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SHORT COMMUNICATION

Effect of Chronic Hyperglycemia on Cardiac Parasympathetic Functions in Type-2 Diabetes

Nanda Kumar L.G.[1], Kaveri N.K.[1] and S. Ravishankar[2]

[1]Department of Physiology, MNR Medical College, MNR Nagar, Sangareddy, Medak-502295 Andhrapradesh, India and [2]Department of Physiology, MIMS, Vijayanagaram, Andhrapradesh, India

Abstract: *Objective:* To evaluate effects of chronic hyperglycemia on cardiac parasympathetic functions in type 2 diabetics. *Research Design and Methodology:* HBA1c was estimated and Average Blood Glucose (ABG) was calculated in 100 type 2 diabetics fulfilling the study criteria, were subjected to cardiac parasympathetic function tests i.e. Resting Heart Rate(RHR), Heart Rate Variation to Deep Breathing (HRV) and Valsalva ratio. They were placed in two groups, group 'A' (n=60) diabetics with HbA_{1c} <8% [ABG <180 mg/dl] and group 'B' (n=40) diabetics having HbA_{1c} >8% [ABG >180 mg/dl]. *Results:* The mean HbA_{1c} of group A was 7.423% (SD±1.194), group B was 11.82% (SD±1.974). The ABG of group 'A' was 162.55 (SD±40.32), group 'B' was 316.8 (SD±79.25). RHR of group 'A' was 87.56 (SD±10.99), group 'B' was 93.09 (SD±14.07). The HRV of group 'A' was 19.5 (SD±9.76), group 'B' was 10.1 (SD±6.54). The Valsalva ratio of group 'A" was 1.3244 (SD ± 0.1555), group 'B' was 0.06 (SD ± 0.0036). *Conclusion:* Current study evaluated the existence of parasympathetic neuropathy in relation to the glycemic status irrespective of the duration of diabetes.

Key words: Chronic hyperglycemia, Parasympathetic neuropathy

Introduction

Diabetes mellitus is one of the leading causes of mortality and morbidity in our country. Mortality and morbidity is due to a high levels of blood glucose (hyperglycemia) (RBS>180 mg/dl) [1]. Chronically elevated levels of glucose in the blood or achieving poor glucose control may lead to complications of diabetes over time [2]. Chronic hyperglycemia predicts the likelihood of future neuropathy, retinopathy and nephropathy [3]. Incidence of diabetic autonomic neuropathy is as high as 60–80% [3]. Autonomic neuropathy carries a higher mortality in diabetics [4]. Functional disturbance in peripheral and autonomic nerves, are often present even at the time of diagnosis [5]. Diabetes Control and Complication Trial & United Kingdom Prospective Diabetes Study have concluded that lowering of blood glucose level (HbA_{1C}) resulted in lowering of morbidity, mortality and cost of living [6-7].

Material and Method

As per the study guidelines and Institutional Ethical Committee permission, 100 age matched type 2 diabetics belonging to both sexes, with a variable duration of diabetic history were taken up for study. Smokers, alcoholic and patients having history of hypertension were excluded from the study. After an overnight fast, their blood was

collected and sent for estimation of HbA_{1C} and Average Blood Glucose [8]. The existence of chronic hyperglycemia can be made out by the estimation of $HbA_{1C,}$ which gives the glycemic status for the last three months. They were subjected to parasympathetic autonomic function tests [9] which included

1. *Resting Heart Rate (RHR)* which is obtained by recording a resting ECG in lead II at a paper speed of 50 mm/sec. From which the heart rate is calculated.
2. *Heart Rate response to Valsalva Manoeuvre* was performed with patient blowing into a mouth piece connected to a sphygmomanometer with clipped nostrils and holding at a pressure of 40 mm Hg. for 15 seconds while a continuous ECG was recorded [result is expressed as Valsalva Ratio which is the ratio of longest R-R interval after the manoeuvre to the shortest R-R interval during the manoeuvre]. *Normal ratio* : $\geq$1.20 *Borderline*: between 1.11 to 1.20 *Abnormal*: $\leq$1.10
3. *Heart Rate Response to Deep Breathing (HRV)*: The patient breathes at 6 breaths/min. (5 sec. in & 5 sec. out) and a continuous ECG is recorded with a marker to indicate the point of inspiration and expiration. [max. and min. R-R intervals during each breathing cycles were measured and converted to beats/min.] *Normal ratio*: $\geq$ 15 beats/min. *Borderline*: between 11 to 14 beats/min. *Abnormal*: $\leq$10 beats/min.

