REPORT

Screening ROP in the University Hospital Ostrava

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SUMMARY

Objective: to analyze the group of premature infants who were examined by an ophthalmologist in screening for ROP (retinopathy of prematurity) at the University Hospital in Ostrava.
Methods: A retrospective observational case series. We reviewed and analyzed clinical records of all the premature infants born before the 32nd gestational week examined by ophthalmologist in ROP screening at the University Hospital in Ostrava in the period from 1. 9. 2011 to 31. 8. 2012. Children's gestational age at birth, birth weight, postconceptional age (PCA) of the child at the time of the first ocular inspection, at the time of diagnosis ROP and at the time of any intervention, possible risk factors of ROP (Apgar score in the 1st minute, duration of oxygen therapy, FiO2 (%) (percentage fraction of oxygen in the inspired gas mixture), duration of mechanical ventilation, transfusion of erythrocytes (resuspended leukodepleted), presence of sepsis / infection in the perinatal period and duration of phototherapy) were evaluated. Eye examination was performed in local anesthesia with the use of an eyelid retractor, in artificial mydriasis, using an indirect ophthalmoscope and digital imaging system RetCam 3.
Results: 138 premature infants with an average gestational age at birth of 29.8 weeks, average birth weight 1385 g, were included in this study. Thirty-four children (24.6 %) were diagnosed with ROP, in all cases 1st stage at the time of diagnosis. An ophthalmologist indicated and subsequently implemented intervention (cryotherapy / laser treatment) in the case of five children (14.7 %) with ROP under general anesthesia. Average duration of oxygen therapy at infants with ROP was 371 hours, in the group without ROP 84 hours. The difference between the average values was statistically significant [t (37) = -3.69, P <= 0.0007]. Average time of mechanical ventilation in the case of children with ROP were 229 hours, in the group without ROP 41 hours [t (35) = -2.99, P <0.005]. In the case of children with ROP, we noticed on average 3 transfusions of erythrocytes, in the group without ROP 1 transfusion [t (40) = -3.94, P <= 0.0003]. The average value of the Apgar score in the 1st minute of children with ROP group was 6.3 and children without ROP 7.8. The difference between the average values of Apgar score in the 1st minute was between both groups statistically significant [t (136) = 4.06, P <= 0.00008]. Sepsis / infection in the perinatal period occurred in 30 (88.2 %) children with ROP, in comparison with 46 (44.2 %) children with sepsis / infection without ROP. Average duration of phototherapy in infants with ROP was 42.4 hours, in the group without ROP 53.6 hours [t(136) = 1,21, P<= 0,2]. Conclusion: This study demonstrated statistically significant correlation of Apgar score in the 1st minute, duration of oxygen therapy, duration of mechanical ventilation, transfusion of erythrocytes and presence of sepsis / infection on the onset and progression of ROP at premature infants in our group. No effect of FiO2 (%) and duration of phototherapy on the onset and progression of ROP was demonstrated.

Key words: ROP, retinopathy of prematurity, ROP screening, RetCam 3, risk factors of ROP

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INTRODUCTION

Retinopathy of prematurity (ROP) was first described in 1942 by Terry as greyish white non-translucent retrolental membranes (retrolental fibroplasias). He assumed that the cause was proliferation of the embryonic hyaloid system [17]. The term retinopathy of prematurity was first used in 1953 by Heath, who described three histopathological stages of this disorder in his work – primary disease of the retina, secondary affliction of the retina caused by changes in the vitreous body and atrophy of the eye as a consequence of reparation processes [6].
According to the current view, retinopathy of prematurity is a vasoproliferative disorder afflicting especially prematurely born infants with low birth weight. The etiology of ROP is complex and multi-factorial. The main risk factors are the degree of prematurity and low birth weight, which predict the incidence, course and prognosis of ROP [12]. However, a range of other factors may also participate in the incidence of ROP, and their significance is supported by several studies [9, 11, 14, 15].
RetCam 3 is a digital imaging system enabling a modern alternative to scree-

ning of afflicted retinas in infants. The main advantage of this system is the possibility of a 130-degree view of the retina in comparison with the 30-degree view which can be attained by the classic method of indirect ophthalmoscopy. Studies have demonstrated the higher sensitivity of this method of examination in comparison with the sensitivity of conventional indirect ophthalmoscopy [19].
The aim of our work was to identify possible risk factors of ROP in prematurely born infants in the Moravian-Silesian region.

METHOD

We conducted a retrospective analysis of medical documentation in all infants born before the 32nd week of gestation, examined by an ophthalmologist within the framework of ROP screening in the University Hospital Ostrava within the period from 1 September 2011 to 31 August 2012. The population did not include infants with/without ROP who had not reached the 40th week of post-conception age (PCA) within the monitoring period. The observed parameters covered the gestation age of infants at the time of birth, post-conception age of the infant at the time of the first eye examination, at the time of determining of the ROP diagnosis and at the time of any applicable intervention, also birth weight, possible risk factors of ROP (Apgar score in 1st minute, duration of oxygen therapy, FiO2 (%) (percentage fraction of oxygen in inhaled gas mixture), time of APV (artificial pulmonary ventilation), transfusion of ERL (erythrocytes resuspended leukodepleted), presence of sepsis / infection in the perinatal period, length of phototherapy). An eye examination was conducted on all the infants under local instillation anaesthesia (oxybuprocaine hydrochloride 0.4% gtt.) using an eyelid speculum (Katena K1-5401 / K1-5677) in artificial mydriasis (phenylephrine hydrochloride 2.5% gtt. + tropicamidum 0.5% gtt.) The fundus was examined by an indirect opththalmoscope using a 28D lens and digital imaging system RetCam 3 [fig. 1a – 1e]. A Student t-test was used for determination of the statistical significance of the compared results between the groups of infants with / without ROP (statistical program of Microsoft Office Professional Edition, 2003). The indicator of statistical significance was the value $P < 0.05$.

RESULTS

The population was composed of 138 infants (77 boys, 61 girls), with an average gestation age at the time of birth of 29.8 weeks (median 30 weeks, SD ± 2.16, interval 24-32 weeks, with an average birth weight of 1385 g (median 1400 g, SD ± 404.78, interval 460-2200 g). The average age of the infants at the time of the first eye examination was 33 PCA (median 33 PCA, SD ± 0.96, interval 29th-35th PCA). In 34 infants (24.6%) ROP was diagnosed by an ophthalmologist, in all cases the 1st stage at the time of designation of the diagnosis. The average age of these infants at the time of designation of the diagnosis was the 37th PCA (median 36th PCA, SD ± 3.86, interval 32nd--47th PCA), average birth weight 1040 g (median 990 g, SD ± 250.86, interval 460-1490 g). The individual stages of ROP in the prematurely born infants in the population during the observation period are shown in summary by the photographic documentation obtained in the University Hospital Ostrava by the digital imaging system RetCam 3 [fig. 2a – 2f]. In 5 infants (14.7%) with ROP the ophthalmologist indicated and

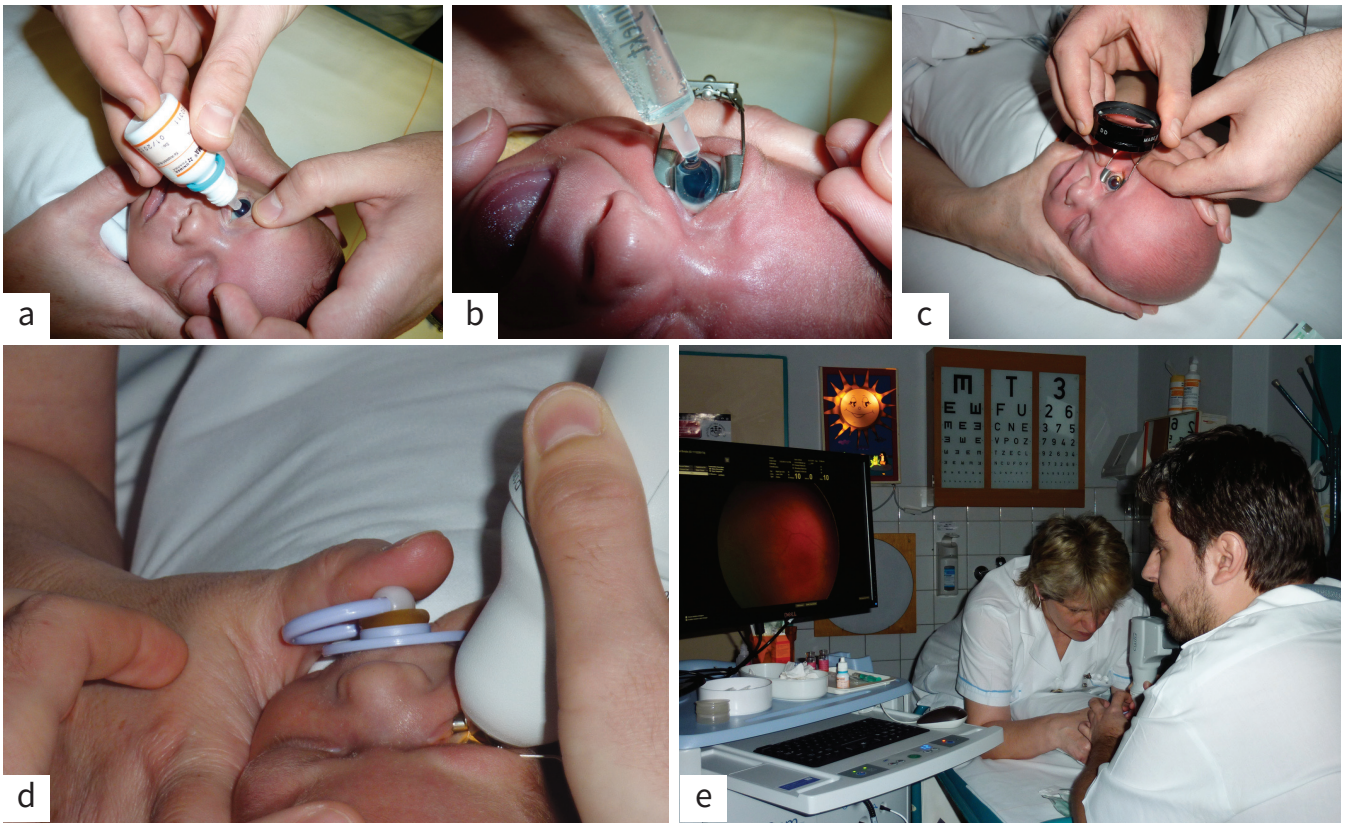


Fig. 1 Eye examination was conducted on all infants under local anaesthesia (fig. 1a), using an eyelid speculum (fig. 1b), in artificial mydriasis. Examination of fundus by indirect ophthalmoscope with use of a 28D lens and digital imaging system RetCam 3 (fig. 1c, d, e,)

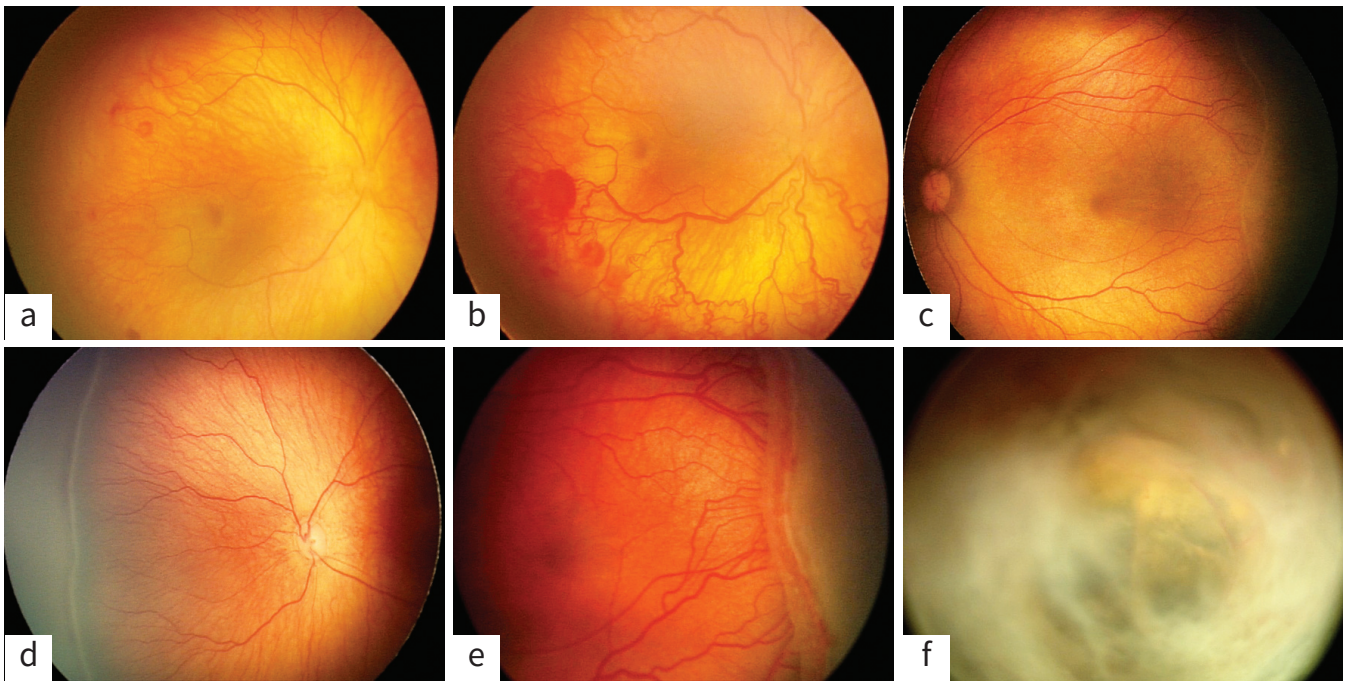


Fig. 2 Progression stages of ROP (retinopathy of prematurity) – photo documentation obtained in the University Hospital Ostrava by digital imaging system RetCam 3. Image of immature vascularisation of retina – progressive constriction of retinal capillaries in the direction towards the periphery (fig. 2a), "plus disease" form of ROP – dilated and coiled capillaries (fig. 2b), ROP stage 1 – a demarcation line separating vascularised and avascular part of retina (fig. 2c), ROP stage 2 – elevation of a demarcation line and formation of the so-called wall (fig. 2d), ROP stage 3 – a ridge-like demarcation line with neovascularisations and incipient extraretinal fibroproliferation (fig. 2e), ROP stage 4 – partial retinal detachment, ROP stage 5 – terminal stage – total retinal detachment (fig. 2f).

subsequently performed intervention (cryotherapy/laser treatment of the retina) under general anaesthesia. The average age of the infants at the time of the intervention was 36th PCA (median 36th PCA, SD ± 2.28, interval 34th-40th PCA), birth weight 946 g (median 960 g, SD ± 205.26, interval 690-1250 g). The intervention was conducted under direct monitoring by RetCam 3. The course of cryotherapy and laser photocoagulation of the avascular part of the retina by transscleral diode laser under monitoring by RetCam is displayed in summary in the images [fig. 3a – 3f]. The average time of oxygen therapy in infants with ROP was 371 hours (median 156 hours, SD ± 441.3, interval 0-1560 hours), in the group without ROP 84 hours (median 5 hours, SD ± 185, interval 0-1000 hours). The difference between the average values was statistically significant [t(37) = -3.69, P < 0.0007] [graph 1]. The average value of FiO2 (%) was 42.5% in infants with ROP (median 37.5%, SD ± 20.8, interval 0-100%) compared to 34.9 % in infants without ROP (median 29 %, SD ± 22.2, interval 0-100 %). The difference between both groups was statistically insignificant [t(136) = -1.78, P < 0.08] [graph 2]. The average time of APV in infants with ROP was 229 hours (median 44 hours, SD ± 360.3, interval 0 – 1530 hours), in the group without ROP 41 hours (median 0, SD ± 102, interval 0 – 700 hours) [t(35) = -2.99, P < 0.005] [graph 3]. In the infants with ROP we recorded an average of 3 ERL transfusions (median 3 transfusions, SD ± 2.8, interval 0-10), in the group without ROP 1 transfusion (median 1, SD ± 1.5, interval 0-9) [t(40) = -3.94, P < 0.0003] [graph 4]. The average value of the Apgar score in the 1st minute in infants in the group with ROP was 6.3 (median 6, SD ± 2.3, interval 2-10), in infants without ROP 7.8 (median 8.5, SD ± 1.8, interval 1-10). The difference between the average values of the Apgar score in the 1st minute was statistically significant between the two groups [t(136) = 4.06, P < 0.00008] [graph 5]. 30 infants (88.2%) with ROP suffered sepsis / infection in the perinatal period, compared with 46 infants (44.2%) suffering sepsis / infection without ROP [graph 6]. The last observed possible risk factor of ROP in prematurely born infants in the population was the average duration of phototherapy. In infants with ROP this was 42.4 hours (median 44.5 hours, SD ± 38.9, interval 0-148), in infants without ROP 53.6 hours (median 49 hours, SD ± 49.6, interval 0-210). The difference between both groups was statistically insignificant in the case of this factor [t(136) = 1.21, P < 0.2] [graph 7].

