Original Research Article

An observational study of ocular motor nerve palsies in diabetes mellitus

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Abstract

Background: Cranial mononeuropathy is a well-documented complication in people with diabetes with almost 7.5-fold increased incidence compared to the non-diabetic population. Cranial nerves III and VI appear to be involved more frequently and spontaneous recovery usually occurs within 3-6 months.

Aim of the study: The present study was conducted to assess the pattern of ocular motor nerve palsy in diabetes mellitus, its correlation with glycemic control and other microvascular complications, and to study the recovery pattern.

Materials and methods: 51 patients within the age group of 21-70 years with ocular motor nerve palsies who also had T2DM of any duration were included in this study. The patients underwent thorough clinical and ophthalmological examination and lab investigations and were followed up every 2-3 weeks for a period of 6 months to analyze the recovery pattern.

Results: The ocular cranial nerve palsies were more common in the 51 to 60 years age group. Overall, males were affected more than females except with third nerve palsy, which showed a slight female preponderance. Sixth nerve involvement was most common and none of the patients had fourth nerve

palsy. The left eye was involved more frequently. There was no significant correlation between the level of glycemic control and incidence of ocular motor nerve palsy though retinopathy and nephropathy were seen to occur more with poorer glycemic status. More than three fourth of the patients had complete or partial recovery implying a good prognosis.

Conclusion: Ocular cranial nerve palsy, though a common complication of diabetes mellitus, has a good prognosis. Good glycemic control is of paramount importance for earlier and complete recovery.

Key words

Ocular motor nerve palsy, Type 2 Diabetes mellitus, Recovery.

Introduction

Perfect alignment between the motor system of two eyes is responsible for viewing an object as a single. The extraocular muscles of both eyes work in coordination. When any one or more of these falter, it may manifest as double vision, drooping of eyelids, deviation of eyes or sometimes with pain [1]. Patients may present to the ophthalmologist for one of these complaints, may be referred by another physician or be seen accidentally while they come for a routine checkup [2]. This may be one of the first manifestations of a multisystem disease like diabetes mellitus or may occur at any time during the natural course of this disorder [3]. The features of third nerve palsy may be complete or incomplete and it may be congenital or acquired. Ptosis is due to paralysis of levator palpebrae superioris. The eyeball is turned down, out and slightly intorted due to unopposed action of the lateral rectus and the superior oblique. There is a restriction of ocular movements like adduction, elevation, depression, and extortion. The pupil is fixed and dilated due to paralysis of sphincter pupillae. Accommodation is completely lost due to paralysis of the ciliary muscle. Crossed diplopia appears on manually raising the eyelid, which occurs due to paralytic divergent squint [4]. If the pupillary area is uncovered the head takes a posture consistent with the directions of actions of paralyzed muscle i.e. head is turned to the opposite side, titled towards the same side and chin is slightly raised [5]. The pupillomotor fibers of the III nerve travel in the outer layers of the nerve and are therefore closer to the nutrient blood supply enveloping the nerve [6]. The outer fibers are supplied by the pial plexus whereas the inner fibers are supplied by the vasa nervorum. This explains why in people with diabetes (where the vasa nervorum is affected) there exists pupillary sparing in 80% and similar is the case in any ischemic vascular etiology. On the contrary, when compressive lesions involve the III nerve the superficial fibers are affected, resulting in pupillary involvement in 90% [7]. Most patients with ischemic III nerve paresis demonstrate improvement in motility measurements within one month or may have complete recovery by 3 months (maximum: 6 months) [8]. Cranial imaging like MR scanning – MRI, MRA, four-vessel angiography and Lumbar puncture are recommended if the pupil is involved i.e. dilates or becomes dilated in the initial 5-7 days after onset, no significant improvement in 3 months, the patient develops signs of aberrant regeneration of III nerve or other neurologic findings develop [9]. In IV nerve palsy there is hyperdeviation due to the weakness of superior oblique. This becomes more obvious when the head is titled towards the ipsilateral shoulder (Park Bielchowsky head tilt test) [10]. Depression is limited in adduction. Intorsion is also limited. Vertical diplopia occurs on looking down. To avoid diplopia head adopts a posture such that the action of superior oblique is less needed i.e. face is slightly turned to the opposite side, the chin is depressed and the head is tilted towards the opposite side. Features of ocular motor nerve palsies in diabetes include a commonly affected III nerve, greater occurrence in the elderly, and is remarkably pupillary sparing in nature because the peripherally situated pupillary fibers supplied by the pial plexus are spared whereas the centrally located

