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A Study of Magnesium Supplementation on Amplitudes of Sensory and Motor Nerves in Patients of Diabetic Neuropathy

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Abstract

To Study the effect of magnesium supplementation on amplitudes of sensory and motor nerves in patients of diabetic neuropathy.

This study was conducted on 60 diabetic neuropathy patients attending the neurology o.p.d between february 2009 to august 2010. These patients were segregated into two groups. group I (n=30) receiving magnesium and metformin therapy for a period of 16 weeks. Group II (n=30) receiving only metformin therapy.

The blood samples were collected and analyzed for s. magnesium and fasting blood glucose at 0,4,8,16 weeks, respectively. Measurement of amplitudes of sural and common peroneal nerves were done at 0,4,8,16 weeks, respectively.

Average age of males in group I was 54.36±1.18yrs and of females was 53.09±1.47yrs and in group II was 55.94±1.62yrs and of females was 52.83±1.58yrs.

Mean baseline value for amplitude of sural nerve in group I was 4.90±0.34uV and after treatment values at 4, 8 and 16 weeks were 6.19±0.29, 7.56±0.34 and 9.64±0.59uV respectively. In Group II mean baseline value for amplitude of sural nerve was 5.13±0.50uV and after treatment values at 4, 8 and 16 weeks were 4.97+0.48, 4.85±0.51, 4.86+0.49uV respectively. Mean baseline value amplitude of common peroneal nerve in group I was 2.49±0.21mV and after treatment values at 4, 8 and 16 weeks were 3.31±0.23, 3.91+0.19 and 4.24±0.19mV respectively. In group II, mean baseline value for amplitude of common peroneal nerve was 2.58±0.25mV and after treatment values at 4, 8 and 16 weeks were 2.61±0.24, 2.64±0.24 and 2.77±0.24mV respectively.

Statistically significant difference was observed in group I, patients' amplitudes of sural and common peroneal nerves, before and after treatment values at 16 weeks ($p<0.05$). Statistically insignificant difference was observed in group II patients before and after treatment values at 16 weeks ($p>0.05$). This study thus concludes that anti-diabetic therapy when combined with magnesium supplementation shows improvement in amplitudes of sensory and motor nerves.

Keywords: *Diabetic neuropathy, magnesium supplementation, amplitude (sural and common peroneal nerve).*

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Introduction

Globally, an estimated 422 million people are suffering from diabetes in 2014. Separate data for type 1 and type 2 diabetes mellitus doesn't exist but the majority of these adults are affected by type 2 DM.[1] Majority of people with diabetes will eventually

develop peripheral neuropathy, making it the leading known cause of neuropathy. Diabetic neuropathy is one of its most common complication and great source of morbidity and mortality. Hyperglycemia being the major causative factor leading to neuropathy.

Magnesium is known to be necessary for nerve conduction; deficiency is known to cause peripheral neuropathy symptoms and studies suggest that a deficiency in magnesium may worsen blood glucose control in type 2 diabetes.

Chu C et al (2016) suggested that serum magnesium levels were significantly lower in type 2 DM patients with abnormal nerve conduction studies, and significantly associated with lower amplitude, furthermore indicating the possible affect of magnesium on axonal degeneration.[2] Amighi j.et.al (2004) stated that magnesium is known to be necessary for nerve conduction.[3] Engelen w et.al (2000) substantiated that under unchanged metabolic control supplementation with could improve nerve conduction.[4]

Material and Method

This study was carried out in the Department of Physiology and Department of Neurology, S.N. Medical College and Associated Hospitals, Agra, over a period of 18 months in Diabetic neuropathy patients who were attending neurology O.P.D of S.N Medical college, Agra from February 2009 to august 2010.

All participants were subjected to detailed history taking and thorough clinical examination after obtaining their consent. Special focus was given to neurological examination and detailed examination of both the upper and lower extremities were done. Patients with at least two of the followings were included in the study:

1. Symptoms of paraesthesia or dysesthesia.
2. Diminished vibratory sense below the knee.
3. Decreased ankle jerk compared to knee jerk.
4. Reduced discrimination and light touch sense distally in the legs.

