ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Etiology and Treatment Outcomes in Patients with Binocular Diplopia: Experience of a Tertiary Center

Binoküler Diplopi Hastalarında Etiyoloji ve Tedavi Sonuçları: Üçüncü Basamak Bir Merkezin Deneyimi

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ABSTRACT Objective: Diplopia is a common symptom in ophthalmologic and neurological diseases. In the presence of binocular diplopia, investigation should be made for differential diagnosis. Detection of the underlying etiology provides early diagnosis of accompanying neurological diseases and facilitates the treatment of diplopia. In this study, we aimed to evaluate the causes of binocular diplopia, treatment modalities and treatment outcomes in a tertiary center. **Material and Methods:** Medical records of patients with binocular diplopia were reviewed. Demographic features and ophthalmological examination findings were noted. Etiological differential diagnoses of diplopia were elucidated according to the results of full ophthalmological examination and neuro-radiological evaluation with cranio-orbital magnetic resonance imaging. Treatment modalities and responses to these treatments were noted. **Results:** A total of 70 patients were evaluated. Thirty-six patients (51.4%) had cranial nerve palsies. Of 36 patients, 61.1% had 6th nerve palsy, 22.2% 3th nerve palsy and 16.7% 4th nerve palsy. Patients without cranial nerve palsies were also grouped according to the type of deviations. The most common deviations were acute-decompansated esotropia (21.2%) and age-related esotropia (18.2%). Diplopia recovered in 8 patients (11.4%) after treatment of the underlying etiology. Nineteen (27.1%) patients were not treated due to spontaneous recovery. Prism glasses were prescribed in 22 (31.4%) patients. Twelve patients (17.1%) were operated. Six (8.6%) patients received Botulinum-A toxin injections. **Conclusion:** In the presence of binocular diplopia, cranial nerve palsies should be investigated. Diplopia can resolve spontaneously. In cases with persistant diplopia, prism glasses, Botulinum toxin-A injection and surgery can be performed.

Keywords: Abducens palsy; binocular diplopia; cranial nerves; oculomotor nerve diseases; strabismus; trochlear nerve diseases

ÖZET Objective: Diplopi, oftalmolojik ve nörolojik hastalıklarda sık izlenen bir semptomdur. Binoküler diplopi varlığında ayırıcı tanı için gerekli araştırmalar yapılmalıdır. Altta yatan etiyolojinin tespiti hem eşlik eden nörolojik hastalıkların erken tanısını sağlamakta hem de tedaviyi kolaylaştırmaktadır. Bu çalışmada, üçüncü basamak sağlık merkezine başvuran binoküler diplopili hastalarda, etiyolojinin tespit edilmesini, tedavi yöntemlerinin belirlenmesini ve tedaviye alınan yanıtın değerlendirilmesini amaçladık. **Gereç ve Yöntemler:** Binoküler diplopili hastaların medikal kayıtları incelendi. Hastaların demografik özellikleri ve oftalmolojik muayene bulguları kaydedildi. Oftalmolojik ve nöro-radyolojik muayene sonuçlarına göre etiyolojik ayırıcı tanılar yapıldı. Tedavi yöntemleri ve sonuçları değerlendirildi. **Bulgular:** Toplam 70 hasta çalışmaya dahil edildi. Hastaların 36'sında (%51,4) kranial sinir felci vardı. Kranial sinir felci olan hastaların %61,1'inde 6. sinir felci, %22,2'sinde 3. sinir felci, %16.7'sinde ise 4. sinir felci mevcuttu. Kranial sinir felci olmayan hastalar kayma tipine göre sınıflandırıldığında, en sık görülen kayma, akut-dekompanze ezotropya (%21,2) ve yaşa bağlı ezotropya (%18,2) idi. Altta yatan hastalığın tedavisi ile 8 (%11,4) hastada diplopi düzeldi. On dokuz (%27,1) hastada ise spontan düzelme izlendi. Yirmi iki (%31,4) hastaya prizmatik gözlük verilirken, 12 (%17,1) hasta ameliyat edildi. Altı (%8,6) hastaya ise Botulinum-A toksin enjeksiyonu yapıldı. **Sonuç:** Binoküler diplopi varlığında, kranial sinir felçleri ayırıcı tanıda düşünülmelidir. Diplopi kendiliğinden düzelebilir. Devam eden diplopisi olan hastalarda prizmatik gözlük, Botulinum-A toksin enjeksiyonu ve cerrahi uygulanabilir.

