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Research Article

The Effect of Combined Vitamin B Therapy on the Outcome of Diabetic Isolated Abducent Nerve Palsy

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Abstract

Objective: To evaluate the effect of vitamin B combined therapy on the recovery of acquired abducent nerve palsy of variable severity in the early stages of the disease.

Subjects and Methods: Ninety-three cases of diabetic sixth nerve palsy presented to the neuro-ophthalmology clinic of the National Eye Center of Egypt and the ophthalmology outpatient clinic of Beni Suef University Hospitals, from June 2007 to march 2010 were included in the study. Only cases with less than one month complaint were included in the study. Combined vitamin B therapy were applied by intramuscular injections to all cases using the same formula by the same time scheme and dosage for a minimum period of 1 month and a maximum period of 3 months. All cases had minimum follow up period of six months.

Results: Uncontrolled diabetes caused Sixth nerve palsy in 90 cases in this study while the disease was controlled only in 3 cases at the time of presentation. The recovery was achieved in 80 cases while surgery was indicated in 4 cases. Partial recovery was achieved in 9 cases. This study included only one cases of bilateral simultaneous diabetic 6th nerve palsy that had full recovery during the study period. One cases had third cranial nerve palsy 7 months after recovery from 6th nerve palsy. The earliest full recovery came after 3 weeks while the latest recovery came after 4 months and 3 weeks. The rate of recovery was variable. Full diabetic control was achieved in all cases combined with instituted therapy. All cases that had full recovery received treatment within 4 weeks of the onset of the disease while all cases that needed surgery received treatment after 4 weeks of the onset of sixth nerve palsy.

Conclusion: Combined Vitamin B therapy used in the early stage of diabetic sixth nerve palsy have a good result on the rate of recovery as well as the overall outcome of cases of diabetic sixth nerve palsy.

Keywords: *Vitamin B, Diabetic, Abducent Nerve Palsy*

Introduction

Abducent nerve palsy is one of the most common cranial nerve palsies, and may be the commonest amongst all cranial nerves. This may be due to the long course of the nerve and its vicinity to many structures during its course to the supply the lateral rectus muscle. Thus, Isolated abducent nerve palsy is hardly central in origin, and in the vast majority due to peripheral nerve involvement [1].

The sixth nerve is very commonly as a diabetic cranial mononeuropathy and may be the commonest cause of isolated sixth cranial nerve palsy [2]. The etiological factors of this cranial nerve varied greatly from one study to the other [3,4]. The one study in Saudi Arabia, diabetes was the commonest etiological factors for ocular motor cranial nerves and the abducent nerve was the commonest cranial nerve to be affected [5]. In their study to determine the risk factors in ischemic ocular motor cranial nerve palsies, Jacobson and his colleagues reached the same conclusion, with 6th nerve being the commonest nerve to be affected [2]. Moster and his colleagues found that the commonest cause of isolated cranial 6th nerve palsy is the systemic vascular disease and in this group diabetes was the commonest cause [3]. Savino., *et al.* 1982 found that diabetes is the commonest cause of chronic 6th nerve palsy but they emphasized the importance of possible

presence of other serious risk factors including mass lesion [6]. In Indian and Iranian population the same conclusion was reached by the investigators [7,8].

Vitamin B complex was advised for the treatment of diabetic neuropathy in general [9] and there are reports that vitamin B metabolism may be affected in diabetic. There are other reports that vitamin B complex is deficient in diabetic tissues in animal models [10]. Thiamine (vitamin B1) deficiency was suggested to be the key to vascular complications in diabetic patients [11] while its high dosage was linked to beneficial effect in the same category of patients [12]. Pyridoxine (vitamin B6) was linked to improved glucose tolerance curve [13] and carbohydrate metabolism [14]. The pyridoxine deficiency was linked to diabetic neuropathy in many reports [15,16]. The vitamin was reported to alleviate vascular complications in diabetic rates [17].

Cobalamines or Vitamin B 12 deficiency in diabetic patients was linked to the use of metformin in the treatment of diabetes [18] but another study found that vitamin B 12 was deficient in patient with metformin therapy and in patient without meformin therapy [19]. Vitamin B 12 deficiency was strongly linked to diabetic neuropathies. The correction of vitamin B 12 complex deficiency was suggested as treatment for diabetic patient with diabetic neuropathy [20,21,22].

Although abducent nerve palsy in diabetic patients is due a medical cause, a few reports of medical treatment are available. No report of vitamin B therapy in diabetic 6th nerve palsy was recorded in the literature. Most reports wait for spontaneous improvement [23,24] and with failure of this improvement to occur, surgical options are done, including Botulinum toxin injection [25,26,27].

The aim of our study is to study the effect of Vitamin B complex therapy on the outcome of abducent nerve palsy with recent presentation.

Subjects and Methods

All cases presenting to the neuro-ophthalmology clinic of the National Eye Center and the ophthalmology outpatient clinic of Beni Suef University Hospitals, with acute isolated 6th nerve palsy were included in the study.

Inclusion Criteria

Only cases with less than 3 months' complaint were included in the study. Cases with diabetes mellitus as the recognized risk factor with known history of diabetes under treatment or cases newly diagnosed as diabetes during the investigation for the etiology of 6th nerve palsy were included in the study. Cases with combined diabetes and other systemic vascular condition were included in the study including hypertension. There was no age limit in this study.

Exclusion Criteria

Cases with etiology other than diabetes as brain tumors and pseudo tumor cerebri were excluded. Cases with 6th nerve palsy with a period longer than 3 month between onset and presentation were excluded. Cases with any contraindication to combined vitamin B therapy were excluded from the study.

Ninety-three cases of diabetic sixth nerve palsy presented to the neuro-ophthalmology clinic of the National Eye Center of Egypt from June 2007 to march 2010 were included in the study.