The Results obtained were analyzed by 'z' test.

Result

They were segregated into two groups. Group 'A' [N=60] consisted of patients having average plasma glucose less than 180 mg/dl (HBA_{1c} < 8 mg%). Group 'B' [N=40] consisted of patients having average plasma glucose of more than 180 mg/dl (HBA_{1c} >8%). The general characteristics are shown in table-1.

Table-1: Showing General characteristics of both the groups

General characteristics	Group 'A' [HbA_{1c} < 8%]	Group 'B' [HbA_{1c} > 8%]
Age (years)	48.033	48
Gender (F:M))	1 : 2.157 [19/41]	1 : 1.857[14/26]
Duration of diabetes (years)	6.2	7.38
FBS (mg%)	160.2	238

There was a statistically significant variation in parasympathetic function tests between the two groups and are shown in table-2.

Table-2: Showing the variations in both groups

	Group 'A' [HbA_{1c} < 8%]	Group 'B' [HbA_{1c} > 8%]	Statistical Significance
HBA_{1c} (%)	7.423 (SD$\pm$1.194)	11.82 (SD$\pm$1.974)	P<0.01
Average Blood Glucose (mg/dl)	162.55 (SD $\pm$ 40.32)	316.8 (SD $\pm$ 79.25)	P<0.01
Resting Heart Rate (RHR) per min.	87.56 (SD$\pm$10.99)	93.09 (SD$\pm$14.07)	P<0.01
Heart Rate Variability to deep breathing (HRV)	19.5 (SD$\pm$9.76)	10.1 (SD$\pm$6.54)	P<0.01
Valsalva Ratio	1.3244 (SD$\pm$0.1555)	0.06 (SD$\pm$0.0036)	P<0.01

Discussion

Hyperglycemia is considered the principle cause of diabetic complications. As long as the average blood glucose level is normal it leads to normal glucose metabolism, without any complications. In conditions of sustained hyperglycemia, the proportion of glycated hemoglobin is increased [10-11]. Studies have shown that HbA_{1C} is the index of mean blood glucose, which includes both fasting and post prandial blood glucose levels, over the preceding weeks to months [12]. Persistent elevated glucose levels leads to formation of glucotoxins by various biochemical pathways, which produce end organ damage such as neuropathy, nephropathy, retinopathy and cardiovascular complications [13]. Its deleterious effects are attributable to the formation of glucose derived substances called advanced glycated end products (AGEp). In diabetic vascular tissue the concentration of AGEp is four times than the normal more so when blood sugar levels are chronically elevated [13]. Autonomic neuropathy is one among the microvascular complications. Early detection and treatment of which postpones these complications. It is to remember that the parasympathetic pre-ganglionic fibres are long and are prone of damage very early in diabetics due to prolonged hyperglycemia even before the development of diabetic complications [13]. As pancreatic beta cells are also innervated by parasympathetic nerves, hyperglycemia stimulates pancreas to augment insulin secretion and hyperinsulinemia [14] and insulin resistance. Studies have shown that when glucose levels are lowered towards the normal range, microvascular complications of type 2 diabetes are reduced [15]. Target level of HBA_{1c} level is <7% and the 'take action' level is >8% [15]. By keeping HbA1c within normal delays parasympathetic autonomic neuropathy and a reduction in microvascular complications.

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*All Correspondence: Dr. Nanda Kumar LG, Professor, Department of Physiology, MNR Medical College, MNR Nagar, Sangareddy, Medak (AP) 502295 Email : dranusri@yahoo.com