ORIGINAL RESEARCH PAPER

Physiology

CROSS SECTIONAL STUDY OF CO-RELATION B/W ANEMIA AND NEUROPATHY IN TYPE -2 DIABETES MELLITUS

KEY WORDS: Diabetic Peripheral Neuropathy, Unpaired T- Test, Nerve Conduction Study

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ABSTRACT

Anemia is a common complication of diabetic peripheral neuropathy. Nerve conduction study parameters of diabetic peripheral neuropathy with anemia are deranged. **Material and Method:** 400 female subjects of age group 20-40 years in JLN Hospital, Ajmer OPD and IPD were randomly selected for this study. Glycemic profile, complete blood count and nerve conduction study of these patients are done forming 2 groups (200 diabetic peripheral neuropathy patients without anemia and 200 diabetic peripheral neuropathy patients with anemia). Chi- Square, Unpaired t- test & Z- test were used. Level of significance was set at P≤0.05. **Result:** The result of present study suggests that with increasing HBA1C & decreased hemoglobin levels; latency increased, amplitude and velocity decreases. **Conclusion:** In present study diabetic peripheral neuropathy patients with anemia had lower nerve conduction velocity and amplitude of sensory nerves when compared to those without anemia. Hence the treatment of anemia should be considered in diabetic peripheral neuropathy patients while treating the other possible risk factors.

INTRODUCTION:

Diabetes mellitus is a syndrome characterized by impaired carbohydrate, protein and fat metabolism resulting from either deficiency of insulin or reduced tissue sensitivity to insulin. Gestational diabetes mellitus is diagnosed in second or third trimester of pregnancy due to malnutrition or unrestricted intake of calories.

Among the micro vascular complications of diabetes; diabetic neuropathy occurs in more than 50% of individuals. The pathogenesis of diabetic peripheral neuropathy is inflammatory and oxidative stress which occur due to metabolic dysfunction that damages the neuronal cells.

Anemia is common manifestation in diabetes mellitus. The prevalence of anemia is 2-3 times higher in diabetic patients compared to healthy population. Since anemia causes reduction in oxygen carrying capacity of blood; impaired oxygenation causes endo neural hypoxia which could damage the neurons.

Approximately 40% of diabetics are affected by kidney disease. Due to the development of diabetes mellitus, nephropathy may arise which undermines the renal production of erythropoietin hence resulting in anemia. Furthermore pro-inflammatory cytokines due to kidney disease also interferes with intestinal iron absorption resulting in anemia.

MATERIALS & METHODS:

- The present study was conducted in Neurophysiology lab at JLN Medical College &Hospital Ajmer (Rajasthan). 400 female subjects of age group 20-40 years with history of diabetes mellitus type 2 for >1 year were taken in JLN Hospital, Ajmer OPD and IPD and were selected for this study.
- At the beginning we take their general information.
- Than we performed investigations: HBA1C, Fasting Blood Sugar, Post-prandial blood sugar, Complete Blood Count.
- Diagnosis of diabetic peripheral neuropathy is made by symptoms such as numbness, burning sensation, aching pain in feet, leg, toes, and signs such as symmetrical reduction in distal sensation & absent or reduced ankle reflexes.
- We formed two groups: Group A - 200 Diabetic peripheral neuropathy patients without anemia (Hb- 12gm/DL or More)
- Group B – 200 Diabetic peripheral neuropathy patients with anemia (Hb - <12gm/DL).
- Now nerve conduction studies of these groups were conducted.

Statistical Analysis: Chi-square test used for association of various factors with respect to nerve conduction test interpretation. Unpaired t- test used for calculating mean latency, amplitude & conduction velocity of various nerves. Z-test calculating the confidence interval of latency, amplitude & conduction velocity of various nerves. Level of significance was set at P≤0.05.

RESULT:

Sensory nerve conduction study variables such as latency, amplitude, and nerve conduction velocity are compared between group A (Diabetic peripheral neuropathy without anemia) and group B (Diabetic peripheral neuropathy with anemia). The baseline characteristics and clinical profile of the subjects were compared between the two groups. Comparison of continuous variables between the two groups are made using unpaired "t"test.

Statistical analysis are made using IBM SPSS software version 25. p-value<0.05 is considered to be statistically significant and value< 0.01was considered as statistically highly significant.