Age ranged from 26 years to 71 years with average age of 53.8 years. Twelve patients were 40 years of age or less. Twenty patients came in the 41 to 50 years' age group while 31 patients came in the 51 to 60 age group. Twenty-seven patients came in the 61 to 70 age group while only 3 patients were above 70 years of age (Figure 1). There were 51 females and 42 males in this series of cases (Figure 2).

Full ophthalmological examination was done to all patients including anterior segment examination, dilated fundus examination, and full ocular motility and diplopia examination.

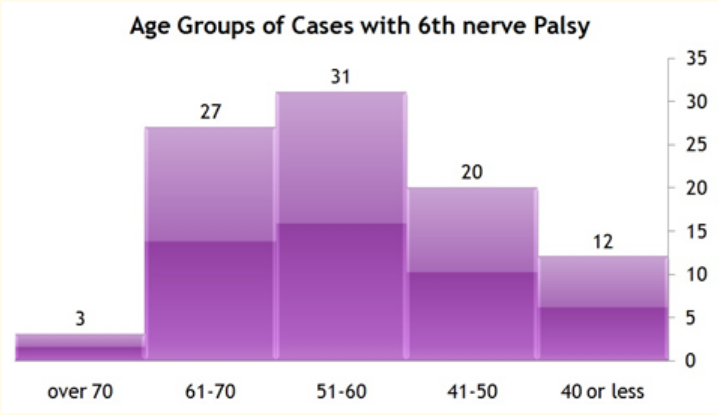

Figure 1: *Showing the age groups of cases with 6th cranial nerve palsy with a peak at the 51-60 years' age group.*

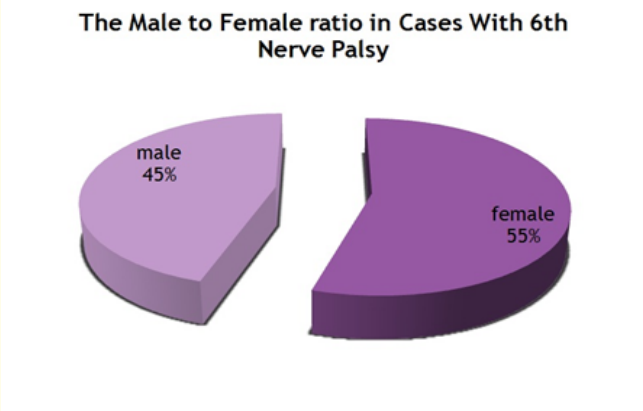

Figure 2: *Showing the male to female ratio with slight female predominance.*

General medical consultation was done for every patient with full medical history. In case of known diabetic patients, the diabetic control of the patient was recorded but controlled and uncontrolled cases were included in the study. All cases presenting with 6th nerve palsy had measurement of fasting blood sugar and postprandial testing of diabetes on weekly basis with control of diabetes in uncontrolled cases. All uncontrolled cases were committed to strict diabetic control.

Controlled diabetes was diagnosed when fasting blood sugar is below 105 mml and the postprandial level of 140 or less. The pattern of diabetic control was obtained through detailed history of the patient about the previous pattern of blood glucose level and the period of diabetes. On the diagnosis of new cases of diabetes, the same parameters were taken and immediate control was started.

Fasting blood sugar and postprandial testing were done every week for the first month then 2 weekly thereafter to ensure optimum control over DM.

Neuroimaging was requested in 31 cases of 6th nerve palsy with 20 cases having MRI and 11cases having CT imaging of the brain.

The follow period ranged from 6 months to 19 months with mean follow up of 8.7 months. The patients were committed to weekly visits for 2 months and 2 weekly visits for 2 months and longer follow up periods were committed to monthly visits. Full ophthalmological examination was done in each visit.

Combined vitamin B therapy was applied by intramuscular injections to all cases using the same formula. Vitamins B1, B6, B12 were injected by intramuscular injection every 3 days for a minimum period of 1 month. After 1 month, the injections were given weekly for a maximum period of 3 months.

Evaluation of the Degree of Abducent Nerve Palsy

The degree of nerve paralysis was evaluated using the amount of movement of the globe beyond the orbital midline. The anatomical landmarks used are the pupil and the limbus. The corneal light reflex method was combined with the anatomical landmarks to make a simple clinical grading method to evaluate the degree of sixth nerve palsy.

With the patient stimulated to direct his eye towards the side of the affected nerve with maximum effort judged by the movement of the contralateral agonist, the medial rectus of the other eye. The evaluation depends not only on the excursion of the affected medial rectus beyond the orbital medline but also on obtaining the maximum action of the yoke muscle of the other eye to ensure the maximum nerve impluse to both muscles.

On attempted lateral gaze towards the affected side the contralateral medial rectus assumes maximum adduction and the corneal light reflex is at or outside the limbus in the sound eye. The affected eye will show a position that reflects the degree of the palsy (Figures 3 & 4).

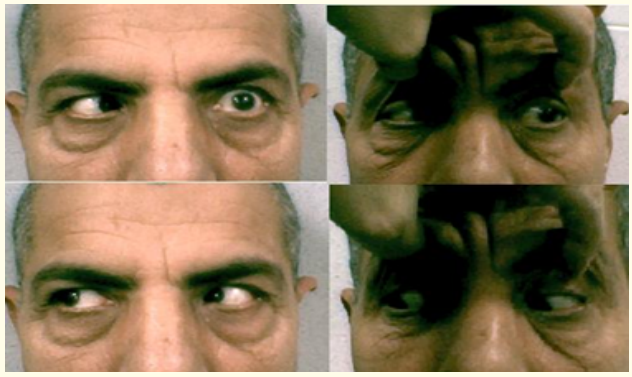

Figure 3: *Showing case number 4 with complete or grade 0 6th nerve palsy with complete recovery following treatment with the correct method applied with full excursion of the contralateral medial rectus.*