After examination, participants were investigated for fasting blood sugar, S. magnesium, blood urea and serum creatinine at first visit (0 weeks) and subsequently these tests were repeated at 4, 8,16 weeks respectively.

A nerve conduction study (NCS) is a test commonly used to evaluate the latency, amplitude, duration and conduction velocity of electrical impulses from the motor and sensory nerves of the human body. The amplitude, i.e. the size of the response, represents the number of axons that are conducting action potentials. Thus, decrease in amplitude depicts axonal degeneration.

Sensory NCS was performed by electrical stimulation of a peripheral nerve and recording from a purely-sensory portion of the nerve. Sensory amplitudes are much smaller than the motor amplitudes and measured in the microvolts (uV) range. *Motor NCS* was performed by electrical stimulation of a peripheral nerve and recording from the muscle supplied by this nerve. Motor amplitudes were measured in millivolts (mV).

In all the participants, nerve conduction study of lower limb was carried out - amplitudes of sural nerve (sensory nerve) and common peroneal nerve (motor nerve) of right leg were measured on DOS-based two channel NCV/EMG machine (M/S Recorders & Medicare System, Chandigarh, India). For evaluating the level of improvements in the peripheral neuropathy, the type II Diabetic neuropathy patients (n=60) who were attending O.P.D of neurology clinic S.N Medical college, Agra were segregated into two groups:

Group-I: was given 300 mg/day of magnesium supplementation (magnesium chloride sustained release tablets) along with metformin for a period of 16 weeks. Average dose of metformin was 1.5 g/day.

Group-II: was given only metformin for a period of 16 weeks. Group II patients were of comparable ages, of normal weight for height, on usual diet with no drugs taken at the time of examination.

Electrophysiological examination of the tested nerves (i.e. sural nerve and common peroneal nerve of right leg) was carried out four times, for patients of both the groups, at first visit and then subsequent examinations at the end of 4, 8 and 16 weeks.

Inclusion Criteria:

1. Known case of diabetes mellitus.
2. Probable case of diabetes mellitus after being investigated for fasting and postprandial blood sugar.
3. Patients with signs/symptoms suggestive of

diabetic poly neuropathy.

Exclusion Criteria:

1. Those with altered sensorium or disturbed mental state.

2. Those having any other diseases known to cause peripheral neuropathy like chronic renal failure, liver failure, hypothyroidism, leprosy, porphyria etc.

3. Patients on drugs that are known to cause peripheral neuropathy like isoniazid, phenytoin or those who are chronic alcoholics.

4. Patients showing abnormal levels of blood urea, S. creatinine, abnormal liver function tests.

Observation

Table no. L: Age and Sex Distribution of Diabetic Neuropathy Patients

Age	Group-I (n=30)				Group II (n=30)				Total I±II (n=60)			
	M	F	Total	%	M	F	Total	%	M	F	Total	%
41-50	4	3	7	23.3	4	5	9	30	8	8	16	26.7
51-60	13	7	20	66.7	9	5	14	46.6	22	12	34	56.7
61-70	2	1	3	10.00	4	2	6	20	6	3	9	15.0
>70	0	0	0	0	1	0	1	3.4	1	0	1	1.6
	19 63.3%	11 36.7%	30	100	18 60%	12 40%	30	100	37	23	60	100

Table No.l depicts the age and sex wise distribution of Diabetic neuropathy patients.

In Group I - Percentages of neuropathy patients belonging to 41-50, 51-60, 61-70 and >70 years age groups were 23%, 66.7%, 10% and 0%, respectively. Number of males in aforementioned age groups were 4, 13, 2 and 0, respectively. Number of females were 3, 7, 1 and 0, respectively. Out of 30, 19 Males(63.3%) and 11 females(36.7%) were present.

In Group II- Percentages of neuropathy patients belonging to 41-50, 51-60, 61-70 and >70 years age groups were 30, 46.6, 20 and 3.4%, respectively. Number of males in aforementioned age groups were 4, 9, 4 and 1, respectively. Number of females were 5, 5, 2 and 1, respectively. Out of 30, 18 males(60%) and 12 females(40%) were present.

