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Original Article

Comparative study of cardiac autonomic status by heart rate variability between under-treatment normotensive and hypertensive known type 2 diabetics

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ABSTRACT

Background: Co-existence of hypertension is known in three quarter of Indian type 2 diabetics, this duo having adverse additive effect on cardiovascular health including dysautonomia. Later can be measured by simple 5 min heart rate variability (HRV) using simple electrocardiogram, which if reduced indicates cardiac risk.

Objective: We compared HRV parameters between hypertensive and normotensive type 2 diabetics, looking for significant difference if any.

Materials and methods: 98 hypertensive and 40 normotensive type 2 diabetics treated as outpatients were evaluated for disease control and risk stratification. 5 min resting HRV was measured by Variowin HR, software based instrument, using standard protocols to record time domain, frequency domain and Poincare plot parameters. They were compared between groups for difference with $p < 0.05$ defining statistical significance.

Results: Mean age was 56 and 51 years, duration 6 years and 4 years respectively in hypertensive (HT) and normotensive (NT) group of type 2 diabetics, which did not significantly differ in distribution of risk factors. There was poor glycaemic control (one third only) in both groups and good pressure control in HT group. Both groups revealed all reduced HRV parameters with significant difference in-between only for LF/HF ratio (1.29 in HT vs 2.61 in NT group).

Conclusion: Our findings of HRV suggest that in type 2 diabetics with poor glycaemic and good pressure control, hypertension as a co-existing factor does not make significant difference in cardiac dysautonomia emphasizing residual risk despite antihypertensive treatment and need for early HRV screening, strict glycaemic control and other interventions.

1. Introduction

India stands second globally in type 2 diabetes mellitus (T2DM) with alarming future prediction[1] and co-existence of hypertension (HTN) and T2DM is in 75% cases.[2] Both have a threatening synergistic effect[3] with majority of sub-optimal disease control[4,5] and same is evident in T2DM subjects of our regions as per our previous study.[6] Cardiac autonomic neuropathy is common yet overlooked complication which contributes to residual risk for cardiovascular morbidity and mortality.[7] Heart rate variability (HRV), measured by simple 5 min recording provides reliable status of cardiac autonomic balance.[8] Reduced HRV is seen in both HTN and T2DM individually and known to be an independent risk factor for cardiovascular health.[9] But only few studies like Takahashi et al.[10] have focused their synergistic effect, perhaps none from India. Indian hypertensives are very peculiar[4] and we hypothesize to assess the effect of coexisting hypertension on HRV in known type 2 diabetics.

2. Materials and methods

2.1. Study design

This case control study was conducted in the Department of Medicine with the help of Department of Physiology, Government Medical College, Bhavnagar, Gujarat, India during a period from 15th October 2014 to 15th January 2015.

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2.2. Study subjects

After approval from the Institutional ethical Committee and written informed consent from each subject, volunteers were recruited for this study. Of total number of subjects that attended the Out Door Clinic, all the adult subjects were screened for presence of type 2 diabetes. Subjects coming to clinic with record of treatment of diabetes were also included in this screening for confirmation. Of total number of patients with type 2 diabetes, observed during the recruitment period ($n = 300$), 138 patients were randomly selected for this study. Sample size was calculated by software Raosoft (Raosoft, Inc. free online software, Seattle, WA, USA). A sample of 138 subjects for a population of 6 lakhs with 7.33% prevalence of type 2 diabetes mellitus in our region gave us 95% confidence level, leaving 5% margin of error.

2.3. Inclusion and exclusion criteria

We included type 2 diabetic patients, with minimum duration of one year and known glycaemic control, aged 30–70 years, of either sex, taking regular treatment (through chart review), not taking insulin, ready for written consent.

Exclusion criteria were; those patients with less than one year duration of diabetes ($n = 12$), taking irregular treatment of diabetes ($n = 18$), age more than 70 years ($n = 127$), patients having cancer ($n = 0$), chronic dysentery ($n = 0$), chronic renal failure ($n = 3$), type 1 diabetes ($n = 9$), on pace maker ($n = 0$), past history of intervention, drug therapy influencing autonomic function ($n = 11$) and non-volunteers ($n = 1$) were excluded.