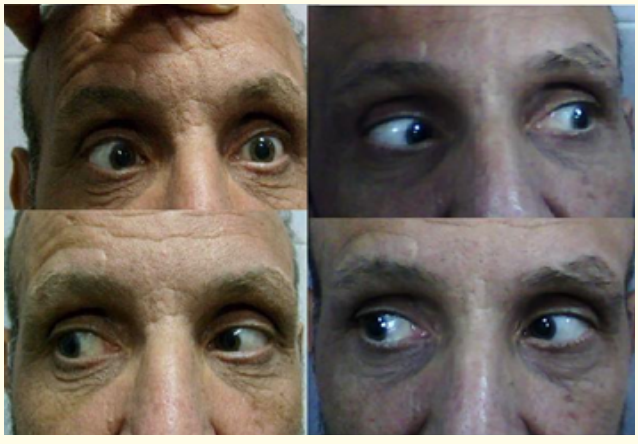

Figure 4: *Showing case 36 with incorrect excursion of the contralateral medial rectus as a part of the diplopia avoidance mechanism and with full recovery after treatment.*

If the nerve palsy is complete, the affected globe will not exceed the orbital midline and the angle of movement is zero. The corneal light reflex will remain within the pupil while the light reflex of the other eye will be at or outside the limbus. If the patient has sixth nerve paresis with full range of motility, the excursion of the affected lateral rectus will be full and coinciding with the affected eye.

Using the old rule of measuring the angle of deviation using the corneal reflex method, the when the corneal light reflex is at the papillary border, the amount of movement is 15 degrees. If the affected globe has a lager excursion so that the corneal light reflex is midway between the papillary border and the limbus, the amount of movement will 30 degrees. When the movement is full and the reflex is at or outside the limbus and the amount of movement is about 45 degrees.

The reference point is the other eye full adduction ensuring maximum excursion making sure that the nervous impulse is maximum to both eyes (Figure 5).

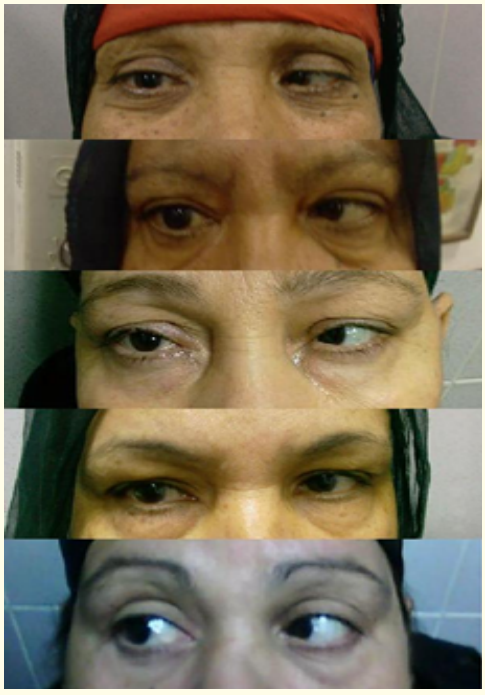

Figure 5: *Showing The different grades of 6th nerve palsy starting with grade 0 at the top picture and ending with grade 4 at the bottom picture.*

Using this method sixth nerve palsy was divided according to severity into:

Grade 0: Central corneal light reflex with no movement of the affected globe with zero angle of movement.

Grade 1: Corneal light reflex within the pupil; very weak excursion with less than 15 degrees of movement.

Grade 2: Corneal light reflex at the papillary border; Weak excursion with 15 degrees of movement.

Grade 3: Corneal light reflex midway between the pupil and the limbus. Moderate excursion with 30 degrees of movement.

Grade 4: Corneal light reflex at the limbus. Full excursion with 45 degrees or more of movement.

This method was applied for all cases during the primary diagnosis and during the follow up visits. Each patient was given a grade for each visit measuring the rate of improvement. The final outcome of all patients was recorded using the same method.

Results

The Presentation

Ninety-three cases of sixth cranial nerve palsy matched the inclusion and exclusion criteria defined. All cases presented with isolated sixth nerve palsy with horizontal diplopia with or without limited abduction in the affected side. Ninety-two cases presented with unilateral palsy while one patient had bilateral simultaneous sixth nerve palsy. The involved eyes in this study are 94 eyes of 93 patients.

Seventy-one cases had diplopia in the primary position while 22 cases had diplopia on side gaze towards the affected side (Figure 6).

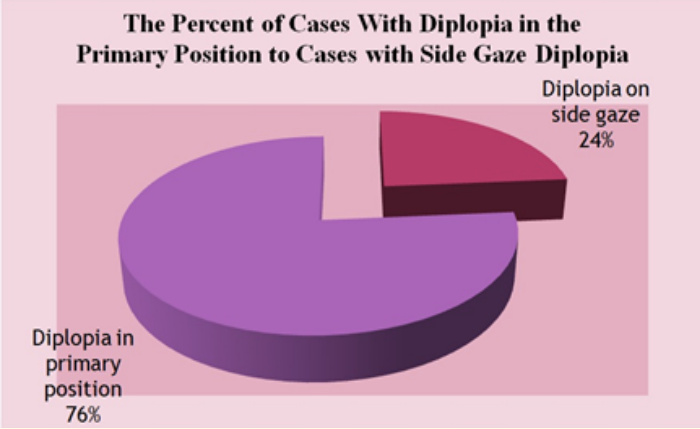

Figure 6: *Showing the percentage of diplopia in the primary position to diplopia of side gaze in cases of 6th nerve palsy in this study.*

Abnormal head posture was adopted in 53 (56.9%) cases with head tilting towards the affected side. Esotropia in the primary position was presented in 67 (72%) cases in the while 26 (27.9%) cases head no tropia in the primary position without cover testing (Figure 7 & 8). The secondary angle of deviation was more than the primary angle in only 18 (19.4%) cases.

