ASSESSMENT OF AUTONOMIC SYMPTOMS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Background:Cardiovascular autonomic neuropathy results from damage to autonomic nerve fibres that result in abnormalities in HR control and vascular dynamics commonly seen disease like DM. Aim and objectives: To assess autonomic symptoms in patients with type 2 DM.Measure response of BP and HR to handgrip test in patients with DM.
Methodology: 40 type 2 Diabetic were selected. HR and BP were recorded three times at rest, immediately after release of handgrip test and after one minute of rest.
Results: there is no significant variation in heart rate (p=0.2748) and quite significant variation in diastolic blood pressure(p=0.0990) and extreme significant variation in systolic blood pressure(p=0.0001) which shows there is autonomic symptoms present in patients with type 2 DM.
Conclusion: patients with type 2 DM have cardiovascular autonomic symptoms.
Keywords: type 2 DM, autonomic symptoms, handgrip strength test.

Introduction

The autonomic nervous system is the part of the nervous system that is responsible for regulation and integration of internal organs' functioning. Together with the endocrine and immunological systems it determines the status of the internal environment of the organism and adjusts it to its current needs, thus enabling adaptation of the internal environment to changes in the external environment1.

Pathophysiology

The metabolic hypotheses for diabetic complications include polyol pathway hyperactivity and its related myo-inositol deletion, increased diacylglycerol-protein kinase C cascade, oxidative stress, and nonenzymatic glycation. Metabolic abnormalities cause functional alterations of neural cells and finally lead to structural alterations in nerve tissues. Vascular deficit-induced ischemia and hypoxia also cause functional and structural abnormalities in nerve tissues.

Among all the metabolic pathways, the polyol pathway hypothesis has been considered as the leading metabolic contender for neuropathy. Multiple etiology of DAN leads to autoimmune damage and neurovascular insufficiency. Chronic hyperglycemia leads to activations of polyol pathway which in turn activates sorbitol and fructose accumulation and reduces sodium-potassium ATPase levels. This alter fatty acid metabolism and increase the accumulation of advanced glycated end products and oxidative stress. These pathways ultimately cause neuronal damage and decrease neuronal blood flow. Elevated glucose level stimulates Diacylglycerol (DAG) which in turn activates Protein Kinase C (PKC). Activation of PKC reduces neuronal blood flow resulting in worsening of DAN. Upon activation of PKC, MAPKs (mitogen activated protein kinases) are activated which phosphorylate transcription factors and thus alter the balance of gene expression. Inhibition of PKC-? reduces oxidative stress and normalizes blood flow and nerve conduction deficits in diabetic rats.

Non-enzymatic protein glycation by glucose is a complex cascade of reactions yielding a heterogeneous class of compounds, collectively termed as AGEs. AGEs disrupt the function of neurons in DAN by acting on cell surface specific receptors named RAGEs. AGEs activate Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase, Mitogen-Activated Protein Kinases (MAPK), stimulate cell division and activate various transcriptional factors like Nuclear Factor-Kappa B (NF-?B) to induce local inflammatory cascades, which execute diabetic vascular complications.

The balance between the rate of free radical generation and elimination is important, however, if there is a significant increase in radical generation, or a decrease in radical elimination from the cell, oxidative cellular stress ensues. Increased production of Reactive Oxygen Species (ROS) induces oxidative stress in both type

of diabetes. Diabetic autonomic neuropathy involves alteration of metabolic pathways which in turn alters redox capacity of the cell.
Furthermore these pathways also trigger damage through expression of inflammation proteins leading to impaired neural function, gradually heading to apoptosis of neurons, Schwann and glial cells of peripheral nervous system. The disease arises from a combination of microvascular and neuronal deficits. Oxidative stress can contribute significantly to these deficits as a direct result of prolonged hyperglycemia. Increased oxidative stress causes vascular endothelium damage and reduces nitric oxide availability. Excess nitric oxide production leads to the formation of peroxynitrite which causes nerve damage (Nitrosative stress).
All these pathways in combination, results in reduced endoneural blood flow and nerve hypoxia leading to altered nerve function2.
Autonomic dysfunction occur when there is damage to the nerves that manage every day body functions such as blood pressure, heart rate, sweating, bowel and bladder emptying, and digestion. Disorders of autonomic regulation are described in multiple and diverse diseases, both those that directly afflict the nervous system as well as those afflicting other organs, where they trigger or enhance pathological symptoms2.
Clinical symptoms of these disturbances are frequently non-characteristic. Diabetic autonomic dysfunction is among the least recognized and understood complications of diabetes despite its signi?cant negative impact on survival and quality of life in people with diabetes3.
The patient's history and physical examination are ineffective for early indications of autonomic nerve dysfunction, and thus recommendations for the use of noninvasive tests that have demonstrated ef?cacy are warranted. Integrity of autonomic system can be assessed by means of hand dynamometer, a device that measures the force of hand grip. The hand dynamometer is static muscular exercise. The Static muscular exercises produce a significant rise in systolic and diastolic arterial pressures and heart rate. The normal response is rise of diastolic pressure >16mmHg, whereas a response of <10mmHg is considered abnormal1.After the contraction ends, the blood pressure and heart rate quickly return to control values in normal circumstances3.