Anahtar Kelimeler: Abdusens felci; binoküler diplopi; kranial sinirler; okülomotor sinir hastalıkları; şaşılık; troklear sinir hastalıkları

Diplopia is a common symptom in ophthalmological and neurological diseases and this symptom affects the quality of life to a great extent. Once the patient is disturbed from diplopia, it must be determined whether diplopia is monocular or binocular. While monocular

diplopia is associated with ocular pathologies such as refractive errors, media opacities and optical aberrations, binocular diplopia may be caused by systemic diseases such as neurological pathologies.[1] In the presence of binocular diplopia, it should be investigated for differential diagnosis. Multiple etiologies such as neuro-ophthalmologic, strabismic and iatrogenic pathologies can cause binocular diplopia by misaligning the visual axes.[2] Detection of the underlying etiology provides early diagnosis of accompanying neurological diseases and facilitates the treatment of diplopia.

In this study, we aimed to evaluate the causes of binocular diplopia, treatment modalities and treatment outcomes in a tertiary center.

MATERIAL AND METHODS

The medical records of 70 patients who had binocular diplopia between May 2016 and May 2018 were reviewed retrospectively. Patients who suffered from monocular diplopia and those with a follow-up period of less than 3 months were excluded from the study.

Demographic features of the patients (gender, age at onset of diplopia), follow-up period, accompanying systemic diseases, diagnoses of patients and treatment modalities were noted. Etiological differential diagnoses of diplopia were elucidated according to the results of full ophthalmological examination and neuro-radiological evaluation with cranio-orbital magnetic resonance imaging (MRI).

Ophthalmological examination included; visual acuity, alternate prism cover test in all gaze positions for near and distance, Bielschowsky head tilt test and Maddox rod test. Hess screen test was not performed. Ocular motility was evaluated by the examination of ductions and versions. Worth 4 Test for near and distance was performed to evaluate the presence of diplopia. Anterior segment and fundus examination, retinoscopy and pupil examination (presence of anisocoria, light reaction and relative afferent pupil defect) were also noted.

Patients were divided into 2 groups according to the presence of cranial nerve palsies. Patients without cranial nerve palsies were grouped according to the type of deviation such as esotropia and exotropia and etiologies of diplopia were evaluated separately for these groups. Differential diagnosis of acute decompansated esotropia and age related esotropia was made by the history and orbital MRI imaging of patients.

Treatment modalities and responses to these treatments were noted. Yoked prism glasses were given to the patients with less than 20 PD of deviation. For horizontal deviations, operation was planned for the patients who had more than 20 PD and who was stable for at least 6 months. Patients who suffered from 6th nerve palsy with an amount of deviation more than 20 PD were performed Botulinum toxin-A injection to the medial rectus muscle firstly. Of them, who did not recover for more than 6 months underwent surgery. Adjustable suture was performed to the patients with postoperative unpredictable amount of deviations such as orbital myositis and thyroid ophthalmopathy.

Distribution pattern of continuous variables was tested by using Kolmogorov-Smirnov test and the results of normally distributed variables were reported as mean±standard deviation and abnormally distributed variables as median (minimum-maximum). The data of categorized variables was presented as percentage (%).

This retrospective study has been approved by local ethic committee protocol (Ankara University Ethic Committee, Protocol Number: 18-1191-18) and adhered to the Declaration of Helsinki.

