Therapeutic results in sixth nerve palsy

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Abstract: Authors aim to assess through a retrospective study the efficiency of different therapeutic methods used in VIth nerve palsy. 60 patients with VIth nerve palsy, admitted and treated in Oftapro Clinic, were divided into two groups: a group with partial dysfunction (paresis) of sixth nerve and a group with the complete abolition of neuromuscular function (VIth nerve palsy). Initial examination included assessment of neuromuscular function, binocular vision and existence of medial rectus muscle contracture (ipsi- and contralateral) and contralateral lateral rectus inhibitory palsy. Neuromuscular dysfunction was graded from - 8 (paralysis) to 0 (normal abduction). Therapeutic modalities ranged from conservative treatment (occlusion, prism correction), botulinum toxin chemodenervation and surgical treatment: medial rectus recession + lateral rectus resection, in cases of paresis, and transposition procedures (Hummelscheim and full tendon transfer) in cases of sixth nerve palsy. Functional therapeutic success was defined as absence of diplopia in primary position, with or without prism correction, and surgical success was considered obtaining orthoptic alignment in primary position or a small residual deviation (under 10 PD). 51 patients had unilateral dysfunction, and 9 patients had bilateral VI-th nerve dysfunction. 8 patients had associated fourth or seventh cranial nerves palsy. The most common etiology was traumatic, followed by tumor and vascular causes. There were 18 cases of spontaneous remission, partial or complete (4-8 months after the onset), and 6 cases enhanced by botulinum toxin chemodenervation. 17 paretic eyes underwent surgery, showing a very good outcome, with restoration of binocular single vision. The procedure of choice was recession of medial rectus muscle, combined with resection of lateral rectus muscle. All patients with sixth nerve palsy underwent surgery, except one old female patient, who refused surgery. Hummelscheim procedure was applied in 19 cases, and full tendon transfer in 6 cases. In 13 cases partial results were obtained, who needed further prismatic correction or reintervention. In 12 cases the outcome was very good, with restoration of binocular single vision, without prismatic correction. Therapeutic success in sixth nerve palsy depends on accurate assessment of neuromuscular dysfunction and appropriate choice of therapeutic modality for each case. Interdisciplinary collaboration is mandatory for correct etiologic diagnosis of sixth nerve palsy.
Key words: paresis, paralysis, nerve VI, recession, resection, botulinum toxin.

Introduction

Sixth nerve palsy is one of the most common cranial nerves palsies, because of the long intracranial route of this nerve. Patel, Mutyala, Leske, Hodge, and Holmes found an incidence of 11,3/100000 in a population – based study (1). The most frequent causes they described are: undetermined (26%), hypertension alone (19%), coexistent hypertension and diabetes (12%), trauma (12%), multiple sclerosis (7%), neoplasm (5%), diabetes alone (4%), cerebrovascular accident (4%), post neurosurgery (3%), aneurysm (2%), and other (8%). Peters et all. founded in their work central nervous system mass lesions and multiple sclerosis as the most common causes for a sixth nerve palsy in a 20 – 50 years age group (traumatic cases were excluded) (2). They reported that patients with tumoral etiology had the lowest rate of spontaneous recovery (3). In other publication trauma was the most common etiology, followed by viral infections, tumors and cerebral ischemia. Although positive diagnosis is obvious in almost all cases, sometimes differential diagnosis may raise difficulties. Thyroid eye diseases, myasthenia gravis, Duane's syndrome, spasm of the near reflex, and medial orbital wall fracture may mimic an isolated sixth nerve palsy (4). Treatment may be conservative and/or surgical, but a waiting period of at least 6 months to 1 year should be consider prior to any surgery, for the eventuality of spontaneous recovery (5).

Objective

The authors aim to assess trough this retrospective study the efficiency of different therapeutic methods used in sixth nerve palsy.

Material and methods

The records of 60 patients with sixth nerve palsy, admitted and treated in Oftapro Clinic between January 2009 and December 2013, were reviewed, in order to assess the efficiency of different therapeutic methods used in sixth nerve palsy. The etiology was correlated with age and the degree of neuro-muscular dysfunction. In the evaluation criteria of sixth nerve palsy were included: measuring of primary and secondary deviation (in prism diopters), evaluating the degree of abduction (from 0 = full abduction, to – 8 = complete abolition of abduction, with the eye immobilized in extreme adduction), finding of ipsilateral and contralateral medial rectus contracture and contralateral lateral rectus inhibitory paresis (active and passive duction tests). The associated neuro-muscular dysfunctions were, also, noted (other cranial nerves paresis or palsies), as association of optic nerve atrophy (partial or total). The treatment was differentiated according to degree of neuro-muscular dysfunction, to the purpose and the intended result, and according to patient's expectations and options. Conservative treatment consisted of alternating occlusion, follow up and/or prismatic correction. Minimally invasive treatment meant botulinum toxin chemodenervation. Surgical treatment were applied as follows: ipsilateral medial rectus recession, combined with ipsilateral lateral rectus resection in cases with partial neuro-muscular dysfunction and transfer procedures (Hummelscheim, combined or not with contralateral medial rectus recession, full tendon transfer simple or augmented, or combinations of these). Surgical success was