DISCUSSION

In comparison with foreign studies [13, 18], which state a 68% incidence of ROP in infants with birth weight below 1250 g, the incidence of retinopathy of prematurity in our perinatological centre, nominally in the Moravian-Silesian region, was considerably lower (24.6%, birth weight of infants under 1490 g). The comparison is not completely precise due to the difference in the use of input criteria of the particular studies, but it is sufficient for orientation. We expect that the lower incidence is linked to the marked improvement in ophthalmological-neonatal care of prematurely born infants which has indisputably occurred in the last decade, not only in Europe but worldwide. This is also confirmed by studies from South America (Brazil), in which the incidence of ROP is described in retrospective and prospective studies in 20-23 % infants with low birth weight [8, 16]. Compared to the work of colleagues from Plzeň [9], who observed the above risk factors over a period of 12 years, the incidence of ROP in infants with a birth weight below 1490 g in our workplace is higher (24.6% in comparison with 9%). The significant difference in the incidence of both perinatological centres is most

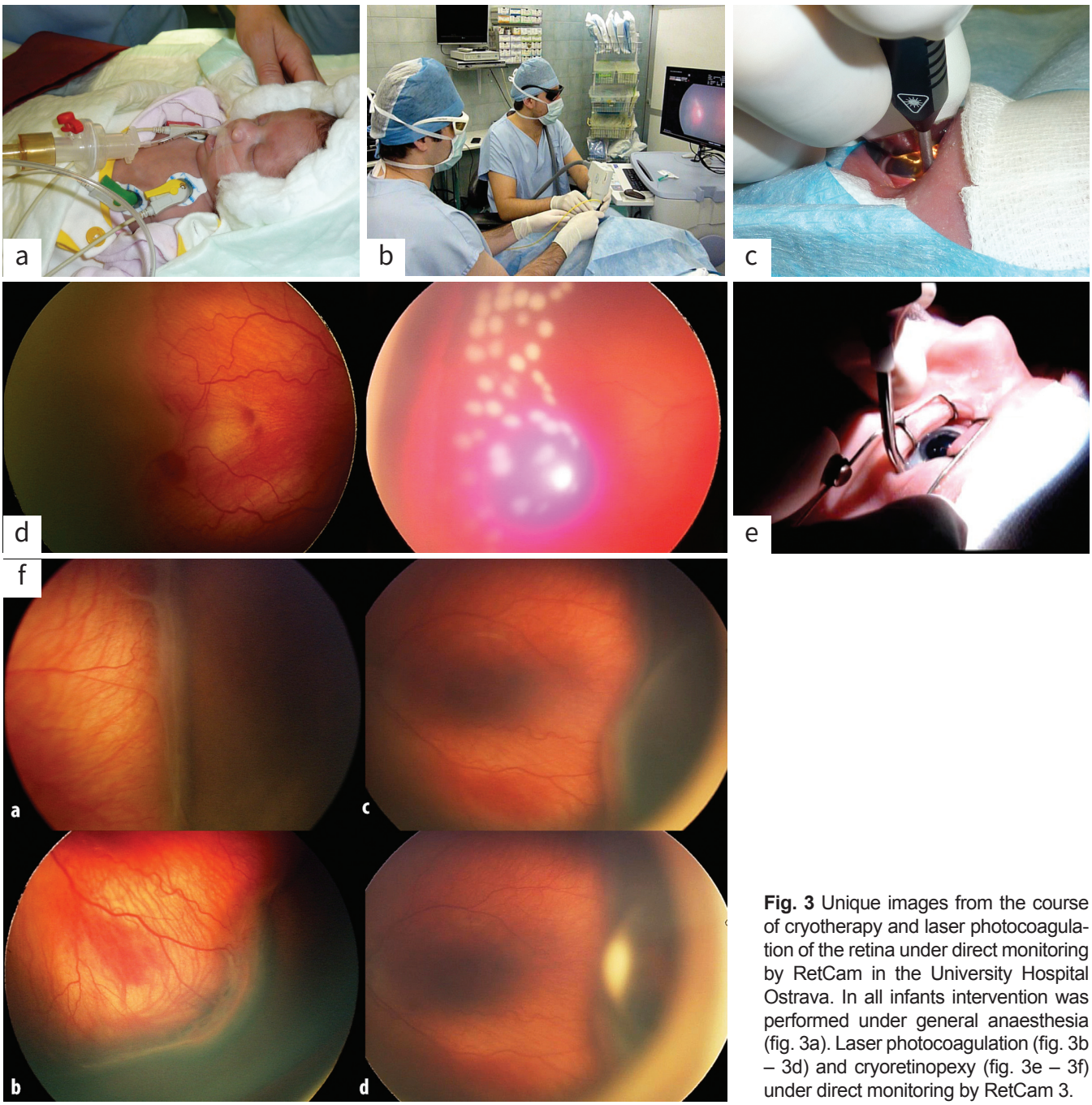
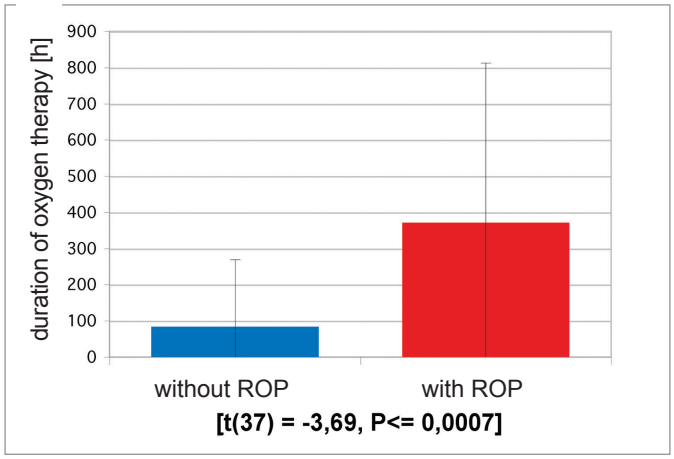


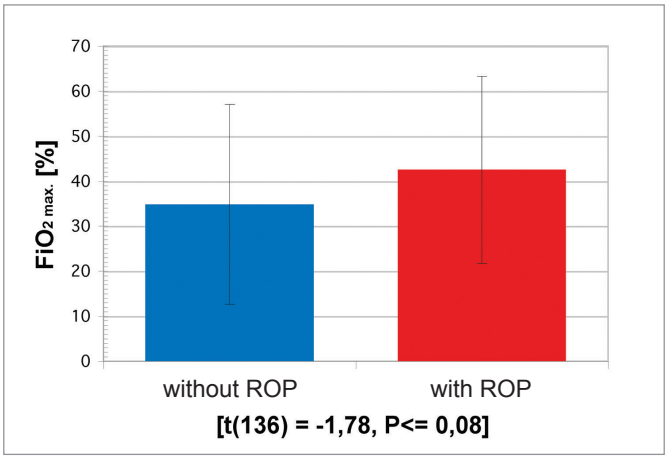
Fig. 3 Unique images from the course of cryotherapy and laser photocoagulation of the retina under direct monitoring by RetCam in the University Hospital Ostrava. In all infants intervention was performed under general anaesthesia (fig. 3a). Laser photocoagulation (fig. 3b – 3d) and cryoretinopexy (fig. 3e – 3f) under direct monitoring by RetCam 3.

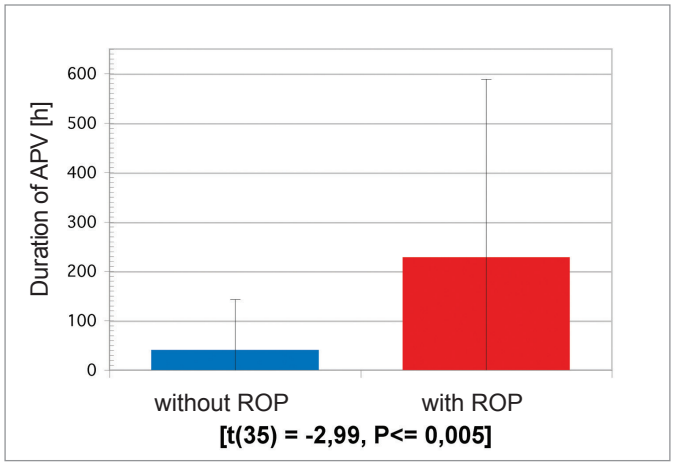
probably due to the length and scope of the study and the number of the observed infants. The higher identification of ROP in the Moravian-Silesian region is probably caused by the higher identification of lower degrees of ROP, which may be contributed to by the introduction of routine examination of prematurely born infants by the digital imaging system RetCam 3, which has become an integral component of the screening process at our workplace.

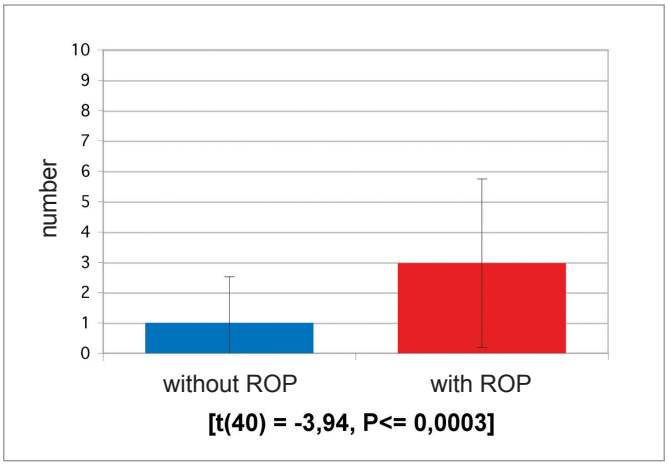
Duration of oxygen therapy and artificial pulmonary ventilation also has an influence on the progression of ROP in prematurely born infants and infants with low birth weight. Mehmet et al. in their study described a significant difference in the length of oxygen therapy in infants with ROP in comparison with infants without affliction of the retina (average 7 ± 13.6 days [10]). Our retrospective trial in the perinatological centre at the University Hospital Ostrava confirms a significant difference in the need for oxygen therapy and duration of artificial pulmonary ventilation of infants with ROP (average 6.5 ± 18.4 days). This fact is confirmed also by other studies [5, 7].

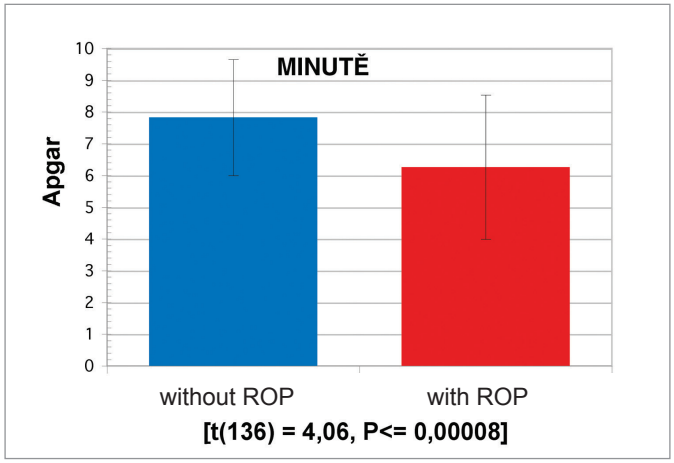
Administration of transfusion is a further risk factor in the incidence of ROP in prematurely born infants. Authors of studies from Italy and Bangladesh have also reached a similar conclusion [1, 3]. On the other hand, a prospective study from the USA conducted in 1999 did not demonstrate a significant influence of transfusion on the incidence of ROP [2]. In our study we recorded a statistically significant difference in the number of administered transfusions in infants with ROP (in infants with ROP the number of administered transfusions was 3, in comparison with 1 transfusion on a child without affliction of the retina). For an unequivocal conclusion as to whether or not the influence of transfusion is a risk factor for the incidence and progression of ROP it would be necessary to conduct a more extensive study with

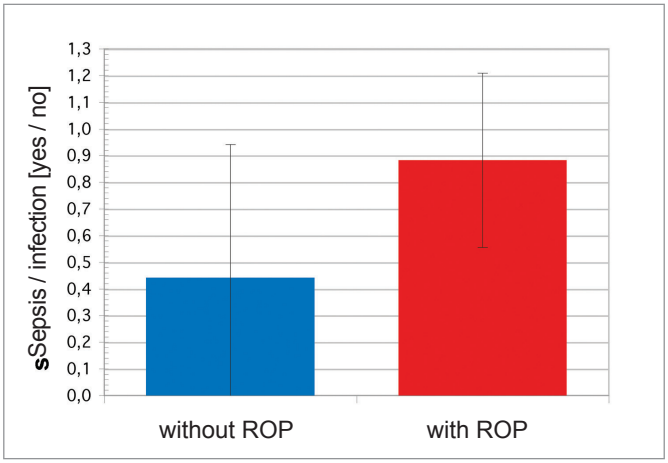


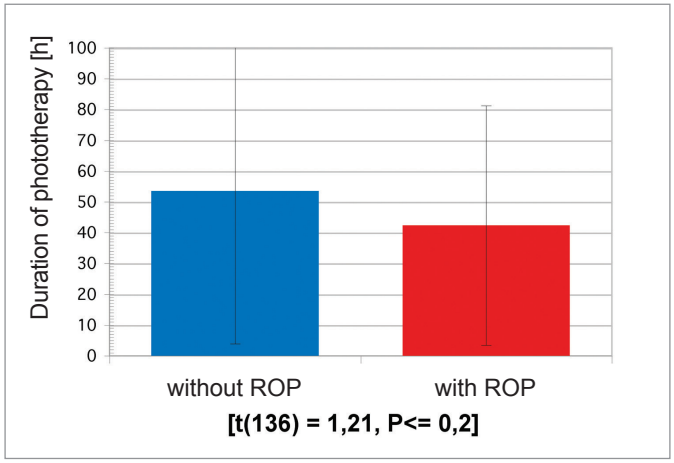












Graphs 1-7 Comparison of average length of oxygen therapy, maximum percentage fraction of oxygen in inhaled gas mixture FiO2 max (%), average length of APV, number of ERL transfusions, Apgar score in 1st minute, presence of sepsis/infection in perinatal period and average length of phototherapy in prematurely born infants examined by ophthalmologists within the framework of ROP screening at the University Hospital Ostrava in the period from 1 September 2011 to 31 August 2012.

precisely defined and comparable criteria and larger populations of patients.
Some foreign studies [4] demonstrate an influence of phototherapy on the progression of ROP. In our study no influence of phototherapy on the progression of ROP was demonstrated, the difference between the length of phototherapy in infants with ROP and infants without affliction of the retina was not significant in our population. The result is most probably linked to the measures which we adhere to during phototherapy of newborns. This primarily concerns thorough covering of the eyes with canvas patches as prevention against damage to the retina by blue light. The lack of demonstration of an influence of phototherapy on the progression of ROP is positive feedback for us, indicating that the above-indicated measures are justified.
From the development and improvement of intensive care of premature newborns it ensues that there is a need for increased ophthalmo-neonatological care and constant improvement thereof according to current trends, which include the digital imaging system RetCam 3. The system enables us to obtain photo documentation or a video recording from the examination, comparison of images in time and observation of the dynamics of progression of the disorder or effect of applicable treatment, the possibility of connection to the computer network, sharing and consultation of the obtained photo documentation with another workplace, in particular for borderline cases, and last but not least provides credible, defensible medical-legal documentation. Since December 2011 we have been using this equipment also for therapeutic interventions (laser photocoagulation/cryotherapy of the retina), and so far we have not encountered similar utilisation of this system in the literature. The obtained data shall be the subject of further analysis.

CONCLUSION

In our retrospective trial, in addition to the low birth weight and short gestation period of prematurely born infants, we identified also the length of oxygen therapy and the duration of artificial pulmonary ventilation as the main risk factors. Further risks are administration of transfusion, postnatal adaptation in the 1st minute of the child after birth and the presence of sepsis/infection in the perinatal period. No influence of phototherapy or the percentage fraction of oxygen in the inhaled mixture of gas on the progression of ROP was demonstrated. Our results do not differ significantly from the previously conducted studies from other regions of the Czech Republic and worldwide, but it would undoubtedly be of benefit to conduct at least a multicenter study. A more profound analysis of the individual risk factors could then improve the precision of the prognostic parameters of the incidence and progression of ROP.
This represents an area of care which has been developing very dynamically, with the typical example being the routine use of the RetCam 3 system, in particular in the precision of diagnostics and data processing. In addition, this system opens up new possibilities also in the therapeutic area – in the sense of performance of intervention under direct monitoring by RetCam.

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ORIGINAL ARTICLE

New Possibilities for Screening of Refractive Errors among Children

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SUMMARY

Purpose: To establish early detection of refractive errors among children in Slovakia. Different screening methods have been evaluated and compared in this work.
Materials and methods: we have been working on a prospective study. Pre-school children in kindergardens in Central Slovakia were checked up between years 2009–2011. Effectiveness of various screening methods was compared within 2 groups, using test-type and Plusoptix Vision Screener. Parent´s of children positive to refractive errors were recommended to consult a paediatrician ophthalmologist.
Results: 3982 children were examined. As a result, 13–14.1% of children who have not been examined by the specialist, were positive. 53.3% of them went to see the doctor afterwards.
Conclusion: establishment of early refractive errors screening is an important method how to prevent strabismus and amblyopia. It is very important to improve parent´s knowledge about the risk of refractive errors and also to improve screening methods with collaboration with kindergarten teachers.

Key words: refractive errors, children, screening

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INTRODUCTION

Refractive anomalies (ametropias) are very frequent disorders of the dioptric system of the eye, in which the sharp image is not projected to the place of sharpest vision (5, 6). The visual functions develop to the age of 6-8 years of childhood age (10). Early screening and correction of refractive error in pre-school age is important as prevention against strabismus and amblyopia (5, 6). In the past, screening of refractive errors in childhood age was also shared by orthopaedic nurses at children's eye clinics or eye nurseries. At present this activity is performed by a first contact paediatrician. The first examination of the child should be performed in accordance with the professional directive of the Ministry of Health of the Slovak Republic in the maternity hospital. The next referential examination should be performed by a paediatrician at the age of 3 years, in which special attention should be devoted to parents with an incidence of strabismus and amblyopia (5), and it is important to send the child for examination at a specialised children's eye clinic sufficiently in time.
In this work we present the results of professional screening of refractive errors and disorders of the position of the eye in children of pre-school age that were not discovered during paediatric preventive checks. We compare various methods of screening and draw attention to the importance of professional screening from the perspective of effectiveness and education possibilities and co-operation with teachers in nursery schools in preventing amblyopia and strabismus.

Fig. 1

MATERIAL AND METHODOLOGY

Population No. 1
In the school year 2009/2009 we resumed screening of visual disorders in children at nursery schools in Banská

Table 1 Identification rate of visual disorders in Population No. 1

	n	%
Examined children	350	100
Identification rate	45	13

Table 2 Specification of visual disorders in Population No. 1

	n	%
Presumed refractive error	34	75.6
Position error	11	24.4
Total	45	100.0

Bystrica. After the informed consent of the parents had been obtained, children aged 4-6 years were examined during their attendance at a nursery school, at the time of the examination they did not wear glasses, thus no visual disorder had been discovered in them either by the local paediatrician or by their parents. In the case of a suspected visual disorder, the parents were given a recommendation for a specialised examination at the nearest children's eye clinic. We examined visual acuity using a portable optotype and the position and activity of the eyes using a motivation rod and a cover test. In the population we also evaluated the number of children who had actually undergone a professional eye examination after a positive screening.

Population No. 2

In the period from January to December of 2011 we conducted screening examinations in nursery schools in Banská Bystrica using noncontact determination of refraction in children from a distance of 1 metre using a Plusoptix Vision Screener instrument. The examination was conducted on children aged 4-6 years, who had not previously attended a specialised eye examination. We supplemented the examination with a cover test. The observed parameters were refraction and position of the eyes. We defined measured values of dioptres without cycloplegia of +1.00 Ds ± 1.00 Dcyl, or <0.00 Ds as a positive result. In such a case the parents were given a recommendation for a specialised examination at the nearest children's eye clinic. We statistically evaluated the results and compared them with the results of screening in the previous school year.

RESULTS

Population No. 1

In the school year 2009/2010, over the course of 10 months we examined 350 with an average age of 4.5 years. The identification rate of suspected visual disorders was 13% (45 children) (table 1). Of the 45 children (100%) with a suspected visual disorder, 34 children (75.6%) had a nonspecific refractive error and 11 children (25.5%) (table 2) had a disorder of position and activity. Of the 45 referred children only 24 (53%) were subsequently treated at a children's eye clinic (table 3).

Table 3 Health awareness of parents and teachers in Population No. 1

	n	%
Referred children	45	100
Children examined at children's eye clinic within 3 months of screening	24	53.3
Total	45	100.0

Population No. 2

In 2011, over the course of 12 months, we examined 3632 children. The average age of the children was also 4.5 years. The criteria for a positive screening were met by 513 children (14.1%) (table 4).

We identified a refractive error in 511 children (99.6%), of which 503 children (98.1%) had a refractive error without a disorder of position of eyes, whilst 8 children (1.6%) had a refractive error with a disorder of position of eyes. We determined hypermetropia in 494 children (96.3%), of whom 178 children had hypermetropia in combination with astigmatism. We determined myopia in 4 cases (0.8%), of whom in 1 child this was in combination with astigmatism. We determined only astigmatism of an equal or greater value than 1 Dcyl without measured spherical dioptre in 13 children (2.5%). In 10 children (1.9%) we determined a disorder of the position of eyes, in which 2 of these children (0.4%) had this disorder of position without a determined refractive error (table 5).

