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Physiology

THE INFLUENCE OF GENDER DIFFERENCES IN ECG DERIVED INDEX QT DISPERSION AND SPIROMETRIC PARAMETERS IN INDIAN COPD PATIENTS: COMPARATIVE ANALYTICAL STUDY.

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. The risk factors as far as gender difference in COPD is concerned are different.Biomass combustion is a major risk factor among Indian women from rural area and Smoking, tobacco in males.

Method: 50 diagnosed COPD patients of chronic bronchitis and emphysema was compared with 50 healthy control and between male (n=50) & female (n=50). ECG parameters and pulmonary function tests were compared by using unpaired 't' test. Correlation was done by Pearson's co-relation coefficient and p value was calculated.

Observations and Results: There is no statistically significant difference in QT dispersion, FEF (25-75) & FEV1 as far as male and female COPD patients are concerned. There is negative correlation of QT with various spirometric parameters

Conclusion: There is no effect of influence of gender difference as far as QT dispersion & spirometric parameters like FEF (25-75) & FEV1 are concerned.

KEYWORDS : QT dispersion, Biomass smoke, COPD, Lung function tests.

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death, affects more than 10 million people in the United States and about 2.7 -million people in India.[1] About 3 billion people, are exposed to smoke from biomass fuel compared with 1·01 billion people who smoke tobacco, which suggests that exposure to biomass smoke might be the biggest risk factor for COPD globally.[2].

The term Chronic Obstructive Pulmonary Disease (COPD) refers to a spectrum of disease characterized by cough, sputum production, dyspnoea, air flow limitation and impaired gas exchange. [1] The spectrum of cardiovascular disease in COPD includes Right ventricular dysfunction, pulmonary hypertension, Coronary Artery disease & Arrhythmias [3] Pathogenesis of tachyarrhythmia in COPD patients is multifactorial and includes a number of risk factors such as hypoxemia, acidosis, & reduced FEV1[4]

The risk factors as far as gender difference in COPD is concerned are different.Prolonged exposure to smoke produced by biomass combustion, a common mode of cooking appears to be a significant risk factor among Indian women from rural area. Smoking & tobacco are the major causes of COPD in male patients.

There is paucity of information on QT dispersion in COPD patients as far as gender difference is concerned.

Aim of the present study is to evaluate & compare the ECG derived indices like QT interval, QT dispersion in COPD patients and control group and to correlate these ECG parameters with spirometric parameters like FEV1, FEV1/FVC, FEF (25-75) in male & female COPD patients.

MATERIALAND METHODS:

Present study was conducted inCOPD patientsattending chest OPD Sassoon general hospital, Pune.Written informed consent of subjects and local Ethical committee approval was taken.

Study Design: Comparative analyticalstudy.

Study type: Comparative and correlative.

Study group:100 diagnosed COPD patients (both male and female)35-70 yrs. of chronic bronchitis and emphysema were selected. Diagnosis is done according to GOLD criteria (FEV1<80% & FEV_1/FVC< 70%) after takingbronchodilator therapy.

Inclusion criteria:50 COPD males were smokers (n=35), tobacco chewers (n=8), flour mill workers(n=7),50 COPD females were using chulha as mode of cooking, since 10 to 15 years.

Exclusion criteria: Acute respiratory infection, diabetes, hypertension, LVH, IHD, obesity (BMI < 24.9 kg/m²).

Data collection : BMI was calculated by using formula **BMI[2] = Weight in Kg / (Height in meters)²** Vital parameters like Pulse rate , Blood Pressure was recorded in supine position. ECG was recordedusing Clarity **Med ECG 50-1 CH**.

Methods for measurement: Participants were instructed not to smoke or consume alcohol, tea coffee or to engage in strenuous physical activity 12 hours prior to ECG recording.12 lead ECG was taken after 10 minutes of rest in supine position at the same time of the day (10 a.m.-1p.m.) followingECG derived indices were measured

(1) QT interval (QT)[5]:-Time interval between beginning of Q wave to the end of T wave i.e. reaching to baseline in all 12 leads, measured manually and average of 3 readings was taken.

(2)Corrected QT interval (QTc)[6]:calculated manually by Bazett's Formula:QTc =QT/ RR.QTcrepresents the QT interval corrected for heart rate.RR iscalculated from the onset of one QRS complex to the onset of next QRS complex.

(3) QT dispersion (QTd) [7]: QT dispersion was calculated from the difference between maximum & minimumQT interval.

SPIROMETRY: The pulmonary function parameters were measured using a computerized portable RMS Helios 702(Chandigarh) spirometer.This spirometer is automated and has a flow sensor which converts the airflow signals to digital signals. Values obtained were in litres & compared with the existing data base for the normal healthy Indian population depending on age, sex, height and weight. The tests were conducted according to the American Thoracic Society [8]/ European Respiratory Society (ATS/ERS) task force guidelines.

