

Original Research Article

A study to assess the efficacy of metabolic control of diabetes in the development of neuropathy

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ABSTRACT

Background: The metabolic syndrome is a deadly combination of hypertension, diabetes, heart disease, and dyslipidemia due to abdominal obesity. The causes this is both bad genes and bad environment. The objective of this study was to assess the efficacy of metabolic control of diabetes in the development of neuropathy.

Methods: The present hospital based cross sectional study was conducted at MNR Medical College and Hospital, Sangareddy. The study was undertaken between October 2012 to May 2014 both in inpatient and outpatient department. Diabetic patients seeking consultation for the symptoms suggestive of neuropathy were screened and labeled as suffering from diabetic neuropathy based on the inclusion and exclusion criteria.

Results: Diabetic neuropathy was common in the age group of 56 to 65 years in both male and female (33.3%). Average duration of diabetes was 8.7 years. Overall the rate of irregularity was much more (78%). Maximum (78%) patients reported presence of sensory symptoms. Diminision or loss of both ankle jerks was present in all 60 cases while 28 patients showed sluggish or absent knee jerks in total 60 patients. Maximum patients (60%) had distal symmetrical neuropathy.

Conclusions: Longstanding diabetes and poor glycaemic control are particularly associated with an increased risk of neuropathy in diabetes mellitus.

Keywords: Diabetes, Efficacy, Metabolic control

INTRODUCTION

The spreading diabetes epidemic is a major health threat for India and threatens to bankrupt our nation. According to recent estimates, presently India has 62 million diabetic subjects, and this is projected to increase to 100 million i.e. rise by 250% by the year 2035. In the CUPS study, 12% of individuals above age of 20 years in Chennai were found to be diabetic in the year 1997.¹ The prevalence of diabetes is increasing rapidly and it is estimated that the number of diabetics' worldwide will

double by the year 2020 projection published. In 1997 by the international diabetes institute indicates that there will be more than 400 million people with diabetes by 2020. And the majority of these will have type-2 diabetes.² More than 95-97% of elderly diabetics are of type II diseases.

The metabolic syndrome is a deadly combination of hypertension, diabetes, heart disease, and dyslipidemia due to abdominal obesity. The causes this is both bad genes and bad environment.

Vascular complications both micro and macrovascular predominate the features of Indian diabetes due to delayed diagnosis and late presentation of the syndrome. Diabetic foot accounts for one of the largest inpatient admissions in India, diabetic nerve related disorders and directly and indirectly contribute to morbidity and mortality in a big way, simple measures like good glycemic control and neuro-adjuvants, visual inspection of feet and footcare can save and salvage feet at risk.

Diabetic neuropathy is one of the most common troublesome complications of diabetes mellitus. The prevalence of neuropathy is related to age, duration of diabetes and the quality of metabolic control, by the time a diabetic patient has severe neuropathy, retinopathy and albuminuria are also usually present. It is the most common form of neuropathy in the developed countries of the world, accounts for more hospitalisation than all the other diabetic complication and accounts for 50-70% of non-traumatic amputation.¹

DCCT study proved that a glycosylated hemoglobin (HbA1c) reduction from 9 to 7% for a mean follow up of 6.5 years was able both to reduce the onset of diabetic neuropathy (from 9.6% to 2.8%) and to slow its progression.^{3,4} Euglycemia is only able to halt the progression, rather than reverse it, once the nerve damage has established.^{5,6}

The primary pathological role of hyperglycemia in diabetic complications is well established. With the increasing knowledge that maintenance of euglycemia greatly reduces, if not prevents the risk of diabetic complications and at times helps even in regression of such complications, monitoring the control of diabetes is essential for the successful management of the diabetes. The responsibility of the patient and his physician in close monitoring control of diabetes and tailoring the various components in their management have assumed greater significance.⁷ Present study was conducted to assess the efficacy of metabolic control of diabetes in the development of diabetic neuropathy.³

METHODS

The present study was a hospital based cross sectional study conducted in the Department of General Medicine, MNR Medical College and Hospital, Sangareddy

between October 2012 to May 2014. In outpatient and inpatient department of General Medicine during the study period, it was possible to study the 60 patients as per inclusion and exclusion criteria

Inclusion criteria

- Known cases of diabetes
- Giving consent to participate in the study

Exclusion criteria

- Alcohol intake
- Uremia
- Hemoglobinopathies
- Recent Blood Transfusion

The Institutional Ethics Committee permission was sought after submitting the protocol and taking proper approval from the committee with due procedure before the start of the study. As per the ethics committee norms and the consent form issued by them, individual patient consent was taken in the prescribed consent form taken from the ethics committee.

