Jurnal Oftalmologi 2021, Vol. 3, No. 3.
E-ISSN.2541-4283

Characteristics of Retinoblastoma Patients Treated with Transpupillary Thermotherapy from January – December 2020 in Cicendo National Eye Hospital

Annisa Rahayu[1,2], Grimaldi Ihsan[1,2], Made Indra[1,2], , Erwin Iskandar[1,2], Primawita O. Amiruddin[1,2], Arief S. Kartasasmita[1,2], Rova Virgana[1,2]
[1]Pusat Mata Nasional, Rumah Sakit Mata Cicendo, Bandung
[2]Departemen Ilmu Kesehatan Mata, Fakultas Kedokteran Universitas Padjajaran, Bandung
**Korespondensi: Annisa Rahayu, annisarahayuannisa@gmail.com*

ABSTRACT
Introduction: Treatments for retinoblastoma were aimed to preserve the globe and saving the vision. Transpupillary thermotherapy (TTT) has been used to treat several type of small or medium sized tumor, including retinoblastoma.
Purpose: To describe the TTT laser properties for retinoblastoma tumor.
Methods: Retrospective method was selected from the medical records. Total sampling data were collected from the patients with diagnosis of retinoblastoma who underwent examination under anasthesia and transpupillary thermotherapy laser in Cicendo National Eye Hospital from January to December 2020. The data collected consist of the demographic information, retinoblastoma tumor characteristics, and TTT laser properties.
Results: There was eleven eyes from ten patients who underwent TTT session in Cicendo National Eye Hospital from January until December 2020. Majority was male patients with mean age at diagnosis 16.3 ± 17.01 months and mean TTT session 3.54 ± 1.36 for each eye. The mean total laser that applied in every session were 169.25 ± 241.21 times, with mean power 941.35 ± 1894.16 mW, and mean time exposure 1392.89 ± 1349.09 ms. All of the patients were on chemotherapy systemic treatment, with mean frequency 12.2. Ninety percent patients showed regression of the tumor.
Conclusion: Majority of the patients retinoblastoma who treated with TTT were male, bilateral tumor, with mean TTT session 3.54 for each eye. All of the patients treated with systemic chemotherapy. Majority of the eye in this study showed tumor regression.
Keywords: chemotherapy, laser therapy, eye tumor.

INTRODUCTION

Retinoblastoma is the most common primary intraocular malignancy of childhood. Incidence for retinoblastoma approximately 1 in 18.000 live birth worldwide, with mortality 3000 children every year. Mutation in one RB1 allele is constitutional in hereditary bilateral retinoblastoma, whereas somatic mutation in the both allele will rise to the non hereditary unilateral retinoblastoma. The primary goal of treating retinoblastoma is to save the life, followed by preservation of the globe and save the vision. Treatment options consist of chemotherapy, enucleation of the globe, focal treatment with transpupillary thermotherapy, laser photocoagulation, cryotherapy, plaque brachyterapy, external beam radiotherapy, and local chemotherapy. [1-4]

Transpupillary thermotherapy (TTT) has been used to treat several type of small or medium sized tumor. TTT was first used as retinoblastoma treatment by Lagendijk in 1982 using a microwave applicator to deliver whole eye hyperthermia. Laser TTT acts in a subthreshold manner by raising the choroidal temperature slightly, minimizing thermal damage to the RPE and overlying retina. Infrared laser 810 nm is used with beam size 0.8 mm to 3.0 mm, power settings between 250 mW and 750 mW, with 1-minute exposure time.[5,6]

There was no documentation and guidelines about laser TTT properties including power and duration applied for

retinoblastoma cases in Cicendo National Eye Hospital. The purpose of this study is to describe the TTT laser properties that had been applied to treat retinoblastoma tumor in Cicendo National Eye Hospital from January – December 2020.

