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Pulmonary function test in type 1 diabetics

R.N. Gajbhiye* and A.S. Tambe

Department of Physiology, Govt. Medical College, Hanuman Nagar, Nagpur-440003 Maharashtra, India

Abstract: *Objective*: Present study was undertaken to find out the effect of diabetes on the respiratory system. *Background*: Diabetes is a disease with multiple organ involvement. Glycosylation of tissue proteins occur when blood glucose level remain elevated for a prolonged duration. Due to this, there occur irreversible changes in the chemical structure of tissue proteins. Basement membrane and connective tissues in skin, muscles, respiratory system, vascular bed, kidney, peripheral nervous system, etc. are the targets for glycosylation. Pulmonary function testing (P.F.T.) is a valuable tool for evaluating the respiratory system, representing an important adjunct to the patient history, various lung imaging studies, and invasive testing such as bronchoscopy and open-lung biopsy. *Material and Method:* 64 type 1 diabetic subjects and 60 controls were selected for the study. Anthropometric parameters, blood investigations and P.F.T. were performed on all subjects. *Result and Discussion:* Fasting and Post Meal blood glucose levels as well as HbA_1c% were significantly higher in type 1 diabetics as compared to controls. All P.F.T. parameters excepting FEV_1 % were also significantly reduced in type 1 diabetics. Decreased values of P.F.T parameters in type 1 diabetics can be attributed to biochemical alteration of connective tissue constituents particularly collagen and elastin as well as by microangiopathy due to nonenzymatic protein glycosylation induced by chronic hyperglycemia.
Keywords: Type 1 diabetes mellitus, pulmonary function test, glycosylation.

Introduction

Diabetes mellitus is one of the most common endocrine and metabolic disorder. It is ranked fifth as a leading cause of death worldwide, and is responsible for almost 3 million deaths annually [1]. The worldwide prevalence of diabetes is increasing rapidly because of reduced physical activities and changes in food habits among individuals resulting in increased obesity and insulin resistance. Chronic hyperglycemia and related metabolic derangements may be associated with secondary damage in multiple organ systems, especially kidneys, eyes, nerves and blood vessels. The possibility that the lung is also a target organ for diabetic complications was first suggested by Schuyler et al in 1976. Since that time there have been many studies of pulmonary function in diabetic patients with conflicting results. Many have suggested plausible pathophysiological mechanisms also.

Development of these complications can be explained by biochemical alteration of connective tissue constituents particularly collagen and elastin as well as by microangiopathy due to nonenzymatic protein glycosylation induced by chronic hyperglycemia [2-3]. However at the present time there are no reports of functional limitations of activities of daily living, ascribable to pulmonary disease in diabetic patients. Hence the present study is undertaken to evaluate the magnitude of pulmonary dysfunction in diabetic patients.

Material and Methods

Subjects: The present study was carried out in the Diabetic clinic of Indira Gandhi Govt. Medical College and Mayo Hospital, Nagpur. The approval of Institutional ethical committee was obtained. Written informed consent was obtained from all the subjects. All the subjects were males in the age group of 31- 60 years. Study group included 64 type 1 diabetic patients and for comparison age and height matched 60 subjects were selected from the staff members as control group.

	Control	Cases
Age (yrs)	45.26 ± 9.10	45.00 ± 8.92
Weight (kg)	61.36 ± 4.91	58.14 ± 8.63*
Height (mts)	163.65 ± 5.07	163.06 ± 4.62

Each group was supplemented by respiratory questionnaire [4]. Thorough physical examination was done by the Physician to rule out cardiac, respiratory or other diseases that may contraindicate pulmonary function testing. All were non-smokers with no history of smoking in the past. After selection, subjects from both groups were asked to report in the Dept. of Physiology, I.G.G.M.C. Nagpur in the morning hours (10 A.M. – 12.30 P.M.) to avoid the effects of diurnal variation on P.F.T. [5].

Anthropometric measurements and biochemical profile: Standing height was measured by simply making the subject stand bare foot against a wall on which measuring scale is inscribed. Weight was done by KRUPS weighing machine in light weight garments without foot wears. BSA was calculated using Dubois and Dubois (1916) equation [6]. BMI was calculated using formula Weight in kg / (Height in meter)^2. Fasting and post meal blood glucose level was measured using Glucose Oxidase Biosensor assay method by One Touch Horizon Glucose Meter. HbA_1c% was measured using cation exchange resin method (monozyme's glycohemin kit).

