

The Frequency of Autonomic Neuropathy in Type 2 Diabetic Patients

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ABSTRACT:

BACKGROUND:

Autonomic Nervous System Innervates vascular and visceral smooth muscle, exocrine and endocrine glands and parenchymal cells through out the various organ system. Diabetic autonomic neuropathy is classified as subclinical or clinical upon the presence or absence of symptoms. A wide spectrum of symptoms affecting many different organ system can occur including CVS, GUS, pupillary, automotor and neuroendocrine systems.

OBJECTIVE:

To investigate the frequency of diabetic A.N.P as defined by simple non – invasive test in type 2 diabetic Iraqi patients and its relation to the duration of disease.

PATIENTS AND METHODS:

Fifty type 2 diabetic patients, were evaluated with a five bedside tests to detect autonomic neuropathy and a history of related symptoms was taken. There were 30 (60%) males and 20 (40%) females in the age range 30–70 years.

The five tests were carried out were, heart rate variation during deep breathing, HR response to valsalva, HR response to standing, BP response to sustained hand grip, BP fall in response to standing.

Resting ECG (to measure QTc interval) fasting plasma glucose and 2hr., post prandial plasma glucose were done to each patient.

RESULTS:

Of these 50 patients 34(68%) had evidence of neuropathic abnormality of parasympathetic involvement 19(38%) patients 13(26%), patients had evidence of combined parasympathetic and sympathetic involvement and only 2(4%), patients had only sympathetic involvement. Increase incidence was seen in older age group and poor glycemic control. Autonomic neuropathy more common in patients who had the disease for more than 5 yrs. There was no correlation with prolonged QTC intervals.

CONCLUSION:

Diabetic ANP is a common complication and related to poor diabetic control and the duration of diabetes. While it is not associated with prolonged QTC interval.

KEYWORDS: autonomic neuropathy, type II diabetes sympathetic and parasympathetic nervous system

INTRODUCTION:

Autonomic nervous system (ANS)

The ANS supplies and influences every organ in the body and closely integrate vital processes, such as Blood Pressure (BP), temperature and adaptation to environmental change⁽¹⁾.

Accordingly, sensory, motor, visceral and neuroendocrine function can be modulated by this system⁽²⁾.

The clinical signs and symptoms that occur in disturbances of autonomic response which is influenced by the organ involved. The normal balance of sympathetic (ST) and parasympathetic (pst) innervations, the nature of underlying illness and stage of progression of the disease⁽³⁾.

To investigate the prevalence of D.A.N. was defined by simple non- invasive tests in type 2 diabetic Iraqi patients and its relation to the duration of the disease.

Baghdad Teaching Hospital.

PATIENT AND METHODS:

This descriptive cross sectional study includes fifty patients with type 2 diabetes they were studied during the period between December 2014 to October 2015 in Alshahed Asader General hospital.

They were all on oral anti diabetic therapy and none had clinical evidence of any intrinsic heart or respiratory disease nor any one of them on any medication a part from oral antidiabetic therapy.

Thirty healthy non diabetic persons matched for age, height, weight, and BMI were included in this study as control group. Members of the control group had no family history of diabetes and their fasting plasma glucose less than 110 mg /dl, and their postprandial plasma glucose is < 140 mg/dl

METHODS:

Data were collected including name, age, wt., length , BMI , duration of diabetic , treatment and Blood sugar control .

The subjects were asked for any symptoms suggestive of ANP which include dysphagia, nocturnal diarrhoea, constipation, palpitation, postural dizziness, hesitancy, incontinence, impotence, and cold extremities.

Investigations include: fasting plasma glucose, 2hr. post.

Prandial plasma glucose and ECG.

we divided the glycemic control of our patients into three groups which includes good , Fair and poor control according to HbA1C (14)

Tests:

The five standard cardiovascular Ewing tests used for assessment of cardiovascular autonomic neuropathy.

A. Tests to Detect Parasympathetic Involvement

1. HR response to Valsalva maneuver.

The test performed by asking the patient to blow into a mouth – piece connected to modified sphygmo- manometer and holding it at a pressure of 40 mmhg for 15 second , nose clips were used to prevent exhaling through the nose. While heart rate was recorded continuously from ECG (normal person shows reflex tachycardia during maneuver) .

After 15 seconds, the pressure was abruptly relived and the ECG recorded for further 30 seconds (normal person shows reflex Brady cardia after the manoeuvre).

The result is expressed as the valsalva ratio which is the ratio of the longest R.R interval after the maneuver to the shortest R-R interval during the maneuver.

The mean of the three valsalva ratio is taken as the final result.^(5,6,8)

2. heart rate (HR) (R-R interval) variation during deep breathing :

the patient sit quietly and then breathes deeply and even at 6 breath per minute with 5 seconds allocated for each inspiration and expiration to optimize the sinus arrhythmia .