In TOTAL-out of 60 diabetic patients 37 were males (61.7%), 23 were females (38.4%).

Table No. 2: Average Age (in **Year** Mean **± S.e.m) in Both Gender in Different Groups**

GENDER	GROUP-I	GROUP-II
MALE	54.36±1.18 (n=19) S.D = 5.155	55.94±1.62 (n=18) S.D = 6.881
FEMALE	53.09±1.47 (n=11) S.D = 4.888	52.83±1.58 (n=12) S.D = 5.491
TOTAL	53.90±0.9152 (n=30) S.D = 5.013	54.7±1.178 (n=30) S.D = 6.450

Table no.2 depicts the average age of males and females in both the groups.

In the present study, In group I, average age of males was 54.36±1.18 years and of females was 53.09±1.47 years.

In group II, males were of 55.94±1.62 years and females were of 52.83±1.58 years.

In group I, Average age of was 53.90±0.9152 years and in group II, it was 54.7±1.178 years.

TABLE NO. 3: AMPLITUDE OF SURAL NERVE (microvolts) BEFORE AND AFTER TREATMENT

	GROUP I (n=30)				**GROUP II (n=30)**			
	Before treatment	**After Treatment**			**Before treatment**	**After Treatment**		
		4 weeks	**8 weeks**	**16 weeks**		**4 weeks**	**8 weeks**	**16 weeks**
Mean	4.90	6.19	7.56	9.64	5.13	4.97	4.85	4.86
S.D	1.86	1.59	1.84	3.22	2.73	2.61	2.77	2.66
S.E.M	0.34	0.29	0.34	0.59	0.50	0.48	0.51	0.49
% Change Over Baseline				96.7%				5.3%
p Value				$p<0.05$				$p>0.05$

Table No. 3 depicts the baseline values (before treatment) of amplitude (microvolts) of Sural N. and after treatment values for group I and group II at 4, 8 and 16 weeks, respectively.

In group I, mean baseline value for amplitude of sural nerve was 4.90±0.34 and after treatment values at 4, 8 and 16 weeks were 6.19±0.29, 7.56±0.34 and 9.64±0.59, respectively. Differences in values of amplitude of sural nerve before and after treatment with magnesium and metformin were considered extremely significant ($p<0.05$).

In group II, mean baseline value for amplitude of sural nerve was 5.13±0.50 and after treatment values at 4, 8 and 16 weeks were 4.97+0.48, 4.85±0.51 and 4.86±0.49 respectively. These differences in values of amplitude of sural nerve before and after treatment with metformin for 16 weeks were not significant ($p>0.05$).

Table No. 4: Amplitude of C.P.N (Millivolts) Before and After Treatment

	GROUP I (n=30)				**GROUP II (n=30)**			
	Before treatment	**After Treatment**			**Before treatment**	**After Treatment**		
		4 weeks	**8 weeks**	**16 weeks**		**4 weeks**	**8 weeks**	**16 weeks**
Mean	2.49	3.31	3.91	4.24	2.58	2.61	2.64	2.77

Cont... **Table No. 4: Amplitude of C.P.N (Millivolts) Before and After Treatment**

S.D	1.15	1.27	1.02	1.02	1.34	1.30	1.30	1.32
S.E.M	0.21	0.23	0.19	0.19	0.25	0.24	0.24	0.24
% Change Over Baseline				70.3%				7.4%
p Value				P<0.05				p>0.05

Table No. 4 depicts the baseline values (before treatment) of amplitude (millivolts) of C.P.N and after treatment values for Group I and GROUP II at 4, 8 and 16 weeks respectively.

In group I, before treatment value for amplitude of common peroneal N. was 2.49±0.21 and after treatment values at 4, 8 and 16 weeks were 3.31±0.23, 3.91+0.19 and 4.24±0.19 respectively. In this group we observed that increase in the amplitude of common peroneal N. values before and after 16 weeks of magnesium supplementation were considered extremely significant ($p<0.05$).

In group II, before treatment value for amplitude of C.P.N was 2.58±0.25 and after treatment values at 4, 8 and 16 weeks were 2.61±0.24, 2.64±0.24 and 2.77±0.24, respectively. In this group we observed that amplitude of C.P.N values before and after 16 weeks of treatment were not statistically significant.