fibers supplied by vasa nervous are affected [11]. They usually recover spontaneously and completely in months. It can manifest as multiple episodes of transient ophthalmoplegia affecting different muscles of either one or both eyes and ocular motor nerve palsies in diabetes can be painless or painful [12]. The sixth cranial nerve is the most frequent cause of an isolated ocular motor palsy; it typically presents as horizontal diplopia that worsens on ipsilateral gaze, especially viewing at distance. The abduction deficit is typically associated with an esodeviation that increases with gaze to the affected side [13]. An ischemic mononeuropathy is the most common cause of isolated sixth nerve palsy. Treatment includes lifestyle modification and tight glycemic control with insulin. At each visit diplopia charting, Hess charting, recording of deviations in nine gazes is done. During the course of recovery, the patient is greatly disturbed by diplopia, so some nonsurgical modalities are practiced for symptomatic relief. It no resolution occurs after about 8-12 months then surgery is considered [14].

Materials and methods

The cases studied included 51 patients with neurogenic ocular motor nerve palsies who presented to the Outpatient Departments of Institute of Diabetology and Regional Institute of Ophthalmology and Govt. Ophthalmic Hospital, Madras Medical College in the year 2018. All age groups and both sexes with any duration of type 2 diabetes were included in this study. A complete ophthalmological workup was done.

Inclusion criteria: Age of 21-70 years. All infranuclear ocular motor nerve palsies with T2DM.

Exclusion criteria: All supranuclear, nuclear nerve palsies, myogenic and restrictive neuropathies. Associated combined condition like heart disease, were excluded.

After obtaining informed consent from the 51 patients included in the study, a detailed history was recorded according to a questionnaire. The patients were subjected to a thorough clinical and ophthalmological examination and investigations were done including plasma glucose, HbA1c, urine proteins and fundus examination of the eye. Plasma glucose was assessed by glucose oxidation method, HbA1c by high-pressure liquid chromatography, serum creatinine by Jaffe's method and urine proteins were determined by the turbidimetric method using 3% sulfosalicylic acid. Radiological and serological tests were done where indicated. Patients were followed up every 2-3 weeks for a period of 6 months to achieve and maintain good glycemic control and to record their recovery pattern**.**

Statistical analysis

All the data were expressed in numbers and percentages. Data were analyzed using XLStat. Statistical significance was set at $p<0.05$. All statistical analyses were conducted by using SPSS version 17.0.

Results

51 cases of diabetic ocular motor nerve palsies were evaluated of which 29 were males and 22 were females.

Table - 1 shows in this study, the highest proportion of patients were affected with sixth nerve palsy (62.74%) followed by III nerve palsy (35.29%) and the least in frequency was multiple ocular motor nerve palsy (1.96%). There was no patient with fourth nerve involvement. Regarding the age distribution, considering all the nerve palsies in total, the maximum number of patients belonged to 51-60 years age group (56.86%) followed in frequency by 41-50 years age group with 17.6% of patients, 61-70 years age group with 15.68% patients and 31-40 years age group with 7.84% patients. The least number was seen in the age group of 20-30 years (1.96%). Considering each nerve palsy, with regard to the third nerve, the maximum number was in the age group of 51-60 years (23.52%) followed in frequency by the age group of 61-70 years

(7.84%). With regard to sixth nerve palsy, the maximum number was in the age group of 51-60 years (33.33%) followed by 41-50 years age group (13.7%). Multiple cranial ocular motor nerves were affected in one patient of the age group 41-50 years.

Table – 1: Age distribution.

Age group (Years)	III Nerve	IV Nerve	VI Nerve	Multiple Nerves	Total
21-30	0	0	1	0	1
31-40	1	0	3	0	4
41-50	1	0	7	1	9
51-60	12	0	17	0	29
61-70	4	0	4	0	8

Table – 2: Sex distribution.