In population No. 1 we used a portable optotype and cover test to examine 350 children over the course of 10 months, on average 35 children per month. In population No. 2 we used a Plusoptix instrument and a cover test to examine 3632 children over the course of 12 months, on average 302.6 children per month. We identified more children with a possible visual disorder which we were able to specify in more detail. As with population No. 1, we referred the children for an examination at the nearest children's eye clinic (table 6).

Table 4 Identification rate of visual disorders in population No. 2

	n	%
Examined children	3632	100
Identification rate	513	14.1
Total	45	100.0

Table 5 Specification of visual disorders in population No. 2

	n	%
Position error	10	1.9
Refractive error	511	99.6
Astigmatism	13	2.5
Hypermetropia	494	96.3
Without astigmatism	316	
With astigmatism	178	
Myopia	4	0.8
Without astigmatism	3	
With astigmatism	1	

DISCUSSION

Ametropias are very frequent disorders of the dioptric system of the eye in children. Their timely identification and treatment is prevention against serious complications such as strabismus and amblyopia. Paediatricians should be the first doctors to examine children, and in addition to an objective finding of deteriorated vision or disorder of the position of the eye, the data from the anamnesis of the parents on the occurrence of strabismus and amblyopia in the family should not be underestimated either (5, 6, 10). In our study we focused on an examination of children who were to undergo a referential visual examination in pre-school age but were not referred for a specialised examination.

In the first year of the study we examined sight using financially available tools such as portable optotypes, coloured pencils or a motivation rod with a picture. In the second year of the ongoing study we verified new possibilities for screening of children using a

Table 6. Effectiveness of examination

	Number of examinations	Duration	Number of examinations per month
Population No. 1	350	10	35
Population No. 2	3632	12	302.6
Total	45	100.0	

Plusoptix Vision Screener instrument. Although the observed parameters in the individual sample groups partly differed, their common aim was to identify visual disorder in children of a pre-school age.

The identification of a refractive error or position disorder of the eyes was similar in the observed populations (13% and 14.1%), which demonstrates the equal value of the used examination methods. 13% and 14.1% identification in a professional eye examination as against negative identification upon examination at a paediatric check demonstrates the need for professional screening.

The effectiveness of the examination methods differed markedly in the examined populations. Although we did not focus on determining of CVA (central visual acuity) of children in population no. 2, the equipment enabled us to increase the effectiveness of the screening and examine an equal number of children within a shorter time, in which according to the published studies this equipment is equally effective at detecting risk factors of amblyopia in children (2, 3, 7, 8). Although the stricter selected positivity criteria for screening increased the sensitivity of the examination at the expense of specificity (possibility of increasing the number of false positive cases), we nevertheless believe that subsequent specialised preventive eye examination will not cumber doctors, parents or the children themselves, and are justified in accordance with the recommendations for the most timely possible correction of ametropia in children (9).

Examination in cycloplegia is the gold standard in the diagnostics of refractive errors. However, ever greater effort is being spent on the development of instruments which would enable reliable examination even without cycloplegia, especially for the requirements of mass screening (2, 6).

As the manufacturer of the Plusoptix Vision Screener instrument states – this instrument is designated for providers of first contact healthcare and eyesight screening programmes. In our opinion it would be of benefit in every general paediatric clinic, where although it will not replace examination of the patient on an optotype, it may indicate a visual disorder far earlier and in the case of worse co-operation of the child. In addition, as Joost et al. state, the correlation of the spherical equivalent upon examination by Plusoptix from a distance of 1 meter without cycloplegia and subsequently in cycloplegia is comparable. In the above-stated study, 296 children within an age range of 0.5 – 6 years were examined, and on the basis of these measurements sensitivity of examination was up to 90% and specificity up to 95% (6). According to a statement from doctors of the American Association for Pediatric Ophthalmology, examination by Plusoptix without cycloplegia does not traumatise the patient and has a 98% negative predictive value (1).

We evaluate our own experience with the Plusoptix instrument very positively. Operation of the instrument is very easy, in its appearance and sound effects it

Fig. 2

captures the attention of the child and enables examination at a distance of 1 metre at an interval of 1.5 – 20 seconds (6, 8). In the group of examined children we did not record a patient on whom an examination could not be performed.

Our opinion is in accordance with similar studies which have been conducted abroad in the past (2, 3, 6, 7, 8, 9).

The ratio of identified refractive errors in population No. 2 by the examination instrument Plusoptix correlates with the literary data. We shall continue to monitor the real number of identified ametropias from the number of patients referred for a specialised eye examination in co-operation with outpatient ophthalmologists. According to current publications, refractive errors are reported most frequently in children aged 4-6 years in the sense of hyperopia (5) (in our group 96.3% of patients), whilst we identified myopia in only 0.8% of the examined children. Astigmatism without linkage to a spherical refractive error appears only rarely in children, occurring more frequently in connection with a spherical refractive disorder (5).

The prevalence of strabismus is stated within the range of 3-8% (11). In our population it is 1.9-3.4%.

In the population No. 1 we determined a colour sense disorder in 2 children (4.4%). The average incidence of dyschromasia is stated at 8 % in men, 0.4 % in women (4).

CONCLUSION

Our results demonstrate a high occurrence of visual disorders in children of pre-school age and the insufficient identification thereof at preventive paediatric check-ups. The Plusoptix Vision Screener instrument markedly increases the effectiveness of screening, which enables examination of a greater number of children and improves the availability of professional examination and consultation. Professional screening of visual disorders in nursery schools using the Plusoptix instrument is at present the optimum method of prevention of amblyopia and strabismus. It enables the dissemination of education and co-operation in care of children with visual disorders also to teachers at nursery schools, who may supervise and help ensure that children with a visual disorder wear visual aids and use them correctly.

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ORIGINAL ARTICLE

The Importance of Angle Kappa for Centration of Multifocal Intraocular Lenses

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SUMMARY

Purpose: To evaluate patient satisfaction with multifocal intraocular lens (MIOL) implants (AcrySof Restor) in relation to the size of angle kappa and precise centration of the MIOL.
Methods: Fifty-two eyes of 26 patients were included in this study. All patients underwent bilateral phacoemulsification and multifocal intraocular lens implantation (AcrySof Restor) from January 2008 to April 2010. Preoperative and postoperative examinations included slit lamp biomicroscopy, near and distance uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA), contrast sensitivity and measurement of angle kappa. Precise centration of the IOL with respect to the centre of the pupil was evaluated postoperatively. Subjective photic phenomena were evaluated separately for each eye and the patients were asked to compare the perception between the right and left eye.
Results: Angle kappa was positive in all cases, ranging from +1° to +7°. The mean angle kappa was 2.78° and 2.10° in the right and left eye, respectively. The IOL was centred exactly to the centre of the pupil in 40 eyes. In twelve eyes there was a slight decentration of the IOL (3 nasal, 4 temporal, 2 superotemporal, 2 superior, 1 inferior). Different subjective perception of photic phenomena between the two eyes was recorded only in five patients. All these patients were among those with a decentred IOL. Temporal and superotemporal decentration of the IOL caused pronounced photic phenomena in five cases – in four cases there was a greater angle kappa of +3° to +4°. In one case of temporal decentration and a small angle kappa (+1°), the patient failed to observe a difference between both eyes. In the cases of inferior, superior and nasal decentration of the IOL, no difference between both eyes was seen.
Conclusion: According to our results, temporal decentration of the IOL is associated with the greatest risk in multifocal IOL implantation, particularly in cases with a higher angle kappa. An evaluation of angle kappa should be a part of preoperative examination before MIOL implantation. Patients with a high angle kappa should be excluded because of a higher risk of postoperative photic phenomena.

Key words: angle kappa, multifocal intraocular lens, photic phenomena

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INTRODUCTION

Implantation of multifocal intraocular lenses (MIOL) in cataract surgery or refractive replacement of the lens is currently a frequent solution for patients who wish to remain independent of correction by eyeglasses following the surgery. There is now a whole range of MIOLs of various designs available on the market. A large amount of space is devoted in the literature and in frequent discussions on professional forums to the issue of selection of a suitable patient for this procedure (10), since intolerance of MIOL and the applicable necessity of its explantation always represents a highly unpleasant complication both for both the patient and the surgeon.
The path to achieving an optimum result and subjective satisfaction of patients following implantation of MIOL is strewn with several obstacles. At present the most important factors which may lead to patient dissatisfaction are considered to be the following: residual ametropia and astigmatism, secondary cataract and pupil larger than 3 mm (6). A large subjective problem and reason for intolerance of MIOL may also be perception of photic phenomena, in particular light circles around point sources of light. The occurrence and intensity of perception of photic phenomena is linked in the literature with decentration of the intraocular lens, with a left fragment of the lens, opacities of the posterior chamber, dry eye, postoperative astigmatism, postoperative spherical equivalent and high refractive index of materials of certain intraocular lenses (13, 14). Only in the last few years greater attention has been devoted also to the possible significance of angle kappa for the implantation and centration of multifocal intraocular lenses (12). In regular practice, examination of angle kappa before implantation of the MIOL is not yet a standard component of preoperative examination.
In our study we focused precisely on the possible relationship between the size of angle kappa, centration of the multifocal intraocular lens AcrySof ReSTOR with regard to the centre of the cornea and subjective perception of photic phenomena.

MATERIAL AND METHODOLOGY

Design of study

The study included patients who had undergone bilateral cataract surgery or refractive replacement of a lens with bilateral implantation of a multifocal intraocular lens AcrySof ReSTOR

Table 1. Data of patients who perceived different photic phenomena in right and left eye in relation to centration of lens and size of angle kappa

Patient	Direction of decentration of lens	Subjective perception of photic phenomena	Size of angle kappa
no. 1 right eye left eye	temporally 0	worse	+4° +3°
no. 2 right eye left eye	0 temporally	worse	+3° +3°
no. 3 right eye left eye	0 temporally	worse	+4° +4°
no. 4 right eye left eye	superotemporally 0	worse	+3° +3°
no. 5 right eye left eye	superotemporally 0	worse	+1° +1°

Table 2. Data of patients with decentred lenses who did not perceive different photic phenomena in right and left eye in relation to centration of lens and size of angle kappa

Patient	Direction of decentration of lens	Subjective perception of photic phenomena	Size of angle kappa
no. 1 right eye left eye	0 nasally	same	+3° +3°
no. 2 right eye left eye	temporally nasally	same	+3° +1°
no. 3 right eye left eye	0 nasally	same	+1° +3°
no. 4 right eye left eye	0 upwards	same	+2° +1°
no. 5 right eye left eye	upwards 0	same	+2° +3°
no. 6 right eye left eye	downwards 0	same	+1° +2°

(SN6AD3, SN6AD1) within the period from January 2008 to April 2010. In all cases a thorough preoperative examination was conducted, which covered examination of the anterior segment on a slit lamp, examination of the fundus, best uncorrected (UCVA) and corrected (BCVA) visual acuity for distance and near vision, and examination of contrast sensitivity. The preoperative examination also included an educational interview in which the patients were familiarised thoroughly with the advantages and possible risks of implantation of multifocal lenses. The exclusion criteria were any pathology in the anterior or posterior segment, astigmatism greater than 1D, unrealistic expectations or frequent driving of a motor vehicle at night. The operation itself was performed on all patients by one doctor, and using an identical surgical procedure. During the surgery, it was inadmissible for any peroperative complications to be noticed (e.g. loose suspension apparatus, rupture of posterior capsule etc.). For the purposes of our study, the postoperative check-up was conducted after 6 to 28 months following the operation. The same parameters were evaluated as before the operation. In addition, we paid attention to centration of the multifocal lens with regard to the centre of the pupil. The examination included photo documentation. The size of angle kappa was measured on a troposcope. Patients completed a subjective satisfaction questionnaire and were asked to describe subjective complaints and perception of photic phenomena. They subsequently evaluated photic phenomena in isolation with each eye separately upon observing a candle flame at a distance of 4 metres in a darkened room. They compared the perception in the right and left eyes.

The aim of our work was to evaluate subjective patient satisfaction and perception of photic phenomena following the implantation of AcrySof Restor – multifocal single-piece intraocular lens. This lens, made of hydrophobic acrylate, uses adiposation, diffraction and refraction, all in a six-millimetre optic section with a yellow filter, in which the adiposed surface has a diameter of 3.6 mm in the centre of the optic section and is formed by concentric ramps, the height of which progressively declines in the direction towards the periphery. We focused especially on the potential relationship between the size of angle kappa, centration of the multifocal intraocular lens with regard to the centre of the pupil and subjective perception of photic phenomena. We evaluated perception of the right and left eye in isolation on each patient. The basic inclusion criterion was therefore a bilaterally implanted multifocal lens AcrySof ReSTOR. From the resulting evaluation, patients in whom perception of photic phenomena could be influenced by factors other than the observed parameters – loosing the normal round shape of the pupil, secondary cataract, any pathology in the anterior segment, vitreous body or retina – were excluded. If a residual refractive error was noticed, the pati-

ent evaluated photic phenomena with each eye separately, both naturally and with best correction with glasses.

RESULTS

Initially 56 eyes of 28 patients were included in the study. Two patients were excluded from the resulting evaluation. The reason for this in one case was diagnosis of incipient asteroid hyalosis in the vitreous body in one eye upon the check-out, and in the other case it was a pronounced secondary cataract in one eye. Therefore 52 eyes of 26 patients were included in the resulting evaluation.

In all cases we measured only positive values of angle kappa within the range of +1° to +7°. The average value of angle kappa was +2.78° in the right and +2.10° in the left eye. We did not find a negative angle kappa in a single case. The intraocular lens was centred precisely at the centre of the pupil in 40 eyes. We recorded slight decentration against the centre of the pupil in 12 eyes of 11 patients (3x nasally, 4x temporally, 2x superotemporally, 2x upwards, 1x downwards). In the entire sample group of patients the preoperative average best uncorrected visual acuity for distance vision was 0.3 and near vision 11.2. The postoperative best uncorrected visual acuity for distance vision was 0.9 and near vision 1.6.

No difference in perception of photic phenomena by the right and left eye before the actual examination was stated by a single patient, either spontaneously or following targeted questioning. During the examination in a darkened room upon observation of a candle flame with the right and left eye separately, however, this difference was noticed by a total of 5 patients. Correction of small residual refractive error (up to 0.5 D of spherical equivalent) in two patients had no impact on the subjective perception of photic phenomena. All patients were from the group with slightly decentred lenses in one eye. In all five cases the patients stated a more impaired perception in the eye with the decentred lens – 3x temporally and 2x superotemporally. In four cases a larger angle kappa was also present (+3° to +4°) (table 1).

Other six patients in whom we recorded decentration of the lens against the centre of the pupil did not notice the difference in perception of photic phenomena by the right or left eye. In one patient the lens was decentred in one eye temporally with a small angle kappa (+1°) and in the second eye nasally with a larger angle kappa (+3°). In two cases the lens in one eye was decentred nasally, in two cases upwards and in one case downwards (table 2).

DISCUSSION

The kappa angle is the angle between the axis of vision and the pupillary pathway (fig. 1). The axis of vision is defined as a line joining the fixation point and the fovea. The pupillary pathway is a line leading through the centre of the pupil perpendicular to the cornea. The angle kappa is indicated as positive if the axis of vision passes nasally from the pupillary pathway, and negative if the axis of vision passes temporally from the pupillary pathway (fig. 2). In the great majority of patients we find a physiologically positive angle kappa up to +4° to +5° (4, 8). With this physiological angle kappa, the corneal reflex is therefore not centred precisely on the centre of the cornea, but is decentred approximately 1 mm nasally from the vertical meridian and approximately 0.5 mm above the horizontal meridian (7) (fig. 3). A pathologically positive angle kappa occurs upon dislocation of the macula temporally, e.g. during retinopathy of prematurity. Nasal dislocation of the macula as a consequence of a scar between the macula and the optic nerve occurs only rarely, and therefore a negative pathological angle kappa is not a frequent finding.

The significance of angle kappa is very well known in strabology and its evaluation is an important part of preoperative examination. A high angle kappa is one of the causes of pseudostrabismus. If a positive angle kappa is greater than +5° (corneal reflex is decentred nasally), an impression of divergent strabismus is generated. Conversely, if a negative angle kappa is greater than -5° (corneal reflex is decentred temporally), this creates an impression of convergent strabismus. In a work dealing with the size of angles kappa in various types of strabismus (3), significantly higher values of angle kappa were demonstrated in patients with exotropia in comparison with the group of patients with esotropia and the control group (3).

The significance of angle kappa is very well known also in the field of refractive surgery. It is very important in centration of the ablation zone, especially in hyperopic laser refractive procedures (11).

The significance of angle kappa in the implantation of intraocular lenses began to come to the forefront together with innovation in surgical procedures and the development of new types of intraocular lenses. Kottler (9) referred a patient with a phakic toric intraocular lens (Verisyse) and a high angle kappa, in whom decentration of the lens according to the axis of vision improved the postoperative result. Prakash (12) in his study confirmed the association of photic phenomena with the size of the angle kappa following implantation of a MIOL (ReZoom). A probable reason for the potential higher incidence of photic phenomena in the case of a high angle kappa following implantation of a MIOL of diffraction type (ReZoom, AcrySof ReSTOR) may be the fact that the ray directed into the fovea does not pass directly through the centre of the MIOL in the case of a high angle kappa, but approaches the edge of the first concentric ring (fig. 4). This issue has not yet been referred to in the Czech literature.

The aim of our work was not to evaluate the intensity of perception of photic phenomenon on a scale, but to compare perception from the right and left eye in connection with the observed parameters. A difference in “vision” between the right and left eye before the actual objective examination was stated by a number of patients, in all cases however this was linked to different UCVA between the right and left eye as a consequence of a residual refractive error. None of our patients were aware of any difference in perception of photic phenomena by the right and left eye in our population before the actual examination. During the examination in a darkened room, upon observation of a candle flame, 5 patients were surprised that they perceived the “rings” around the flame more pronouncedly in one eye. In three cases the patients had excellent UCVA in both eyes for both near and distance vision. In two cases, UCVA for distance vision was slightly reduced in the eye in which the photic phenomena were perceived more markedly. However, the different perception of photic phenomena did not change with correction. Our finding of the aspects of subjective perception correlates with the results of published studies (12, 13), in which it was confirmed that one of the most important factors for patient satisfaction following implantation of MIOL is attaining the best UCVA. This is very

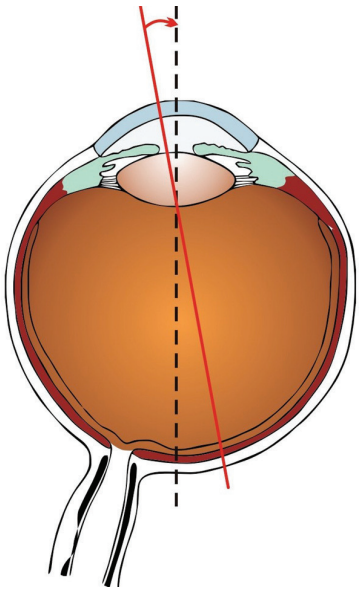

Fig. 1. Angle kappa is the angle formed by the axis of vision (a joining line between fixation point and fovea) and the pupillary pathway (pathway leading through the centre of the pupil perpendicular to the cornea)

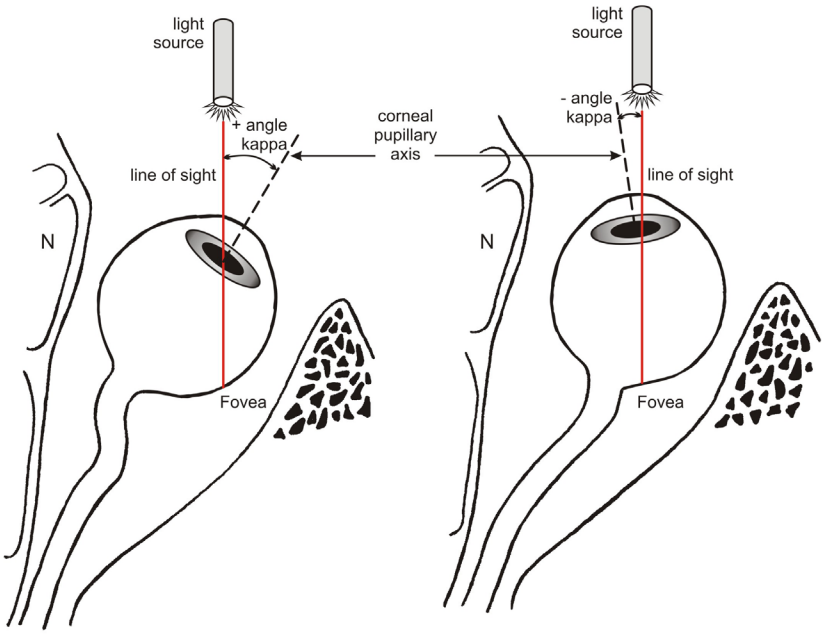

Fig. 2. Schematic picture of positive and negative angle kappa

probably because whilst patients perceive photic phenomena to varying degrees only under certain light conditions, they are aware of reduced UCVA throughout the day. It is therefore possible to assume that patients notice a difference in UCVA between the right and left eye rather than different perception of photic phenomena. An interesting secondary finding, which however was not the aim of our study and has not been quantified in any manner, was the reaction of patients and the description of intensity of photic phenomena after lighting the candle flame upon its observation with both eyes. In certain cases the photic phenomena were entirely trivialised, in other cases the "rings and lights" were described very dramatically.