Comparison Of Baseline Characteristics Between Groupa (Diabetic Peripheral Neuropathy Without Anemia) And Group B (Diabetic Peripheral Neuropathy With Anemia)

Base line characteristics of the study participants in both groups

Variables	Diabetic peripheral neuropathy without anemia (Group A) n=200	Diabetic peripheral neuropathy with anemia (Group B)n=200	P-value
	Mean ± SD	Mean ± SD	
Mean age (years)	31.50 ± 3.51	32.01 ± 2.36	0.089

The p-value is 0.089 and the difference is statistically not significant. Hence these diabetic patients were recruited to study the effect of anemia on nerve conduction parameters.

Comparison Of Clinical Profile Between Group A (Diabetic Peripheral Neuropathy Without Anemia) And Group B (Diabetic Peripheral NeuropathyWith Anemia)

Clinical characteristics of the study participants in both groups

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Hemoglobin (g/dL)	14.78 ± 2.05	9.40 ± 1.65	0.0001
Mean Corpuscular Volume (fL)	87.12 ± 4.12	80.32 ± 7.12	0.0001
Mean Corpuscular Hemoglobin (pg)	28.04 ± 2.12	27.19 ± 2.89	0.0009
Duration of diabetes (years)	5.95 ± 1.34	6.40 ± 3.51	0.0915
Fasting Blood Sugar (mg/dL)	124.12 ± 20.12	128.12 ± 25.52	0.0825
Postprandial Blood Sugar (mg/dL)	184.67 ± 18.23	187.12 ± 20.45	0.2067
HbA1c (%)	7.83 ± 0.77	8.10 ± 0.95	0.0019

Hemoglobin values of group B were reduced when compared to group A and the difference of means is statistically significant (p-value is 0.0001).

Glycemic Index

Duration of diabetes in DPN without anemia is 5.95 ± 1.34years and that of DPN with anemia is 6.40 ± 3.51years. The difference in mean between the two groups is not statistically significant (p-value 0.0915).

Fasting blood sugar of DPN without anemia is 124.12 ± 20.12mg/dl and that of DPN with anemia is 128.12 ± 25.52mg/dl. The difference in mean between the two groups is not statistically significant (p-value 0.0825).

The postprandial blood sugar of DPN patients without anemia is 184.67 ± 18.23 mg/dl and that of DPN patients with anemia is 187.12 ± 20.45mg/dl. The difference in means is not statistically significant (p-value 0.2067).

HbA1c of DPN patients without anemia is 7.83 ± 0.77and that of DPN patients with anemia is 8.10 ± 0.95. The difference in means is statistically significant (p-value 0.0019).

Hence these variables except HbA1c don't have a significant effect on the study results and the variations in nerve conduction studies produced between the two groups might be considered to be due to anemia in these diabetic patients.

Comparison Of Sensory Nerve Conduction Variables Between Group A (diabetic Peripheral Neuropathy Without Anemia) And Group B (diabetic Peripheral NeuropathyWith Anemia)

Right Median Nerve

Sensory nerve conduction variables of Right Median nerve between Diabetic peripheral neuropathy without and with anemia

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	4.68 ± 1.04	4.82 ± 1.31	0.2373
Amplitude (μV)	16.42 ± 3.17	15.89 ± 3.64	0.1213
Nerve Conduction Velocity (m/s)	48.44 ± 1.56	45.04 ± 3.32	0.0001

Left Median Nerve

Sensory nerve conduction variables of Left Median nerve between Diabetic peripheral neuropathy without and with anemia

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	4.21 ± 0.87	4.36 ± 1.07	0.1248
Amplitude (μV)	16.12 ± 3.43	15.95 ± 2.95	0.5954
Nerve Conduction Velocity (m/s)	48.86 ± 0.97	45.90 ± 2.02	0.0001

Right Ulnar Nerve

Sensory nerve conduction variables of Right Ulnar nerve between Diabetic peripheral neuropathy without and with anemia

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	4.14 ± 1.21	4.39 ± 1.39	0.0558
Amplitude (μV)	16.94 ± 3.34	16.18 ± 2.46	0.0113
Nerve Conduction Velocity (m/s)	46.56 ± 6.60	42.41 ± 5.93	0.0001