Measurement of lung volumes: P.F.T. was determined using MEDSPIROR - Recorder and Medicare system. Necessary instructions were given to the subjects before performing P.F.T. They were asked to execute fast forcible expiration as much as possible at the end of deep full inspiration. Subjects were asked to perform the test till they become accustomed to the procedure. Then, three consecutive readings were obtained and the best was selected for the study. One single expiratory effort gives many readings, out of them FVC, FEV_1, FEV_1 %, FEF 25-75%, FEF 0.2-1.2L, PEFR were selected for the study. After the rest of 15 minutes, the test to obtain Maximum Ventilation Volume was carried out. Subjects were asked to inhale and exhale as deep and as fast as possible for twelve seconds. The in-built calculation in the Medspiror gives MVV which was repeated for three consecutive times with a period of rest for ten minutes between each effort and best reading was selected for the study.

Statistical Analysis: Mean and Standard Deviation were calculated and significance of difference was tested statistically by unpaired student's t test [7]. Correlation coefficients were calculated and tested for statistical significance. Data is exhibited in the tables.

Results

The results of pulmonary function test were compared between the cases (type 1 diabetics) and the controls. Values are expressed as Mean ± SD in the tables. Table No. 1 shows that fasting and post meal blood glucose levels as well as HbA1c % are significantly higher in type 1 diabetics as compared to controls. Also all P.F.T. parameters excepting FEV_1 %, are significantly reduced in type 1 diabetics.

Table-1: Showing comparison of blood parameters and P.F.T. parameters in cases (type 1 diabetics) and controls (Values are expressed as Mean ± SD)

Parameters	**Controls** (Mean ± SD)	**Cases** (Mean ± SD)
Fasting (mg %)	92.48 ± 7.97	172.76 ±56.49*
Post Meal (mg %)	126.46 ± 7.63	285.42 ±80.58*
HbA_1c %	4.29 ± 0.95	9.35 ±1.24*
FVC (Litre)	2.99 ± 0.26	2.37 ± 0.46*
FEV_1 (Litre)	2.57 ± 0.26	2.04 ± 0.35*
FEV_1 %	85.9 ± 3.39	86.93 ± 5.83
FEF 25-75 % (L/sec)	3.31 ± 0.55	2.74 ± 0.67*
FEF 0.2-1.2 L (L/sec)	6.10 ± 0.87	3.98 ± 1.16*
PEFR (L/sec)	7.24 ± 0.94	5.36 ± 1.29*
MVV (L/min)	116.10 ± 15.37	91.42 ± 15.14*
*p < 0.001 (highly significant)		

Table-2: Showing correlation between various anthropometric and lung function parameters in cases (type 1 diabetics) and controls

		FVC	FEV_1	PEFR	FEF 25–75%	FEF 0.2-1.2L	FEV_1 %	MVV
Age	Cases	-0.4053*	-0.4574*	-0.0605	-0.282*	-0.2871*	-0.02	-0.1768
	controls	-0.5696*	-0.5374*	-0.1215	-0.3939*	-0.2575*	-0.12	-0.677*
Weight	Cases	0.073	0.022	0.111	0.022	0.064	-0.19	0.0936
	controls	0.264	0.132*	0.17	0.104	0.117	-0.22	0.1009
Height	Cases	0.1824	0.2018	0.0442	0.0833	0.1202	-0.03	0.0872
	Controls	0.2191	0.0904	0.0365	0.1692	0.1183	-0.26	0.2409
BMI	Cases	0.008	-0.049	0.116	-0.0006	0.0364	-0.19	0.0731
	Controls	0.1139	0.078	0.1626	-0.0216	0.0316	-0.02	-0.0997
BSA	Cases	0.1174	0.0754	0.1054	0.0353	0.0832	-0.19	0.1115
	Controls	0.2763*	0.129	0.1303	0.1467	0.1341	-0.27	0.1754

*$p < 0.001$ (highly significant)

Table No. 2 shows the values of correlation coefficient (r value) between the various anthropometric and lung function parameters in cases (type 1 diabetics) and controls. A significant negative correlation was observed between age and FVC, FEV_1, FEF 25-75%, FEF 0.2-1.2L in both cases and controls. A significant negative correlation was observed between age and MVV in controls. Also a positive correlation was found between weight and FEV_1 & BSA and FVC in controls.