Nerve	Male	Female	Total
III	7	11	18
IV	21	11	32
Multiple	1	0	1
Total	29	22	51

Table – 3: Laterality.

Nerve	Right	Left
III	7	11
VI	13	19
Multiple	0	1
Total	20	31

Table – 4: Glycemic control and microvascular complications in iii nerve palsy.

HbA1c%	III Nerve	Urine – Alb	Retinopathy
<6	1	0	1
6.1 – 8.0	8	0	2
8.1 – 10.0	8	2	5
> 10	1	1	1

Table – 5: Glycemic control and microvascular complications in VI nerve palsy.

HbA1c%	VI Nerve	Urine – Alb	Retinopathy
<6	1	0	0
6.1 – 8.0	19	3	6
8.1 – 10.0	7	0	3
> 10	1	1	1

Table - 2 shows in the study there was a slight gender difference, with males outnumbering females – 56.8% males against 43.13% females. The incidence of III nerve palsy was higher in females (21.56%) compared to males (13.7%). With regard to VI nerve palsy, the incidence was higher among males (41.17%) compared to females (21.56%). The patient with multiple

nerve palsy was a male patient. The ratio of III nerve to VI nerve involvement among males was 1:3 whereas in females it was 1:1.

Table - 3 shows left eye involvement was common, with 31 out of 51 patients presenting with left side nerve palsy (60.70%). 19 patients with sixth nerve palsy and 11 patients with third nerve palsy had left-sided involvement. Multiple cranial nerve palsy patient was affected on the left side. Laterality difference was not statistically significant.

Table – 6: Recovery pattern.

Recovery	III	VI	Multiple	Total
Full	10	20	0	30
Partial	3	7	1	11
No Recovery	1	2	0	3
Lost follow up	4	3	0	7

Table - 4 shows in this study, at the time of presentation the glycemic control was assessed by fasting and postprandial blood glucose and glycosylated hemoglobin levels. It was observed that, with regard to III nerve palsy with HbA_{1C} less than 6, one patient developed retinopathy. In the group of 8 patients with HbA_{1C} 6.1-8.0 two had retinopathy (25%). With HbA1c between 8.1-10, 5 of 8 patients had retinopathy (62.5%) whereas 2 had nephropathy (25%) Only one patient had HbA_{IC} > 10 and had both nephropathy and retinopathy (100%).

Table - 5 shows with regard to VI nerve palsy, patients with HbA_{IC} less than six showed no nephropathy or retinopathy. In the group of 19 patients with HbA_{IC} between 6.1-8.0, six patient had retinopathy (31.57%), and 3 patients had nephropathy (15.78%). 7 patients had HbA_{IC} between 8.1-10.0 and of these 3 had retinopathy (42.85%) and none had nephropathy. Only one patient presented with HbA_{IC} of more than 10.0% and had nephropathy (100%) and retinopathy (100%) both. One patient with multiple palsy i.e. III and VI nerve involvement had HbA1C of 9% and showed the presence of both retinopathy and nephropathy.

Table - 6 shows the recovery pattern of the ocular motor nerve palsy due to Diabetes mellitus was varied. Follow up was done at 2-3 weekly intervals for 6 months. 58.8% of the patients showed full recovery, 21.5% showed partial recovery, 5.8% showed no recovery and 13.7% were lost to follow up. The recovery was noted in 4 months in most cases, which was almost complete in 6 months.

Discussion

In this study of 51 cases of Diabetes mellitus with ocular motor nerve palsies, the widest range was associated with sixth nerve palsies. The majority of patients with either III nerve (23.52%) or VI nerve palsy (33.33%) belonged to 51-60 years age group. In a study of 22 cases of III nerve palsy by Rafael E, et al. the average age was 62 years. In our study, the sixth nerve was the commonly affected nerve, whereas in literature the third nerve palsy is the most commonly affected followed by the sixth and seventh nerve. In III nerve palsy, the pupil is usually spared. The cause is thought to be vascular with a localized infarct involving the brain stem nuclei or the emerging nerve root [15]. Older people are commonly affected. In this study, there was an overall slight gender difference with male preponderance 56.86% males compared to 43.13% females. Incidence of third nerve palsy was observed to be higher in females (21.56%) compared to males (13.7%) whereas the incidence of sixth nerve palsy was more among males (41.17%) compared to females (21.56%). The patient with multiple nerve palsy was a male patient. The ratio of III nerve to sixth nerve involvement among males was 1:3 whereas in females it was 1:1. In our