METHODS

Retrospective method was selected from the medical records using International Classification of Diseases (ICD)-10 and ICD-9. Total sampling data were collected from the patients with diagnosis of retinoblastoma (ICD-10 code C69.2) who underwent examination under anasthesia (EUA) (ICD-9 code 95.04) and transpupillary thermotherapy laser (ICD-9 code 14.54 and 14.34) in Cicendo National Eye Hospital from January to December 2020.

The clinical information of the patients were collected from the medical records including the demographic information, retinoblastoma tumor characteristics, and TTT laser properties. Demographic data consist of gender, age at the first time of diagnosis, diagnosis of retinoblastoma at the first time and last time of admission. Retinoblastoma tumor characteristics including laterality of the eye tumor, number of tumors, size of tumor at the first and last examination, feeding vessels and calcification of the tumor, regression of the tumor, and atrophic scar formation. Laser TTT characteristic in this study including number of TTT procedures for each eye, total laser applies, power and time exposure applied.

The exclusion criteria were incomplete medical records and the eye with retinoblastoma who underwent enucleation at the first time of examination under anasthesia. Data were presented in tables and calculated with Microsoft Office Excel 2016.

RESULTS

Eleven eyes from ten patients were included in this study, whereas another nine eyes were planned to undergo enucleation at the first time of visit. The ratio between male and female patients were 9:1. The mean age at the first time of retinoblastoma diagnosis was 16.3 ± 17.01 months. Ninety percent patients had bilateral retinoblastoma, and ten percent unilateral retinoblastoma. Nine patients (90%) underwent unilateral TTT procedure, whereas one patient (10%) had TTT for both eyes. Characteristics of the patients in this study are recorded in Table 1.

Table 1. Characteristics of the patients

Variables	n	%
Number of patients	10	
Number of eyes	11	
Gender		
Male	9	90%
Female	1	10%
Age first diagnosed		
Mean (months)	16.3 ± 17.01	
Laterality of tumor		
Bilateral	9	90%
Unilateral	1	10%
Laterality of TTT		
Bilateral	1	10%
Unilateral	9	90%
Laterality of TTT		
Right eye	8	72%
Left eye	3	28%
Retinoblastoma Classification (at the first of admission)		
Grade A	1	9.1%
Grade B	2	18.2%
Grade C	6	54.5%
Grade D	2	18.2%
Retinoblastoma Classification (at the last follow up)		
Grade A	0	0%
Grade B	2	18.2%
Grade C	7	63.6%
Grade D	1	9.1%
Grade E	1	9.1%
Chemotherapy		
Yes	10	100%
No	0	0%

The retinoblastoma diagnosis classification at the first time of admission

and the last follow up also recorded, based on International Classification of Retinoblastoma. Grade A are for small intraretinal tumors less than 3 mm and away from foveola and disc. Grade B are tumors more than 3 mm in macular or juxtapapillary location, or with subretinal fluid. Grade C are tumors with focal subretinal or vitreous seeding within 3 mm of tumor. Grade D are tumors with diffuse subretinal vitreous seeding more than 3 mm from tumor. Grade E is for Extensive retinoblastoma occupying >50% of the globe with or without neovascular glaucoma, hemorrhage, extension of tumor to optic nerve or anterior chamber. At the first time of admission, 9.1%, 18.2%, 54.5% and 18.2% eyes were classified into grade A, grade B, grade C and grade D respectively. At the last follow up, 18.2%, 63.6%, 9.1% and 9.1% eyes were classified into grade B, grade C, grade D and grade E retinoblastoma. All of the patients underwent systemic chemotherapy, with the mean chemotherapy frequency was 12.2 times.

There were total 39 TTT procedure in 2020 that had been done in 11 eyes from 10 patients. Data of the tumor characteristics and TTT properties are summarized in Table 2. The mean of number of tumor mass in every eye were 2.44 ± 1.78 tumors. The mean size of the tumor at the first time of examination was 5.35 ± 3.51 in disc diameter (DD) or 420.90 ± 214.02 µm. After undergo several TTT procedures and several dosage of systemic chemotherapy, the mean size of tumor at the last examination under anasthesia (EUA) were 3.00 ± 2.78 DD or 288.10 ± 163.39 µm.