Left Ulnar Nerve

Sensory nerve conduction variables of Left Ulnar nerve between Diabetic peripheral neuropathy without and with anemia

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	4.45 ± 0.85	4.62 ± 1.15	0.0936
Amplitude (μV)	17.15 ± 4.24	16.32 ± 3.21	0.0279
Nerve Conduction Velocity (m/s)	44.92 ± 5.53	41.25 ± 4.51	0.0001

Right Sural Nerve

Sensory nerve conduction variables of Right Sural nerve between Diabetic peripheral neuropathy without and with anemia

Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	4.01 ± 0.82	3.88 ± 0.95	0.1437
Amplitude (μV)	10.95 ± 2.32	6.42 ± 1.27	0.0001
Nerve Conduction Velocity (m/s)	50.92 ± 8.20	42.33 ± 4.28	0.0001

Left Sural Nerve

Sensory nerve conduction variables of Right Median nerve between Diabetic peripheral neuropathy without and with anemia			
Variables	Diabetic peripheral neuropathy without anemia (n=200)	Diabetic peripheral neuropathy with anemia (n=200)	P-value
	Mean ± SD	Mean ± SD	
Latency (ms)	3.82 ± 0.98	3.65 ± 1.05	0.0949
Amplitude (μV)	7.67 ± 1.89	5.06 ± 1.02	0.0001
Nerve Conduction Velocity (m/s)	52.73 ± 10.02	38.84 ± 8.54	0.0001

Pearson's Correlation Between Hba1c And Sensory Nerve Conduction Study Variables In Diabetic Peripheral Neuropathy

Table 9: Pearson's Correlation Between Hba1c And Sensory Nerve Conduction Variables In Diabetic Peripheral Neuropathy (n=400)

Sensory nerve conduction variables	Correlation coefficient (r)	p-value
Median Nerve		
Right Median Latency (ms)	0.144	0.221
Right Median Amplitude (μV)	-0.225	0.0723
Right Median NCV (m/s)	-0.011	0.9601
Left Median Latency (ms)	0.039	0.1701
Left Median Amplitude (μV)	-0.007	0.9794
Left Median NCV (m/s)	-0.139	0.2549
Ulnar Nerve		
Right Ulnar Latency (ms)	0.349	0.0025
Right Ulnar Amplitude (μV)	-0.062	0.7029
Right Ulnar NCV (m/s)	-0.012	0.9443
Left Ulnar Latency (ms)	0.013	0.9279
Left Ulnar Amplitude (μV)	-0.275	0.0945
Left Ulnar NCV (m/s)	-0.186	0.3818
Sural Nerve		
Right Sural Latency (ms)	0.105	0.1273
Right Sural Amplitude (μV)	-0.205	0.4615
Right Sural NCV (m/s)	-0.098	0.6577
Left Sural Latency (ms)	0.143	0.3085
Left Sural Amplitude (μV)	-0.291	0.0875
Left Sural NCV (m/s)	-0.219	0.4128

Latency, amplitude and nerve conduction velocity (NCV) of right median nerve had a correlation coefficient (r) of 0.144, -0.225 and -0.011 respectively and that of left median nerve had a correlation coefficient (r) of 0.039, -0.007 and -0.139 respectively with HbA1c. This implies that with increasing HbA1c; latency increases, amplitude decreases, and velocity decreases. The correlation is not statistically significant.

Latency, amplitude, and NCV of right ulnar nerve had a correlation coefficient ® of 0.349, -0.062 and -0.012 respectively and that of left ulnar nerve had a correlation coefficient (r) of 0.013, -0.275 and -0.186 with HbA1c, which means that with increasing HbA1c; latency increases, the amplitude decreases, and velocity decreases. The correlation of right ulnar nerve latency with HbA1c alone is statistically significant (p- value is 0.0025).

Latency, amplitude, and NCV of right ulnar nerve had a correlation coefficient (r) of 0.105, -0.205 and -0.098 respectively and that of left sural nerve had a correlation coefficient (r) of 0.143, -0.291 and -0.219 respectively with HbA1c. which implies that with increasing HbA1c; latency increases, amplitude decreases and velocity decreases. The correlation is not statistically significant.

