Ablastic Improvement of Retinoblastoma Eyes Enucleation

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Abstract

Purpose: Increasing the ablaticity of retinoblastoma (RB) eyes enucleation by the new surgical technologies using high-frequency electric welding of biological tissues (HEWBT).

Materials and Methods: Primary enucleation was performed in 72 children (72 eyes) aged 2 - 84 mo (average 34.21 ± 20.11 mo) with monolateral RB T3-T4 stage. The surgery was carried out using the EK-300M1 and EKV Z-300 PATONMED devices and special instruments.

Results: Two methods of enucleation in advanced stage RB have been elaborated using the high-frequency electric welding (HEWBT) for optic nerve (ON) and its orbital part resection using “cutting” and “cutting + welding” modes. No bleeding, tissue edema and other complications were observed during the operation, which made possible to perform ON resection on maximal distance from the eye ball with perineural spaces welding, exclude the orbit tamponade and significantly reduced the surgery time. Intraorbital polytetrafluoroethylene implant of various sizes was implanted simultaneously after enucleation.

Histopathology revealed RB with optic nerve invasion in 22 eyes (30.5%), including: intralaminar - 15 (20.8%), retrolaminar - 5 (6.9%), surgical margin - 2 (2.8%), while in one case RB cells were also detected in the removed orbital ON fragment. Remote observations from 12 to 82 mo (ave 46.04 ± 18.07 mo) were followed in 47 children. There were no cases of orbital relapse, invasion into the brain and distant metastases, no deformities and cicatricial changes of the conjunctival cavity. All children demonstrated good cosmetic effect with regular prosthesis replacement.

Conclusion: The elaborated new methods of RB eyes enucleation using various modes of HEWBT for optic nerve cutting make the operation in cases of advanced RB safer, less traumatic and the most important, increased its ablaticity. The absence of any serious complications in children in the remote terms after enucleation (orbital relapse, cranial cavity spreading, distant metastasis) indicates the high efficiency of the applied methods of enucleation with the HEWBT impact on the ON.

Keywords: Retinoblastoma (RB); High-Frequency Electric Welding of Biological Tissues (HEWBT); Optic Nerve (ON)

Introduction

The only way to save the life of the child with advanced retinoblastoma (RB) is to enucleate the eye affected by tumor. The frequency of primary enucleation worldwide ranges from 10 to 95% [1,24,34]: in unilateral RB - 66 - 91%, in bilateral - 17 - 43% [24,27,29].

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Basic requirements for RB eyes enucleation are:

- Intervention ablasticity which provides preservation of eyeball integrity, optic nerve (ON) resection at the maximum distance from the eyeball, minimizing bleeding and externalization of RB cells;
- Histopathology of the enucleated eye to determine the presence of invasion and their spread.

RB cells spread more often at the ON - 29 - 56% [2,5,8,14,24,27,30]. The survival prognosis for the child depends on the level of ON invasion. Only 31% of children with RB cells spread beyond the lamina cribrosa and 25% with tumor elements presence along the line of the ON surgical incision survive 5 years [12]. There are also the hematogenous pathway for tumor metastases spread - through the blood vessels when the tumor invades the choroid, at bleeding and pressure on the eyeball during enucleation.

Therefore at the RB eye enucleation the especial importance is attached to cut off the ON from the eyeball as far as possible and to minimize bleeding from a.ophthalmica.

Purpose of the Study

Increasing the ablasticity of RB eyes enucleation by the new surgical technologies using high-frequency electric welding of biological tissues (HEWBT).

Materials and Methods

Primary enucleation was performed in 72 children (72 eyes) aged 2 - 84 mo (average 34.21 ± 20.11 months) with monolateral RB of T3-T4 stage by TNM-classification (WHO, 1982). The surgery was carried out using special PATONMED devices EK-300M1 and EKV Z-300 with the set of electric welding tools, developed at the Institute of electric welding by E.O. Paton (Kyiv, Ukraine) (Figure 1). These devices are automated electric welding complex. The alternating voltage with a frequency of 66 kHz is generated at the device outlet. Voltage amplitude up to 200V, amperage up to 0.3A, impact exposition up to 3 seconds. Maximum output power up to 350 watts. The HEWBT principle is based on the coagulation transformation of the tissue being welded under the influence of high frequency current. The different regimens were used: "cutting" mode (amperage 1.5A, voltage 200V, power 350W, frequency 66 kHz, exposure up to 3 seconds) and "welding" mode (amperage up to 0.3A, voltage 40 - 60V, frequency 66 kHz, exposure up to 3 seconds). The histopathology were performed of the enucleated eyes. Remote follow up were in 47 children at the terms from 12 to 82 mo (46.04 ± 18.07 mo on average).