defined as orthoptic alignment in primary position or a residual esotropia, less than 12 PD, and surgical failure was considered when postoperative deviation was greater than 12 PD. Functional therapeutic success was defined as absence of diplopia in primary position, either partial, in which cases binocular single vision was achieved by prismatic correction for distance or for both, distance and near, or complete, with no need for prismatic correction.

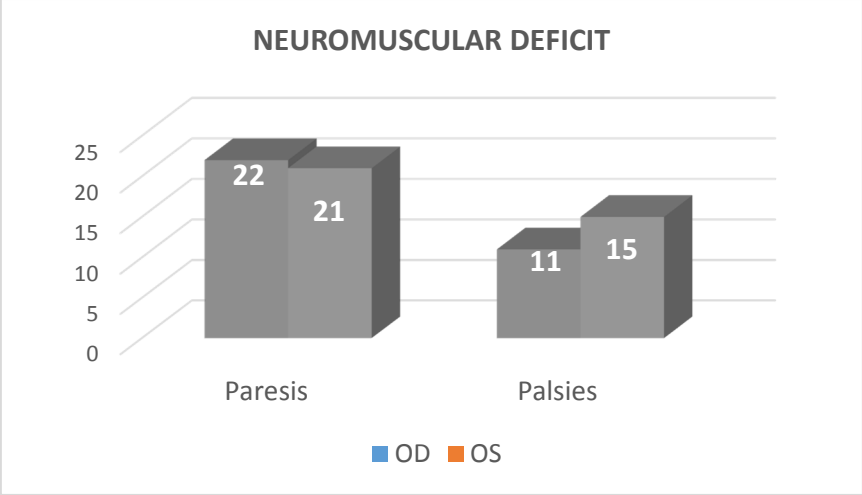
Results

31 men and 29 women, aged between 4 months and 81 years, had sixth nerve palsy, unilateral in 59 cases and bilateral in 9 patients (59 eyes). In 43 eyes the deficit was partial (paresis) and 26 eyes manifested complete abolishment of neuro-muscular function (sixth nerve palsy). Most cases had traumatic etiology (32 patients), especially by car crashes (24 cases), followed by fall from height (7 cases) and one perinatal craniocerebral trauma. Next frequent etiology was vascular (12 cases), HTA being most commonly incriminated, either alone (6 eyes), or in association with diabetes mellitus, dyslipidemia and/or cardiac insufficiency (6 cases). Tumoral etiology had almost equal frequency, involving 11 eyes. Multiple sclerosis was not insignificant, being responsible of 5 cases of sixth nerve palsy. In 2 cases, sphenoidal sinusitis was incriminated as etiology, one case after empyema and Klebsiella meningitis, one case after repeated febrile relapses with seizures, and one case post immunization. The etiology were unable to be determined in 3 cases (to note that among these, one female patient gave birth to 10 times).

TABLE I

Etiology (age related)

ETIOLOGY	AGE							
	<10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	>71 years
Car crashes	0	1	5	7	2	2	2	0
Fall from height	0	1	1	2	0	1	0	0
Perinatal trauma	1	0	0	0	0	0	0	0
CNS tumors	2	1	2	1	2	1	1	0
HTA	0	0	0	0	0	0	3	3
HTA in association	0	0	0	0	0	1	2	3
Multiple sclerosis	0	0	1	1	2	1	0	0
Sphenoidal sinusitis	0	1	1	0	0	0	0	0
Empyema	1	0	0	0	0	0	0	0
Febrile seizures	1	0	0	0	0	0	0	0
Postvaccinal	0	1	0	0	0	0	0	0
Multiparity	0	0	0	1	0	0	0	0
Unknown	0	0	1	1	0	0	0	0



Graph 1 - Neuromuscular deficit on each eye

Both tumors and trauma had predilection for younger ages (third and fourth decades), while vascular etiology was most frequent among the elders. Traumatic etiology interested a little more male than female patients (14 of 25), and was responsible for all bilateral cases and for most cases with complete abolition of abduction (17 of 32 eyes). Tumoral and vascular causes produced more paresis. 8 patients had associated neuromuscular dysfunctions: 4 of them had a fourth nerve palsy, and the other 4 had an associated seventh nerve palsy. 5 patients had optic atrophy in the affected eye (4 partial and one total optic nerve atrophy).