Other factors which may have an impact on resulting patient satisfaction following implantation of the MIOL according to the literature include a high residual cylinder and induced aberrations of higher degrees (1, 2). The risk of perception of photic phenomena is linked to a higher spherical aberration. A higher coma is associated with a high angle kappa (15). Patients with a higher value of cylindrical correction were not included in the study population. We also did not conduct a wavefront analysis postoperatively.

In the population, more pronounced perception of photic phenomena was linked to decentration of the lens in the temporal direction. With regard to the fact that all the patients simultaneously had a positive angle kappa, this represented decentration against this angle. Decentration of the lens nasally (thus in the direction of a positive angle kappa) did not lead to a deterioration of perception of photic phenomena in a single case. This observation confirmed the theory of the significance of angle kappa upon implantation of MIOL.

Upon implantation of a diffraction type

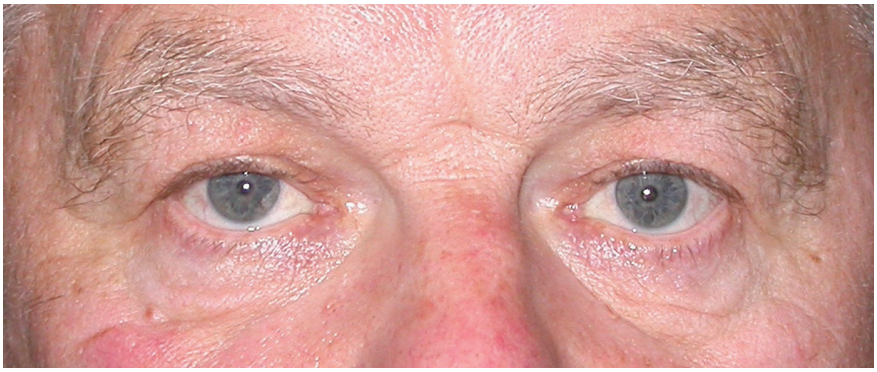

Fig. 3. Patient with positive angle kappa – corneal reflex is not precisely in the centre of the pupil, it is decentred nasally

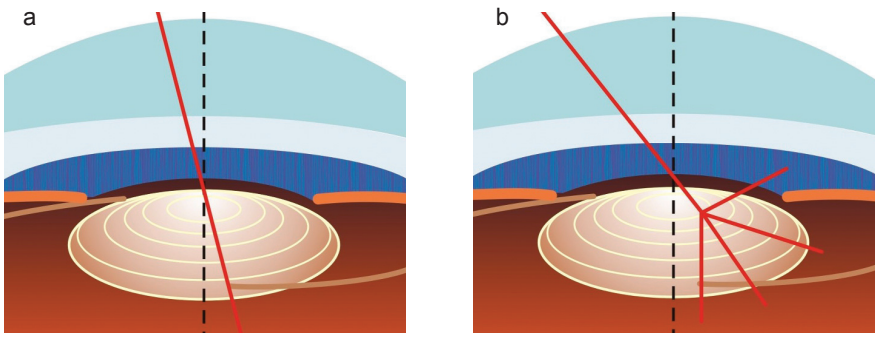

Fig. 4. In the case of a small angle kappa the ray directed to the fovea passes through the central part of the lens (a). In the case of a large angle kappa it passes close to the edge of the concentric ring of the MIOL (b), which may cause more pronounced photic phenomena.

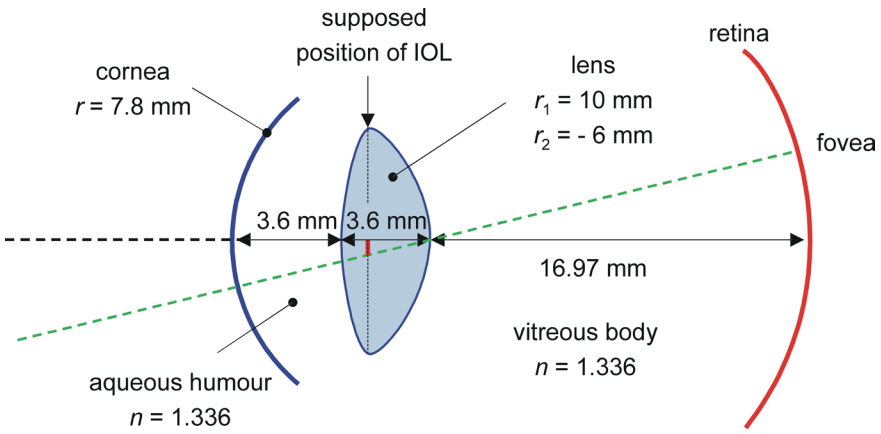

Fig. 5. Gullstrand's simplified schematic model of the eye

MIOL (AcrySof, ReSTOR, ReZoom) it is currently recommended to place the haptics vertically for numbers 6 and 12 and to decentre the lens slightly in the direction of the axis of vision – in the case of a positive angle kappa, which we find in the great majority of cases, thus in a nasal direction. With regard to a whole range of factors which may influence the definitive position of the lens in the final result (irregularity of capsulorhexis, contraction of capsule upon released suspension apparatus, rotation of lens as a consequence of memory of haptics etc.), it is not however possible to guarantee that a lens which is peroperatively decentred nasally according to the axis of vision will remain in this position also in the postoperative period (12). A high angle kappa thus represents a very important risk factor in the implantation of these lenses. However, we have not found an answer in the literature to the question of how a large angle kappa represents a risk for implantation of AcrySof ReSTOR (if we assume centration of the lens to the centre of the pupil). On the basis of detailed knowledge of the parameters of the AcrySof ReSTOR lens and with the use of geometric optics, we performed an optical construction of the passage of rays through the nexus point following implantation of AcrySof ReSTOR on an appropriate theoretical model of the eye (Gullstrand's simplified schematic eye) (fig. 5).

With this model of the eye, a ray directed into the fovea would pass through the edge of the first ring at an angle kappa of up to 9° to 10°. This value is nevertheless variable depending on the change to the individual parameters of the eye (axial length of eye, depth of anterior chamber, corneal curvature, optical power of implanted MIOL). We experimentally altered the individual parameters. The most important factor in our calculations was shown to be the depth of the anterior chamber or effective position of MIOL in the eye. In the case of a shallowing anterior chamber even a fundamentally smaller angle kappa may represent a risk. We are currently working on confirming and verifying this theory.

CONCLUSION

According to our results, the greatest risk upon implantation of multifocal intraocular lenses is represented by their temporal decentration, in particular in the case of a high angle kappa. On the basis of the performed calculations we believe that a further risk factor in connection with a high angle kappa is a shallow anterior chamber. Even a small decentration of the lens in a temporal direction could lead to a more pronounced perception of photic phenomena in these cases. Examination of angle kappa should be an integral part of preoperative examination before the implantation of multifocal lenses. Patients with a high angle kappa should be notified of the greater risk of perception of photic phenomena following implantation of multifocal lenses of the AcrySof ReSTOR type, or another type of implant should be selected.

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ORIGINAL ARTICLE

Myopia or Hypermetropia?

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SUMMARY

Introduction: The study describes cases of patients screened for worse vision and headaches. We are trying to point out we can measure minus diopters even at latent hypemetropes. These patients come to a doctor for a variety of problems that may be caused by inadequate correction of ametropia. It is necessary to know about this possibility, and rather perform cycloplegia in sporadic cases.
Methods: Patients were measured at autorefractometer without mydriasis, and then after using UNITROPIC 1% or CYCLOGYL 1%. Both of these substances induce cycloplegia. Visual acuity with the best correction was tested with and without cycloplegia.
Results: After cycloplegia, a significant change in both objective and subjective refraction was detected in most of the selected patients. This change was within the meaning of a shift to hyperopia. Subsequent adjustment correction led to resolving of problems.
Conclusion: The work should highlight the necessity of an individual approach of prescription of the best correction. Not always an autorefractometer gives correct information, the real-needed correction is completely different in some cases.

Key words: myopia, hyperopia, cycloplegia, spectacle correction

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INTRODUCTION

In our work at the general eye outpatient clinic, we encounter patients who come to us with various conditions. Some of them (poor distance vision, poor near vision, headache) can be caused by inadequate correction of ametropia, in certain cases also with subsequent excessive strain on the accommodating apparatus of the eye. It is necessary to consider this possibility and in sporadic cases rather to conduct an examination in cycloplegia.

Theory

According to the relationship of the focal spot to the retina we differentiate two spherical ametropias: myopia and hypermetropia (hyperopia).
Myopia (short-sightedness) – the focal point of the non-accommodated eye lies in front of the retina. As a rule it is caused by excessive growth of the eye (normal length approximately 24 mm, difference of 1 mm corresponds to approximately 3 dioptres). In these patients we use the weakest correction with which the patient can read the smallest value of the optotype from the prescribed distance. Although overcorrection would cause the patient to see with perfect sharpness, it would be necessary for the patient to engage accommodation upon distance vision, and this increased accommodating exertion would lead to complaints such as headaches or migraines, fatigue etc. (11).
Hypermetropia (long-sightedness) – the focal spot of the non-accommodated eye lies behind the retina. A part of total hypermetropia is compensated for by the individual permanent tone of the ciliary muscle – here we are referring to latent hypermetropia. The remaining part is termed manifest hypermetropia. This may have two components – facultative and absolute hypermetropia. Absolute hypermetropia is no longer corrected in any way by the eye, and is thus manifested in a reduction of vision. Facultative hypermetropia can be corrected by an increased accommodating exertion, which may cause asthenopic complaints. Absolute hypermetropia, i.e. latent plus manifest component, can be determined only after complete elimination of the accommodating apparatus of the eye, in cycloplegia (11).
At present there is a range of substances on the market which we can use for cycloplegia (13). However, there is no clear consensus as to which substance is optimal in order to attain cyclopledia for the purposes of examination of refraction (1, 2, 6, 7, 8, 12, 13, 15). Amongst the most frequently used are tropicamide, cyclophenolate, atropine, homatropine, also used is phenylephrine, or a combination of these substances (1, 2, 4, 7, 12, 13). Cycloplegic refraction is important in order to detect refractive errors, primarily in children (6, 15). However, its significance in adults is underestimated. Inadequate cycloplegia can lead to an overestimation of myopia or an underestimation of hypermetropia (6, 14).

RESULTS

In our practice we relatively frequently encounter patients whose complaints in some way do not correspond with other circumstances such as age, and often the value of the dioptres examined by autorefractometer. Young patients aged around 20-30 years with myopic refraction determined by autorefractometer complain of deteriorated near vision, headaches during work on computer and epiphora. They also state poor distance vision. However, this is not as deteriorated as it may seem according to the results of the autorefractormeter, and myopic correction does not have the expected effect. Some of them are even sent from the neurology department due to cephalea in order to eliminate congestion papilla in intra-cranial hypertension.

Patients were measured on a SPEEDY-K autorefractometer produced by the Nikon company, first without mydriasis, subsequently in mydriasis created with the help of tropicamide (UNITROPIC 1%, UNIMED PHARMA s.r.o., Bratislava, Slovakia) or cyclophenolate (CYCLOGYL 1%, Alcon Laboratories, Puurs, Belgium). Both of these substances induce cycloplegia. Best corrected visual acuity was examined both naturally and in cycloplegia.
We present several examples here. In all there was an objectively physiological ocular finding.

Patient 1 (female), 28 years old

For approximately six months subjectively states worse distance vision. Visual acuity values VRE: 0.2 naturally, s -1.25 = 1.0, VLE: 0.3 naturally, s -0.75 = 1.0, near vision in both eyes J no. 1 naturally and with correction. Result of measurement by autorefractometer naturally RE: -2.25 = -0.25ax.2, LE: -1.5 = -0.25ax.162. Following the examination myopia modica bilaterally was diagnosed, glasses were prescribed RE: -1.0, LE: -0.5. With this correction visual acuity was 1.0.
The patient came for the next check two months later due to the following complaints: she sees worse to distance with the new glasses, and suffers headaches during longer periods of reading. The values of vision were surprising. VRE: 0.2 naturally, correction not improved, VLE: 0.3 naturally, s 0.75 = 1.0. The results of the subsequent examination in mydriasis (tropicamide) were unexpected. The values measured by auto refractometer showed RE: +0.5 = +0.25ax.90, LE: +0.25 = -0.25ax.5. The diagnosis was therefore amended to latent bilateral hypermetropia. The patient obtained new glasses with +0.5 dioptre and was instructed of the necessity of gradual acclimatisation to them, initially mainly during work close up. At a check-up after six months she is satisfied with the correction.

Patient 2 (female), 20 years old

Subjectively eyes are often fatigued, focuses poorly, wears contact lenses received from optician, right -0.5m, left -0.75. The patient would like glasses for driving a motor vehicle. Vision RE: 0.8 naturally, s -0.75 = 0.9, LE: 0.9 naturally, s -0.5ax.155 = 1.0 partially. Result of autorefractometer: naturally RE: -0.75 = -0.25ax.33, LE: +0.0 = -0.5ax.157. With regard to the uncharacteristic complaints ("suspiciously" good natural vision on these myopic dioptres, correction does not improve as we are generally accustomed to for myopics), an examination was conducted in cycloplegia (tropicamide), in which refraction was determined RE: +1.25 = +0.25ax.114, LE: +1.75 = +0.5ax.76, value of vision V: 0.8 naturally, s +0.75 = 1.0. Latent bilateral hypermetropia was diagnosed. Following instruction the patient received prescribed glasses +0.5. After six months she states that she wears them for close up work, she is satisfied and the complaints have subsided.

Patient 3 (male), 26 years old

Subjectively states asthenopic complaints, epiphora and cephalea. Vision V: 1.0 naturally, J. no. 1 naturally, refraction determined by autorefractometer RE: -0.5, LE: -0.5 = -0.25ax.24. Due to the uncharacteristic complaints (asthenopic complaints in a young person and myopia according to autorefractometer) an examination was conducted in cycloplegia (cyclophenolate). Subsequently the values on the autorefractometer showed RE: +0.75, LE: +0.75 = +0.25ax.112, V: 0.8 naturally, s +0.75 = 1.0. Latent bilateral hypermetropia was again diagnosed. We recommended glasses RLE +0.5 dioptre. Six months later the patient states that he does not wear the glasses for distance vision, but feels relief with glasses when working at computer or reading, complaints with epiphora and headaches have subsided, patient is satisfied.

Patient 4 (male), 34 years old

Sent from neurology department due to cephalea in order to eliminate intra-cranial hypertension. Subjectively states headaches in the area of the temples early morning and afternoon. Neurological finding is within the norm. V: 1.0 naturally, J no. 1 naturally, dioptre measured by autorefractometer naturally RE: -1.5, LE: -2.0. We subsequently conducted an examination in cycloplegia (cyclophenolate), in which the result of the autorefractometer was RE: +1.75, LE: +1.75 = +0.25ax.158, V: s + 1.5 = 1.0. Additionally states in anamnesis that he was examined at an eye department at the age of 4 and instructed to wear glasses but refused them. In our examination congestion papilla was excluded and latent bilateral hypermetropia was diagnosed. Glasses +0.75 dioptre were prescribed. Six months later the patient states that the complaints have ceased. The patient is still being monitored and an increase of correction is planned for the future.

DISCUSSION

As is evident from fig. 1 (5), in myopia with refraction = 1.0 dioptre, the value of natural vision is around 0.3. In addition, in such myopic patients we expect a "wow" effect after applying adequate correction. If the patient had a different condition, for example the values of vision are unexpectedly good with regard to the dioptres, it is necessary to consider this and preferably perform cycloplegia.
In his article "Glasses – a simple matter", Boháč recommends that even for patients who have attained a vision of 1.0 it is advisable try whether the patients can tolerate +0.5 Dsf mononuclear, and in the case that they do not state worse vision, it is possible

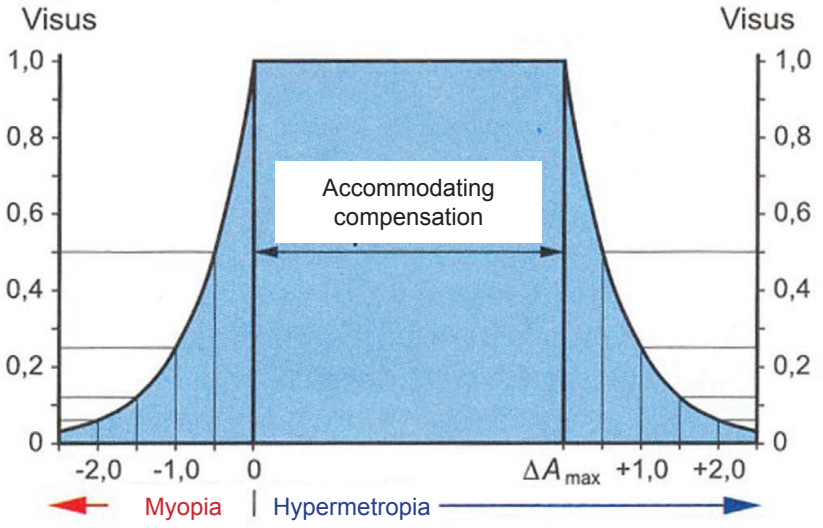

Fig. 1. Author: Diepes, H

to infer the possibility of latent hypermetropia. A second possibility is the performance of the "fogging method" (author professor Sachsenweger). During this we examine each eye separately, placing +2.0D into the glasses frame and allowing the patient to look at an optotype for several minutes. We progressively reduce the values by +0.5D. If we determine that the patient reads better with +1.0 (patients sometimes state that the letters are blacker), this mostly concerns latent hypermetropia (3). In regular practice, however, we are often limited by time. Patients frequently state that their vision is worse even with only weak hyperopic correction upon first view of the optotype. We then obtain the opposite result in cycloplegia. Jones speaks of psychological pseudomyopia. Measurement of objective refraction demonstrates that accommodation is not entirely disengaged even when the stimulus to refraction is zero. He termed this myopic shift psychological pseudomyopia (10). In our opinion this matter also can influence examination on an autorefractometer without the use of cycloplegia, nevertheless this cannot represent the sole fact. If this were the case, hyperopic correction should improve vision even naturally. However, we do not encounter this in these uncharacteristic patients.

