Visual Prognostic Value of Ocular Electrophysiology Tests in Corneal Transplantation

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Objective: *To determine visual prognostic value of electrophysiologic tests in unilateral-eye-disease patients who underwent corneal transplantation.*

Material and Method: *Retrospective charts of the patients who underwent unilateral optical penetrating keratoplasty at Siriraj Hospital from September 2003-June 2009 were reviewed. The amplitude of a-wave and b-wave in dark-adapted bright flash ERG and the amplitude of major positivity (P2) in flash VEP were recorded and compared with the good fellow eye. Area under receiver operating characteristic curve (AUC) was used to determine the best predictor of good visual prognosis. Positive predictive value (PPV) and negative predictive value (NPV) were used to determine the accuracy of the tests.*

Results: *Thirty-nine patients were included. The present study showed that a-wave amplitude was a good predictor (AUC = 0.83). For a-wave amplitude that was equal to or more than 80% and P2 amplitude that was equal to or more than 67%, PPV was 95.65%.*

Conclusion: *The a-wave amplitude and P2 amplitude predict good visual outcome most accurately when changing less than 20% and 33%, respectively, compared to the normal fellow eye.*

Keywords: *Electrophysiologic test, Corneal transplantation*

J Med Assoc Thai 2012; 95 (Suppl. 4): S50-S55
Full text. e-Journal: *http://www.jmat.mat.or.th*

Preoperative clinical evaluation of visual potential after corneal transplantation in the patient with dense corneal opacity remains difficult using only history and biomicroscopic examination. Some studies found that electrophysiologic tests were good predictors of visual prognosis prior to corneal transplantation in as high as 71-92% of cases[1,2]. In the present study, full-field electroretinography (ERG) and flash visual evoked potential (VEP) were used as predictors for visual prognosis prior to corneal transplantation.

Material and Method

The authors reviewed charts of the patients who underwent penetrating keratoplasty (PKP) for optical indication at Siriraj Hospital from September 2003-June 2009. Only the patients that had unilateral PKP and normal fellow eye were included in the present study. The present study was approved by Siriraj Institutional Review Board (SIRB). Demographic data (age, sex), preoperative diagnosis, preoperative best-corrected visual acuity (BCVA), operative procedure and postoperative BCVA were recorded for each patient. The amplitude of a-wave and b-wave in dark-adapted bright flash ERG and the amplitude of major positivity (P2) in flash VEP in both eyes were recorded. The results of normal fellow eye were used as a normal value for each patient. Postoperative BCVA was divided into 2 groups. As in a previous study by Wendel et al[1], if postoperative BCVA was equal to or better than 6/24, it was classified as good visual acuity and if postoperative BCVA was less than 6/24, it was classified as poor visual acuity. This BCVA was used as a cut-off point because it was the vision that was better than low vision definition. Mean, standard deviation (SD), median, range, number and percentage were used to describe demographic data. Area under the receiver operating characteristic curve (AUC) was used to determine the best predictor of good visual prognosis after corneal transplantation. Positive predictive value

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(PPV) and negative predictive value (NPV) were used to determine the accuracy of the tests.

Results

Forty-nine charts of the patients who had undergone PKP were reviewed, only 39 patients (23 males, 16 females) with the mean age of 59.38 years (range 12 to 89 years) were included (Table 1). Preoperative diagnosis were corneal decom-pensation (15 cases), bullous keratopathy (9 cases), corneal scar (9 cases), graft rejection (3 cases), lattice dystrophy (2 cases) and ICE syndrome (1 case) (Table 2). Operative procedures included simple PKP, PKP with extracapsular cataract extraction with intraocular lens (IOL) implantation and PKP with scleral fixation IOL.

Preoperative BCVA ranged from hand motion to 6/24 and postoperative BCVA ranged from light perception to 6/6 (Fig. 1). Thirty-two patients (82.1%) achieved good visual acuity with a mean follow-up period of 14.18 months (range 1 to 61 months).

The present study compared among a-wave amplitude in dark-adapted bright flash ERG (a-wave amplitude), b-wave amplitude in dark-adapted bright flash ERG (b-wave amplitude), P2 amplitude in flash VEP (P2 amplitude) to determine postoperative visual acuity, the cut-off point of these waves that would make the best sensitivity and specificity were as follows:

A-wave amplitude > 79.79 gave sensitivity 0.75 and specificity 0.867.

P2 amplitude > 73.70 gave sensitivity 0.688 and specificity 0.867.

B-wave amplitude > 93.19 gave sensitivity 0.656 and specificity 0.724.

Then AUC was used to estimate magnitude of each parameter a-wave amplitude, b-wave amplitude, P2 amplitude to predict the visual prognosis after corneal transplantation. The present study found that a-wave amplitude was a good predictor (AUC = 0.83) while P2 amplitude and b-wave amplitude were fair predictors with AUC 0.75 and 0.72, respectively (Fig. 2).