Pearson's Correlation Between Hemoglobin Values And Sensory Nerve Conduction Variables In Diabetic Peripheral Neuropathy With Anemia

Table 11: Pearson's correlation between hemoglobin and sensory nerve conduction variables in Diabetic peripheral neuropathy (n=400)

Sensory nerve conduction variables	Correlation coefficient (r)	p-value
Median Nerve		
Right Median Latency (ms)	-0.276	0.1647
Right Median Amplitude (μV)	0.312	0.1022
Right Median NCV (m/s)	0.327	0.0921
Left Median Latency (ms)	-0.212	0.2212
Left Median Amplitude (μV)	0.483	0.0089
Left Median NCV (m/s)	0.171	0.4381
Ulnar Nerve		
Right Ulnar Latency (ms)	-0.119	0.5602
Right Ulnar Amplitude (μV)	0.398	0.045
Right Ulnar NCV (m/s)	0.202	0.1782
Left Ulnar Latency (ms)	-0.186	0.4845
Left Ulnar Amplitude (μV)	0.224	0.1287
Left Ulnar NCV (m/s)	0.417	0.0178
Sural Nerve		
Right Sural Latency (ms)	-0.241	0.2708
Right Sural Amplitude (μV)	0.191	0.3528
Right Sural NCV (m/s)	0.572	0.0001
Left Sural Latency (ms)	-0.403	0.0295
Left Sural Amplitude (μV)	0.122	0.6809
Left Sural NCV (m/s)	0.455	0.0103

Latency, amplitude and nerve conduction velocity (NCV) of right median nerve had a correlation coefficient (r) of -0.276, 0.312 and 0.327 respectively and that of left median nerve had a correlation coefficient (r) of -0.212, 0.483 and 0.171 respectively with hemoglobin. This implies that as hemoglobin level decreases; latency increases, amplitude decreases, and velocity decreases. The correlation is statistically highly significant for the amplitude of the left median nerve with hemoglobin with a p-value of 0.0089.

Latency, amplitude, and NCV of right ulnar nerve had a correlation coefficient (r) of -0.119, 0.398 and 0.202 respectively and that of left ulnar nerve had a correlation coefficient (r) of -0.186, 0.224 and 0.417 respectively with hemoglobin. This implies that with a fall in hemoglobin values; latency increases, amplitude decreases, and velocity decreases. The correlation of right ulnar nerve amplitude with hemoglobin (p-value 0.0450) and left ulnar nerve conduction velocity with hemoglobin (p-value 0.0178) were statistically significant.

Latency, amplitude, and nerve conduction velocity of right sural nerve had a correlation coefficient (r) of -0.241, 0.191 and 0.572 respectively and that of left sural nerve had a correlation coefficient (r) of -0.403, 0.122 and 0.455 respectively with hemoglobin. This implies that with decreasing hemoglobin; latency increases, amplitude decreases, and velocity decreases.

The correlation of right sural NCV with hemoglobin (p-value 0.0001) and left sural NCV with hemoglobin (p-value 0.0295) were statistically highly significant. The correlation is statistically significant for the latency of left sural nerve with hemoglobin with a p-value of 0.0103.

DISCUSSION:

Nerve conduction study is the most sensitive and specific method for detection of peripheral neuropathy.

This study shows nerve conduction velocity of right median, right ulnar, right and left sural nerve in diabetic peripheral neuropathy patients with anemia were significantly reduced when compared to diabetic peripheral neuropathy patients without anemia.

Axonal degeneration and demyelination affects the impulse conduction in a nerve.

Our study is supporting the research work of Fan Wu ,et al showing amplitude of left ulnar , right and left sural nerve in diabetic peripheral neuropathy patients with anemia were significantly decreased when compared to non-anemic patients.

Limitations of Study: confounding factors were best avoided but insufficient vitamin b12 and folate levels could not be excluded.

CONCLUSION:

In present study diabetic peripheral neuropathy patients with anemia had lower nerve conduction velocity and amplitude of sensory nerves as compared to non-anemic. Sensory nerve conduction velocity of sural nerve which is a lower limb nerve was reduced when compared to upper limb nerves.

Latency of sensory nerves was positively correlated with HBA1C and Hemoglobin levels.

Hence treatment of anemia should be considered in diabetic peripheral neuropathy patients while treating the other possible risk factors.

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