In children the difference between manifest refraction and refraction in cycloplegia is generally known. This has been dealt with for example by Rotsos, who in his work compared these parameters in 69 true myopic and 73 emmetropic and hyperopic eyes. He determined that in the case of a negative spherical value of the dioptres, its strength was far higher naturally than in cycloplegia and vice versa (14).

Opinions vary on how many drops to apply and at what intervals in order to attain cycloplegia. Bhatia works with one drop of 1% tropicamide or 2% homatropine with measurement of refraction after 45 minutes (tropicamide) or 60 minutes (homatropine) (2). Bagheri compared the difference between the effect of one, two and three drops of 1% cyclophenolate. He did not demonstrate a statistically significant difference between the groups (1). By contrast, Mohan compared the effect of 1% cyclophenolate applied once, twice and three times in 51 hyperopic patients. According to his work, there is a statistically significant difference between the application of one and three drops, whilst the difference between the application of two and three drops is no longer statistically significant, from which he concludes that the application of 1% cyclophenolate twice within a ten minute interval is sufficient (12). Fotouhi uses two drops of 1% cyclophenolate at a 5 minute interval, with subsequent measurement of refraction 25 minutes after the second drop (7).

Tropicamide was used until recently in our workplace, now we have cyclophenolate available. Tropicamide is a blocker of the acetylcholine receptors, which has a short term cycloplegic and mydriatic effect (2). Cyclophenolate is a synthetic anticholinergic substance, an antagonist of the muscarine receptors (4). We apply tropicamide twice within an interval of ten minutes with subsequent measurement of refraction twenty minutes after the last drop, cyclophenolate twice within an interval of ten minutes with subsequent measurement of refraction thirty minutes after the second drop. We do not have statistically processed results due to the relatively small number of patients, in the majority of cases however the difference between cycloplegic refraction attained using tropicamide and cyclophenolate is slightly in favour of the latter substance.

The difference between the effect of tropicamide and cyclophenolate was compared by Hofmeister et al. in their study on 30 myopic patients before a refractive procedure (average age 35.4 years). There was not a statistically significant difference between cycloplegic reaction after the application of tropicamide and cyclophenolate. In three eyes of five patients the difference in refraction was 0.5D and higher, the smaller myopia was after instillation of cyclophenolate. Upon testing of refraction to near vision a smaller residual accommodation was determined upon use of cyclophenolate. The great majority of patients preferred tropicamide (8).

The effect of 1% tropicamide in 76 eyes and 2% homatropine in 28 eyes is compared by Bhatia in his work, with the results evaluated using an a-scan. The average reduction in the thickness of the lens after application of tropicamide was 0.21 mm (from an original thickness of 3.92. SD 0.34), after application of homatropine the width of the lens was reduced on average by 0.24 mm (from an original 3.87, SD 0.29). Both of these differences are statistically significant. Flattening of the lens occurred as a consequence of cycloplegia (2).

The validity of non-cycloplegic refraction was the subject of the Tehran study (Fotouhi). Measurement was conducted on 3501 persons aged over 5 years, in all of whom refraction was measured without and in cycloplegia (2 drops of 1% cylcophenolate applied at an interval of 5 minutes, measurement of refraction 25 minutes after the second application). Fotouhi found that sensitivity of non-cycloplegic myopia was 99%, whereas specificity is only 80.4%. By contrast, sensitivity in hypermetropia was only 46.9%, but specificity 99.4%. In all age categories, non-cycloplegic refraction overestimated myopia and underestimated hypermetropia. Overestimation of myopia was greatest in the age groups of 21-30 years and 31-40 years. Underestimation of hypermetropia was greatest in the group aged under 50 years, declining by 8% to the age of 70 years (0%). From this Fotouhi concludes that errors may have occurred in the case of measurement of non-cycloplegic refraction, except the group of patients aged 50-60 years (7). Our experience also corresponds to these results, in which virtually all patients examined in cycloplegia due to uncharacteristic complaints belong in the category of 21-40 years.

The necessity of performing cycloplegia up to the age of 45 years is emphasised by the work of the French author Jeddi. In this prospective study, together with his colleagues he examined 164 eyes of 82 patients suffering from headaches. In cycloplegia (cyclophenolate), hypermetropia was significantly the most frequent ametropia. After examination full correction was applied to the patients, eliminating headaches in 76.5% of cases (9). In our workplace we do not apply full correction immediately, according to our experience this correlation can transitionally diminish distance vision, a better procedure seems to us to be progressive increase of dioptres and gradual acclimatisation, in most cases initially upon work close up.

The importance of examination of refraction in cycloplegia is mentioned also by the work of the author Ebri, who compared the effectiveness of three different cycloplegic drugs (1% cyclophenolate, 1% cyclophenolate + 0.5% tropicamide, 1% atropine) on Nigerian children. The main aim was to determine residual accommodation. Significantly the lowest residual accommodation was after administra-

tion of atropine, followed by a combination of 1% cyclophenolate + 0.5% tropicamide and then cyclophenolate alone (6). It is certainly appropriate in a range of cases to know which cycloplegic drug works best, though for regular practice the minor differences between them are not fundamental. As we have already stated, we do not apply full correction immediately, we always begin to accustom patients first of all to the values of +0.5 to +0.75 dioptre. For this reason it is not necessary to know the refraction "precisely to quarters of the dioptre". In addition, it seems inappropriate to us to burden adult patients in productive age with atropine (outside of therapeutic use).

CONCLUSION

Examination of refraction in cycloplegia before prescribing spectacle correction is not a regular necessity for adult patients. The majority of myopias are true myopias, and this applies also to hypermetropias. However, it is necessary to consider this possibility, and in the case of discrepancies rather conduct an examination. We also encounter cases in which we would expect potential latent hypermetropia, but it is not demonstrated in cycloplegia. It is however better to confirm that this is a genuine case of myopia than to prescribe inappropriate spectacle correction. In our experience it is then appropriate to correct these patients progressively, and if they are sufficiently instructed they will not invest unnecessarily large amounts in the first pair of glasses, after which subsequent strengthening is only of benefit.

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ORIGINAL ARTICLE

HDR 192Ir Brachytherapy in Treatment of Basal Cell Carcinoma of the Lower Eyelid and Inner Angle – Our Experience

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SUMMARY

Purpose: First experience and evaluation of relapses in group of patients after surgery with applied adjuvant HDR brachytherapy for recurrent tumor after incomplete excision of basal cell carcinoma of the lower eyelid and inner angle.
Methods: Patients with recurrent basal cell carcinoma of the lower eyelid in year 2010. In 3 male patients with recurrent finding of basal cell after surgery we applied adjuvant HDR 192Ir brachytherapy. The isodose curve chosen to prescribe the dose was 5 mm away from the skin surface.
Results: In the year 2010 we applied adjuvant HDR 192Ir brachytherapy in 3 male patients with recurrent basal cell carcinoma. The average age was 58 years (52 to 75 years). From group of 41 patients with non melanotic malignant tumors of the eyelids in 3 patients (7.3 %) with relapse after incomplete excision of the basal cell carcinoma of the lower eyelid we applied after removal of stitches after surgery adjuvant HDR 192Ir brachytherapy. For each patient was made individual orfit mask that bore plastic applicators. Tungsten eye shield applicator was applied to protect the eye globe. Treatment of 10 fractions of 4.5 Gy single dose (5 times weekly) were scheduled within 2 weeks. Patients received outpatient treatment.
Conclusion: Acute toxicity postradiation erythema of eyelid and skin around relieved by standard symptomatic treatment within a few days after completion of radiation therapy. In 2 year interval after HDR 192Ir brachytherapy we did not record the occurrence of late complications such as corneal ulcers. Our preliminary experience shows excellent early skin tolerance. After 2 years of follow-up at 6 month interval we did not recognize relapse in our group of patients. The proposed technique of HDR 192Ir brachytherapy after surgery should be considered a new clinical treatment in patients with recurrent non melanotic eyelid cancer. Its main advantage lies in the usefulness in all types of basal cell and squamous cell carcinoma and sebaceous carcinoma of the eyelids, without restriction by site, dimension, clinical or histological type, or the patient's general status.

Key words: HDR 192Ir brachytherapy, basal cell carcinoma, eyelid carcinoma treatment

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INTRODUCTION

The incidence of tumours in the area of the eyelids (dg. C44.1) has increased in recent years, and with it there has also been an increase in the incidence of malignant skin tumours in other localisations, in which we are recording the highest occurrence of these diseases in the group of patients aged from 70 to 74 years (15). The most frequently occurring nonmelanocytic tumours of the eyelids are basocellular carcinoma (basal cell carcinoma), spinocellular carcinoma, mucoepidermoid carcinoma, sebaceous carcinoma and Merkel cell carcinoma. Tumours which simultaneously afflict the conjunctiva and the eyelids are squamous cell carcinoma, lymphomas and leukemic infiltrates (1, 13).
Basal cell carcinoma is the most frequent malignant tumour of the eyelids, blameful for 90% of malignant tumours in this area. Its incidence has also been increasing in recent decades. It originates from the basal cells of the epidermis and hair follicles. Histopathologically we can find several forms of basal cell carcinoma: multicentric, sclerodermiform, fibroepithelial, keratinising, metatypical and intraepidermal. We classify them in histopathological stages from G1 – G4. In clinical practice, basal cell carcinoma is most often identified in stage T1 or T2 (5, 6, 7).
It is a tumour resembling the basal layers of the squamous epithelium. Macroscopically it is very diverse, beginning from minor resistance of the eyelid or medial angle, later exulcerates and infiltrates into the surrounding area. It is distinguished by invasive growth, low mortality and a low tendency towards formation of metastases. Basal cell carcinoma is the main representative of the category of dg. No. C44 MKCH-10 (other malignant skin tumours), the incidence of which was 69/100 000 persons in Slovakia last years (13). It is possible to stipulate a definitive diagnosis of basal cell carcinoma only on the basis

of a histological examination. Upon differential diagnostics it is possible to confuse basal cell carcinoma with adnexal epitheliomas, the presence of melanin must not lead to such confusion. The most important etiological factors in the occurrence of basal cell carcinoma are actinic radiation, genetic influences, carcinogens, scars and chronic damage to skin (1, 4, 8).

Primary therapy of basal cell carcinoma in the area of the lower eyelid and the medial angle is in principle surgical. Broad excision of the deposit with loose resection edges (at least 2-3 mm) is a highly effective solution, with a 5 year rate of local recurrence of less than 10% (16). With regard to the size of the defect after primary excision, it is necessary to continue with a reconstructive surgery for 80% of patients. Some advanced lesions require extensive surgical interventions and it is necessary to embark upon mutilating procedures – orbital exenteration (10). In the case of positive resection edges following insufficient primary excision (e.g. by inexperienced surgeon), the indication of re-excision is considered. In the case of pronounced locally advanced basal cell carcinomas in this area with a high risk of local recurrence after excision or an unacceptable expected cosmetic effect, in patients of advanced age or with repeatedly recurring lesions, the definitive radiotherapy is an appropriate solution. In certain exceptional cases, where a surgical procedure is impossible, isolated radiotherapy may also be a definitive alternative (12).

In the past, especially in the 1970s, external radiotherapy in monotherapy (mostly 60Co) was used as a standard in the treatment of basal cell carcinomas in the area of the lower eyelid and medial angle. This procedure has now been surpassed with regard to the post-radiation scar changes in the surrounding area, whilst in certain other localisations this treatment is considered highly effective to this day (5, 8, 14).

After incomplete excision, in the case of recurring malignant tumours of the lower eyelids or in the case of impossibility of a surgical solution, high dose rate (HDR) brachytherapy is currently coming to the forefront (2). The advantage of brachytherapy is the possibility of concentrating the dose of radiation into a small volume and the sharp gradient of the dose into the surrounding area with potential sparing the surrounding tissues. Brachytherapy has a theoretical advantage in comparison with surgery in the fact that it enables coverage of a larger area of the skin with a high dose (macroscopic disease, microscopic disease, safety margin), without the necessity of irreversible damage to the surrounding tissues. Brachytherapy in the treatment of skin tumours may be implemented via the interstitial pathway (surgical introduction of brachytherapeutic applicators directly into the tumour tissue by puncture), or superficially. Superficial brachytherapy is implemented by using standard applicators (e.g. Leipzig Applicator, Brock Applicator, Nucletron BV, Holland), or moulages made to measure. Standard applicators are distinguished by their simplicity of use, good reproducibility of treatment, but they do not enable use for irregular deposits or in a "crooked" irregular terrain such as the periocular area (9, 11).

Individually made surface moulages enable us to overcome the above-mentioned circumstances, but require longer preparation. The principle of moulage lies in preparation of a vessel of the appropriate depth, which sufficiently copies the surface of the respective area and bears the plastic applicators for brachytherapy. The vessel can be made of various materials, e.g. dental or thermoplastic materials. Plastic applicators respecting the shape and depth of the target volume are subsequently fixed to the vessel at a distance of 5-10 mm. Planning systems which reconstruct the spatial distribution of the individual applicators and create an isodose plan at the selected levels are used for calculation of the dose distribution. The resulting dose distribution is specified by a summary of doses in the single path positions of 192Ir radiation. Subsequent use of an individually made applicator is simple, easily reproducible, comfortable for the patient, and the entire treatment may be conducted in an outpatient form.

MATERIAL AND METHODOLOGY

In 3 patients (7.3%) with recurring basal cell carcinoma of the medial angle and lower eyelid, after incomplete excision of the lower eyelid and after confirming recurrence by histological examination, we indicated the outpatient adjuvant HDR 192Ir brachytherapy.

We indicated radiation therapy after removing stitches in the form of surface individually made moulage on the area of the scar and recurrence with a margin of 5-10 mm. An individual thermoplastic mask (Orfit industries, Belgium) was made as a vessel for each patient, onto which plastic applicators for brachytherapy were fixed (Flexible implant tube 6F, Nucletron, Holland). There followed 2D orthogonal reconstruction and calculation of the dose

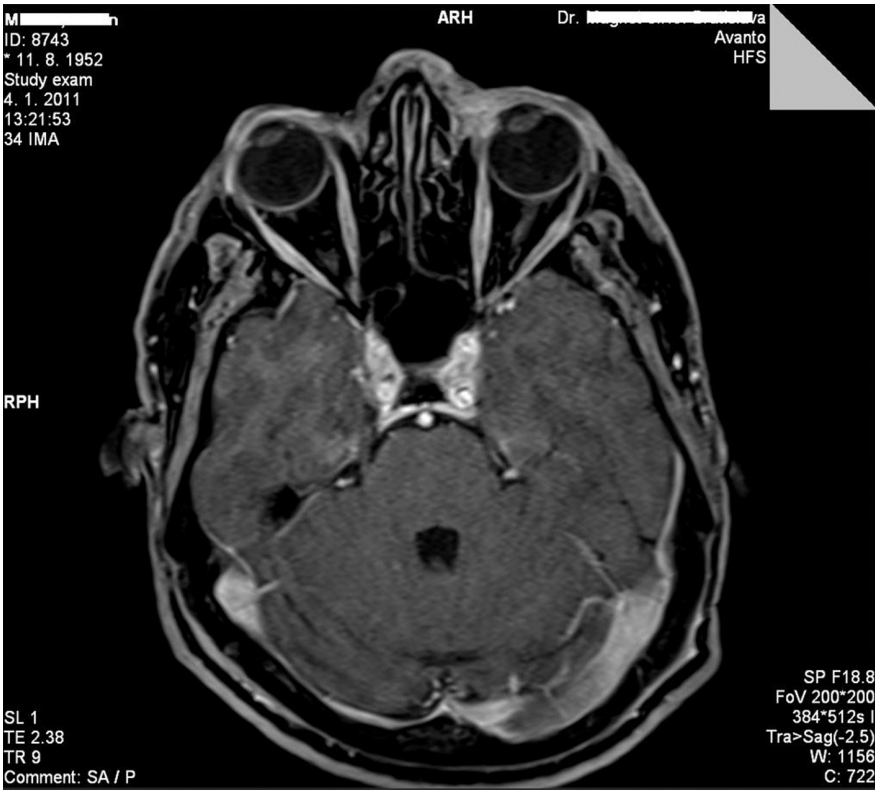

Fig. 1. MRI examination of orbit in patient with infiltration of medial angle of left eye before HDR brachytherapy

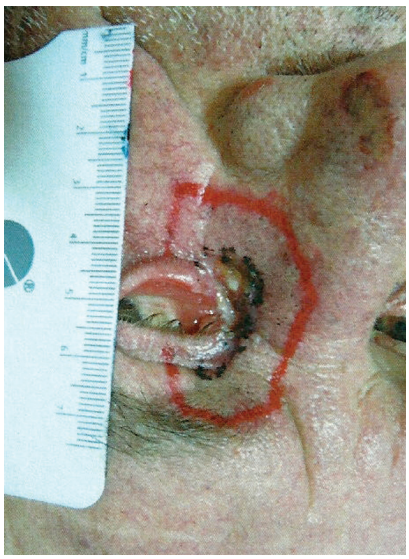

Fig. 2 Plotting of recurring deposit (black colour) with margin 5-10 mm (red colour) before creation of Orfit mask

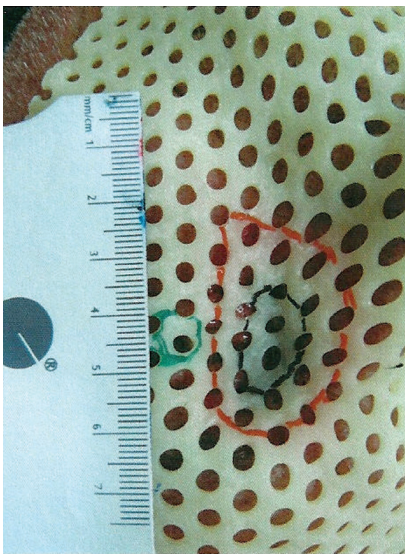

Fig. 4. Placement of protection on surface of eyeball (Tungsten eye shield)

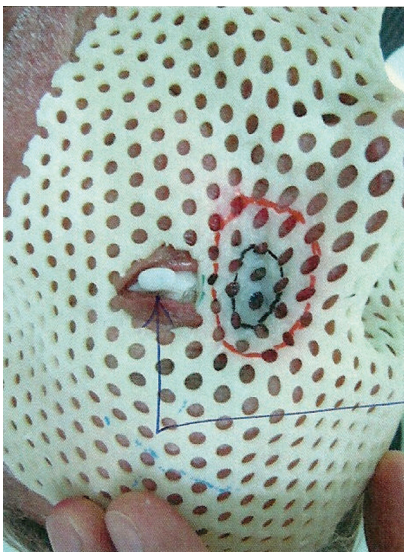

Fig. 5. Treatment position of patient with applied individually made surface moulage

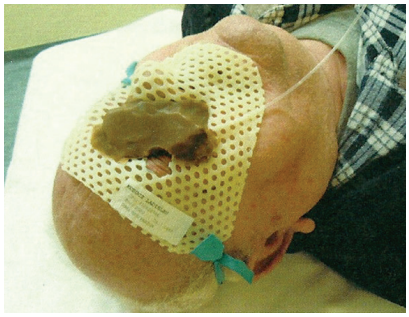

Fig. 3. Indication of target volume (red colour) and lens (green colour) on Orfit mask

with subsequent geometric optimisation. In all 3 patients we applied an individual dose of 4.5 Gy in 10 fractions (1 fraction per day, 5 fractions per week), which biologically represented a dose per tumour of 54.4Gy EQD2 (α/β =10, LQ model). During treatment the eyeball was covered as standard by a Tungsten eye shield applicator (Civco, USA). All patients underwent treatment as outpatients.