RESULTS

Of 70 patients included, 40 (57.1%) were female and 30 (42.9%) were male. Mean age was 45.2 (range: 11-83) years and median follow-up period was 13.2 (range:3-24) months. Fifty-one (72.8%) patients suffered from horizontal diplopia, 14 (20%) from vertical diplopia and 5 (7.2%) from both horizontal and vertical diplopia.

Of 70 patients, 36 (51.4%) had cranial nerve palsies (Table 1). Sixteen (22.9%) patients had esotropia and 10 (14.3%) had vertical deviation in the group of patients without cranial nerve palsies. Five (7.1%) patients had heterophoria (Table 2).

TABLE 1: Diagnoses of the patients with cranial nerve palsies.

Diagnoses of the patients	Number of the patients n (%)
6th nerve palsy	22 (61.1)
Vascular	8 (22.2)
Idiopathic	6 (16.7)
Elevated intracranial pressure	5 (13.9)
Intracranial lesion	2 (5.6)
Venous sinus thrombosis	2 (5.6)
Pseudotumor cerebri	1 (2.7)
Traumatic	2 (5.6)
Carotico-cavernous fistula	1 (2.7)
3rd nerve palsy	8 (22.2)
Vascular	4 (11.1)
Idiopathic	2 (5.6)
İntracranial aneurysm	1 (2.7)
Elevated intracranial pressure (subdural hemorrhage)	1 (2.7)
4th nerve palsy	6 (16.7)
Idiopathic	4 (11.1)
Traumatic	1 (2.7)
Hydrocephalus	1 (2.7)
Total	36 (100)

Diplopia recovered in 8 (11.4%) after treatment of underlying etiology (Table 3). Complaints of these patients except one patient with Myastenia Gravis (MG), decreased after etiological treatment. This patient was operated for vertical deviation. Nineteen (27.1%) patients were not treated due to spontaneous recovery (Table 4). Mean period of spontaneous recovery was 4 (1-6) months. Diplopia improved in 2 (2.8%) patients with convergence insufficiency and 1 (1.4%) patient with acute-decompansated esotropia recovered after correction of refractive error. Prism glasses were prescribed in 22 (31.4%) patients (Table 5). Of these 22 patients, complaints of 20 (90.9%) decreased, however 2 patients (9.1%) had no benefit. Surgical procedures were planned for these 2 patients who had 4th nerve palsy and operation for nasal cavity malignancy.

TABLE 2: Diagnoses of the patients without cranial nerve palsies.

Diagnoses of the patients	Number of the patients n (%)
Esotropia	16 (48.5)
Acute-decompansated	7 (21.2)
Age-related	6 (18.2)
Orbital myositis	1 (3)
Myastenia Gravis	1 (3)
Postoperative (Retinal detachment surgery)	1 (3)
Hypotropia	6 (18.2)
Thyroid orbitopathy	2 (6)
Orbital blow out fracture	2 (6)
Brown Syndrome	1 (3)
Orbital myositis	1 (3)
Hypotropia + Exotropia	3 (9.1)
Thyroid orbitopathy	1 (3)
Orbital myositis	1 (3)
Postoperative (Malignancy of nasal cavity)	1 (3)
Exotropia	2 (6.1)
Internuclear ophthamoplegia	1 (3)
Intermittant exotropia	1 (3)
Hypertropia	1 (3)
Myastenia Gravis	1 (3)
Heterophoria	5 (15.2)
Convergence insufficiency	4 (12.1)
Divergence insufficiency	1 (3.1)
Total	33 (100)

TABLE 3: Diagnoses and treatment modalities of the patients who were treated for underlying etiology.

Diagnoses of the patients	Number of the patients/n	Treatment Modalities
6th nerve palsy	3	
Intracranial tumor	1	Chemotherapy
Pseudotumor cerebri	1	Lumbar puncture+ acetazolamide
Carotico-cavernous fistula	1	Fistula embolization
Myastenia Gravis	3	Medical treatment
3rd nerve palsy (Subdural hematoma)	1	Hematoma drainage
Orbital blow-out fracture	1	Fracture repair
Thyroid orbitopathy	1	Corticosteroid

TABLE 4: Diagnoses of the patients with spontaneous recovery.