An ECG is recorded through out the period of deep breathing.

With marker to indicate the onset of each inspiration & expiration the result is then expressed as the mean difference between maximum & minimum heart rate for six measured cycles in beat per minute.

3. Immediate heart rate response to standing: the test is performed with the patient lying quietly on couch while the HR is recorded continuously on an ECG. The shortest R-R interval at or around the 15th beat and the longest R-R interval at or around the 30th beat after starting to stand is measured.

The characteristic heart rate response is expressed by 30: 15 ratios (R-R interval of the 30th to the R-R interval of the 15th)

B- Test to Detect Sympathetic Involvement:

1. Blood pressure response to standing: the test is performed by measuring the patient's blood pressure with sphygmomanometer while he is lying down, and again, when he stands up for three minutes. The postural fall in blood pressure is taken as the difference between systolic blood pressure lying and systolic blood pressure standing.

2. Blood pressure response to sustained handgrip: Here sphygmomanometer cuff is used. Hand grip is then maintained at the 30 % of that maximum for as long as possible up to 5 minutes. Blood pressure is measured three times before and at one – minute interval during hand grip. The result was expressed as the difference between the highest diastolic blood pressure during hand grip exercise and the mean of the three diastolic blood pressure reading before hand- grip began.

Statistical analysis

All data arranged and tabulated in NO. , % , mean \pm SD between different variable measured by chi-square , t- test , analysis of variance (ANOVA) by using statistical package for social science (SPSS) version 17.

$P \leq 0.05$ consider as level of significance.

RESULTS:

A total fifty diabetic patients were include in this study their mean \pm SD of age 48.5 ± 10.5 .

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The mean duration of their diabetic since diagnosis 9.76 ± 4.6 .

A thirty (60%) of patients was males and twenty (40%) of patients was females with male : Female ratio 3:2.

There was no significant statistical difference between 50 diabetic and 30 control subjects regarding the age and BMI.

distribution of patients according to symptoms. It shows that the sweating , tingling , palpitation were the more prevalent symptoms 62%, 54% and 52% respectively, the least prevalent symptoms was nocturnal diarrhea , dysphagia & hesitancy 18%, 8%,6% respectively. While no patient was +ve regarding incontinences.

Table below : shows the frequency of the symptoms suggesting of autonomic neuropathy in relation to the patients and controls . it shows that the most common symptoms in group2 patients were sweating , Tingling ,palpitation and Impotence.

there had no postural dizziness. While in group 3 postural dizziness was present in association with other symptoms . symptoms of incontinence were not seen in any of our patients .

For the control group all of them were a symptomatic except for palpitation was (3) patients .

Constipation (2) patients and one patient was for impotence & sweating .

Table the frequency of symptoms of autonomic neuropathy in relation to the result of the tests in the patient and for the control Studing The result

of distribution of Age of 50 Diabetic patients with Autonomic neuropathy it shows that the Abnormalities of autonomic function increase with age. In this study, this was observed in 14.2% in the 3rd decade which increased to 93.3% in the 7th decade of life.

While The presence of autonomic neuropathy in various grades of metabolic control of diabetes.

According to the result of this study there was significant association between grades of metabolic control and autonomic neuropathy.

Patient with good control only 30% have autonomic involvement while those patients with fair control 66.6% have autonomic abnormalities this percentage increased to 84% in those patients with poor control.

In the studying of patients according to QTC interval with autonomic tests. According to the result of this table.

Patients with -ve test both PST & ST have only (1) (7.1 %) patient with $QTC > 0.44$ and (15) (92.9%) with $QTC \leq 0.44$.

In patients with +ve pst only have (2) (9.5%) patients with $QTC \geq 0.44$ & (17) 90.5% patients with $QTC \leq 0.44$.

Patients with +ve both PST and ST test have (3) (15.4%) patients with $QTC \geq 0.44$ while (10) (84.6%) patient with $QTC \leq 0.44$. For patients with + ve ST test there is no patients with prolong QTC interval. So there is no significant relation between autonomic dysfunction and prolongation of QTC intervals.

Table the frequency of symptoms of autonomic neuropathy in relation to the result of the tests in patients and for the control group.