Data of TTT properties that were recorded in the medical records including times, power, and also time exposure in every laser session. The mean TTT procedure for each eye were 3.54 ± 1.36 times. The mean total laser that applied in every session were 169.25 ± 241.21 times, with mean power 941.35 ± 1894.16 mW, and mean time exposure 1392.89 ± 1349.09 ms. Scar are formed in all of the eyes in this study with the partial regression occured in nine eye, total regression in one eye, whereas one eyes not showed any regression yet. Four eyes in this study record the regression type of the tumor, two patients had regression type II and two eyes had regression type IV. One eye from the study was enucleated after 3 session of TTT, before enucleation the patient showed tumor regression type II.

Table 2. Characteristics of Tumors and TTT Laser Properties.

Variables	n	%
Number of tumors	2.44 ± 1.78	
Size of tumor (DD)		
First examination	5.35 ± 3.51	
Last examination	3.00 ± 2.78	
Size of tumor (µm)		
First examination	420.90 ± 214.02	
Last examination	288.10 ± 163.39	
TTT sessions/eye	3.54 ± 1.36	
TTT characteristics		
Times	169.25 ± 241.21	
Power (mW)	941.35 ± 1894.16	
Time exposure (ms)	1392.89 ± 1349.09	
Scar formation	11	100%
Regression		
Not regressed yet	1	9.1%
Partial regressed	9	81.8%
Total regressed	1	9.1%

DISCUSSIONS

There were total 11 eyes from 10 patients that were included in this study with male to female ratio was 9:1. The ratio between male and female in this study showed difference with other study. Epidemiology study in Taiwan showed male to female ratio for retinoblastoma patients were 6:4. Golda et al showed that in Indonesia there was an equal incidence between male and female patients. The mean age at the first time of diagnosis in this study were 16.3 ± 17.01 months. Abramsom et all showed that the mean age

at diagnosis was 3 months with median 2 months. Golda et al showed 53.8% patients mean age at diagnosis of retinoblastoma was 3-5 years, whereas Su Li et al found that majority of cases appeared by 5 years old of age and 68.2% of them showed at 2 years of age. Ninety percent patients in this study had bilateral disease and only one patient had unilateral tumor. Study of Abramsom et al from 24 patients revealed that all of the patients had bilateral disease.[5,7,8]

The mean initial tumor base in this study was 5.35 ± 3.51 DD or 420.90 ± 214.02 µm. This size of tumor quite larger compared to another study. Abramsom et al study showed the mean initial tumor size before TTT session was 0.67 DD with range of 0.1-1.5 DD. In recent years, TTT has become widely used for small to medium sized retinoblastoma. In Shields study, thermotherapy is used for relatively small retinoblastomas without associated vitreous or subretinal seeds. Smaller tumor <3.0 mm at initial base showed 85.6% regression in 12 months follow up. Larger tumor > 3.0 mm base required greater energy and time than did small tumor. [5,9]

Transpupillary thermotherapy aim is to deliver the heat directly to the tumor using 810 nm infrared laser. The temperature will rise between 45 until 60 C, below the coagulative threshold and spare coagulation of retinal vessels. The heat itself has cytotoxic effects to the tumor and induced alteration to micro- environment of the tumor, heat shock protein expression, apoptosis induction and regulation, signal transduction, drug resistance modulaton and carboplatin uptake increase into tumor cell above 44 C. Chawla et al found that laser power should start at 200 mW and increased or decreased at 50 mW increments, until an adequate, slow-onset take is observed in the mass. Power and time exposure of this study showed a huge variability with mean power applied 941.35 ± 1894.16 mW and mean time exposure 1392.89 ± 1349.09 ms. Power and time exposure of TTT that will be used in Cicendo National Eye Hospital should be agreed to gain an uniformity of procedure.[1,6,9]