study, the male to female ratio for the incidence of III nerve palsy was 1:1.57 and for sixth nerve palsy, it was 1.9:1 [16]. Comparing with the study by Goldstein and Cogan for third nerve palsy where the male to female ratio was 1:1. Left eye involvement was found to be common (60.78%) of which 37.25% of patients had sixth nerve palsy, 21.56% of patients had third nerve palsy and 1.96% was multiple cranial nerve palsy. Bilaterality was not observed in this study. The laterality does not seem to have significance in the study Reddy P Siva, et al. where right and left eye were equally affected [17]. There was left eye preponderance in our study. Glycosylated Hemoglobin was taken to assess the overall glycemic control of the patient at the time of incidence of the specific cranial nerve palsy [18]. There is a large body of evidence that Glycated Hemoglobin relates to integrated preceding glycemic control. It is now recognized that Glycated Hemoglobin is the weighted measure of preceding glycemia with recent events contributing more than distant ones. In our study, only one patient was seen with third nerve palsy with an HbA1c of less than 6%. This implies overall good glycemic control in the past three months but this patient had mild non-proliferative diabetic retinopathy which may be explained by the duration of diabetes being more than 12 years [19]. There were 8 patients with HbA1c from 6.1% to 8.0% of whom 25% had retinopathy and none had nephropathy. In the group with HbA1c between 8.1 to 10%, there were 8 patients, of whom 62.5% had retinopathy and 25% had nephropathy. Only one patient in this series had HbA1c of more than 10% and she had both nephropathy and retinopathy. This implies that the patients with poorer control indicated by higher HbA1c had a higher incidence of microvascular complications like nephropathy and retinopathy but there was no correlation between HbA1c and ocular motor cranial nerve palsies [20]. With regard to VI nerve, only one patient had HbA1c less than 6% and had no evidence of retinopathy or nephropathy. This patient had diabetes for 2 years. In the group with HbA1c from 6.1% to 8.0%, there were 19 patients of whom retinopathy was found in 6 patients (31.8%) and 3 patients had nephropathy (15.78%). When glycated hemoglobin was in the range of 8.1 to 10%, 7 patients had VI nerve palsy with 3 patients having retinopathy (42.85%) and none had nephropathy. The only patient with HbA1c of more than 10% had both nephropathy and retinopathy. The sole patient with multiple palsy had an HbA1c level of 9% with both microvascular complications [21]. This again went in for favor to imply that glycemic control did not relate to ocular motor cranial nerve palsies. 30 patients (58.8%) showed complete recovery of whom 10 had III nerve palsy (55.5%) and 20 had VI nerve palsy (62.5%). The partial recovery in the series was seen in 21.5% patients of whom 3 suffered from III nerve palsy (16.6%) and 7 with VI nerve palsy (21.87%). No recovery was seen in 5.88% of total patients of whom one belonged to III nerve palsy (5.55%) and 2 with VI nerve palsy (6.25%). 7 patients were lost to follow up. Patients who showed no recovery by the end of 6 months were further evaluated. In this study, the recovery pattern was found to be good with more than three-fourths of the patients recovering fully or partially [22].

Conclusion

The diabetic ocular motor nerve palsies occur in a wide range of age but are more common in the age group of 51-60 years. Overall males were affected more than females except in third nerve palsy which showed a slight female preponderance. Left eye involvement was common. Sixth nerve palsy was more common than third nerve palsy. Fourth nerve involvement in diabetes mellitus is comparatively rare and no patients were detected with IV nerve palsy. A careful history, general and complete ophthalmological workup with necessary basic investigations is enough to diagnose patients with diabetic ocular motor nerve palsies. Further evaluation and specialist opinion are necessary when there is a deviation from the normal pattern of recovery.

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