Diagnoses of the patients	Number of the patients/n
6th Nerve Palsy	6
3rd Nerve Palsy	4
4th Nerve Palsy	3
Convergence Insufficiency	2
Acute Decompensated Esotropia	2
Thyroid Orbitopathy	1
Orbital Myositis	1
Total	19

TABLE 5: Diagnoses of the patients who were prescribed prism glasses.

Diagnoses of the patients	Number of the patients/n
6th nerve palsy	5
Age related esotropia	5
4th nerve palsy	3
Acute decompensated esotropia	1
Postoperative (Retinal detachment surgery)	1
Divergence insufficiency	1
Brown Syndrome	1
Internuclear ophthamoplegia	1
Orbital myositis	1
Thyroid Orbitopathy	1
Postoperative (Malignancy of nasal cavity)	1
Postoperative orbital blow out fracture	1
Total	22

TABLE 6: Diagnoses of the patients who underwent surgery.

Diagnoses of the patients	Number of the patients / n
6th nerve palsy	2
3rd nerve palsy	3
Acute Decompensated Esotropia	4
Intermittant exotropia	1
Orbital myositis (Hypotropia, exotropia)	1
Myastenia Gravis (Hypertropia)	1
Total	12

Twelve patients (17.1%) who had deviation larger than 20 prism diopters (PD) and a stable deviation for at least six months were operated (Table 6). Postoperatively, 7 (77.8%) of these 9 patients regained fusion and diplopia improved. Postoperative residual symptoms of 3 (4.3%) patients with the diagnoses of 3rd nerve palsy decreased by prism glasses. Botulinum-A toxin injection to the medial rectus muscle was performed to 6 (8.6%) patients with the diagnoses of 6th nerve palsy and all of them recovered.

DISCUSSION

When a patient presents with diplopia, the first step should be determining whether diplopia is monocular or binocular, as underlying etiologies and treatment modalities of monocular and binocular diplopia are different. In the presence of diplopia; a detailed history should be taken; a full ophthalmological examination should be performed and differential diagnosis of monocular and binocular diplopia should be carried out. Binocular diplopia is more common than monocular diplopia and its frequency is up to 88.5% among all diplopia patients.[3,4] Detection of the underlying pathology of binocular diplopia allows early diagnosis and treatment of accompanying systemic diseases which can be life-saving in situations like intracranial lesions and vascular diseases. Furthermore, treatment of underlying etiology can resolve diplopia.

The most common cause of binocular diplopia is isolated cranial nerve palsies (40-67%).[3-5] In our study we found cranial nerve palsies in 51.4% of our patients, of these 31.4 % were sixth nerve palsy, 11.4% third nerve palsy and 8.6% fourth nerve palsy. Merino et al. similarly found the most frequent cause, as cranial nerve palsies and in their study, sixth nerve palsy was the most frequent.[6] The frequency of isolated nerve palsies was 53.7% in the study of O'Colmain and of these, 25.5% were sixth nerve palsies, 16.1% fourth nerve palsies and 12.1% third nerve palsies.[5]

In early childhood, in the presence of acute esotropia, patients usually do not suffer from diplopia because of suppression. However, if acute esotropia develops in older ages, patients usually complain of diplopia.[7] Decompensation of pre-existing esophoria may result in acute esotropia and binocular diplopia in adults. Decompensated strabismus was the most

common cause of binocular diplopia after cranial nerve palsies in the study of Merino et al. In the study of O'Colmain, decompensation of a pre-existing heterophoria was the cause of acute diplopia in 8.1% of patients.[5,6,8] Similar to their results, frequency of decompensated strabismus was 10% in our study, and it was the most common cause of binocular diplopia after cranial nerve palsies.

