European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 07, Issue 10, 2020

Determination of cardiovascular autonomic neuropathy in type II DM patients

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ABSTRACT:

Background: The diabetic neuropathy, including the cardiovascular autonomic neuropathy (CAN), is a common complication of type 1 and 2 diabetes that leads to high mortality and morbidity. The present study was conducted to determine CAN in type II DM patients.

Materials & Methods: 168 type II DM patients of both genders were recruited. Resting heart rate, blood pressure, and body mass index (BMI), systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, fasting lipid profile (low-density lipoprotein/LDL, high-density lipoprotein/HDL, triglycerides/TG) and cardiac autonomic function was evaluated with the CAN system analyzer as early, definite and advanced CAN.

Results: CAN was seen in 66 patients. The mean age (years) was 45.2 and 44.5, duration of diabetes (years) was 6.1 and 12.3, SBP (mm Hg) was 130.4 and 134.5, DBP (mm Hg) was 86.2 and 87.6, resting heart rate (beats/min) was 76.3 and 87.4, LDL (mg/dl) was 102.4 and 98.6, HDL (mg/dl) was 40.5 and 38.1 and TG (mg/dl) was 165.2 and 184.6 in CAN- and CAN+ patients. The difference was non- significant (P> 0.05). Severity of CAN found to be early in 20%, definitive in 45% and advanced in 35%. The difference was significant (P< 0.05).

Conclusion: Type II diabetes patients had high prevalence of cardiac autonomic neuropathy.

Key words: Cardiac autonomic neuropathy, Diabetes, Lipid profile

INTRODUCTION

Type 2 diabetes mellitus (DM2) has high morbidity and mortality and great socioeconomic impact, having affected 150 million individuals in the year 2000, with an expectancy of affecting 336 million by 2030. The diabetic neuropathy, including the cardiovascular autonomic neuropathy (CAN), is a common complication of type 1 and 2 diabetes that leads to high mortality and morbidity.[1] Cardiac autonomic neuropathy (CAN) is often an under-diagnosed

complication of diabetes mellitus (DM) and is associated with increased mortality and morbidity. The prevalence of CAN is approximately 31–73% in type 2 DM and the annual incidence has been reported to be 2%. CAN pathogenesis is complex and multifactorial. CAN is initially subclinical and becomes symptomatic only in the later stages of the disease. Identifying patients with CAN is important as early initiation of intensive interventions targeting lifestyle, glycemic control, and cardiovascular risk factors can slow the progression of CAN and may be reversed if diagnosed soon after onset.[2]

Hyperglycemia plays an important role in the pathogenesis of diabetes-related microvascular complications, and hence it is not surprising that hyperglycemia has an unfavorable impact on the development and progression of CAN. DCCT showed a 50% decrease in CAN incidence over a 6.5-year follow-up in its intensive-therapy cohort.[3] The benefits of intensive glycemic control during DCCT persisted for at least 14 years after the end of the study, despite glycated hemoglobin (HbA1c) differences between the intensive- and conventional-therapy arms disappearing after the end of randomization.[4] Furthermore, participants in the DCCT intensive-therapy group who were free from CAN at the end of the study had a 31% reduction in risk of incident CAN when compared to those in the control arm. However, those individuals diagnosed with CAN at the end of DCCT showed a higher risk of suffering CVD events in follow-up, which was not independent of previous glycemic exposure or the effect of metabolic memory.[5] The present study was conducted to determine CAN in type II DM patients.

MATERIALS & METHODS

The present study comprised of 168 type II DM patients of both genders. Enrollment of subjects was done after obtaining their written consent.

Demographic data such as name, age, gender etc. was recorded. All patients underwent a thorough physical examination, including measurement of resting heart rate, blood pressure, and body mass index (BMI). Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg. Fasting lipid profile (low-density lipoprotein/LDL, high-density lipoprotein/HDL, triglycerides/TG) and creatinine levels were measured with an automatic analyzer. Glycosylated hemoglobin (HbA1c) was determined by the high-performance liquid chromatography. The cardiac autonomic function was evaluated with the CAN system analyzer as early, definite and advanced CAN. Results were statistically analyzed considering $p<0.05$ as significant.

RESULTS

Table I Clinical and biochemical assessment

Variables	CAN- (102)	CAN+ (66)	P value
Age (years)	45.2	44.5	0.12
Duration of diabetes (years)	6.1	12.3	0.01
SBP (mm Hg)	130.4	134.5	0.15
DBP (mm Hg)	86.2	87.6	0.21
Resting heart rate (beats/min)	76.3	87.4	0.09
LDL (mg/dl)	102.4	98.6	0.16
HDL (mg/dl)	40.5	38.1	0.82
TG (mg/dl)	165.2	184.6	0.07