Patients		Group 1 -ve test	Group 2 + ve pstonly	Group 3 + ve pst and ST	Group 4 + ve ST only	(B) control
Postural Dizziness	No	16	19	2	2	30
	Yes	-	-	11	1	-
Palpitation	No	12	9	1	2	27
	Yes	4	10	12	-	3
Nacurnal Diarrhea	No	16	15	8	2	30
	Yes	-	4	5	-	-
Constpation	No	10	11	6	2	28
	Yes	6	8	7	-	2
Dysphagia	No	16	18	10	2	30
	Yes	-	1	3	-	-
Sweating	No	12	4	1	2	29
	Yes	4	15	12	-	1
Hesitancy	No	16	18	11	2	30
	Yes	-	1	2	-	-

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Incontinency	No	16	19	11	2	30
	Yes	-	-	-	-	-
impotence	No	13	8	5	2	29
	Yes	3	11	8	-	-
Cold Extr.	No	14	15	6	1	30
	Yes	2	4	7	1	-

DISCUSSION:

Complications of diabetes mellitus continue to account for increased morbidity and mortality.

Measurement of peripheral and autonomic nerve functions in diabetic patients help in establishment of prospective natural history, its pathogenesis and predict the beneficial effects of various drugs⁽⁴⁾.

According to the result of our study there are no significant statistical differences between 50 diabetic and 30 control subject regarding the age and BMI. These match the study which was done nationally, by Dr. Ala'a Abid- Awn the prevalence of autonomic neuropathy in Insulin dependent diabetic Iraqi patients and it's relation to diabetic nephropathy & retinopathy.⁽¹⁵⁾

Regarding the symptoms of autonomic neuropathy, the symptoms of postural dizziness was not seen in patients that had only parasympathetic dysfunction but occur in the latter stage of disease as the patients had sympathetic dysfunction and this match the study by [Ewing D.J the natural history of diabetic autonomic neuropathy]⁽⁶⁾

The symptoms of incontinence is not seen in our patients, however, cyst metric a abnormality can be demonstrated in some diabetic patients without obvious symptoms [Ellenberger and Weber (1967); Faerman, maler, jadzinsky, Alvarez, fox, zilbervarge, ciberia and calinus (1971); Buck, McCrae reed and Chisholm (1973)].

The prevalence of diabetic autonomic neuropathy in our patients with duration of diabetic < 20 yrs.) was 68% , 38% had only parasympathetic involvement, 26% had both parasympathetic and sympathetic dysfunction and only 4 % had atypical pattern as had sympathetic involvement this match the findings of Ewing D.J, the value of cardiovascular autonomic function. Tests: 10 yr. experience in diabetic⁽⁵⁾

In this study also shows that the parasympathetic abnormalities occur earlier than sympathetic involvement and this is in agreement with other study.^(5,6,7)

This can be explained by that the parasympathetic involvement occur earlier in natural history of diabetic autonomic neuropathy or whether it is simply that the cardiovascular

reflex heart rate tests (pst) are rather more sensitive than the blood pressure tests⁽⁵⁾.

In our study we found that there is significant relationship between autonomic neuropathy with mean duration of diabetes.

A various follow up studies have shown that the incidence of autonomic neuropathy may increase with the duration of disease^(11,12).

Abnormalities of autonomic function increase progressively with age.

In this study, this was observed in 12.5% of cases in the 3rd decade which increased to 93.5% in the 7th decade.

This is probably related to the increased incidence of disease per se with age and to the duration of DM. This match the study by Kasthuri AS, Yadar RPS cardiac autonomic neuropathy in diabetes mellitus Medical Journal forces of India⁽¹⁶⁾.

A higher percentage of patients with diabetic A.N. found in our study. this may be due to poor control of Blood sugar in our patients. As there were paper published in U.S revealing an association of decrease in the activity of cardiovascular autonomic nervous system with poorly control diabetes^(9,10).

So better metabolic control improve the result of neurological tests⁽¹²⁾.

In our study we also found the higher percentage of prolonged QTC was found in combined sympathetic and parasympathetic autonomic neuropathy. Although it is statistically in significant so we can not regard it as markers of ANP.

Therefore it might be considered as an overall index for complication and not for pure autonomic impairment. this match with other study by takebayashi; -k, Aso, -y, sugita; -r; takemura, -Y; Inukai, -T. clinical usefulness of corrected QT in intervals in diabetic autonomic neuropathy in patients with type 2 diabetic.⁽¹³⁾

CONCLUSION:

1. Symptoms of ANP in type 2 diabetic patients found to be correlated with the duration of the diseases.
2. The symptoms of ANP in type 2 diabetic patients; it is not significantly correlated with diabetic control according to HbA1C result.

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3. The parasympathetic ANP occur earlier than the sympathetic ANP in type 2 diabetic patients.
4. There is significant relationship between ANP and duration of diabetes.
5. ANP increase progressively with the age of diabetic patients.
6. Poor diabetic control is a significant risk factor for the development of diabetic ANP.
7. There is no significant prolongation of QTc interval in the diabetic patients with ANP- yet the prolonged QT interval can be considered as an index of complication of ANP in type 2 diabetic patients

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