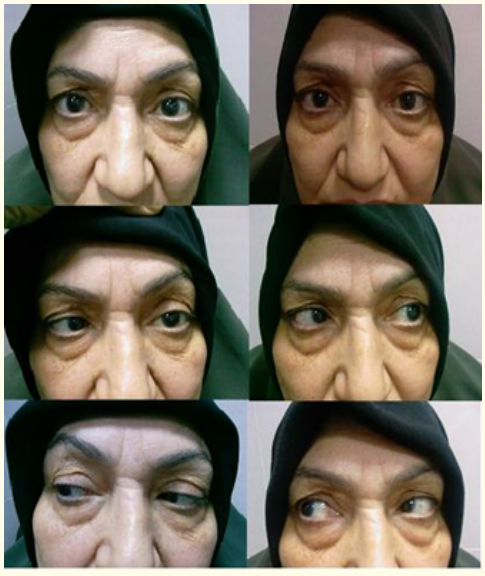

Figure 7: *Showing case 77 with grade 1 6th nerve palsy with minimal lateral rectus excursion and without tropia in the primary at presentation and with complete recovery.*

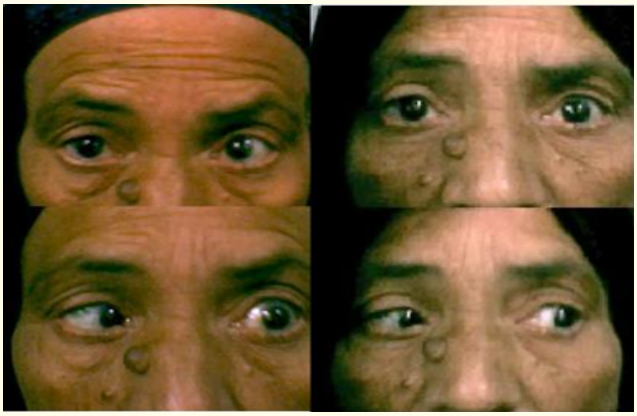

Figure 8: *Showing case 10 with left 6th nerve palsy grade 0 with esotropia in the primary position with complete recovery.*

Variable angle of deviation occurred in the primary presentation in the same setting of examination in both primary and secondary angle of deviation in 23 patients (24.7%). The variability did not exceed 10 degrees in any case.

Variable excursion of the lateral rectus muscle occurred in the same setting in 3 (3.2%) patient in the primary examination of the case. Using the suggested grading the variability in the excursion of the lateral rectus did not exceed one grade in any cases.

One case had oculomotor third cranial nerve palsy 7 months after the onset of 6th nerve palsy in the same side. Investigations showed no abnormality including MRI and MRA of the brain and also CT and MRI of the orbits.

The laterality: fifty patients had an affected left while forty-two patients had affected right eye, one patient had both eyes affected. There was no significant deviation towards one side.

Diplopia induced ptosis with present in 11 cases in this study with 9 cases showing bilateral ptosis while only 2 cases having unilateral ptosis. Cases showed improvement of ptosis with the improvement of diplopia (Figures 9 & 10).

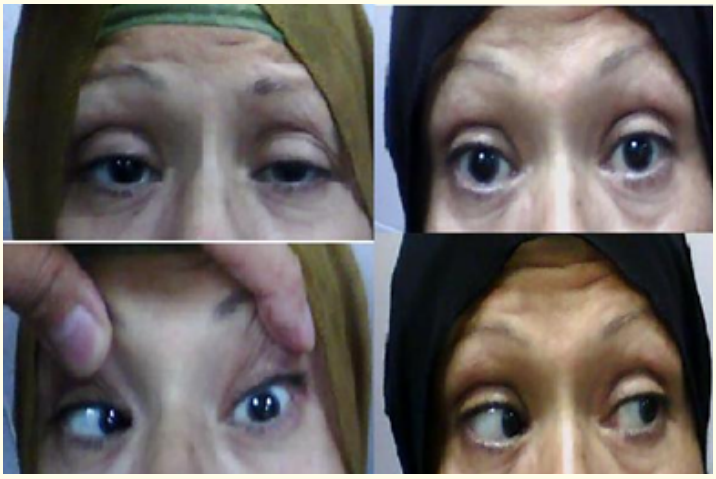

Figure 9: *Showing the right top and bottom picture of case 14 presenting with complete or grade 0 left 6th nerve palsy with left unilateral ptosis with complete recovery of both ptosis and the 6th nerve palsy.*

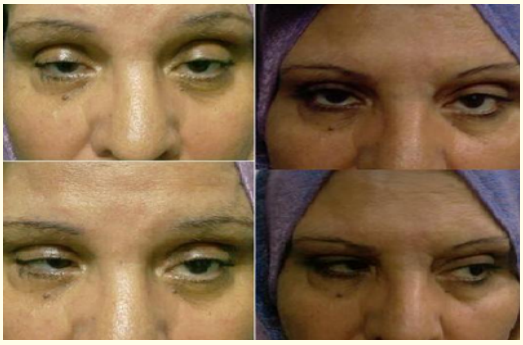

Figure 10: *Showing case 22 with complete grade 0 6th nerve palsy with bilateral ptosis induced by diplopia that showed complete recovery of both following treatment.*

The Onset to Presentation Period

The period between onset and presentation ranged from within 1 week of onset to within 12 weeks of onset of 6th nerve palsy. The average time was 2.8 weeks. The period between the onset and presentation was correlated to the results of therapy. Each patient was given a delay factor according to his delay to present and this was correlated to prognosis.

The Evaluation of 6th Nerve Palsy

According to the evaluation scheme followed in this study, cases of sixth nerve palsy can be divided into:

Grade 0: Complete 6th nerve palsy without any movement of the globe. Thirty-four (36.5%) patients with unilateral presentation came in this category (Figure 5).