Over the age of 60 years, incidence of strabismus increases. Previous studies have reported increase in incidence of paralytic strabismus and MG with age.[9-12] In the absence of paralytic strabismus or MG, the incidence of strabismus increases due to orbital pulley abnormalities. With age, lateral rectus-superior rectus band gets thinner and lateral rectus muscle displaces inferiorly.[13] Fusional range decreases with normal aging process and this condition also causes age related esotropia. Therefore, age related pulley abnormalities and decrease in fusional range should be considered in the presence of a new onset strabismus and diplopia in elderly patients. Kawai et al. suggested that binocular diplopia was often caused by orbital pulley disorders in elderly patients.[13] In our study, we did not group the causes of diplopia by age, but when we evaluated the causes for all ages together, age-related esotropia was the third most common cause (8.6%).

Myastenia Gravis is another diagnosis to remember in the presence of diplopia. Approximately 90% of patients with MG have weakness of extraocular muscles at the onset of the disease.[14] Especially in the presence of diplopia that does not fit with a specific pattern, MG should be considered. In our study 3 (4.3%) patients with diplopia had the diagnosis of MG. While types of deviations in 2 patients were hypertropia and esotropia, 1 patient was ortophoric at all gazes with discrepancy in saccadic velocities. This patient was diagnosed as MG in Neurology Department with single fiber electromyelography test.

The first step in the management of diplopia is to find out the underlying cause and to treat it. Diplopia will improve when the causative factors are eliminated. However, underlying causes may not be treated in some patients or diplopia persists even after treatment. These cases should be treated to relieve complaints. There are different treatment modalities including occlusion therapy, fusional vergence exercises, prism glasses and surgery. The main purpose of treatment is to restore single binocular vision.

When the deviation is not too large, some patients can compensate diplopia with small head tilt, face turn and chin elevation/depression. These patients can be followed without any treatment, if they do not feel discomfort from diplopia.[2] Also, if spontaneous resolution is expected in a patient with a small deviation, occlusion therapy can be given to relieve the symptoms. Prism treatment has a great importance in the management of diplopia. Correction of diplopia with prism is associated with improvement in reading and general function.[15] In the study of Tamhankar et al. 72% of patients reported complete or partial resolution of diplopia after prism use for restrictive strabismus.[16] If the deviation is too large to correct with prisms and stable for at least six months, extraocular muscle surgery can be performed.

In Merino's study spontaneous resolution was observed in 31.6% of patients, 20% was treated with botulinum toxin, 15% was operated.[6] Prism glasses were prescribed only in 3.3% of the patients. In their study 53.3% obtained good results with resolution of diplopia with or without treatment at the end of the study. In our study 27.1% of the patients had spontaneous resolution similar to Merino's study. The most common treatment modality was prism glasses (31.4%) and in 90.9% of these patients, diplopia complaints decreased or completely resolved. We performed surgery to 17.1% of patients and Botulinum toxin-A injection to 8.6% of patients. In 77.8% of the patients who underwent surgery and all of the patients with Botulinum injection, diplopia improved.

CONCLUSION

Patients with diplopia should be examined by an ophthalmologist firstly. A detailed history and ophthalmological examination are crucial to define the underlying etiology. Ocular pathologies should be

considered in the presence of monocular diplopia. Although binocular diplopia may be caused by systemic pathologies, it can be treated by ophthalmologists. For the treatment of diplopia, the etiologic factor should be eliminated first if possible. In case of persistent diplopia, treatment modalities include prism glasses, Botulinum toxin-A injection and surgery.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Huban Atilla, Pınar Bingöl Kızıltunç;* ***Design:*** *Huban Atilla;* ***Control/Supervision:*** *Huban Atilla;* ***Data Collection and/or Processing:*** *Pınar Bingöl Kızıltunç;* ***Analysis and/or Interpretation:*** *Huban Atilla;* ***Literature Review:*** *Pınar Bingöl Kızıltunç;* ***Writing the Article:*** *Pınar Bingöl Kızıltunç;* ***Critical Review:*** *Huban Atilla;* ***References and Fundings:*** *Huban Atilla, Pınar Bingöl Kızıltunç;* ***Materials:*** *Huban Atilla.*