![Image of PATONMED device EK-300M1](image_url)

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Results

Two methods of RB advanced stages eyes enucleation using the method of HEWBT were elaborated at the Pediatric Ophthalmopathology Department of the Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine.

Method 1: The difference from classic enucleation methods consist at the section of the ON, which performed at the possible distance from the posterior pole of the eye globe by special tool using the HEWBT device in the “cutting” mode (Figure 2), with additional resection of orbital ON fragment using the same instrument at the same “cutting” mode (Figure 3A and 3B) [23].

Method 2: Enucleation in RB eyes with a high risk of the ON invasion. The improvement consist in the usage of two regimen of HEWBT during ON section: before cutting of the ON and additional orbital ON fragment performed “welding” mode HEWBT, after that by the same tool the section in the “cutting” mode instantly makes. Additionally, the ON stump remaining in the orbit is affected by the “welding” mode HEWBT [7].

The HEWBT method utilization during the operation allowed to carry out bloodless during operation, ON cutting at the maximum possible distance (10 mm) from the eye globe, visualize the orbital tissues, additionally cut off an orbital ON fragment (10 mm); together it consist of 20 mm, thereby increasing the likelihood of tumor removal within healthy tissues and preventing the continued growth of RB at the ON and perineural spaces into the brain. At the combined utilization of 2 modes of HEWBT increase the extension of the high-frequency current coagulation effect, both on the removing ON orbital fragment and on its remainder in the orbit. Simultaneously the perineural spaces of the ON are welded. Usage of two HEWBT regimens, increase the length of “dry” necrosis of ON tissue [4], which, in turn, provides additional prevention of tumor spread by the ON into the cranial cavity. All this manoeuvres increase the treatment effectiveness and survival of children in cases with RB increased risk of tumor dissemination.

No bleeding, tissue edema, hematomas and other complications were observed during the operation (Figure 4). This allowed to exclude orbital tamponade and significantly reduce the time of surgical intervention. During the operation after eyeball removal, the loco-motor stump was formed using orbital polytetrafluoroethylene implant “Ekoflon” of various sizes. No complications were noted at the postoperative period, healing occurred by primary intention and good cosmetic effect were achieved.

![Figure 4: Orbital cavity after the eye and optic nerve fragment removal using HEWBT. No bleeding and tissue edema.](image)

60 eyes with RB were enucleated using the first method and 12 eyes with high-risk RB, using the second method. The indications for second method of enucleation were the following clinical signs, testifying the possibility of a high-risk ON invasion: large tumor sizes - H

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≥ 10.3 and L ≥ 16 mm (95.6%), completely covering the optic disc, secondary high total retinal detachment (31.2%), anterior segment lesion (60%), secondary glaucoma (53.3%) [5].

The histopathology of enucleated eyes in all cases verified the RB diagnosis with the invasion presence in 42 cases (58.3%) (Table 1). The tumor cells invasion of the ON were observed in 22 eyes (30.5%), including: intralaminar - 15 (20.8%), retrolaminar - 5 (6.9%), surgical margin - 2 (2.8%), while in one case RB cells were also detected in the removed orbital ON fragment. Choroid invasion was noted in 23 eyes (31.9%), in episclera - 8 eyes (11.1%). Mixed invasion at the ON and other eye structures - 12 (16.7%). In cases of invasive RB growth, intravenous chemoreduction (CEV-protocol) and/or external-beam radiotherapy were prescribed for prophylactic purposes, depending on the level and extent of the invasion.