Grade 1: Partial 6th nerve palsy with very weak excursion with less than 15 degrees of movement. Fifteen (16.1%) patients with unilateral presentation came in this category.

Grade 2: Partial 6th nerve palsy with weak excursion with 15 degrees of movement. Nineteen (20.4%) patients with unilateral presentation came in this category.

Grade 3: Partial 6th nerve palsy with moderate excursion with 30 degrees of movement. Twenty eyes (21.2%) of nineteen patients (20.4%) came in this category.

Grade 4: Partial 6th nerve palsy with full excursion with 45 degrees or more of movement. Six patients (6.4%) with unilateral presentation came in this category (Figure 11).

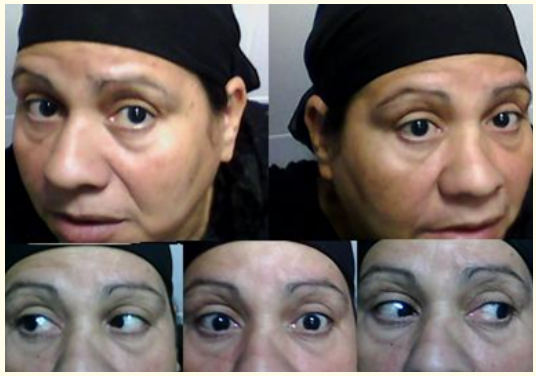

Figure 11: Showing case 78 with full range of lateral rectus motility on both sides with compensatory head rotation towards the affected side with right lateral rectus paresis uncovered by reversing the compensatory head posture.

The above evaluation showed that 63.5% of cases had partial 6th nerve palsy of variable degrees while complete 6th nerve palsy constituted 36.5%. Only 6.4% of cases had 6th nerve palsy with full range of ocular motility (Figure 12).

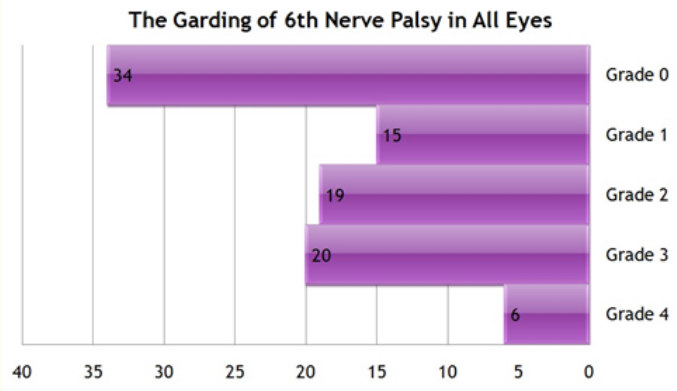

Figure 12: *Showing the number of eyes in each category of the 6th nerve palsy according to the evaluation scheme suggested in this study.*

In this study 13 cases had partial or no recovery, 9 started as complete 6th nerve palsy while only 2 had partial 6th nerve palsy.

Visual Acuity

Visual acuity at presentation ranged from 0.2 to 1.0 in the affected eye and from 0.15 to 1.0 in the fellow eye the mean visual acuity was 0.68 in the affected eye and 0.66 in the other with no significant difference.

Associated ocular diseases

1-Cataract: In this study 49 (52.1%) eyes with 6th nerve palsy of 48 (51.6%) patients had cataract that was found in both eyes. In this study, there was no case of unilateral cataract. Forty-five cases showed no cataract in both eye.

2-Diabetic retinopathy: Fifty (53.2%) eyes of 49 (52.7%) patients had non-proliferative diabetic retinopathy (NPDR) while only 7 (7.4%) eyes with 6th nerve palsy had proliferative diabetic retinopathy (PDR). Cases that showed no diabetic retinopathy were 37 eyes with 6th nerve palsy and had this finding in both the presenting and the non-presenting eye.

All cases with NPDR in the presenting eye had also NPDR in the non-presenting eye while 5 patients with PDR had this finding in both the presenting and the non-presenting eye while only 2 patients had PDR in the presenting eye and NPDR in the fellow eye.

Thirty-eight (40.4%) eyes of thirty-seven (39.8%) patients had coexisting cataract and diabetic retinopathy while 11 (11.7%) presenting eyes had cataract without diabetic retinopathy. Nineteen (20.2%) eyes presenting with 6th nerve palsy had NPDR without cataract in the presenting eye. There was no patient that had PDR without cataract in this study.

Associated Systemic Diseases

Thirty-one patients (33.3%) had systemic hypertension associated with diabetes while 14 patients (17.2%) had hyperlipidemia. Only two patients had coronary artery disease and one patient had virus C hepatitis.

The State of Diabetes at Presentation

Only 3 (3.2%) cases had controlled diabetes at presentation with acute 6th nerve palsy while ninety cases (96.8%) had an uncontrolled diabetic state.

The history of diabetic control was obtained through history taking and through previous laboratory investigation if available. The uncontrolled diabetics were divided into 3 groups according to the history of diabetic control:

1-Totally Uncontrolled: these are the patients not taking any medications for their diabetes at presentation. Twenty-eight patients (31.2%) had no medications taken to control diabetes at presentation, 3 (3.2%) cases had their diabetes discovered through investigating 6th nerve palsy while 19 (20.4%) patients were diagnosed as diabetes before the onset of 6th nerve palsy.

2- Irregularly controlled: These are the patients with history of part time control of their diabetes before the onset of 6th nerve palsy. Forty-one patients (44.1%) had irregular diabetic control before the onset of 6th nerve palsy and all of them had uncontrolled diabetes at presentation.

3- Partially controlled: There are the patients with regular diabetic treatment but with blood sugar levels constantly above normal limits. Twenty-one (22.6%) cases had their blood sugar levels above normal limits and nearly within the same limits at presentation (Figure 13).