2.4. Collection of data

All the data were collected by a personal interview by a trained physician via validated questionnaires that included symptoms of cardiac autonomic neuropathy, investigations done, treatment received, salt, alcohol and tobacco intake and physical activity

Specific emphasis was given to identify following 10 risk factors including diabetes itself: (1) hypertension, (2) hyperlipidaemia, (3) smoking, (4) cardiovascular disease (CVD), (5) family history, (6) age $>$ 52 years, (7) male gender, (8) fasting blood sugar (FBS) $>$130 mg/dL, (9) body mass index (BMI) $>$25 kg/m^2, (10) type 2 diabetes mellitus.

Salt intake was the sum of the salt used during preparation of food and added at the table by each subject.[11,12] Added ingestion was from salt added to manufactured foods was taken into account. The physician also measured body weight on each visit independently in light under clothing to the nearest of 0.1 kg, after removing shoes of the subjects. Height was measured without shoe by standing close to scale.

After a 5-min rest, a blood pressure was recorded in a sitting position, on the right arm with a standard mercury manometer. Every subject had two readings, with the average of these reading recorded as the resting blood pressure. To minimize measurement errors, one individual was assigned to measure blood pressure for all the subjects in both the groups. In accordance with the WHO guidelines, if a blood pressure of more than $\geq$140/90 mmHg was recorded, a repeat measurement was obtained after a 5-min rest, with the subject in a supine position.

Physical activity was assessed by a questionnaires detailing occupational, household, and spare time physical activity. Sedentary lifestyle assessment was based on occupational or household activity, along with spare time activity measures as reported earlier.[11] Alcohol and tobacco consumption were recorded by questionnaires.[12] Tobacco consumption was defined as tobacco intake, in any form, for example, chewing or smoking.[12] Alcohol intake was considered in presence of drinking of alcohol at least once per week.[12]

2.5. Definition of disease control

Prehypertension is diagnosed in presence of a systolic pressure from 120 to 139 mmHg or a diastolic pressure from 80 to 89 mmHg. Readings greater than or equal to 140/90 mmHg are considered hypertension.

Hypertension was also diagnosed as per self-reported use of medications and available records of treatment for high blood pressure during the 2 weeks preceding the clinic examination. Participants also brought to the examination all medications they had taken in the preceding 2 weeks.

We defined glycaemic control as per criteria laid by American Diabetes Association 2014[13] and good glycaemic control was defined as (1) HbA1c $\leq$ 7 mg%, (2) FBS $\leq$ 126 mg% and (3) PP2BS $\leq$ 180 mg%.

2.6. Measurement of HRV

The time domain variables and frequency domain variables were measured and taken for comparison by window based software VarioWin HR.[14] Assessment of heart rate variability was carried out between 8.30 and 12.00 am in an isolated examination room. Patients were requested to avoid coffee, tea, cola drinks and smoking for 12 h and alcoholic beverages for 24 h before procedure. We recorded ECG for the analysis of beat-to-beat heart rate variability after supine rest for at least 5 min while the subject was in supine position and breathing freely. The ECG was recorded from the precordial leads and transferred on-line to a microcomputer for the analysis of heart rate variability. Only stationary time series of approximately 5-min durations free of arrhythmia and artefacts were used.

2.7. HRV parameters

In time-domain analysis of HRV parameters included are RR interval, standard deviation of all RR intervals (SDNN), the square root of the mean of the sum of the squares of differences between adjacent RR intervals (RMSSD), standard deviation of successive differences (SDSD) and pNN50, which is the percentage of consecutive RR intervals that differ by $>$50 ms.[15]

The frequency-domain analysis of HRV consisted of the power of high frequency (HF), (0.15–0.40 Hz); low frequency (LF), (0.04–0.15 Hz); and very low frequency (VLF), (below 0.04 Hz) power ranges. LF and HF were presented also in normalized units and as a ratio.[15]

Poincare plot analysis included SD1 and SD1 which are standard deviation of RR interval along major and minor axis respectively. Scatter index was represented as ratio of SD1 to SD2 which reflected the HRV in a non-linear manner.

2.8. Statistical analysis

The data was transferred on Excel spreadsheet and descriptive analysis was expressed as mean $\pm$ standard deviation. All calculations were accomplished by Graph Pad in Stat 3 software (demo version free software of GraphPad Software, Inc. California, USA). We calculated the statistical significance of difference in mean distribution of various parameters amongst various subgroups by Mann–Whitney test or unpaired student t test for quantitative data and by Fisher's exact test for qualitative data. Difference was considered statistically significant with $p < 0.05$.

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