Subsequent checks after the completion of brachytherapy were conducted due to expected acute toxicity at 2-week intervals, later at 3-month intervals or after 1 year at 6-month intervals.

RESULTS

After 2 years of observation at 6-month intervals we did not record recurrence in any of the patients. The results are satisfactory after treatment by HDR 192Ir brachytherapy, we did not record the occurrence of later complications such as corneal ulcer. Acute post-radiation toxicity – erythema of the skin of the eyelids and in the surrounding area subsided after standard symptomatic treatment within a few days of the end of radiation treatment.

DISCUSSION

Data on recurrences after surgical treatment of basal cell carcinoma differs, depending on the use of the operating technique. In the studies known to us, published over the course of the last 10 years, the incidence of recurrences in patients treated without the use of Mohs micrographic surgery or "en--face" frozen incisions peroperatively was within the range of 1.8% to 39%, in the case of longer monitoring of patients the rate of recurrences increased. In epidemiological and clinical studies we find a slight predominance of incidence in men. Within the framework of the possible causes we may consider the smaller amount of attention devoted by this part of the Slovak population to the occurrence of "cosmetic" lesions on the face from the perspective of the layman. The most frequent incidence of recurrences is on the lower eyelid. Local treatment (Imiquimod – Aldara) in localisation close to the margin of the eyelid or the lateral or medial angle is not yet widely used (3, 16, 17).

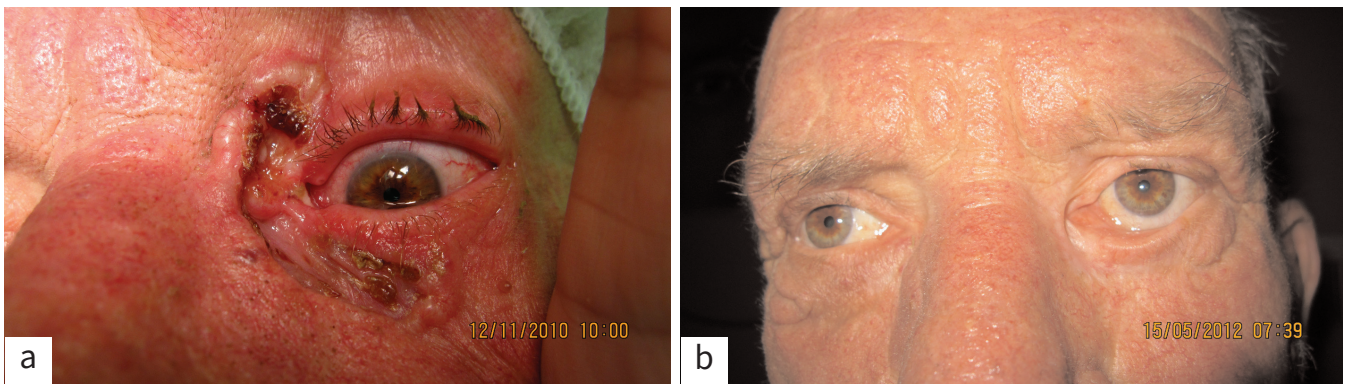

Fig. 6. Patient with recurring basal cell carcinoma of medial angle of left eye before treatment – November 2010 after treatment without recurrence, persisting ectropion – May 2012

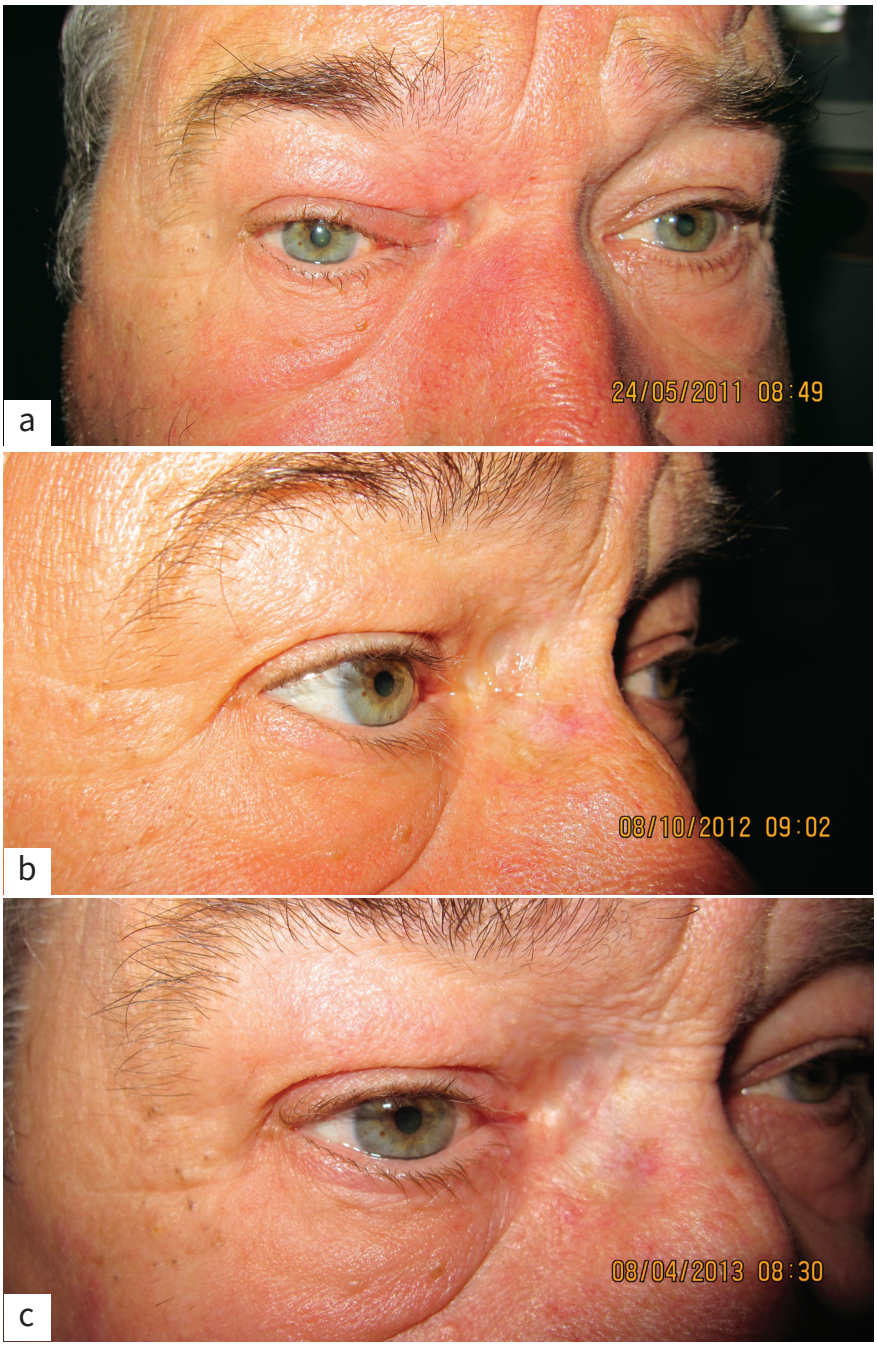

Fig. 7. Patient with microscopically positive resection edge after excision of basal cell carcinoma of the medial angle of the right eye
a) 6 months after brachytherapy erythema of skin persists in the radiation-treated area
b) 22 months after completion of brachytherapy
c) 29 months after completion of brachytherapy

Reconstructive surgeries and plastic surgeries of eyelids following removal of tumour are currently elaborated to the level of a displacement of the chondromucosal septal flap from the upper eyelid. Despite this the orbital exenteration remains one of the alternatives of resolving of an advanced stage of the process (10).
HDR 192Ir brachytherapy was developed in the treatment of basal cell and squamous cell carcinoma of the eyelids in the 1990s. Newer methods of brachytherapy are applied in the treatment of nonmelanotic lesions on the face using the method of HDR electronic brachytherapy (electronic BT).
However, the first reports of HDR brachytherapy in the treatment of basal cell carcinomas of the eyelids did not appear until 2007 (11).
Guix (9) referred to 136 patients with basal cell carcinoma or spinocellular carcinoma in the facial area. Nineteen patients were treated using standard Brock applicators and 117 patients were treated using individually made polymethylmethacrylate applicators obtained by making a casting of the patient's face. For lesions with a size of up to 4 cm the minimum dose was 60 to 65 Gy in a dose to a fraction of 1.8 Gy (EQD2 58.4-63.7 Gy), which is a slightly higher dose than we used on our patients. Lesions larger than 4 cm were irradiated up to a total dose of 75-80 Gy (EQD2 72 – 78 Gy). In the entire group they recorded 3 recurrences, only one patient suffered recurrence upon treatment of the primary tumour, in two patients this concerned relapse in the case of recurrent tumours. At a time interval of 5 years 98% of patients were without recurrence, for patients with primary tumours the 5-year local check-up showed 99% without recurrence, for patients with recurrent tumours 87%. Tolerance of the treatment was excellent in all cases, no serious, early or later complications were detected.
The radiobiologically converted total dose in the treatment scheme we used in the treatment plan (10 fractions of 4.5 Gy) was lower in comparison with the above-presented work (EQD2 54.4 v.s. EQD2 58.4 Gy) and also brought a complete remission of the disorder. However, the short monitoring period (2 years) and the small number of our patients unfortunately does not enable us to evaluate this therapeutic regime reliably with regard to effectiveness.

CONCLUSION

Within the framework of ophthalmo-oncology, increased attention is being devoted to the problem of malignant nonmelanocytic tumours of the eyelids, because in the case of growth into the orbit, an untreated tumour may cause loss of the eye or even orbital exenteration. Primary surgical treatment and subsequent reconstructive surgery of advanced stages represents a repeatedly serious aesthetic intervention.
Radiotherapy represents a highly effective modality in the treatment of skin carcinomas in the facial area. Adjuvant brachytherapy is the method of choice in the case of incomplete excisions or of recurring nonmelanocytic malignant tumours of the eyelids. Our first experience demonstrates that no recurrence of basal cell carcinoma occurred within the monitored interval of 2 years after treatment.

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CASE REPORT

Vogt-Koyanagi-Harada Syndrome in Children

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SUMMARY

Vogt-Koyanagi-Harada (VKH) syndrome is a multisystemic disease characterized by granulomatous panuveitis with exsudative retinal detachment and often associated with neurological and skin symptomatology.
In the paper is presented a rare case of probably VHK syndrome in 11-year old caucasian race boy in which was found the bilateral granulomatous panuveitis with exsudative retinal detachment without other systemic symptomatology with typical clinical characteristics and course. Systemic corticosteroid therapy in a patient gradually improved the state, which was then complicated by the occurrence of juxtapapillary subretinal neovascular membrane on both eyes. The following administration of intravitreal injection anti-VEGF (bevacizumab) was modified visual acuity and reduced neovascular membrane.

Key words: Vogt-Koyanagi-Harada syndrome, children, juxtapapillary choroidal neovascular membrane, anti-VEGF, bevacizumab.

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INTRODUCTION

Vogt-Koyanagi-Harada (VKH) syndrome is an idiopathic multisystem T-lymphocyte mediated autoimmune disease attacking antigenic components of melanocytes, causing inflammation of the tissues containing melanocytes such as the uvea, ears, skin and meninges (14). It is characterised by granulomatous panuveitis with exudative retinal detachment and is frequently associated with neurological and skin manifestation (4). The syndrome occurs most frequently in darkly pigmented races, in Asians, American Indians, Hispanics and black people. The age of manifestation is most frequently between 20 and 50 years. From the quantity of published works, the occurrence in children aged under 16 has been less than 5%. In the literature there are only a few documented cases of VKH syndrome in children; in our work we present a case of an 11-year-old patient with VKH syndrome, which was complicated by the formation of a juxtapapillary choroidal neovascular membrane.

CASE STUDY

An 11-year-old boy of Caucasian race was sent to our workplace with a 2 week anamnesis of sudden deterioration of vision in both eyes. In the past he had not been treated for any eye disorders, had not suffered an eye injury or undergone an operation. Two weeks before the beginning of the problems he was vaccinated with the PRIORIX vaccine. The only symptom was a visual disorder, he had no other general complaints. At the first examination with his ophthalmologist his central visual acuity (CVA) was 5/30 bilaterally and upon examination of the fundus hyperaemia of the disc of the optic nerve (DON) was diagnosed. He was subsequently admitted at the district eye clinic and sent for a brain scan by nuclear magnetic resonance (NMR), where a finding of an extra axial cystic lesion in the pineal area was determined. Due to the MRI finding the patient was transferred to the Paediatric Neurology Clinic at the Paediatric University Hospital and Clinic in Bratislava. No neurological, skin or hearing manifestations were found, and a cerebrospinal fluid scan (CFS) did not find any abnormalities.
The first eye examination at the Paediatric Ophthalmology Clinic at the Paediatric University Hospital and Clinic determined a persisting disorder of CVA 5/30 bilaterally and bilateral panuveitis with multifocal serous retinal detachment (fig. 1) and with impairment of the visual field (fig. 2). At the same time a suspicion of probable VKH syndrome was expressed. Other causal linkage with another inflammatory or infectious disease was diagnostically excluded. HLA typification determined HLA class I: HLA A2, A11, B51, B7 and HLA class II: DR01 and DR11. For the patient the ultrasonographic (USG) image (fig. 3), the finding on optical coherence tomography (OCT) (fig. 4) and fluorescence angiography (FAG) corresponded to the uveitic stage of VKH syndrome. Initiated was the pulse corticoid therapy with methylprednisolone 500 mg intravenously for 3 days with subsequent oral administration of prednisone in a dose of 1 mg/kg/day.
After 1 month a control MRI scan determined a finding of cisterna magna permagna and a cyst of the epiphysis. The neurosurgeon stated that this concerned a possible ordinary finding without a clinical correlation to visual disorder. During general corticosteroid treatment the patient recorded a progressive improvement of CVA in a period of 1.5 months to 5/7.5 in the right eye and 5/10 in the left eye, as well as an improvement in the visual field, subsidence of retinal detachment and attenuation of anterior uveitis. Oedema of the DON persisted in the ophthamoscopic image, as well as disorders of the pigment retinal epithelium (PRE), which was destroyed in the macula. Depigmentations occurred in the periphery and central periphery (fig. 5), to which the FAG image also corresponded (fig. 6), and on

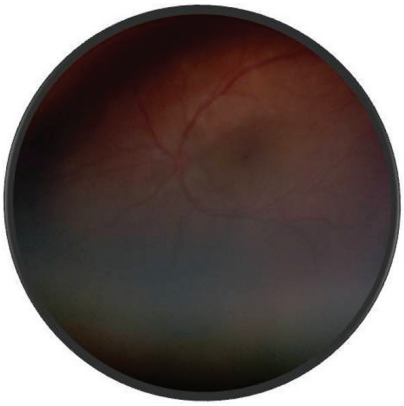

Fig. 1. Photograph of fundus o. sin – multifocal serous retinal detachment – the uveitic stage of VKH syndrome

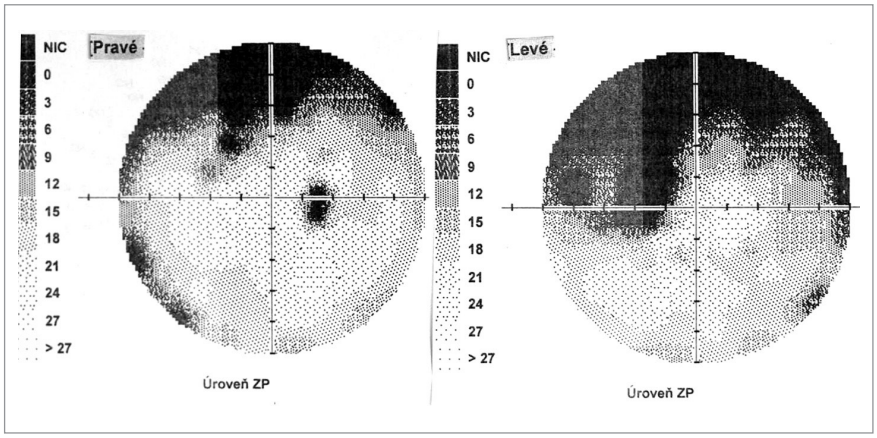

Fig. 2. Perimetric finding – the uveitic stage of VKH syndrome

OCT retinal detachment had attenuated (fig. 7 a, b). The values of intraocular pressure were within the norm. We evaluated the state as a chronic stage of VKH syndrome.

After 3 months from the prodromes of the illness, CVA is 5/5 bilaterally, in the clinical picture there is recurrence of anterior uveitis, without manifestations of posterior uveisits, oedema of the DON persists; the patient has been left on general corticoid therapy in a dose of 10 mg/day.

After 6 months from the beginning of the disease, the patient in the clinical picture has no manifestations of anterior uveitis, a fundoscopic examination revealed formation of a juxtapapillary choroidal neovascular membrane (CNVM) at the temporal edge of the DON bilaterally. Its presence was confirmed by a FAG and an OCT examinations. CVA was 5/5 bilaterally, on the perimeter an extended blind spot (fig. 8).

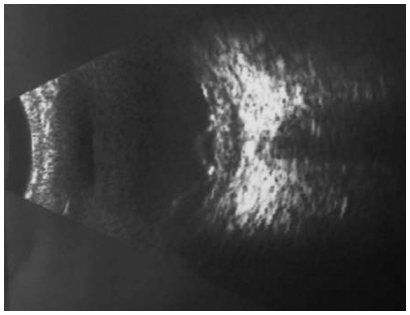

Fig. 3 USG finding in o. sin – the uveitic stage of VKH syndrome

10 months after the beginning of the disease the patient had no manifestations of anterior uveitis. Fundoscopic examination revealed progression of the juxtapapillary CNVM at the temporal edge of the DON bilaterally, which extended into the macula (fig. 9 a, b). Peripapillary, hyperfluorescence spreading temporally from the disc was seen on the FAG image, extending into the area of the macula with delayed infiltration (fig. 10). The OCT image determined a juxtapapillary CNVM with submacular fluid, with a central macular thickness (CMT) of 381 μm in the right eye and 364 μm in the left eye (fig. 11a, b). CVA was 5/10 bilaterally, the perimetric finding showed paracentral scotoma with an extended blind spot. For this reason, after obtaining informed consent from the legal representative of the patient, we applied 1 injection of anti-VEGF bevacizumab intravitreally in a dose of 0.75 mg/0.1 ml into the right eye and 1.25 mg/0.1 ml into the left eye.