The present Hospital based cross sectional study was conducted at MNR Medical College and Hospital, Sangareddy. The study was undertaken between October 2012 to May 2014 both in inpatient and outpatient department. Diabetic patients seeking consultation for the symptoms suggestive of neuropathy were screened and labeled as suffering from diabetic neuropathy based on the inclusion and exclusion criteria.

Statistical analysis

The data was entered in the Microsoft Excel Worksheet and analyzed using proportions. Appropriate statistical tests are used whenever necessary with a p value of less than 0.05 as significant statistically.

RESULTS

Average age group was 52.18 years. Out of 60 cases studied 36 (62.6%) were males and 24 (38%) were female. Diabetic neuropathy was common in the age group of 56 to 65 years in both male and female (33.3%).

Table 1: The age and sex distribution of the cases.

Age in years	Male	Female	Total	Percentage
< 25 years	0	3	3	15
26-35 years	1	1	2	3.33
36-45 years	11	3	14	23.3
46-55 years	7	4	11	1.6
56-65 years	12	8	20	33.3
66 and above	5	5	10	16.6
Total	36	24	60	100

Table 2: Distribution of patients as per type and duration of diabetes.

Duration of diabetes (years)	No. of IDDM patients	No. of NIDDM patients	Total no. of diabetes patients	Percentage
< 5	0	18	18	30
6-10	01	23	24	40
11-15	0	13	13	21.6
> 15	01	04	05	8.4
Total	02	58	60	100

Average duration of diabetes was 8.7 years. NIDDM was more common (58 out of 60 than IDDM). Maximum i.e. 40% of patients had a duration of 6-10 years and only 8.4% of patients had duration of more than 15 years.

A total of 32% of patients were on insulin and 48% were on OHA. 20% were on both OHA and insulin. Among those who were taking insulin, 75% were taking irregular treatment. Among those on OHA, 75% were having irregular treatment. Overall the rate of irregularity was much more (78%).

Table 3: Distribution of patients as per regularity of their treatment.

Nature of treatment	Regular	Irregular	Total
Insulin	04 (25%)	12 (75%)	16 (32%)
Oral hypoglycaemic agents (OHA)	06 (25%)	18 (75%)	24 (48%)
Both OHA and insulin	01 (10%)	09 (90%)	10 (20%)
Total	11 (22%)	39 (78%)	50 (100%)

Maximum (78%) patients reported presence of sensory symptoms followed by motor symptoms in 33.3% of cases. Autonomic symptoms were reported by 16.6% of cases and only 3.3% reported cranial nerve symptoms.

Table 4: Distribution of cases as per neurological symptoms.

Symptoms	Number	Percentage
Sensory	47	78
Motor	20	33.3
Cranial nerve symptoms	02	3.3
Autonomic symptoms	10	16.6

Diminution or loss of both ankle jerks was present in all 60 cases while 28 patients showed sluggish or absent Knee Jerks in total 60 patients.

Maximum patients (60%) had distal symmetrical neuropathy followed by distal symmetrical sensory-motor neuropathy in 40% of cases.

Table 5: Distribution of study subjects as type of reflex.

Reflexes	Sluggish	Absent	Total
Ankle jerk	03	57	60
Knee jerk	08	20	28

Table 6: The types of neuropathy observed in patients.

Type of neuropathy	Number	Percentage
Distal symmetrical sensory neuropathy	36	60
Distal symmetrical sensory-motor neuropathy	24	40
Autonomic neuropathy	18	30
Cranial neuropathy	02	3.3
Proximal motor neuropathy/poly radiculopathy	01	1.7

Autonomic neuropathy was seen in 30% of cases and cranial neuropathy was seen in 3.3% of cases. Only one patient was seen with proximal motor neuropathy/poly radiculopathy.