Discussion

Average age of males was 54.36±1.18 years and of females was 53.09±1.47 years in group I. In group II, average age of males was 55.94±1.62 years and of females was 52.83+1.58 years. Mean duration of diabetes in group I was 15.516±1.066 as compared to 15.290±1.237 in group II.

In present study, mean value for amplitude of sural nerve in group I before treatment was 4.90±0.34uV as compared to 9.64±0.59uV after 16 weeks of treatment. This difference was considered extremely significant ($p<0.05$).

In group II before treatment mean value for amplitude of sural nerve was 5.13±0.50uV as compared to 4.86±0.49uV after treatment (i.e after 16 weeks). This difference was considered statistically insignificant ($p>0.05$).

In present study, mean value for amplitude of common peroneal nerve in group I before treatment was 2.49±0.21mV and after 16 weeks was 4.24±0.19mV. This difference was found to be statistically significant ($p<0.05$).

In group II, before treatment mean value for amplitude of common peroneal nerve was 2.58±0.25mV and after treatment was 2.77±0.24mV. This difference was statistically insignificant ($p>0.05$).

Almost similar results were obtained by the following studies:

Ivo De Leeuw *et al.* (2004) observed that in Mg depleted type 1 diabetic patients, long term magnesium supplementation is a favourable influencer in the natural evolution of neuropathy. They also noticed that chronic Mg depletion in Tldm has been associated with Polyneuropathy (PNP).[5]

Engelen W *et al.* (2000) observed that Mg supplementation increasing Mg RBC, in younger patients with a short duration of diabetes and presenting with early signs of the neurological complication, might improve nerve conduction and amplitude measured by electromyography.[4]

Sophie Begon *et al.* (2000) observed that magnesium could be an alternative for the treatment of neuropathic pain in patients of diabetic neuropathy.[6]

Elamin A *et al.* (1990) observed that appropriate magnesium supplementation might prove beneficial in normalizing the low plasma and tissue magnesium levels and prevent or retard the development of vascular & neural complications in diabetic patients.[7]

Conclusion

This study concludes that anti-diabetic therapy when combined with magnesium supplementation shows improvement in amplitudes of sensory and motor nerves and hence improves the symptoms of diabetic neuropathy patients. Limitation of our study was its small sample size.

Conflict of Interest: None

Source of Funding: self-funded study

Ethical Clearance: Approval of institutional ethical committee was taken for this study.

References

1. Global report on diabetes, Geneva: World Health Organization; 2016.
2. Chu C, Zhao W, Zhang Y, Li L, Lu J, Jiang L *et al.* Low serum magnesium levels are associated with impaired peripheral nerve function in type 2 diabetic patients. *Sci. Rep. 6*, 32623; doi: 10.1038/srep32623 (2016).
3. Amighi J, Sabeti S, Schlager O, Mlekusch W, Exner M, Lalouschek W et al. Low serum magnesium predicts neurological events in patients with advanced atherosclerosis. *Stroke.* 2004 Jan; 35(1): 22-7. Epub 2003 Dec 04.
4. Engelen W, Bouten A, De Leeuw I, De Block C. Are low magnesium levels in type 1 diabetes associated with electromyographical signs of polyneuropathy?. Magnes Res. 2000 Sep;13(3):197-203.
5. Ivo De Leeuw, Wendy Engelen, Christophe De Block, Luc Van Gaal. Long term magnesium supplementation influences favourably the natural evolution of neuropathy in MgDdepleted type 1 diabetic patients (Tldm) Magnesium Research. Volume 17, Number 2, 109-14, June 2004, Original article.
6. Sophie Begon, Gisele Pickering, Alain Eschalier and Claude Dubray. Effects of magnesium and MK-801 in two experimental models of neuropathic pain. Brain Research, Volume 887, Issue 2, 29 December 2000, Pages 436-439.
7. Elamin A, Tuvemo T. Magnesium and insulin-dependent diabetes mellitus. Diabetes Res Clin Pract. 1990 Nov-Dec;10(3):203-9.