All of patients in this study were treated with chemotherapy systemic regiments. Shields 2005 performed a prospective non-randomised study in which 28 of 68 tumours were treated by means of systemic chemotherapy alone and 40 of 68 were treated with chemotherapy combined with foveal-sparing TTT. The study findings indicated that recurrence in the group that received chemotherapy alone occurred in 35% of tumours at four years follow-up versus 17% in the combined treatment group. In support of the combined use of TTT and chemotherapy, not only the insufficient role of chemotherapy alone is stated but also the beneficial interaction of heat energy and chemotherapy.[2,10]

Majority of the patients of this study (90.9%) showed regression of the tumor. From medical records, not all of the patients recorded the regression type of retinoblastoma. Four eyes in this study record the regression type of the tumor, two patients had regression type II and two eyes had regression type IV. Regression pattern of retinoblastoma are divided into four types, type 0 no visible remnant, type 1 completely calcified remnant, type 2 completely noncalcified remnant, type 3 partially calcified remnant, and type 4 atrophic chorioretinal flat scar.[1,2]

Limitations of this study are a huge variability of TTT power and time duration that applied to the tumor mass. A further agreement of power and duration of the tumor should be made. Not all the medical record recorded the regression type of the tumor, only four eyes from eleven eyes mentioned the regression type of the tumor. Further analytical study compared between TTT procedure combined with

chemotherapy and chemotherapy alone are needed.

CONCLUSIONS

This study was underwent to assess the characteristic of TTT laser procedure for retinoblastoma patients in our centre. We can conclude that all of TTT procedure in this study was combined with systemic chemotherapy and majority of the eye showed regression process of the tumor. The mean tumor size that included in this study are relatively larger than other studies, therefore further study are needed to assess the TTT alone in small sized or initial retinoblastoma.

Conflict of Interest: There was no conflict of interest in this study

REFERENCES

1. Chawla B, Jain A, Azad R. Review Article Conservative treatment modalities in retinoblastoma Classification System for Retinoblastoma. Indian J Ophthalmol. 2012;61(9):479–85.
2. Id F, Kp J, Aw S, Ms S, Ma R. Focal laser treatment in addition to chemotherapy for retinoblastoma (Review). Cochrane Database Syst Rev. 2017;(6):1–18.
3. Cantor LB, Rapuano CJ, Cioffi GA. Pediatric Ophthalmology and Strabismus. In: Basic and Clinical Science Course. San Fransisco: American Academy of Ophthalmology; 2016. p. 48–56.
4. Liu Y, Zhang X, Liu F, Wang K. Clinical Efficacy and Prognostic Factors of Chemoreduction Combined with Topical Treatment for Advanced Intraocular Retinoblastoma. Asian Pacific J Cancer Prev. 2014;15(18):7805–9.
5. Abramson DH, Schefler AC. Transpupillary Thermotherapy as Initial Treatment for Small Intraocular. Opthalmology. 2004;111(5):984–91.
6. Cantor LB, Rapuano CJ, McCannel CA. Retina and Vitreous. In: Basic and Clinical Science Course. San Fransisco: American Academy of Ophthalmology; 2020. p. 380.
7. Miranda GA, Simanjuntak GWS. Clinical Findings and Demography of Retinoblastoma in a Tertiary Hospital in a Remote Area in a Developing Country. Asia Pacific J Cancer Care. 2018;3(2):37–41.
8. Li S, Chen SC, Tsai C, Sheu S, Yeh J, Tsai C. Incidence and survival of retinoblastoma in Taiwan : a nationwide population-based study 1998 – 2011. Br Med J. 2016;100:839–42.
9. Shields CL, Santos MCM, Diniz W, Thermotherapy Retinoblastoma. Ophthalmol. 1999;117:885– 93.
10. Shields CL, Mashayekhi A, Cater J, Shelil A, Ness S, Meadows AT, et al. Macular Retinoblastoma Managed With Chemoreduction. Arch Ophthalmol. 2005;123:765– 73.