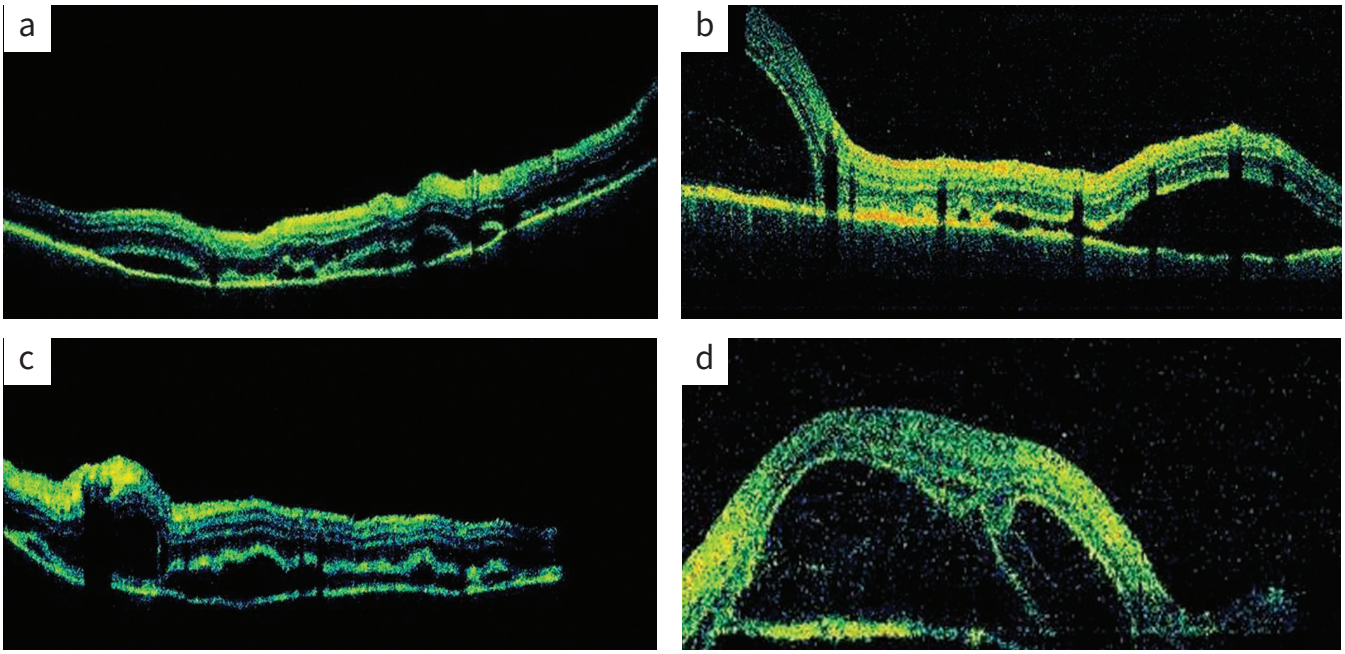

Fig. 4. OCT retinal finding – the uveitic stage of VKH syndrome a) o. dx horizontal scan, b) o. dx vertical scan, c) o. sin horizontal scan, d) o. sin vertical scan

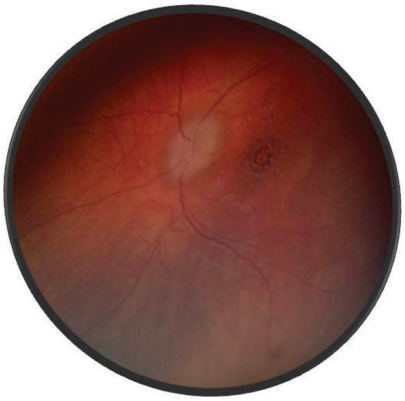

Fig. 5. Photograph of o. sin fundus – the chronic stage of VKH syndrome

Fig. 6. FAG of o. sin – the chronic stage of VKH syndrome

Subsequently within 1 month there was a correction of CVA to 5/5 in the right eye and 5/7.5 in the left eye with regression of the juxtapapillary CNVM visibly on the FAG and OCT examinations (CMT 247/264 μm), though juxtapapillary subretinal fibrosis persists. 11 months after the beginning of the disease, general treatment with prednisone was terminated.

In the 17th and 23rd months from the beginning of the disease two recurrences of anterior uveitis appeared bilaterally, with occurrence of posterior synechieae (fig. 12), which corresponds to a recurring stage of the disease. No manifestations of regression of posterior uveitis were determined. Upon the

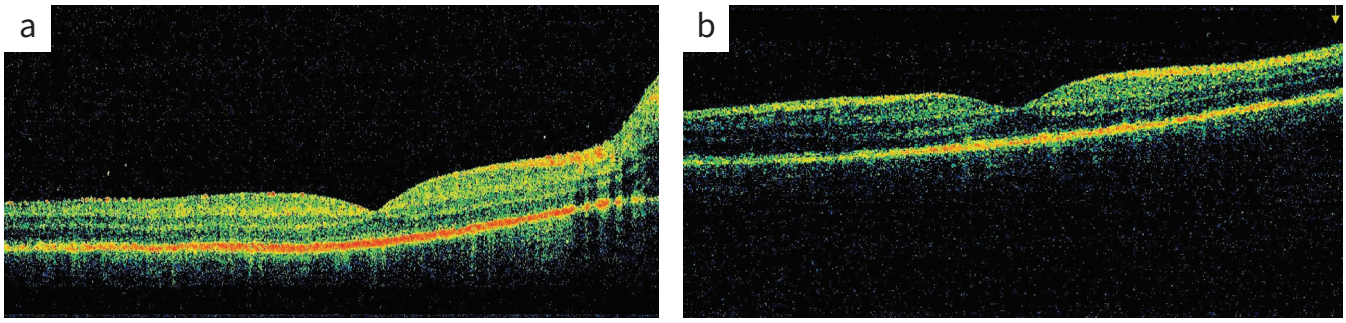

Fig. 7. OCT finding – the chronic stage of VKH syndrome a) o. dx, b) o. sin

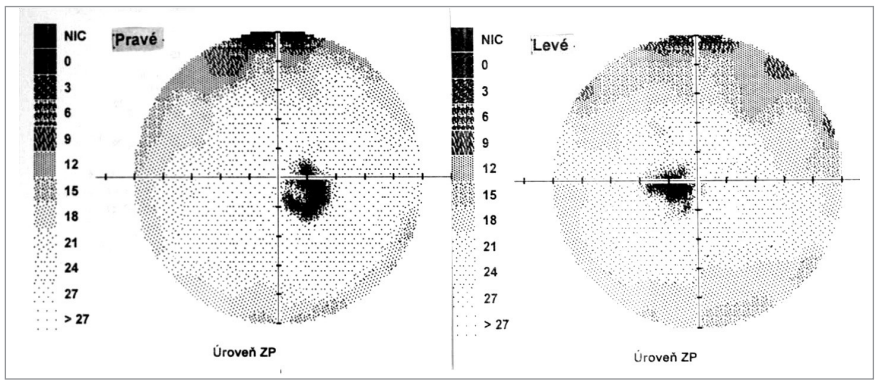

Fig. 8. Perimetric finding – the chronic stage of VKH syndrome

first recurrence the inflammation was managed by a local corticoid therapy, and upon the second recurrence by an oral corticoid therapy with prednisone in a dose of 1 mg/kg with gradual reduction over the course of 2 months. At present, 32 months after the onset of the disease, CVA is 5/5 in the right eye and 5/7.5 in the left eye. The patient has no signs of anterior or posterior uveitis bilaterally. No glaucoma or cataract was found in the patient. However, the patient manifests chronic changes in the anterior and posterior segments, and defocusing of the

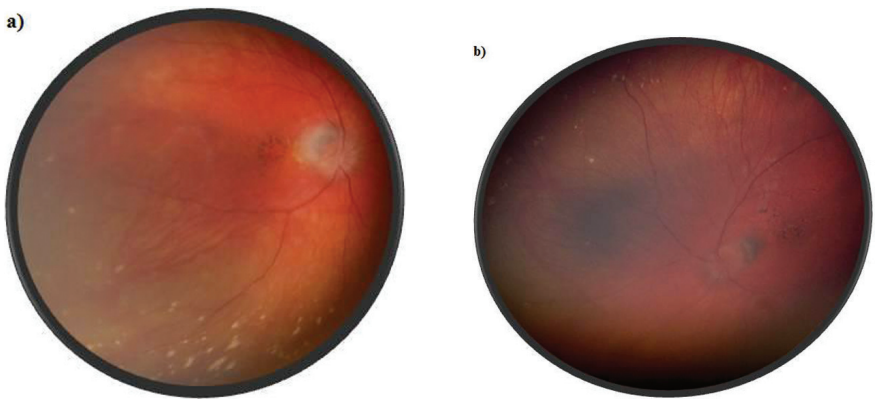

Fig. 9. Photograph of fundus – juxtapapillary CNVM a) o. dx, b) o. sin

Fig. 10. FAG finding of o. sin – classic juxtapapillary CNVM

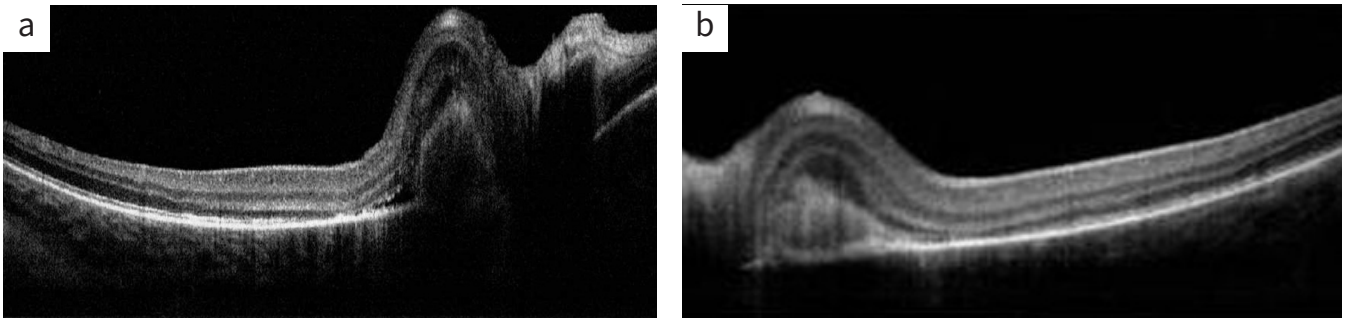

Fig. 11. OCT finding – juxtapapillary CNVM a) o. dx, b) o. sin

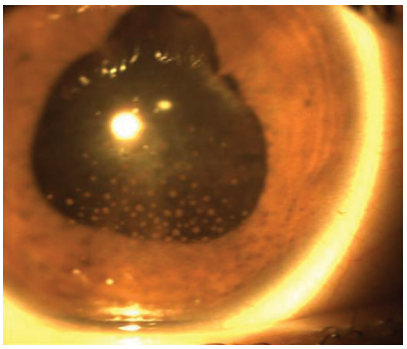

Fig. 12. Photograph of the anterior segment of o. sin – recurring stage

DON is persisting due to the finding of juxtapapillary subretinal fibrosis, paracentral scotoma is persisting in the visual field in the place of the blind spot. Central macular thickness is 249 µm in the right eye and 255 µm in the left eye. The patient remains under our observation.

DISCUSSION

Vogt (1906), Koyanagi (1929), Harada (1926) – independently described a number of patients with bilateral uveitis, exudative retinal detachment, with neurological abnormalities and skin problems. Despite the differences in the individual cases and the assumption that this concerned various different diseases, other authors subsequently came to the conclusion that the disorder could be named Vogt-Koyanagi-Harada syndrome. The international commission for nomenclature set the criteria for diagnosis of VKH syndrome. The revised criteria define 3 categories of the disorder: complete VKH, incomplete VKH and probable VKH disease (4, 20) (table 1). Our patient met the criteria for the probable VKH disease.

The pathogenesis of the disorder is unknown, inflammation and loss of melanocytes was determined in a number of organs – in the skin, the inner ear, meninges and uvea. On the basis of the histopathological findings, the disorder is assumed to have an infectious or autoimmune base. VKH disease most frequently occurs in patients with a genetic predisposition to the disorder. An association was determined with HLA-DRB1, HLA-DR4, HLA-DR5 and HLA-DQ4 (13).

The frequency of incidence of VKH disease is low, most frequently it afflicts people of darkly pigmented races. Pigmentation of the skin alone is not a predisposing factor in the pathogenesis of the disease. Women are afflicted more often than men. The disorder afflicts people between 20 and 50 years of age, most often in the third decade, occurrence in children is rare. In the literature there are only a few recorded cases of occurrence in children (1, 3, 7, 10, 15, 18, 21, 23).

Neurological symptoms may persist for weeks, usually subsiding after corticoids, whilst skin manifestations persist despite the treatment, hearing complaints subside after a corticoid therapy after weeks to months.

Clinical manifestation – we distinguish 4 stages of the disorder (table 2).

Diagnosis of the disease is based on the clinical picture and the symptoms, there are no laboratory tests specific for this disease. FAG, ICG, OCT, USG, MRI, examination of liquor (CSF), eletrophysiological tests and audiometry are useful in diagnosis. HLA typification is not significant for diagnosis and as a result it is not routinely recommended.

The purpose of treatment is to manage uveitis and prevent complications. Treatment of VKH syndrome with systemic corticoids should be started sufficiently in time and aggressively – methylprednisolone up to 1 g/d intravenously for several days, in children 10 mg/kg/d, subsequently predisone 1 mg/kg/d orally, length and reduction of dose individually, sometimes 6-12 months but no less than 3 months due to the risk of recurrence (2, 12, 19). We too respected this recommendation. In patients not responding to corticoids or in whom the treatment produced adverse reactions, an immunomodulation therapy is recommended – methotrexate, cyclosporine, infliximab, tacrolimus, azathioprine, cyclophosphamide (10, 24).

Treatment in children with VKH syndrome is challenging. Various models of treatment have been described in the literature, with varying effects; no definitive treatment module has yet been determined and treatment is usually individual in cases of VKH in children (3). In previous publications, the most useful substances in the treatment of VKH syndrome in children were corticosteroids, whereas combinations of therapy with cyclosporine, methotrexate or azathioprine were used with favourable results in refractory cases (7). In our case the disorder was managed with systemic corticoid therapy, on which the patient was left for 11 months.

In the treatment of complications, it is most often necessary to resolve secondary glaucoma or cataract, which did not occur in our patient, and choroidal neovascular membrane (CNVM). Choroidal neovascularisations occur in 15% of patients with VKH and are associated with an unfavourable prognosis for sight (25). Bevacizumab is a human monoclonal antibody, which binds to all subtypes of vascular endothelial growth factor (VEGF). It has been successfully used in the treatment of secondary CNVM in the case of various disorders. Intravitreally administered bevacizumab is an effective medication in the treatment of CNVM in eyes with VKH syndrome (8, 17, 18, 22). A similar effect in the treatment of CNVM in eyes with VKH syndrome was achieved also upon intravitreal administration of ranibizumab (11). In our case the patient was treated for complicated juxtapapillary CNVM in both eyes with bevacizumab. One intravitreal administration of bevacizumab was sufficient and stabilised CVA. However, persistent subretinal fibrosis

Table 1 Revised criteria for the Vogt-Koyanagi-Harada disease (4, 20)

Complete VKH disease (Criteria 1-5 must be met)
1. absence of penetrative eye trauma and surgery before manifestations of uveitis
2. absence of clinical and laboratory connection with any other eye disorder
3. bilateral affliction of eyes (a. or b. must be met depending on the stage in which we examine the patient)

a. early manifestation of disease
- 1. diffuse choroiditis (without or with anterior uveitis, reaction in vitreous body, hyperaemia of the optic nerve), which may be manifested as
  - a) focal areas of subretinal fluid
  - b) bullous serous retinal detachment
- 2. with subsequent symptoms on fundus (both symptoms must exist)
  - a) focal areas with delayed choroidal perfusion, multifocal areas with point infiltration, large placoid surfaces of hyperfluorescence, with accumulated subretinal fluid, enhancement of optic nerve on FAG
  - b) diffuse choroidal coarsening, without presence of scleritis on USG

b. late manifestation of disease
- 1. anamnestic presumption of presence of symptoms from 3.a, and either (2) or (3) below, or multiple symptoms from (3)
- 2. ocular depigmentation (one of the following is sufficient)
  - a) "sunset glow" fundus
  - b) Sugiura's symptom – perilimbal vitiligo
- 3. other ocular symptoms
  - a) nummular chorioretinal depigmented scars
  - b) RPE clusters or shifts
  - c) recurrent or chronic anterior uveitis

4. Neurological/hearing disorders (may have subsided at time of examination)
a. meningism
b. tinnitus
c. pleocytosis in CSF

5. Skin symptoms (follow after manifestation of CNS or eye affliction)
a. alopecia or
b. poliosis or
c. vitiligo

Incomplete VKH disease (criteria 1-3 and 4 or 5 must be met)
1. absence of penetrative eye trauma and surgery before manifestations of uveitis
2. absence of clinical and laboratory connection with any other eye disorder
3.bilateral affliction of eyes (as defined for the complete VKH disease)
4. neurological/hearing disorders (as defined for complete VKH disease)
5. skin symptoms (as defined for complete VKH syndrome)

Probable VKH syndrome
1. absence of penetrative eye trauma and operation before manifestations of uveitis
2. absence of clinical and laboratory connection with any other eye disorder
3. bilateral affliction of eyes (as defined for complete VKH syndrome)

Table 2 Clinical stages of disorder

1. Prodromal stage	Persists for several days, fever, headache, meningism, nausea, vertigo, tinnitus, dysacusis, CFS pleocytosis, photophobia, epiphora, hypersensitivity of skin and hair. Less frequent paralysis of nerves, neuritis n.II, some patients do not have prodromal symptoms
2. Uveitic stage	Follows prodromal stage after a number of days, frequent deteriorated vision, in 70% bilaterally, if unilaterally the second eye is afflicted a few days later. Bilateral uveitis with retinal oedema, cells in anterior vitreous body, hyperaemia of papilla of the optic nerve or oedema, multifocal serous retinal detachment, granulomatous anterior uveitis with streaked precipitates, Busacca and Koeppe nodules, increase of IOP, the stage persists for several weeks
3. Chronic stage	Typical eye and skin manifestation. Dallen-Fuchs nodules, posterior synechia, pupillary membrane. Subsidence of detachment. Depigmentation of choroidea begins first 3 months from beginning of disease, RPE alteration – depigmentation, hyperpigmentation of fundus, demarcation lines in periphery and central periphery of retina, lesions fade and atrophy. Skin symptoms – vitiligo, poliosis of eyelashes, eyebrows, hair. Dysfunction of inner ear is corrected after several months. Stage persists for several months.
4. Recurring stage	Recurring or chronic anterior uveitis, weaker choroidal inflammation accompanying anterior uveitis diagnosed by ICG angiography (11). Recurrence of posterior uveitis is rare. Ocular complications are frequent – cataract, glaucoma – pupillary block or with closed angle, atrophy of disc of optic nerve, choroidal neovascularisation, neovascularisation of disc of optic nerve and retina, vitreous haemorrhage, subretinal fibrosis.

is a cause of paracentral scotoma in the visual field in both eyes.

Corticosteroids are used due to their angiostatic and antipermeable properties. It is necessary to suppress the inflammation process by immunosuppression. A combination of an intravitreally applied anti-VEGF and a corticosteroid together with a systemic immunosuppressive therapy was effective in the treatment of inflammatory CNVM without serious systemic or ocular side effects (22).