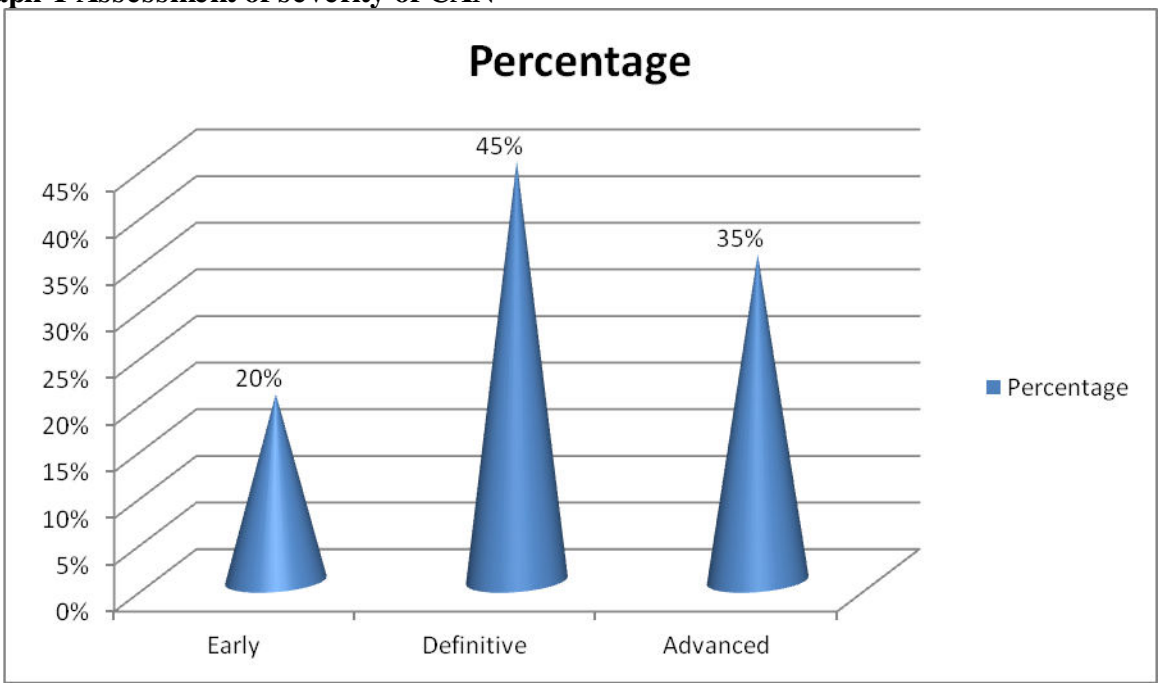
Table I shows that CAN was seen in 66 patients. The mean age (years) was 45.2 and 44.5, duration of diabetes (years) was 6.1 and 12.3, SBP (mm Hg) was 130.4 and 134.5, DBP (mm Hg) was 86.2 and 87.6, resting heart rate (beats/min) was 76.3 and 87.4, LDL (mg/dl) was 102.4 and 98.6, HDL (mg/dl) was 40.5 and 38.1 and TG (mg/dl) was 165.2 and 184.6 in CAN- and CAN+ patients. The difference was non- significant (P> 0.05).

Table II Assessment of severity of CAN

Severity	Percentage	P value
Early	20%	0.05
Definitive	45%	
Advanced	35%	

Table II, graph I shows that severity of CAN found to be early in 20%, definitive in 45% and advanced in 35%. The difference was significant (P< 0.05).

Graph I Assessment of severity of CAN



DISCUSSION

The earliest indicator of cardiac autonomic neuropathy is a reduction in the heart rate variability in response to deep breathing, valsalva, and going from lying to standing position. This test provides a sensitive and non invasive indication of the balance between sympathetic and vagal (parasympathetic) tone on modulating the activity of SA node, and can be useful in predicting the risk of arrhythmia.[6] Resting heart rate is primarily controlled by parasympathetic system, whereas maximal heart rate and blood pressure responses to standing, sustained hand grip and other types of exercise are mainly functions of sympathetic activity.[7] It is considered that parasympathetic dysfunction precedes sympathetic loss. Patients with cardiac autonomic neuropathy have higher resting heart rates and lower maximal heart rates during exercise than diabetic patients without autonomic neuropathy. Abnormally low heart rate variability has been

interpreted as a shift in the sympathetic - vagal balance in favor of sympathetic activity and is associated with poor outcome.[8] After the introduction of cardiovascular reflex tests based on changes in heart rate variability and blood pressure regulation into clinical routine, it became evident that cardiac autonomic neuropathy may be frequently detected at early stages in asymptomatic diabetic patients with autonomic neuropathy.[9] The present study was conducted to determine CAN in type II DM patients.