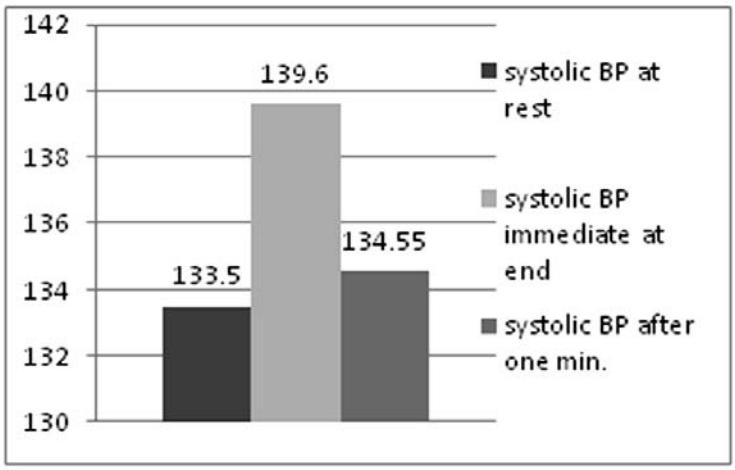
Methodology

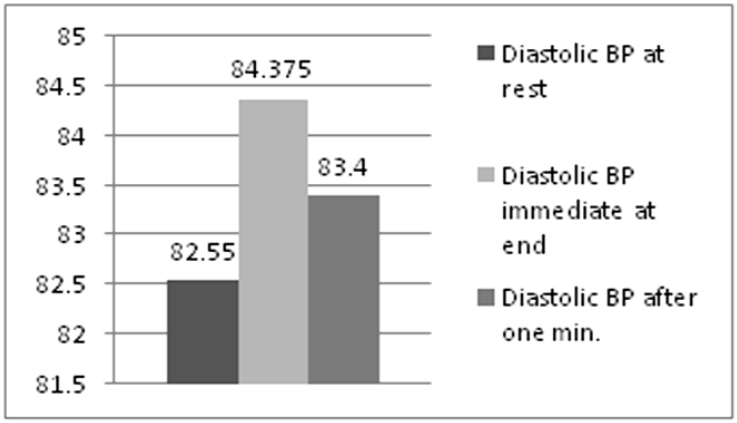
Study design: survey method
Study setting: diabetic care centers and random population of Pune.
Target population: type 2 diabetic.
Sampling method: convenient sampling.
Sample size: 40
Inclusion criteria: type 2 diabetic
Exclusion criteria: type 1 diabetic patients, type 2 diabetic patients with any cardiovascular condition, respira-

tory condition or hypertension and patients with any other metabolic disease.
Materials required: pen, paper, timer and calculator.
Outcome measures: sphygmomanometer and hand dynamometer.

Procedure:
Ethical committee clearance was taken. 40 Patients were approached by convenience and were selected for study according to inclusion and exclusion criteria and consent was taken after explaining the procedure and aim of study.It is assured that the identity of the patient is not disclosed anywhere.Patient is asked to consume medication after the test as medication may influence the results.Subject is seated and asked to use their dominant hand as subjects grip maximally with dominant hand.Adjust the grip bar to fit comfortably within subject's hand. The second joint of fingers should fit under the handle of handgrip dynamometer. Make sure that hand dynamometer is set to zero.Have the subject hold it parallel to the side of body at waist level and forearm at level of thigh.Subject should then squeeze the handgrip dynamometer as hard as possible with care not to hold breath.Test is repeated thrice and highest value of 3 contractions is taken as maximum voluntary contraction (MVC).Handgrip is maintained for as long as possible up to 5mins. Heart rate is recorded by manual palpation and blood pressure by sphygmomanometer .These observations were recorded three times at rest, immediately after release and after 1 min rest.