Although a-wave amplitude was the best predictor of good visual prognosis, a-wave amplitude still represented the response of photoreceptor cells of the whole retina, except the macular area which is the most important area for sharp vision. Then the present study used the P2 amplitude, which reflects macular function in cooperation with a-wave amplitude as a predictor of visual outcome. PPV and NPV from the combination of changing of a-wave amplitude and P2 amplitude by dividing changing of P2 amplitude into 2 groups: P2 amplitude that was equal to or more than 67% and P2 amplitude that was less than 67% when

Table 1. Dermographic data

Variable	n = 39
Male	23 (59%)
Age	
Mean (± SD)	59.38 (± 18.8)
Median (min, max)	65 (12,89)
Preoperative BCVA	
≥ 6/24	1 (2.6%)
< 6/24	38 (97.4%)
Postoperative BCVA	
≥ 6/24	32 (82.1%)
< 6/24	7 (17.9%)

BCVA = Best-corrected visual acuity

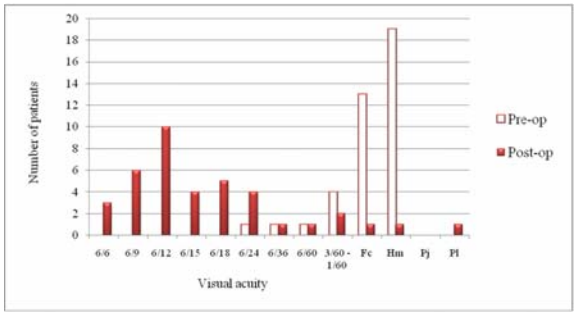

Fig. 1 Preoperative and postoperative best-corrected visual acuity (BCVA) and number of patients

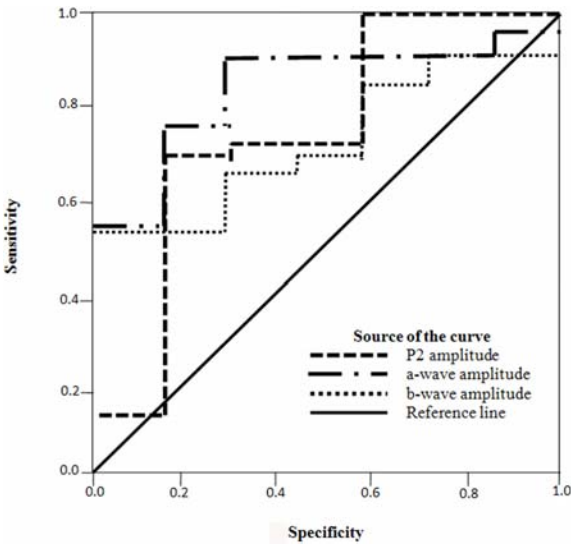

Fig. 2 Receiver operating characteristics (ROC) curve of predictor

Table 2. Patients data

Case	Age	Sex	Diagnosis	Preoperative BCVA	Postoperative BCVA	Dark-adapted ERG		Flash VEP
						Change of a amplitude[a](%)	Change of b amplitude [a](%)	Change of P2 amplitude [a](%)
1	62	F	Lattice dystrophy	Fc1′	6/15	90.8	49.77	-39.38
2	65	M	Bullous keratopathy, Glaucoma	6/60	6/15	7.19	15.16	-3.06
3	76	F	Bullous keratopathy	Hm	6/18	-28.76	-29.86	-25.20
4	65	M	Bullous keratopathyIridocorneal endo thelial dystrophy	2/60	6/15-2	-13.88	36.67	13.54
5	34	M	Leukoma, Amblyopia	Fc1/4′	Fc1′	-42.13	-13.09	-27.65
6	25	M	Corneal decompensation , Glaucoma	Hm	6/18	6.55	9.23	-25.97
7	42	F	Graft rejection, Amblopia	2/60	6/60	-39.40	-27.27	6.37
8	77	F	Corneal scar	1/60	6/12	-4.74	-2.56	-14.51
9	75	M	Corneal decompensation, Glaucoma	Hm	6/9	21.66	17.56	2.78
10	75	M	Corneal decompensation, Glaucama	Hm	6/9	-17.81	-14.94	-2.71
11	40	F	Corneal scar	Hm	6/6	-32.20	11.97	-5.60
12	12	F	Corneal scar	Fc1/2′	6/12	27.33	44.29	-13.71
13	71	M	Bullous keratopathy	Fc1/2′	6/12	32.44	57.95	-40.29
14	73	M	Corneal decompensation, Glaucoma	Hm	6/24	-19.76	0.41	-45.90
15	75	F	Bullous keratopathy	Hm	6/6	9.26	15.15	-19.98
16	69	M	Corneal decompensation	Hm	6/12	-19.37	0.73	2.05
17	75	F	Corneal decompensation, Glaucoma	Fc1/2′	6/9	80.00	58.10	10.89
18	71	M	Bullous keratopathy, Glaucoma	Hm	6/18	-29.26	-17.41	-19.24
19	27	M	Leukoma	6/24	6/9	-32.85	-38.64	-16.95
20	44	M	Corneal decompensation, Glaucoma, Intraocular foreign body S/P surgery	Hm	Hm	-50.01	-19.42	-56.13
21	61	F	Corneal edema, Iridocorneal endothelial dystrophy	Hm	6/36	-34.05	-26.36	-59.79
22	33	M	Leukoma, sensory exotropia	Fc1′	6/9	-14.28	-18.64	-5.88
23	37	M	Leukoma, Glaucoma	Hm	6/24	15.26	-12.69	-50.05
24	74	M	Corneal decompensate, Glaucoma	Fc1′	6/12	-7.68	-6.09	-2.30
25	36	F	Corneal decompensation	Fc1′	6/12	-49.47	-21.90	-36.74
26	55	M	Corneal scar, Glaucoma	6/36	6/12	0.65	10.50	-8.21
27	64	M	Bullous keratopathy, Sensory exotropia	Hm	2/60	-20.65	-0.67	-26.63
28	79	F	Graft rejection	Hm	6/18	58.42	20.63	-17.05
29	63	M	Corneal decompensation	Fc1/2′	6/18	8.41	-2.18	-32.82
30	69	M	Corneal decompensation	Fc1/2′	6/9	4.25	17.87	9.97
31	62	F	Graft rejection	3/60	6/12	6.21	-22.93	-30.97