<table>
<thead>
<tr>
<th>Optic nerve and eye covers invasion</th>
<th>Intra-</th>
<th>Retrolami</th>
<th>Surgical</th>
<th>Fragment</th>
<th>Choroid</th>
<th>Sclera</th>
<th>Mixt</th>
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<tbody>
<tr>
<td>Absent</td>
<td>30</td>
<td>15</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>23</td>
<td>8</td>
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<tr>
<td>n (eyes’ number)</td>
<td>41.7</td>
<td>20.8</td>
<td>6.9</td>
<td>2.8</td>
<td>1.4</td>
<td>31.9</td>
<td>11.1</td>
</tr>
</tbody>
</table>

Table 1

In the follow up period 12-82 mo (ave 46 ± 18 mo), there were no cases of tumor growth orbital relapse, invasion into the brain and distant metastases. No deformities and cicatricial changes of the conjunctival cavity were observed. All children demonstrated good cosmetic effect with regular prosthesis replacement.

Clinical case

Child N., 12 mo/o, was admitted to the Filatov Institute Pediatric Ophthalmology Department on 03.24.2016 with right eye (RE) leukocoria (Figure 5). Visual acuity - light perception, LE - 0.4 according Teller cards. Examination under general anesthesia was performed. RE – cornea is transparent, iris vascularization, mild anterior chamber, slight pupil photoreaction, transparent the lens; total secondary retinal detachment with tumor focuses under it. Normal IOP on both eye. US B-scan RE – big medium and high acoustics density (with calcifications) formation on the papilla opticus and downwards, occupied all vitreous cavity height - 11.0 mm; basic length 17.0 x 17.5 mm (Figure 6).

Figure 5: Child N. Diagnosis RE - monolateral retinoblastoma T3bN0M0, secondary retinal detachment at primary visit.
Diagnosis RE - monolateral retinoblastoma T3bN0M0, secondary retinal detachment; LE - mild hyperopia.

RE enucleation according to the developed technique was performed. The ON was transected by HEWBT in "cutting" regimen at 10 mm distance from the eyeball. Macroscopically the ON was not changed. No bleeding from a. ophthalmica and no tissue edema made it possible to visualize the orbital part of the ON and to perform an additional resection of a 10 mm long its fragment (Figure 7A and 7B). The operation and the postop were without complications, hematomas, orbital tissue edema.
Enucleated eye histopathology: Nondifferentiated RB type with intralaminar ON invasion (Figure 8), Bruch's membrane implantation without choroidal invasion - pT4aN0M0. External beam radiotherapy SD 20gr and 3 chemoreduction courses were performed.
Follow up 60 mo. The last examination was on March 2021. No orbital tumor relapse, progressive growth into the brain and metastasis were observed. No cicatrical changes, deformities of the conjunctival cavity were observed. The child has achieved a good cosmetic effect with regular prosthesis changes (Figure 9A and 9B).

Figure 9: A) Child N. 5y after enucleation, RE - anophthalmos after retinoblastoma T4a eye enucleation with “Ekoflon” implantation and prosthesis; B) Conjunctival cavity after enucleation.

The clinical example demonstrates the effectiveness of the developed enucleation technique in case of advanced RB. Due to neurovascular bundle of the ON section using the HEWBT methods, the bleeding from a. ophtalmica was prevented, the ON was cutted at the maximum possible (10 mm) distance from the eyeball and the orbital part fragment of the ON was additionally excised for 10 mm, which made possible to remove 20 mm of ON within healthy tissues and increase the intervention ablasicity.

Discussion

Despite the significant progress in development of the new methods of RB examination and salvage treatment over the past 20 years, in the most cases of primary visit the advanced T3-T4 by TNM-classification - (D-E) stages (according to the International Intraocular Retinoblastoma Classification (IIRC), 2006) of the disease are diagnosed [1,24,27,29,32]. Because of that fact the primary enucleation to preserve the child's life are recommended. Enucleation, as noted by some authors [18,20] is the first line therapy for most eyes with RB worldwide. As most children without RB family history at the time of primary diagnosis have a disease of group D or E, and more than 50% have unilateral RB, a complete recovery can be achieved after enucleation. According to Dimaras., et al [9], to save the eye in case of A-C tumor stage succeeds in 90% or more cases, in group D - only in half of the patients, and in group E - most eyes require enucleation because they, by definition, carry the risk of extraocular spread, which may be confirmed only by identifying high-risk pathological features at the enucleated eye.