REFERENCES

1. Najem K, Margolin E. Diplopia. StatPearls. Treasure Island (FL); 2018.
2. Bartiss MJ. Nonsurgical treatment of diplopia. Curr Opin Ophthalmol. 2018;29(5):381-4. [Crossref] [PubMed]
3. Comer RM, Dawson E, Plant G, Acheson JF, Lee JP. Causes and outcomes for patients presenting with diplopia to an eye casualty department. Eye (Lond). 2007;21(3):413-8. [Crossref] [PubMed]
4. Morris RJ. Double vision as a presenting symptom in an ophthalmic casualty department. Eye (Lond). 1991;5(Pt 1):124-9. [Crossref] [PubMed]
5. O'Colmain U, Gilmour C, MacEwen CJ. Acute-onset diplopia. Acta Ophthalmol. 2014;92(4): 382-6. [Crossref] [PubMed]
6. Merino P, Fuentes D, Gómez de Liaño P, Ordóñez MA. Binocular diplopia in a tertiary hospital: aetiology, diagnosis and treatment. Arch Soc Esp Oftalmol. 2017;92(12):565-70. [Crossref] [PubMed]
7. Clark AC, Nelson LB, Simon JW, Wagner R, Rubin SE. Acute acquired comitant esotropia. Br J Ophthalmol. 1989;73(8):636-8. [Crossref] [PubMed] [PMC]
8. Ali MH, Berry S, Qureshi A, Rattanalert N, Demer JL. Decompensated esophoria as a benign cause of acquired esotropia. Am J Ophthalmol. 2018;194:95-100. [Crossref] [PubMed] [PMC]
9. Martinez-Thompson JM, Diehl NN, Holmes JM, Mohney BG. Incidence, types, and lifetime risk of adult-onset strabismus. Ophthalmology. 2014;121(4):877-82. [Crossref] [PubMed] [PMC]
10. Tamhankar MA, Biousse V, Ying GS, Prasad S, Subramanian PS, Lee MS, et al. Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study. Ophthalmology. 2013;120(11):2264-9. [Crossref] [PubMed] [PMC]
11. Casetta I, Groppo E, De Gennaro R, Cesnik E, Piccolo L, Volpato S, et al. Myasthenia gravis: a changing pattern of incidence. J Neurol. 2010;257(12):2015-9. [Crossref] [PubMed]
12. Vincent A, Clover L, Buckley C, Grimley Evans J, Rothwell PM; UK Myasthenia Gravis Survey. Evidence of underdiagnosis of myasthenia gravis in older people. J Neurol Neurosurg Psychiatry. 2003;74(8):1105-8. [Crossref] [PubMed] [PMC]
13. Kawai M, Goseki T, Ishikawa H, Hoshina M, Shoji N. Causes, background, and characteristics of binocular diplopia in the elderly. Jpn J Ophthalmol. 2018;62(6):659-66. [Crossref] [PubMed]
14. Kaminski HJ, Maas E, Spiegel P, Ruff RL. Why are eye muscles frequently involved in myasthenia gravis? Neurology. 1990;40(11): 1663-9. [Crossref] [PubMed] [PMC]
15. Hatt SR, Leske DA, Liebermann L, Holmes JM. Successful treatment of diplopia with prism improves health-related quality of life. Am J Ophthalmol. 2014;157(6):1209-13. [Crossref] [PubMed] [PMC]
16. Tamhankar MA, Ying GS, Volpe NJ. Prisms are effective in resolving diplopia from incomitant, large, and combined strabismus. Eur J Ophthalmol. 2012;22(6):890-7. [Crossref] [PubMed]