Table 2. Cont.

Case	Age	Sex	Diagnosis	Preoperative BCVA	Postoperative BCVA	Dark-adapted ERG		Flash VEP
						Change of a amplitude[a] (%)	Change of b amplitude[a] (%)	Change of P2 amplitude[a] (%)
32	67	F	Corneal decompensation. Glaucoma	Hm	6/15	-46.07	-3.25	-4.59
33	68	M	Lattice dystrophy	Fc1′	6/12	21.75	27.41	47.99
34	41	M	Leukoma, sensory exotropia, Glaucoma	Fc1/2′	3/60	-7.00	-1.13	-25.63
35	84	M	Bullous keratopathy, Glaucoma	Hm	6/24	-53.43	-16.40	-35.76
36	39	M	Corneal decompensation	Hm	6/6	-23.08	-19.15	20.04
37	68	F	Corneal decompensation, Glaucoma	Fc1′	6/12	15.85	47.33	-32.13
38	74	F	Corneal decompensation	Hm	6/24	-8.87	-27.79	6.37
39	89	F	Bullous keratopathy, Glaucoma	Hm	Pl	-40.16	-7.53	-77.64

M = Male, F = Female, BCVA = Best-corrected visual acuity, Fc = Finger count (feet), Hm = Hand motion, ERG = Electroretinogram, VEP = Visual evoked potential
a = Percent change of the amplitude compare to the normal fellow eye

compared to the value of the normal fellow eye. The present study showed that a-wave amplitude that was equal to or more than 80% and P2 amplitude that was equal to or more than 67% compared to the value of the normal fellow eye gave a PPV of 95.65%, while the a-wave amplitude that was less than 80% and P2 amplitude that was less than 67% compared to the value of the normal fellow eye gave a NPV of 60%. In the present study showed positive likelihood ratio (LR^+) was 1.69 and negative likelihood ratio (LR^-) was 0.31.

Discussion

For patients with total corneal opacity and need corneal transplantation, it is difficult to visualize the fundus prior to keratoplasty due to the opacity of the ocular media. The assessment of retina and optic nerve function relies on gross tests such as level of visual acuity, color perception and structural tests such as ultrasonography. Electrophysiologic tests are valuable to evaluate the retina, macula and optic nerve function that directly affect the visual outcome after corneal transplantation prior to surgery. The a-wave and b-wave of dark-adapted, bright flash ERG are generated by photoreceptor cells of both rod and cone cells and combination of bipolar and Muller's cells, respectively. The response from dark-adapted, bright flash ERG represents the entire retinal function. Flash VEP is used to evaluate central vision and visual pathway function in poor vision patients (visual acuity less than 6/60)[3]. With both tests, the authors can evaluate both entire retinal function and central visual function. Because the variation among these values depends on both laboratory environment and on the individual person, the authors use the values of the normal fellow eye as the normal value for each patient. Wendel et al[(1)] found that the use of combination of quantitative ERG (assessing ERG wave amplitude) and configurational VEP (value scores of VEP waveform) was able to predict visual outcomes in 92% of cases. Binder et al[(2)] studied the usefulness of the preoperative ERG and VEP to improve physicians' ability to assess the potential for recovery of visual function following corneal transplantation further than perioperative clinical examination alone. They found that these tests were predictive of visual outcome in 71% of all cases but did not provide additional information in the group that was predicted to have a good prognosis from preoperative clinical examination alone.