The primary deviation in paresis cases varied from 12 to 55 PD (prism diopters) esotropia (average 29,30 PD) for distance and from 8 to 50 PD (average 23,67) for near, while secondary deviation was about 30 PD for distance and 27,68 PD for near. In cases of sixth nerve palsy, deviations was greater than in paresis cases, varying from 35 to 80 PD esotropia (average 56,20 PD) at distance and from 30 to 70 PD at near (average 49,20 PD). Secondary deviation was just slightly larger than primary deviation (57,20 PD at distance and 50,2 PD at near) which is explained by the fact that waiting period before surgery was greater, thereby medial rectus contracture and, in some cases, contralateral lateral rectus inhibitory paresis had time to install, reducing thus incomitance. Ipsilateral medial rectus contracture was present in 19 cases and contralateral medial rectus contracture was shown in 13 cases. Contralateral lateral rectus inhibitory paresis developed in 7 cases. Limitation of abduction in paresis ranged from – 1 to – 6 (average – 3,13) and was quasicomplete in palsies – 8 (2 cases with – 7), average – 7,92.

TABLE II

Means of measurements of deviations (in prism diopters)

	Paresis	Palsies
Initial primary ET at distance	29,30	56,2
Initial primary ET at near	23.67	49,29
Initial secondary ET at distance	33	57,20
Initial secondary ET at near	27,68	50,2
Final primary ET at distance	3,34	9,32
Final primary ET at near	1,55	5,4
Final secondary ET at distance	3,82	9,24
Final secondary ET at near	1,97	5,16

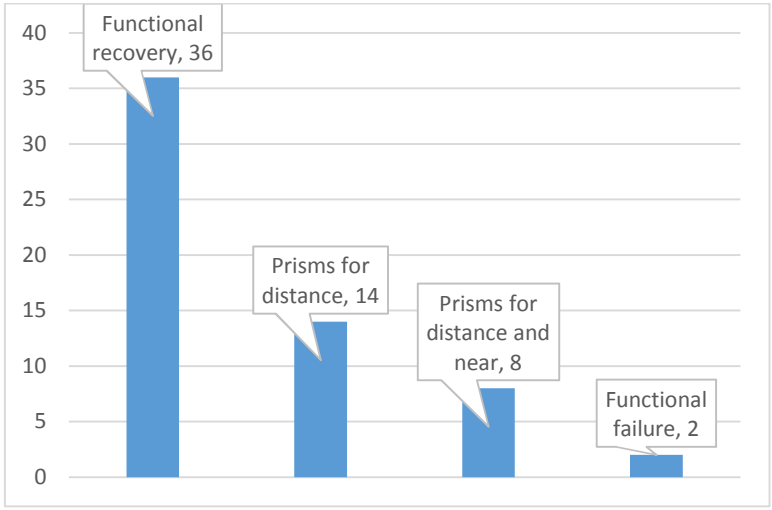
Conservative treatment was applied in 18 cases of sixth nerve paresis, consisting in alternating occlusion (10 cases) with follow up and prismatic correction 8 cases). 7 of these patients showed partial recovery at 5 to 6 months from beginning and needed permanent prismatic correction, for distance (5 patients) or both, for distance and near (2 patients). 11 patients demonstrated complete recovery, without need for prismatic correction, at 3 to 11 months from onset. Spontaneous recovery rate without any treatment but alternating occlusion or prismatic correction was 30%. When botulinum toxin was used to enhance the recovery of neuro-muscular deficit, the rate of remission was raised up to 40%. Vascular and mild traumatic etiology, as well as young patients showed highest recovery rate.

Botulinum toxin chemodenervation was used in 6 paretic and 1 paralitic eyes (one bilateral case paresis – palsy). In all cases, BTX-A potentiated partial (one case) or complete recovery (5 cases), except the last one, who needed further surgery.

The waiting period was at least 8 months before surgery, to permit the chance of eventual spontaneous recovery of deficit. In one case with bilateral sixth nerve paresis after empyema and Klebsiella meningitis, bilateral medial rectus recession was performed, with excellent outcome. In the rest of paretic eyes, medial rectus recession combined with lateral rectus resection was the procedure of choice. In one of these eyes, the surgery was performed after botulinum toxin chemodenervation (at 8 months). An inferior oblique muscle surgery (one inferior oblique recession and one miectomy) was associated in 2 cases. Surgical results were good, except one case who needed further reintervention (lateral rectus re-resection). Functional outcome showed partial recovery in 5 eyes and complete remission in 13 eyes. Postoperative deviations were significantly reduced to an average of 3,34 PD at distance and 1,55 PD at near, thus resulting a correction of approximately 25,96 PD for distance and 22,12 PD for near. Abduction was enhanced from an average of – 3,13 to – 0,53, showing an improvement about 83,06%.