In present study, CAN was seen in 66 patients. The mean age (years) was 45.2 and 44.5, duration of diabetes (years) was 6.1 and 12.3, SBP (mm Hg) was 130.4 and 134.5, DBP (mm Hg) was 86.2 and 87.6, resting heart rate (beats/min) was 76.3 and 87.4, LDL (mg/dl) was 102.4 and 98.6, HDL (mg/dl) was 40.5 and 38.1 and TG (mg/dl) was 165.2 and 184.6 in CAN- and CAN+ patients. Bhuyan et al[10] included 100 patients (60 males and 40 females; age range: 36–72 years) with type 2 DM. Their clinical, biochemical, and metabolic parameters were analyzed and assessment of CAN were done based on the Ewing's criteria. 60 were males and 40 were females. The mean age of the patients was 53.3 ± 10.37 years (36–72 years) and the mean duration of diabetes was 9.03 ± 6.4 years (6 months–25 years). Patients were divided into two groups: "without CAN" (CAN−) and "with CAN" (CAN+). The prevalence of CAN was 70%, with early CAN in 25%, definite CAN in 24%, and severe CAN in 21% cases The patients with CAN were older ($P = 0.0005$), had longer diabetes duration (11.56 vs. 3.13; $P = 0.0001$), higher creatinine ($P < 0.0001$), and lower estimated glomerular filtration rate (eGFR) ($P = 0.0001$) compared to patients without CAN. Retinopathy, peripheral neuropathy, and nephropathy were common in CAN + patients. On multiple logistic regression analysis, duration of diabetes [odds ratio (OR); 6.7, $P < 0.0001$), older age (OR; 1.07, $P < 0.016$), and lower eGFR (OR; 0.97, $P < 0.03$) were risk factors for CAN.

We found that severity of CAN found to be early in 20%, definitive in 45% and advanced in 35%. Patients with chronic complications of DM should be screened for CAN symptoms and signs and in case of the presence tests excluding other drug effects/interactions or comorbidities that could mimic CAN should be performed (level E). CAN assessment can be used for cardiovascular risk stratification and as a marker for increased risk of intraoperative cardiovascular ability.[11] Implementation of tight glucose control as early as possible to prevent or delay the development of CAN in the course of T1DM (class A); consider a multifactorial approach in the course of T2DM (class C). CAN treatment is a complex process, that includes: Lifestyle modification; reducing IR; intensive glycemic control; treatment of DLP; antioxidants, first of all α-lipoic acid (ALA), aldose reductase inhibitors, acetyl- L-carnitine; vitamins, first of all fat-soluble vitamin B1; correction of vascular endothelial dysfunction; prevention and treatment of thrombosis; in severe cases-treatment of OH.[12]

CONCLUSION

Authors found that type II diabetes patients had high prevalence of cardiac autonomic neuropathy.

REFERENCES

1. Yun JS, Park YM, Cha SA, Ahn YB, Ko SH. Progression of cardiovascular autonomic neuropathy and cardiovascular disease in type 2 diabetes. Cardiovasc Diabetol. 2018;17(1):109.

2. Benichou T, Pereira B, Mermillod M, Tauveron I, Pfabigan D, Maqdasy S, et al. Heart rate variability in type 2 diabetes mellitus: a systematic review and meta-analysis. PLoS ONE. 2018;13(4):e0195166.
3. Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care. 2017;40(1):136-54.
4. The Diabetes Control and Complications Trial Research Group, Group TDC and CTR. The effect of intensive diabetes therapy on the development and progression of neuropathy. The Diabetes Control and Complications Trial Research Group. Ann Intern Med. 1995;122(8):561-8.
5. Neil HA, Thompson AV, Thorogood M, Fowler GH, Mann JI. Diabetes in the elderly: the Oxford Community Diabetes Study. Diabet Med. 1989;6(7):608-13.
6. Ziegler D, Gries FA, Mühlen H, Rathmann W, Spüler M, Lessmann F. Prevalence and clinical correlates of cardiovascular autonomic and peripheral diabetic neuropathy in patients attending diabetes centers. The Diacan Multicenter Study Group. Diabete Metab. 1993;19(1 Pt 2):143-51.
7. Ziegler D, Strom A, Kupriyanova Y, Bierwagen A, Bönhof GJ, Bódis K, et al. Association of lower cardiovagal tone and baroreflex sensitivity with higher liver fat content early in type 2 diabetes. J Clin Endocrinol Metab. 2018;103(3):1130-8.
8. Axelrod S, Lishner M, Oz O, Bernheim J, Ravid M. Spectral analysis of fluctuations in heart rate: an objective evaluation of autonomic nervous control in chronic renal failure. Nephron. 1987;45(3):202-6.
9. Maser RE, Mitchell BD, Vinik AI, Freeman R. The association between cardiovascular autonomic neuropathy and mortality in individuals with diabetes: a meta-analysis. Diabetes Care. 2003;26(6):1895-901.
10. Bhuyan AK, Baro A, Sarma D, Choudhury B. A study of cardiac autonomic neuropathy in patients with type 2 diabetes mellitus: A Northeast India experience. Indian J Endocr Metab 2019;23:246-50.
11. Fisher VL, Tahrani AA. Cardiac autonomic neuropathy in patients with diabetes mellitus: current perspectives. Diabetes Metab Syndr Obes. 2017;10:419-34.
12. Balcioğlu S, Arslan U, Türkoğlu S, Ozdemir M, Cengel A. Heart rate variability and heart rate turbulence in patients with type 2 diabetes mellitus with versus without cardiac autonomic neuropathy. Am J Cardiol. 2007;100(5):890-3.