peripheral avascular retina.

CONCLUSION

Eyes with tunica vasculosa lentis have a greater likelihood of unfavourable structural outcome after therapy for threshold ROP.

Cryotherapy can be used safely in eyes with tunica vasculosa lentis.

Dissolution of tunica vasculosa lentis after threshold ROP treatment was directly proportional to favourable fundus outcome.

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