Discussion

Body weight was significantly reduced in type 1 diabetics ($p<0.05$). Insulin is required for the normal utilization of glucose by most cells of our body. There is no insulin secretion in type 1 diabetics, so alternate sources of energy like proteins and fats are being used up. This results in more catabolism of proteins and fats and hence weight loss [8]. B.M.I. and B.S.A. were also found to be significantly reduced ($p<0.05$). Fasting and post meal blood glucose levels as well as HbA_1c% were found to be significantly more in type 1 diabetics pointing to the fact that there is poor glycemic control. This may be because of irregular drug intake, inappropriate drugs, sub-dosing, overeating, lack of diabetic life style discipline, etc. practiced by the patients [9].

HbA_1c% is an indicator of diabetes control. Higher the level of HbA_1c%, poor is the diabetic control i.e. higher level of circulating glucose. If circulating glucose is constantly at a higher level for 3 months (as measured by HbA_1c%), it can lead to more and more non-enzymatic glycosylation of tissue proteins. If respiratory system is a target, this will be reflected in the P.F.T. parameters analysed. FVC and FEV_1 are significantly reduced in type 1 diabetics. But FEV_1 % is not significantly different, in both cases and controls. This signifies that restrictive lung pathology occurs in diabetes. Similar findings were observed by other authors [9-18].

FEF 25-75% is an indicator of force of expiration of gases during middle 50% of forced expiration. In type 1 diabetics FEF 25-75% is significantly reduced compared to controls. Forced expiration is supported by muscular and recoil forces of the respiratory system. But the flow can be decreased even due to obstruction, but this is excluded as FEV_1 % is normal. Thus decrease in muscular and recoiling forces of the respiratory system because of increased glycosylation is responsible for significant decrease in FEF 25-75%. Similar findings were observed in other studies [9,16,19]. FEF 0.2-1.2 L is the initial portion of forced expiratory manoeuvre. First 200 ml of the gas is from the dead space. Remaining 1 litre is exhaled from lung broncho-alveolar tree. This includes some gas from the functional residual

capacity, as normal tidal volume is 500 ml. This extraction of gas is due to compression forces that are built up by the expiratory muscles. But due to glycosylation of connective tissues of the respiratory apparatus, the compression forces built up by the expiratory muscles might be decreased leading to a significant reduction in FEF 0.2-1.2 L in type 1 diabetics. PEFR is the gas exhaled in $1/10^{th}$ of a second during forced expiratory manoeuvre. At this time recoiling forces of the lungs and contractile forces of respiratory muscles are functioning maximally and supporting the expiration to the maximal. But due to glycosylation of the connective tissues of the respiratory apparatus, the recoiling forces of the lungs and the contractile forces of the respiratory muscles might be decreased, leading to a significant reduction in PEFR [16, 18].

MVV is the manoeuvre where maximum ventilator efforts are made. MVV in type 1 diabetics is significantly reduced indicating that muscular forces are weakened causing decrease in lung compliance. This again is due to glycosylation of connective tissues of respiratory apparatus [12,15]. Makkar P. *et al*. [16] studied the pulmonary function tests in type 1 diabetics of Bikaner and observed a significant reduction in FVC, FEV_1, PEFR, MEF 75% and MEF 25%. Irfan M. *et al*. [17] investigated pulmonary functions in Pakistani diabetic patients and observed a significant reduction in the forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) relative to non diabetic controls. Meo S.A. *et al*. [18] in their studies on Saudi diabetic patients showed significant reduction in FVC, FEV_1, and PEF, as compared to their matched controls. Sreeja C.K. *et al.* [19] in their studies of lung function in diabetics of Kerala observed that the expiratory flow rates are reduced in insulin administered patients.

Thus, our study suggests that there is hyperglycaemia which remains chronic. This chronic hyperglycaemia causes increased glycosylation of connective tissues and other proteins. The restrictive lung pathology observed in diabetics is due to an overall effect of glycosylation on collagen and elastic framework of the respiratory apparatus, producing a less compliant lung. Normally the diabetic patient may not appreciate the respiratory muscle weakness as during normal tidal respiration, diaphragm is the mostly used muscle. Therefore tidal work load on non-diaphragmatic respiratory muscles being comparatively less, weakness of respiratory muscles is not much appreciated by the patient in routine life. This does not mean that respiratory muscles are not weakened. Magnitude of restriction will depend upon individual susceptibility and susceptibility of lungs as well. Keeping this individual variation in mind it becomes necessary to test HbA_1c% and P.F.T. at regular intervals to find out early deterioration of lungs in diabetic patients.

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*All correspondences to: Dr. Ratnesh N. Gajbhiye, Department of Physiology, Govt. Medical College, Hanuman Nagar, Nagpur-440003 Maharashtra, India. Email: dr_ratnesh2003@yahoo.com