However, eyeball removal is not a guarantee of getting rid of the tumor process, since, according to histopathology, extraocular spread (invasion of the ON, choroid, sclera, anterior chamber, iris, ciliary body, as well as extrabulbar tumor growth) are found in 18 - 53% of cases [6,11,13,14]. More often, RB cells invade the ON - in 29 - 56%, including retrolaminar invasion - 30.5% - 71.5% and to the level of resection - 0.3 - 23% [2,6,8,14,27,30], which poses a serious threat to the child's life. If at the histopathology the RB cells are detected at the level of ON resection - this means that they persist in the ON stump remaining in the orbit, which is danger for the tumor dissemination and leads to mortality, according to different authors up to 50-81%. Retrolaminar invasion, where the meningeal membrane starts, is the another important risk factor for metastatic RB development with a reported mortality rate of 13 - 69% [15,16,17,19,30]. In some cases the post-op systemic chemotherapy reduces the lethality to 9.1% [25]. In the same time successful enucleation with ON cutting above the tumor spread level provides the survival rate more than 95% [17,26,33]. Thereby, the level of ON section at the course of enucleation get the particular importance.

Various tools and techniques have been proposed with the aim of ON cutting at the maximum distance from the eyeball and bleeding from a.ophthalmica reduction [8,10,28,31], but they have a number of disadvantages.

For the first time in ophthalmology for the enucleation of eyes with uveal melanoma the technology of high-frequency electric welding of biological tissues (HEWBT), developed in Ukraine at the Filatov Institute of Eye Diseases and Tissue Therapy together with the Institute of Electric Welding named after E.O. Paton was proposed [21,22], which we took as a basis for developing a new methods for RB eyes enucleation.

Previously at the experiment of rabbits eyeball enucleation was carried out different modes of HEWBT influence regime - "cutting" and "welding + cutting" for ON section with subsequent histopathological and ultrastructural examination [3,4]. It has been shown that the usage of the HEWBT method for neurovascular bundle of the ON cutting the both in the "cutting" and "welding + cutting" modes leads to the "dry" necrosis development of the ON parenchyma and ON sheaths not only at the site exposed by high-frequency electric current, but also at the distance from it. The length of it depends on the type of regime. Using the HEWBT in the "welding + cutting" mode causes necrosis up to 3 - 4 mm wide in both directions from the site of exposure, increasing up to the 7th day after the operation, which is 2 times higher than the length of necrosis after HEWBT exposure only in the "cutting" mode (about 1 - 2 mm). The phenomena of degeneration and gliosis of the ON in group II ("welding + cutting") spread over a greater distance than in group 1 ("cutting"), reaching the ON head and the sensory part of the retina. The obtained experimental data formed the basis for the development of previously described two methods of enucleation, which have significant advantages over the classical methods. The invented method allow to perform ON cutting at the distance 10 mm or more from the eyeball with additional resection of it orbital fragment up to 10 mm - common about 20 mm length with the absence of bleeding from a.ophthalmica ("dry enucleation"), to increase the length of coagulation necrosis and weld intershell spaces of the ON, reduce the duration and damage of the surgery. This promotes to prevent the RB cells proliferation along the ON and
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hematogenously, hinders the tumor recurrence development in the orbit, continued growth into the cranial cavity and hematogenous RB metastasis, which, in turn, increases the ablasticity of the operation and the survival rate of children with RB.

Conclusion

The utilization of the elaborated new methods RB eyes enucleation using various modes of high-frequency electric welding of biological tissues for ON cutting makes the operation in cases of advanced RB stage safer, less traumatic and, which is most important, increased its ablasticity. The absence of any serious complications in children in the remote terms after enucleation (orbit tumor recurrence, at the cranial cavity spreading, distant metastasis) indicates the high efficiency of the applied methods of enucleation with the HEWBT impact on the ON.

Disclosure

The authors certify that they have no conflicts of financial interest in related instruments or techniques.

Bibliography


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