Laser photocoagulation, photodynamic therapy, surgical excision and corticosteroid therapy have been used in the treatment of secondarily occurring CNVM in VKH with varying degrees of success (5, 6, 9, 16).

The visual prognosis of VKH in adults as well as in children is generally favourable. The clinical finding upon manifestation of the disease, the interval between occurrence of the first symptoms and the initiation of treatment, repeated inflammations, development of complications, use of intravenous corticosteroids and the method of reducing of systemic corticosteroids are significant prognostic factors.

CONCLUSION

VKH syndrome is a serious disease which in rare cases also afflicts children. If extraocular symptoms are not present, the diagnosis may be complicated and treatment of the acute phase requires immediate bolus corticoid therapy. VKH syndrome requires monitoring for several years due to its chronic character. Prognosis quo ad visum is favourable in child patients. The deterioration of visual acuity in patients with VKH syndrome is frequently caused by complications such as cataract, glaucoma and choroidal neovascularisation. Choroidal neovascularisation is the main cause of later loss of sight.

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CASE REPORT

Contraception and Ocular Thromboembolic Episodes

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SUMMARY

The aim of the paper is to warn of the retinal vein occlusion possibility due to the using of hormonal contraceptive pills in young female patients. A case report of 22 years old female patient hospitalized at the Department of Ophthalmology, School of Medicine, Masaryk University, Brno, Czech Republic, E.U., with sudden decrease of the left eye visual acuity is presented. After excluding other causes of visual acuity decrease, the diagnosis of prethrombotic state was made and anticoagulant treatment was started.

Key words: optic disc edema, prethrombotic state, retinal vein occlusion, visual acuity decrease, hormonal contraception

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INTRODUCTION

Retinal Vein Occlusion (RVO) is the second most common vascular disorder of the retina, after diabetic retinopathy. According to the localisation of the vascular occlusion we classify retinal vein occlusions as central (CRVO) and branch (BRVO) ones. A separate clinical form is hemiocclusion, in which the upper or lower half of the retina is afflicted [8]. Within the framework of central occlusions, "prethrombotic state" is sometimes given a separate status. This is characterised by the presence of dilated and tortuous retinal veins and oedema of the disc of the optic nerve. Massive haemorrhages are not evident. Visual acuity is only slightly reduced [11].

Risk factors of retinal vein occlusion include systemic cardiovascular disorders (hypertension, hyperlipidemia, diabetes mellitus, increased BMI), hyperviscous states, vasculitis or hypercoagulation states (Leiden mutation, antiphospholipid syndrome, deficit of C and S protein). The ocular risk factors include glaucoma excavation of the disc of the optic nerve. We consider smoking and certain pharmaceuticals (oral contraceptives, hormonal substitution therapy or diuretics) [10] to represent external risk factors.

Retinal vein occlusion most frequently afflicts patients aged over 50 years, who primarily manifest risk cardiovascular factors. A small proportion of retinal vein occlusions occurs in younger patients [8].

CASE STUDY

In July 2012 a 22-year old female patient came to the emergency department of the outpatient Eye Clinic of Brno University Hospital due to a deterioration of visual acuity in the left eye persisting for several hours.

The patient's anamnesis stated a surgery for strabismus at the age of 3 years in the Paediatric University Hospital in Brno. In childhood she wore an occlusor, at primary school she no longer wore spectacle correction or an occlusor and saw equally well in both eyes and read the last row of Snellen charts. In general, she did not receive treatment for any illnesses. From the age of 16 years she had used oral hormonal contraception, Diane 35 (Ethinylestradiol, Cyproteron acetate). The patient had been a smoker since the age of 16, smoking 10-15 cigarettes per day.

At an objective examination best corrected visual acuity in the right eye was 1.0, in the left eye 0.8, correction did not improve. The anterior segment of the eye was without a pathological finding in both eyes. There was a physiological finding corresponding to age on the fundus of the right eye. A blunted papilla was evident on the fundus of the left eye, with haemorrhages at its edge and pronouncedly dilated and tortuous capillaries (fig. 1). Within the framework of differential diagnosis we in first place considered a prethrombotic state, also intraocular neuritis or anterior ischemia of the optic nerve.

The patient was acutely hospitalised at the inpatient department of our clinic. Upon admittance contraception was discontinued and following consultation with a haematologist a therapeutic dose of LMWH (low molecular weigh heparin) was applied. We administered Fraxiparine (Nadroparinum calcicum 9 500 IU in 1 ml solution) in a dose of 0.6 ml s.c. BID. We recommended that the patient stops smoking. After application of anticoagulation therapy there was a rapid improvement in the finding on the fundus, the oedema of the papilla of the optic nerve gradually subsided, haemorrhages attenuated and the dilation and tortuosity of the capillaries was reduced.

In order to exclude intraocular neuritis we conducted a VEP examination (the finding was within the norm). Within the framework of differential diagnosis we also considered presence of orbital expansion, for this reason a USG examination of the eye socket was conducted with a negative result. There was a physiological finding on the perimeter in both eyes.

The patient also underwent a brain MR in order to exclude demyelination disease and lumbar puncture in order to exclude neuroinfection. Both examinations were negative. Due to suspected thrombophilic disorder the patient underwent a haematological examination with a negative result. With regard to the prethrombotic state on the fundus, the patient underwent an X-ray of the chest area so that we could exclude pulmonary embolism.

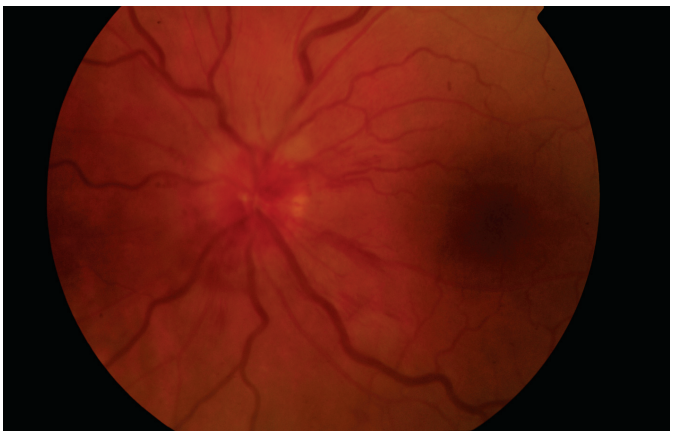

Fig. 1. Fundus of left eye upon initiation of treatment

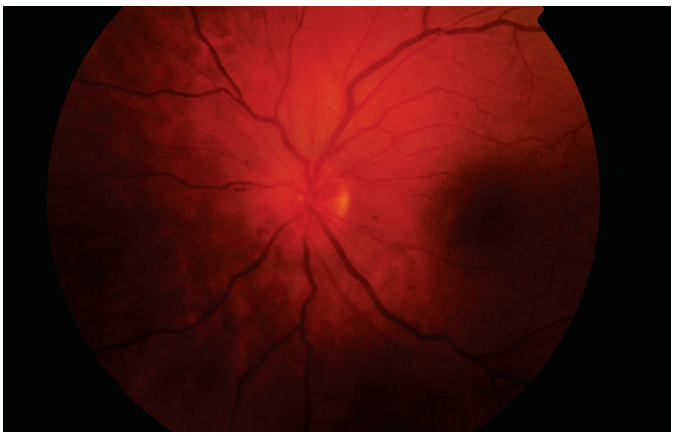

Fig. 2. Fundus of left eye upon discharge

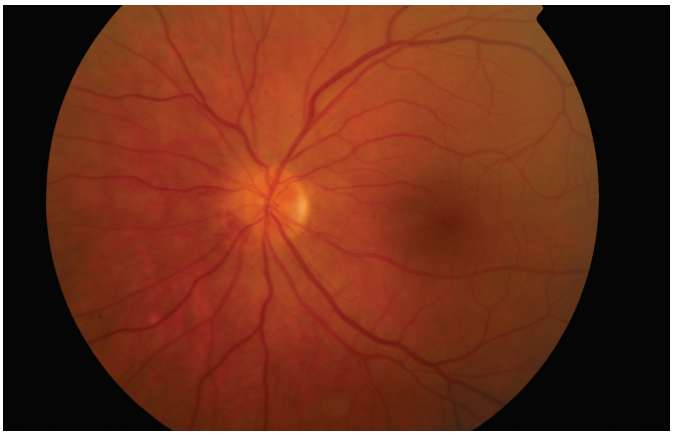

Fig. 3. Fundus of left eye after occurrence of the prethrombotic state

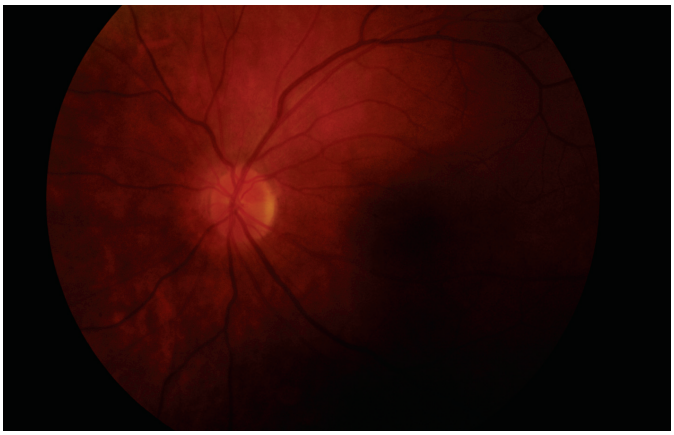

Fig. 4. Fundus of left eye 2 months after occurrence of the prethrombotic state

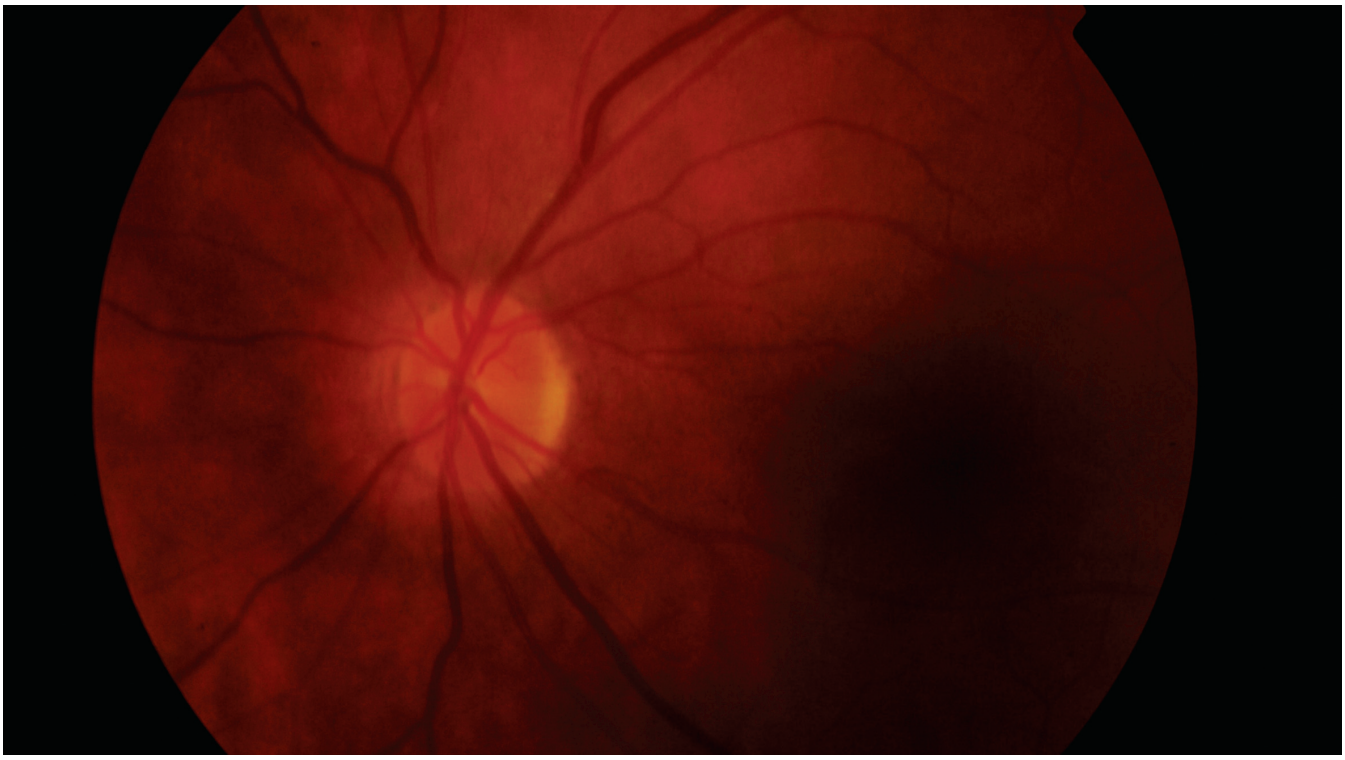

Fig. 5. Fundus of left eye 5 months after occurrence of the prethrombotic state

On the basis of the conducted examinations and with regard to the markedly improved finding following anticoagulation therapy, we concluded that the finding on the fundus of the left eye was a prethrombotic state. Upon discharge (after 7 days of anticoagulation treatment), VA in the left eye was 1.0, we observed a smaller oedema of the papilla on the fundus than upon admission, haemorrhages had subsided and dilation and tortuosity of veins had been reduced (fig. 2). The patient was further left on a therapeutic dose of LMWH (Fraxiparine 0.6 ml s.c. BID per day). The patient was further observed at our outpatient clinic, a further improvement of the finding on the fundus was evident (fig. 3). The dose of Fraxiparine 0.6 ml s.c. BID was continued for a further 20 days after discharge, then reduced to Fraxiparine 0.6 ml s.c. QD day for 10 days and subsequently the patient applied Fraxiparine 0.6 ml s.c. every other day for one month. At a check-up 2 months after the occurrence of the prethrombotic state, visual acuity of the left eye was 1.0 and there was a physiological finding on the fundus (fig. 4). This finding persisted also 5 months after the occurrence of the non-thrombotic state (fig. 5).

DISCUSSION

At present almost 40% of women in fertile age [3] use one of the available hormonal contraceptive preparations (HCP). A large quantity of oral contraceptives is used in clinical practice. Two types of preparations appear in practice: a combination of oestrogen and gestagen or only gestagens [3, 5]. Individual gestagens differ in various preparations, the oestrogenic component is ethinylestradiol or more recently, estradiol valerate [3, 13]. The contraceptive effect is induced by selective inhibition of the function of hypophysis, which leads to a suppression of ovulation. Combined preparations at the same time induce changes in the cervical mucus, the endometrium and in the motility and secretion of the oviducts. The latter changes play the main role in the action of the gestagens [5].

According to the dose of the oestrogen component, we classify HCP as preparations with a high dose (40 Kg of ethniylestradiol), with a low dose (30-37.5 µg) and a very low dose (15-20 µg of ethinylestradiol). Preparations with 15 µg are sometimes classified as preparations with an extremely low dose [3].

The preparation Diane 35, used by our patient contains cyproterone acetate, a gestagen with antiandrogenic activity. It is also used as a dermatological agent in the treatment of disorders conditioned by androgens in women (acne, seborrhea, milder forms of hirsutism, androgenic alopecia) [2, 13].

The mild undesirable effects of the use of HCP include nausea, mastalgia and headache; moderate undesirable effects include uterine bleeding from "penetration", increase in weight, increased skin pigmentation, and amenorrhea after discontinuation of administration of HCP. Serious undesirable effects include vascular disorders (thromboembolic disease, myocardial infarction and cerebrovascular disorders), gastrointestinal disorders and depression [2, 5].

Venous thromboembolism is a rare but potentially very serious complication of use of hormonal contraception. Hormonal contraceptives increase the risk of venous thromboembolis by almost 3-4x, and this risk increases in smokers, with age over 35 years or in obese women [13]. The risk of thromboembolism increases during the first month of use of contraceptives and thereafter remains constant. Within a month after the discontinuation of therapy the level of risk returns to the original values [5]. The incidence of thromboembolism upon use of HCP is linked only to the oestrogen content. During use of HCP there is a substantial reduction of antithrombin III, which is the main plasmatic thrombin inhibitor [5].

Kirwan et al. in their study investigate the relationship between use of hormonal contraception and retinal vein occlusion (RVO). In a population of 588 patients with RVO they recorded 6 patients who used HCP [9]. A study by Harhiu et al. retrospectively processed a population of 60 young patients with branch retinal vein occlusion (BRVO). Women represented 40% of this group (24 women). Of these women, 5 patients (8%, n = 60) [6] used hormonal contraception.

Opinions on the treatment of central occlusion are not constantly equivocal. Treatment may be medicamentous (antiaggregation therapy, rheology, antiocoagulation therapy), laser or surgical (PPV). Acetylsalicylic acid is used as an antiaggregant. Rheological drugs used in the treatment of CRVO include troxerutin or pentoxifylline. To date the effect of any of these preparations has not been confirmed by a large randomised double-blind study [11]. The approach to treatment of central retinal vein occlusion using anticoagulants is not unequivocal either. Except the patients with hypercoagulopathy, the majority of authors consider it to be of little effect, with a high risk of haemorrhaging complications [4, 11, 12].

Two studies have been published which observed anticoagulation therapy using LMWH in patients with acute form of CRVO. The study by Farahvash et al. evaluates 93 patients, of whom one group was treated for 20 days with dalteparin (100 IU/kg subcutaneously) and the second group with acetylsalicylic acid (100 mg/day). The observation period was 6 months. In the group of patients treated with dalteparin, the authors recorded an increase in BCVA by 5.5 ETDRS letters. In the group treated with acetylsalicylic acid the patients had a reduction of BCVA by 14 letters [4]. The second study published on this theme was by the authors Ageno and Catteneo et al. This was a multicentre randomised double-blind study. In all patients there was an interval between the onset of subjective complaints and the diagnosis of less than 15 days. One group of patients (30) received acetylsalicylic acid (ASA) in a dose of 100 mg per day for a period of 3 months, and another group of patients (28) were treated with a fixed dose of parnaparin (12 800 IU for a period of 7 days, subsequently 6 400 IU for 3 months). Functional deterioration was diagnosed in 20.7% of patients treated with parnaparin and in 59.4% of patients treated with acetylsalicylic acid. Recurrence of CRVO was observed in 3 patients treated with ASA. Haemorrhaging complications were identical in both groups [1].

In the Czech literature, Řehák deals with the issue of treatment of CRVO using anticoagulation (initial treatment by LMWH and subsequently with warfarin). He monitored a group of 24 patients, in 9 of whom a non-thrombotic state was diagnosed. Anticoagulation therapy with warfarin was administered to all patients, INR was maintained between 3-3.5. Patients were also treated with pentoxifylline and rutoside with ascorbic acid. In the group of prethromboses, visual acuity better than 6/18 was achieved in 89% of patients. The authors demonstrated that anticoagulation therapy substantially

reduces progression of the non-ischemic form of CRVO to the ischemic one. Their approach to treatment, i.e. timely application of anticoagulation in prethrombosis corresponds with our observations [12].

In January 2013 use of Diane 35 was prohibited in France. On the basis of an assessment of the available data from the French National Agency for Medicines and Health Products Safety ANSM, it was demonstrated that the risk of thromboembolism linked to the use of Diane 35 exceeds the benefits in the treatment of acne. Use of the drug in the indication of hormonal contraception is unsuitable according to ANSM [7].

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