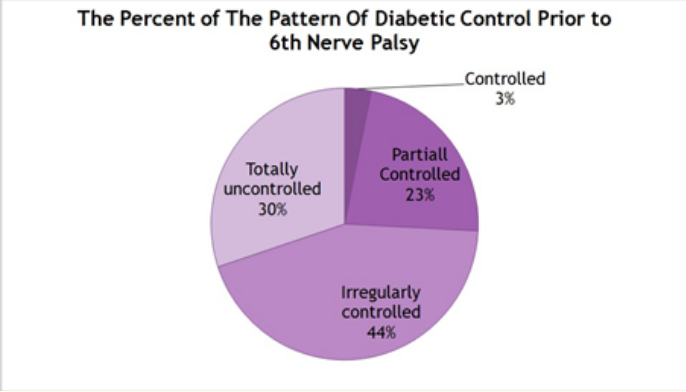

Figure 13: *Showing the pattern of diabetic control in all cases in this study with the minority having control at presentation and the largest group with history of irregular use of treatment.*

The period of diabetes at presentation

The duration of diabetes prior to the onset of 6th nerve palsy in this study ranged from newly diagnosed cases during the investigations for 6th nerve palsy to 26 years of diabetes before the onset of the palsy. The newly diagnosed cases were given the number zero during calculations of period of diabetes in this study.

The mean period of diabetes prior to the palsy was 11.6 years with 40 (43.02%) patients having diabetes for 10 years or less while 41 (44.1%) patients had diabetes from 11 to 20 years and only 12 (12.9%) patients had diabetes for more than 20 years.

There was a homogenous distribution of patients when correlated to the period of DM. There was no significant occurrence of 6th palsy pointing to certain association between the period of diabetes and 6th nerve palsy; however, there was a small peak at 11 years of diabetes with 9 patients having DM 11 years before the palsy. The second point is that there were no patients having diabetes for more than 26 years that presented with 6th palsy during the study period.

For cases with partial or no recovery the period of DM ranged from 0 to 21 years with mean of 11.8 years without significant difference from the mean of all cases.

The recovery of 6th nerve palsy

Full recovery group: Eighty-one eyes (86.2%) of eighty cases (86.02%) had full recovery of 6th nerve palsy. Diplopia completely disappeared in all directions of gaze with full lateral rectus motility (Figures 3, 4, 7-10).

Partial recovery group: partial recovery was achieved in 9 unilateral cases (9.6%). Diplopia disappeared in the primary position in 6 cases with only diplopia on side gaze with full or partial improvement of the excursion of the lateral rectus muscle. In 3 cases the excursion of the lateral rectus improved with diplopia in the primary position and was treated by relieving prism incorporated in the patients' glasses. Eight of the nine cases with partial recovery had complete 6th nerve palsy at presentation (Figure 14).

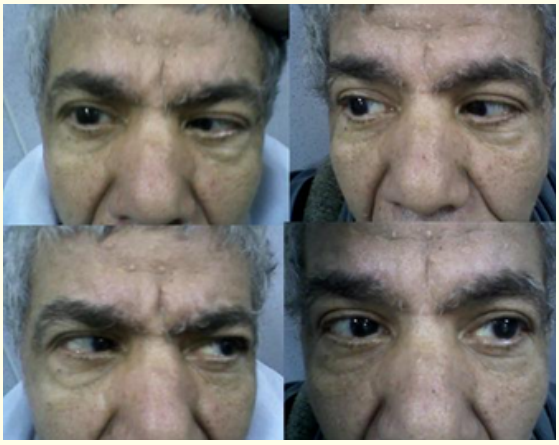

Figure 14: *Showing case 7 presenting with complete right 6th nerve palsy with partial recovery. Notice the slight head rotation towards the right side to avoid diplopia on right gaze after recovery in the top right picture. No further treatment was needed for diplopia management.*

No recovery group: No recovery was found in 4 unilateral cases (4.3%). Surgery was required for all patients in this category. Recess-resect procedure with recovery of diplopia in the primary position was done in 3 cases. One case had muscle transposition surgery with failure of surgery to negate diplopia in the primary position and relieving prisms were prescribed for the patient. Three of the four patients that needed surgery had complete 6th nerve palsy at presentation (Figure 15).

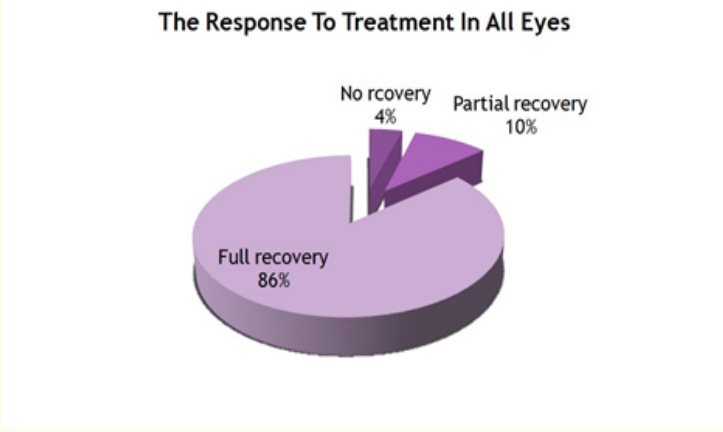

Figure 15: *Showing the response to treatment in all eyes of this work with only 4% failure rate.*

The period of recovery

The period of recovery of all cases with recovery either complete or partial ranged from 3 to 19 weeks with an average of 7.6 weeks. The average period of recovery for cases with full recovery was 7.3 week while average period of recovery for cases with partial recovery was 10.6 weeks.