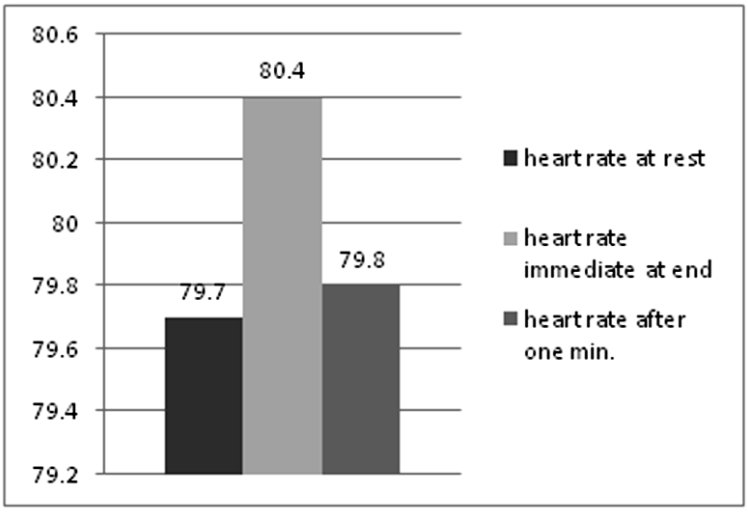
Result
Graph no. 1 shows mean of systolic blood pressure at rest was 133.5mmHg, immediate at end was 139.6 mmHg and after one minute was 143.55 mmHg(p=0.0001) which shows that there is Extreme significant variation in systolic blood pressure
Graph no. 2 shows mean of diastolic blood pressure at rest was 82.55 mmHg, immediate at end was 84.37 mmHg and after one minute was 83.4 (p=0.0990) which shows that there is Quite significant variation in diastolic





blood pressure.

Graph no. 3 shows mean of heart rate at rest was 79.7bpm, immediate at end was 80.4bpm and after one minute is 79.8bpm (p=0.2748) which shows that there was no significant variation in heart rate



Discussion

In this study we found that TYPE 2 diabetics have autonomic symptoms present. This was proven by an objective measure of handgrip strength test.

This study was performed on 40 type 2 diabetic patients approached from Sanjeevan hospital and random population of Pune. Patients were explained about the procedure and aim of the study and were asked to consume medication after the assessment as medication may influence the result. The procedure was followed after the written consent was taken.

D. J. Ewing in his study concluded that the mean diastolic blood pressure rises were smaller both in males and females this was related to a smaller mean MVC. the diabetic subjects had an abnormally low response to sustained handgrip, which was not related to age, duration of diabetes, treatment or control of the disease. damage of the autonomic fibres mediated the response. The findings suggested that sustained handgrip is a useful and simple method of detecting involvement of the autonomic nervous system in dia-

betes.

The handgrip strength test performed by hand dynamometer; three readings were recorded namely systolic blood pressure, diastolic blood pressure and heart rate recorded thrice at rest, immediately at the end of the procedure and after giving rest for a min. after the end of procedure.
On recording the systolic blood pressure the three reading noted ,showed extreme significant variation ($p=0.0001$) with the mean being at rest was 133.5 mmHg, immediate at end was 139.6 mmHg and after one minute was 134.55 mmHg which means there is significant rise in systolic blood pressure after an exercise (static muscular exercise).
On recording of diastolic blood pressure the three readings noted, showed Quite significant variation ($p=0.0990$) with the mean being at rest was82.55 mmHg, immediate at end was84.375 mmHg and after one minute was 83.4mmHg which means there is quite less variation in diastolic blood pressure after exercise (static muscular exercise), in normal circumstances there is rise in diastolic blood pressure more than 16mmHg, whereas a response of <10mmHg is considered abnormal and may be indicative of presence of autonomic dysfunction. As noted in this study there is less than 10 mmHg rise in diastolic blood pressure. So it can be said that there is presence of autonomic dysfunction and patient may be symptomatic or asymptomatic.

On recording heart rate the three readings were noted, showed there is no variation ($p=0.2748$) with mean being at rest 79.7bpm, immediate at end was 80.4bpm and after one minute was 79.8bpm which means there is no variation in heart rate after exercise (static muscular exercise). In normal circumstances there is rise in heart rate in response to increase demand due to exercise which returns to normal after the contraction ends. no variation to heart rate to exercise may lead to exercise intolerance. And no variation in heart rate also shows that there is presence of autonomic dysfunction present in patients with type 2 diabetics.
Autonomic symptoms are present in diabetes mostly because of metabolic insult, neurovascular insufficiency and several different factors.In our future study we can confirm neuropathy by using additional tests for autonomic dysfunction.

CONCLUSION

We concluded that patients with type 2 DM have cardiovascular autonomic symptoms present according to handgrip strength test.

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