For the present study, AUC of receiver operating characteristics (ROC) curve was used to identify the best predictor of postoperative visual

outcome. A-wave amplitude was the best predictor, but as mentioned above the authors chose to use both a-wave amplitude and P2 amplitude for predicting visual outcome after corneal transplantation. In the patients who had P2 amplitude equal to or more than 67% and a-wave amplitude equal to more than 80% compared to the normal fellow eye, 95.96% may have postoperative visual acuity equal to better than 6/24. The authors had one case (case 34) for which P2 amplitude was more than 67% and a-wave amplitude was more than 80%, but had poor vision after corneal transplantation. This case was reviewed and found that this patient had corneal leukoma since he was 8 years old and he had the preoperative diagnosis of amblyopia. This is the same as 2 cases with the diagnosis of amblyopia (case 5, 7) who had poor vision after the operation even when their P2 amplitude was more than 67%. Another case (case 27) who also had poor vision after operation despite good a-wave amplitude and P2 amplitude, had preoperative abnormal color vision and positive relative afferent pupillary defect prior to the operation.

The present study showed high PPV and low NPV because most of the patients for whom electrophysiologic tests were requested prior to corneal transplantation were from the group of patients that were expected to be good candidates for the operation by clinical evaluations and ultrasonography. There were very few cases that had poor visual prognosis from both clinical evaluation and ultrasonography and who underwent penetrating keratoplasty.

Conclusion

Electrophysiologic tests, especially the a-wave amplitude and P2 amplitude, are useful for predicting visual prognosis after corneal transplantation. In the unilateral corneal disease patients who were evaluated as good candidates by clinical evaluation and ultrasonography, the a-wave amplitude and P2 amplitude predict good visual outcome most accurately (95.96%) when changing less than 20% and 33%, respectively, compared to the normal fellow eye. Not only the electrophysiologic tests, but also other factors can influence the visual outcome such as experience of the surgeon, operative technique and patient's compliance after surgery. Carefully taking a history of amblyopia and examining for color vision and pupillary reaction may also be helpful to predict the visual outcome.

Potential conflicts of interest

None.

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การพยากรณ์การมองเห็นด้วยการตรวจคลื่นไฟฟ้าของตาในผู้ป่วยที่ปลูกถ่ายกระจกตา

อติพร ตวงทอง, ภัทนี สามเสน, งามแข เรืองวรเวทย์, ฉันทกา สุปิยพันธุ์

วัตถุประสงค์: *เพื่อพยากรณ์การมองเห็น โดยการตรวจคลื่นไฟฟ้าของตาในผู้ป่วยที่ปลูกถ่ายกระจกตา*
วัสดุและวิธีการ: *ศึกษาย้อนหลังในผู้ป่วยที่ได้รับการปลูกถ่ายกระจกตาเพื่อการมองเห็น ที่โรงพยาบาลศิริราช ตั้งแต่เดือน กันยายน พ.ศ. 2546 – มิถุนายน พ.ศ. 2552 โดยเปรียบเทียบค่าความกว้างของ a-wave และ b-wave ของ dark-adapted bright flash ERG และค่าความกว้างของ P2 ของ Flash VEP ของตาที่ผิดปกติกับตาอีกข้างที่ปกติ Area under receiver operating characteristic curve (AUC) ใช้ในการหาตัวพยากรณ์ที่ดีที่สุด Positive predictive value (PPV) และ Negative predictive value (NPV) ใช้ในการหาค่าความถูกต้องของการตรวจนั้น*
ผลการศึกษา: *ผู้ป่วยทั้งหมดจำนวน 39 คน พบว่าค่าความกว้างของ a-wave เป็นตัวพยากรณ์โรคที่ดี (AUC=0.83) และสำหรับค่าความกว้างของ a-wave ที่มากกว่าหรือเท่ากับร้อยละ 80 ร่วมกับค่าความกว้างของ P2 ที่มากกว่าหรือเท่ากับร้อยละ 67 ให้ค่า PPV เท่ากับ ร้อยละ 95.65*
สรุป: *ค่าความกว้างของ a-wave ร่วมกับค่าความกว้างของ P2 เป็นตัวพยากรณ์การมองเห็นที่ดีและให้ค่าความถูกต้องสูงเมื่อมีการเปลี่ยนแปลงน้อยกว่าร้อยละ 20 และ ร้อยละ 33 ตามลำดับเทียบกับค่าของตาข้างที่ปกติ*