The correlation between onset to presentation (treatment) period and the period of recovery

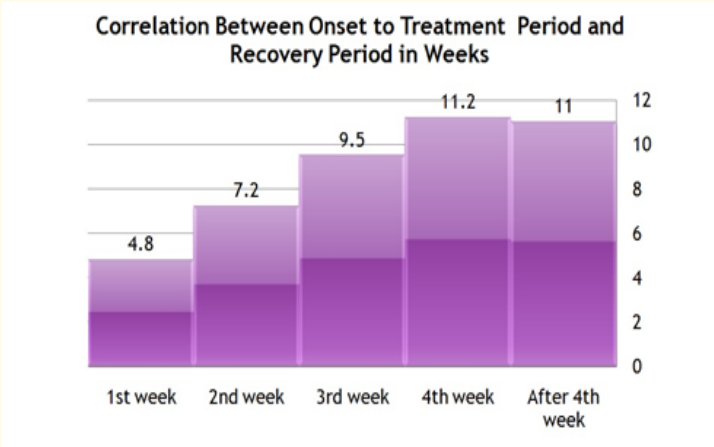

Figure 16: *Showing the correlation between the onset to treatment period and the recovery period showing correlation between early treatment and speed of recovery.*

1. Onset to treatment within the first week: Thirty-two patients came in this category. The period of recovery ranged from 3 to 10 weeks with an average of 4.8 weeks. The recovery was full in all cases presented and received treatment within the first week.

2. Onset to treatment within 2 weeks: Twenty-two patients came in this category. The period of recovery ranged from 4 to 16 weeks with an average of 7.2 weeks. The recovery was full for all cases presented and received treatment within 2 weeks of presentation.

3. Onset to treatment within 3 weeks: eighteen eyes of 17 patients came in this category. The period of recovery ranged from 7 to 19 weeks with an average of 9.5 weeks. Seventeen eyes of 16 patients had full recovery while only one unilateral case had partial recovery for patients presented and received treatment within 3 weeks of presentation.

4. Onset to treatment within 4 weeks: Eleven patients came in this category. The period of recovery ranged from 6 to 16 weeks with an average of 11.2 weeks. Ten cases had full recovery while only one case had partial recovery for patients presented and received treatment within 4 weeks of presentation.

5. Onset to treatment more than 4 weeks: Eleven patients came in this category. No patient in this category had full recovery of the movement of the lateral rectus muscle with 7 patients having partial recovery and 4 patients having no recovery. The average recovery time for patients with partial recovery was 11 weeks.

Discussion

The diabetic 6th nerve palsy is definitely due to a medical metabolic disorder that is needs a long-standing patient compliance to avoid its adverse systemic effects. One of the very well-known complications is diabetic peripheral neuropathy. The etiology of diabetic peripheral neuropathy is supposed to be ischemic however, many authors suggested that it is multifactorial in origin and others suggested an oxidative stress or vitamin deficiency as a proposed etiology.

The good effect of vitamin B complex on the state of diabetic peripheral neuropathy with other reports that vitamin B complex may be deficient in diabetic and the recent reports that some diabetic therapies cause vitamin B12 deficiency made a good point for the rationale of this study. Some about the good effect of pyridoxine (B6) on the vascular complication of diabetic and also the suggested good effect of thiamine (B1) on the glucose tolerance curve made another point towards validating the trial of this combination of vitamins in 6th nerve palsy in diabetic isolated cases.

It is not hidden or concealed that isolated 6th nerve palsy is due to peripheral nerve lesion, infranuclear rather than a central cause, as the central causes almost always not neurologically isolated.

Histopathological studies shown that there is vascular affection of the 6th nerve in DM, however, demyelination was reported in these studies but without any correlation that vitamin B deficiency may the cause for that [28,29].

Although diabetes is a systemic metabolic disorder that causes vascular and neurological complications including 6th nerve palsy, no attempt was done to try to reverse the effect of 6th nerve palsy through medical means and more precisely try to study the effect of strict diabetic control over 6th nerve palsy in diabetics although most reports linked the non-control of diabetics to its systemic vascular complication and also linked diabetic control to improvement of diabetic neuropathy [30,31,32]. Also, there were only few trials for medical therapy for diabetic neuropathy and no trial was directed towards 6th nerve palsy.

The origin, course, anatomical relations, and vascular supply of ocular motor cranial nerves are different and it is not correct to study them collectively as regards the etiology, risk factors, effect of therapy or prognosis. These factors should be studied for each of the cranial nerve alone even if the causative etiology is common, as DM, but it may affect them differently. Also, when trying to understand the prognosis or the effect of therapy, this should be done for each of the ocular motor cranial nerve separately for proper assessment of both of them.

The ptosis that accompanied the sixth nerve palsy was remarkable and cause confusion about the possibility of a central cause of the nerve palsy. The complete recovery of the ptosis either unilateral or bilateral unveiled that it is a diplopia avoidance mechanism that is adopted by the patient and that its recovery was directly correlated to the recovery of diplopia and not due to any central cause.

The commitment of the patient for strict diabetic control was a trial to stop the mechanism that caused the injury and give a chance for the therapeutic agent to show its proper therapeutic effects.

The vascular complication of diabetes are more less chronic in nature and start insidiously, however, 6th nerve palsy in diabetic has an acute onset and this suggest an additional factor that cause the acute palsy, and this factor in our opinion may be deficiency of vitamin B complex below certain levels augmenting the effect vasculopathy caused by DM.

The measurement of the vitamin B levels in the blood or tissue is beyond the scope of this study and needs a prospective trial comparing the diurnal level of vitamin B complex in blood and in tissues compared to the diurnal levels of blood sugar. In our study, we committed our patients to strict diabetic control and this may reverse the proposed vitamin B lowering effect especially when we believe that it had an acute onset rather than a chronic onset. Another point is that the blood changes of vitamin B is different from the tissue levels of the vitamin group which may be the cause of the acute neuropathy rather than the blood levels as suggested by some animal studies [10]. The results of this work recommends that the blood and tissues levels of vitamin B complex should be studied compared to the blood levels and blood glucose levels in patients with diabetic neuropathies, including 6th nerve palsy.