In paralytic group, a 78 years old patient refused surgery, because poor perception of diplopia, due to a very large deviation, and because she was not concerned with aesthetics. Hummelsheim procedure alone was performed in 7 eyes, and in other 7, who developed contralateral medial rectus contracture, it was combined with contralateral medial rectus recession. In another case, Hummelscheim technique was

performed after botulinum toxin chemodenervation (the bilateral case paresis – palsy). 2 patients underwent associated surgery on the inferior oblique muscle, for fourth nerve palsy. One case had a reintervention after failed recession – resection procedure. Full tendon transfer was done in 6 cases one simple, one augmented (Foster technique), 3 combined with ipsilateral medial rectus recession and 1 combined with bilateral medial rectus recession. Reoperation was necessary in one case (with full tendon transfer alone), and bilateral medial rectus recession was done. Surgical failure appeared in 2 cases one above mentioned, and one who refused further surgery. Partial correction was the outcome in 9 cases, 6 of them needed prisms for distance, and 3 patients needed prisms for both distance and near, in order to achieve binocular vision. In 10 cases, a good postoperative result was achieved, with restoration of binocular vision, both for distance and near. Postoperative esodeviation measured an average of 9,23 PD for distance and 5,4 PD at near that means a reduction of 46,88 respective 43,8 PD of esotropia. The degree of abduction was improved from – 7,92 preoperative to – 3,4 postoperative.



Graph 2 - Overall functional results

No operative or postoperative complications were noted.

Discussions

In contrast to literature data, showing the main etiology as vascular or unidentified, we found a higher proportion of traumatic etiology, and, also, a significant number of tumoral causes in our patients (6). This may be due to the fact that many vascular patients arrived first in neurological services, and vascular etiology cases having a higher rate of spontaneous recovery, these patients do not get the ophthalmologist, since they see their condition improves in time. Most of the

patients with sixth nerve paresis have indication for botulinum toxin chemodenervation (7, 8), but many of them refuse this option, because of fear of muscle damage, or because this is a temporary solution and last but not least for financial reasons. Nevertheless, our findings that coincide with literature data, shows that botulinum toxin chemodenervation promotes an accelerated recovery of the deficit, inhibit the development of medial rectus contracture, and relieves symptoms of diplopia (8). The waiting period recommended in specialized books should be respected, as we found many patients (30%) who have recovered their lost function even after 11 months of disease onset. When surgery is recommended, it should be done, as postoperative results are very good, with restoration of binocular vision in most of the cases. Our postoperative results show a very good outcome in 60,60% of cases, 18,18% of patients needed prismatic correction just for distance, and same percent needed prisms for both distance and near. Only 3,03% were considered functional failure. This outcome is in agreement with published results of Holmes et all (5), in which shows an overall surgical success rate of 75%. When cases are carefully selected and surgical indication is well chosen, the results are excellent and reintervention rate is greatly diminished.

Holmes in his studies found some predictive factors for spontaneous recovery and stated that "In acute traumatic sixth nerve palsy or paresis, failure to recover by 6 months after onset was associated independently with inability to abduct past midline at presentation and bilaterality. Although the overall recovery rate is high in acute traumatic sixth nerve palsy or paresis, a complete or bilateral case has a poor prognosis and is more likely to need strabismus surgery." (9)

King et all found a spontaneous recovery rate in their series of 78.4%, but traumatic etiology was excluded (10). On the other hand, Mutyala and Holmes stated that "Spontaneous recovery from isolated traumatic sixth-nerve palsy may be lower than previously reported. A prospective study is needed to provide a more accurate estimate of recovery rate" (11). Volpe searched the mechanism of spontaneous recovery in tumoral sixth nerve palsies and found that "Possible mechanisms for recovery include remyelination, axonal regeneration, relief of transient compression (eg, resorption of hemorrhage), restoration of impaired blood flow, slippage of a nerve previously stretched over the tumor, or immune responses to the tumor" (12).

Conclusions

The functional and surgical success in sixth nerve palsy depends on accurate assessment of degree of neuromuscular dysfunction and appropriate choice of therapeutic modality for each case. A waiting period of at least 6 months to 1 year should be consider prior to any surgery, to track the event of spontaneous recovery of neuro-muscular function.

Interdisciplinary collaboration is mandatory for correct etiologic diagnosis of sixth nerve palsy. Vascular etiology should be remain an exclusion diagnosis, after more serious and life-threatening conditions have been ruled-out. Botulinum toxin chemodenervation for paretic cases should be

encouraged, both by ophthalmologist and neurologist, as it provide the chance for earlier recovery and is a minim invasive and reversible procedure.

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