DISCUSSION

The exact mechanism in the development of neuropathy in diabetes is uncertain. Whether a poor control of the diabetic state hastens the progression of neuropathy is a question that yet to be answered, one of the earlier study to establish relation between glycemic control and neuropathy performed by Pirart which showed that poor control was associated with a higher incidence of neuropathy.⁸ Intensive glycemic control in the DCCT study showed decreased incidence of diabetic neuropathy to 3% in intensively treated patients compared to 10% in group that received conventional treatment.³ Holman et al, concluded that tight control of diabetes retarded or reversed the progression of the neuropathy.⁹

On the other hand, Service et al, found no such correlations.¹⁰ However majority of the authorities Dyck et al, favoured the view that poor control of diabetes is associated with an increased risk of neuropathy.

In the present study, the accurate classification regarding control of the diabetic state as laid down by the recommendations of the American Diabetes Association (1988) could not be done. The reason has been elaborated earlier. However, patients who could be grossly classified as having poor metabolic control outnumbered those who could be classified as having good control (46 Vs 8) in this study.

Though considerable controversy exists regarding the etiopathogenesis of neuropathy in diabetes. It has been conclusively shown by Pirart, that the incidence of neuropathy increases with the duration of the diabetes.¹¹ He also showed that there was a positive correlation between the occurrence of neuropathy and retinopathy. Tesfaye S et al showed a significant correlation between diabetic neuropathy, age; duration of diabetes, diabetic retinopathy, cigarette smoking and prevalence of cardiovascular disease in IDDM patient.^{1,2,12} This fact was brought out in this study.

In the present study 33 (55%) neuropathy patients had retinopathy and the duration of diabetes was long. Also 16 neuropathy patients showed evidence of myocardial infarction and smoking habit observed in 26 neuropathy patients.

This has been observed in the study. All patients who exhibited sensory changes did so in lower limbs. No patients showed sensory loss to touch (large fibre neuropathy), and yet to be firmly established.

The occurrence of proximal motor neuropathy is well known and Garland coined the term as diabetic amyotrophy for this entity.¹³ The exact incidence of this variant is not well established. In the present study only one case of proximal motor neuropathy was observed which associated with DSN.

One of the difficulties encountered in treating IDDM with the older insulins is the "insulin resistance" which is defined as the daily requirement of insulin in excess of 200 units. The older insulins contain varying amounts of glucagons, pro-insulin, altered insulin and other peptides which are largely responsible for the insulin-binding antibodies found in the plasma of all patients treated with these insulins.

These antibodies are particularly related to the development of insulin resistance. Highly purified mono component insulins prepared from pig and cattle pancreases and human insulin, synthesized by recombinant DNA technology, are now available which are superseding the older preparations. They are less likely to cause insulin allergy and lipodystrophy which prevent the potential hazards of patient's noncompliance.

Better methods of treatment like better delivery system and better insulins offer the hope of better control of diabetes and thereby better quality of life.

A recent 1 year multi centre trial of GLA administration to patients with diabetic neuropathy reported improvement in clinical and electrophysiological nerve function.¹⁴

Kurezyn AD suggested that bells palsy (LMN facial palsy) occurs greater than expected frequency in diabetics, however only one case was observed in the present study.¹⁵

In the present study 30% of neuropathy patients had coexisting autonomic dysfunction. The duration of diabetes was long and level of glycemic control was poor (mean value GlycoHb -11.05%).

Several studies showed a positive correlation between Hb A1C and retinopathy, nephropathy and platelet aggregation.

Glucose in Hb A1C is attached to N-terminal of beta chain of HbA which also forms the site for 2,3 diphosphoglycerate (2,3 DPG), a regulator of Hb function. Hb A1C has high affinity for oxygen. Thus, in diabetics elevated Hb A1C and a relative deficiency of 2,3 DPG may result in decreased oxygenation to the tissue. This forms one of the hypothesis for the pathogenesis of neuropathy and other microvascular complications.

CONCLUSION

Longstanding diabetes and poor glycemic control are particularly associated with an increased risk of neuropathy in diabetes mellitus.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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