The methods of evaluation of 6th nerve palsy are discussed in the ophthalmology text very widely and nearly all included in the methods of examination of a case of squint or diplopia, however, there was lack of assessment of 6th nerve palsy in terms of strength of muscle action or reversely the amount of muscle weakness or the degree of paresis. The system of grading 6th nerve palsy suggested in this study allows the quantification of the muscle action in relation to the yoke contralateral medial rectus muscle. The system depends on assessment of the excursion of the lateral rectus muscle when the yoke medial rectus is in full adduction. This system determines accurately the amount of muscle paresis and prevents the variability from one case to the other, from one visit to the other and from one examiner to the other. It offers a reliable method of patient follow up and determining the degree of patient improvement or stability and the response to therapy in a well calibrated clinical method.

The duration of diabetes mellitus in years did not correlate with 6th palsy and homogenous distribution was found. This suggests that there no duration of diabetic illness that correlates in a positive or a negative manner to this type of neuropathy. All diabetics from newly

diagnosed cases to longstanding cases are liable to 6th nerve palsy. This supports the view that 6th nerve palsy in diabetics is due to an acute cause rather than a chronic time-related manner.

The state of diabetic control reflects the concept that diabetic control is related positively to this disorder. Only 3 patients out of 93 patients had controlled diabetes at presentation while the vast majority had either partial, irregular, or no control at all at presentation. Although the data about diabetic control prior to presentation was obtained through history taking but it gave a realistic view about the state of diabetic control in Egypt. When correlating our results to results obtained in countries with the same social characteristics as Saudi Arabia, India, and Iran [5,7,8], it seemed that there is more prevalence of irregular control of diabetes causing increased incidence of diabetic 6th nerve palsy compared to other causes. In the western community, the incidence of diabetic 6th nerve palsy was not always the most common cause, reflecting a better diabetic control in the general population. The DCCT (Diabetes Control and Complications Trial) has shown definitively that in diabetic patients, the risk of diabetic poly neuropathy (DPN) and autonomic neuropathy can be reduced with improved blood glucose control. DCCT data strongly suggest that optimal blood glucose control helps to prevent DPN and autonomic neuropathy in diabetic patients. There have been no definitely positive prevention studies of other risk factor modifications for diabetic neuropathies [30,31,31].

The onset to treatment duration was related positively to the recovery of 6th nerve palsy in response to treatment and also to the duration of recovery. Cases that received treatment within the first 4 weeks of the onset had full recovery with the exception of 2 cases only that had partial recovery. Cases that received treatment after 4 weeks from the onset of 6th nerve palsy showed partial or no recovery at all. In cases with full recovery, the longer the onset to treatment duration, the longer the recovery time. The results of this work suggests that the recovery of 6th nerve palsy is time related and the longer the duration of the palsy prior to vitamin B complex treatment, the lower the probability of recovery.

The term spontaneous recovery was used in many papers claiming that there is a recovery not aided by any factor [23,24]. Most probably 6th nerve palsy and diplopia are so much alarming that the diabetic patient gets into strict control immediately reversing much of the metabolic incidents that caused the nerve palsy, among which probably comes vitamin B complex deficiency. A proper control of this factor in the study is to leave the diabetic patient at his state of uncontrolled diabetes and judge the alleged spontaneous recovery of 6th nerve palsy, something that is ethically unacceptable for human subjects. Also this would be unethical in the evaluation of vitamin B therapy on diabetic 6th nerve palsy.

King and colleagues [24] observed 213 patients over 16 years with unilateral, nontraumatic sixth nerve palsies, and found a 78.4% spontaneous recovery rate after 1 year, with 36.6% recovering by 8 weeks and 73.7% by 24 weeks. Recovery did not occur in 16.4%, with 40% of this group having significant underlying pathology, including aneurysm, Arnold-Chiari malformation, brain-stem stroke, carotid-cavernous fistula, or tumor.

In most studies reviewing cases with 6th nerve palsy there was a mixed etiology with difficultly in correlating the rate of recovery for each specific pathology over the same time interval. In simple words the rate of recovery in our study for diabetic isolated 6th nerve palsy with vitamin B complex treatment exceed any reported rate of spontaneous recovery with an overall shorter duration of recovery denoting the significance of the effect of vitamin B complex on the recovery of 6th nerve palsy combined with diabetic control.

The indication of neurodiagnostic imaging in 6th nerve palsy is controversial [33]. However, for cases with suspected intracranial pathology it is definitely indicated. Diabetic isolated 6th nerve palsy does not necessarily require immediate neurodiagnostic imaging when the cause of the palsy is clear and those investigations are only required when the patient fails to show early recovery or when there associated symptoms as headache or prolonged periocular pain.

The coexistence of hypertension does not appear to be a significant risk factor in the pathogenesis of systemic vascular disorders. Patel and colleagues found that there is six fold increase in the odds of having 6th nerve palsy in diabetics and that there is no increased odds of having 6th nerve palsy in hypertension alone. They found that there is eight fold increase in the odds of having 6th nerve palsy in

patients with combined hypertension and DM. They concluded that the coexistence of isolated 6th nerve palsy and hypertension alone is coincidental [4]. In our study, hypertension was the most common systemic disorder associated with DM in cases with isolated 6th nerve palsy. A proper correlation of 6th nerve palsy and hypertension required a separate study.

The effect of vitamin B on the recovery of 6th nerve palsy may be due to;

1. The compensation for the metabolic defects causing vitamin B deficiency.
2. The improvement of glucose tolerance and metabolism.
3. The compensation for the vitamin B complex deficiency caused by some therapeutic agents.
4. Enhancement of nerve recovery following the metabolic insult or vasculopathy.

In conclusion, the good effect of vitamin B therapy on isolated diabetic 6th nerve palsy in this work suggest that these group of vitamins should be given in the early stage of the disease. A delay of therapy for more than 4 weeks is accompanied by lower prognosis of recovery.

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