Procedure-- The pulmonary functions were recorded in the sitting position. Name, age, sex, height and weight were entered in the spirometer.

Forced Vital Capacity (FVC) manoeuvre was conducted in the following order:

1) Subjects were instructed to hold the mouthpiece in the mouth with

lips pursed around it.

2) After the three normal breaths, they are asked to take deep inspiration and to blow forcefully into the mouthpiece as long as possible without hesitation and coughing. Then without removing the mouthpiece from the mouth, they are instructed to inspire maximally through the mouthpiece.Following Parameters recordedand expressed as predicted value and testvalue.

a. Force expiratory volume in one second (FEV1) in litres.
b. FEV_1/FVC in %.
c. FEF(25-75)%

Statistical Analysis: ECG parameters and pulmonary function tests were compared by using unpaired 't' test. Correlation ofQTd and Pd with pulmonary function parameters was done by Pearson's correlation coefficient and P value was calculated.

OBSERVATIONS AND RESULTS:

Table no. 1 shows comparison of age (59.16 ± 4.26 vs. 59.24 ± 4.78, p>0.05) and BMI (19.68 ± 4.76 vs. 20.41 ± 3.84, p>0.05) inCOPD and control group respectively. BMI is within normal range (18.5 - 24.9 kg/m^2)[9] which rule out obesity. Both groups were comparable with respect to age and BMI. Systolic blood pressure (143.2 ± 4.9 vs 119.72 ± 8.01, p<0.0001), Diastolic blood Pressure (92.84 ± 2.9 vs 75.68 ± 4.68, p<0.0001) and Heart Rate (126.62 ± 5.02 vs 81.26 ± 5.31, p<0.0001) is more in COPD patients compared to control group.

Table no.2 shows decrease QT interval in COPD patients (302.8 ± 8.18 vs.322.72 ± 25.99, p<0.001) as compared to control group. Increased resting heart rate which affect QT interval but after correction with heart rate by **Bazett's formula**[6] corrected QT interval (QTc) is more in COPD patients (431.7 ± 26.6 vs 384.24 ± 33, p<0.0001) as compared to control group which indicates that QT interval is heart rate dependent parameter.QT dispersion (QTd) is found to be significantly increase in COPD patients (65.2 ± 4.5 vs 37.34 ± 5.33, P value <0.0001) as compared to control group.

Table no.3 Shows significantly reduced spirometric parameters i.e.FEV1 (1.80 ± 0.69 vs 2.63 ± 0.46, p<0.0001), FEV1/FVC (77.06 ± 6.97 vs 88.18 ± 5.73, p<0.01) and FEF 25-75 (2.78 ± 0.59 vs 3.33 ± 0.90, p<0.05) in COPD patients compared to control group respectively. This finding indicates obstructive nature of pulmonary involvement in COPD patients. [10]

Table no.4 Shows positive correlation of QTdispersion withHeart Rate (r =0.888, p<0.0001), Systolic Blood Pressure (r = 0.670, p<0.0001) and Diastolic Blood Pressure(r = 0.969, p<0.0001) in COPD patients as compared to control. It indicates autonomic imbalance in COPD patients compared to control group.

Table no.5 Shows negative correlation of QT dispersion with various spirometric parameters like FEV1 (r = -0.874, p<0.0001), FEV1/FVC (r = -0.903, p<0.0001) and $FEF_{(25-75)}$ (r = -0.715, p<0.0001) in COPD patients.It indicates prolonged QT dispersion is associated with obstructive lung pathology.

Table no.6 shows age, BMI, heart rate, systolic and diastolic blood pressure in male & female COPD patients. There was no significant difference (p>0.05) found in both groups.

Table no.7 shows comparison of QT interval, QTc i.e. corrected QT interval, and QT dispersion in male and female COPD patients.

Table no. 8 shows the mean values of FEV1, FEF(25-75), FEV1/FVC in COPD Male and COPD Female group. FEV1/FVC significantly less (p<0.05) infemale patients compared to male.

Table no. 9 shows correlation between QTdwith age, BMI, heart rate, Blood pressure in male and female group.QTd was positively(r<0.0001)correlates with heart rate, systolic and diastolic blood pressure. No correlation of QTd with age and BMI In both groups.

Table no. 10 shows Correlation between QTd with spirometric parameters in male & female COPD.QTd negatively(r<0.0001) correlates with FEV1,FEV1/FVC,FEF (25-75) which is statistically significant.

Table 1: Shows mean valuesof Age, BMI,HeartRate,Systolic BloodPressure & Diastolic Blood Pressure in COPD patients and control group.

Parameters	COPD (n=50)	control (n=50)	t value	p value
	Mean ± SD	Mean ± SD		
Age (yrs)	59.16 ± 4.26	59.24 ± 4.78	0.06	>0.05
BMI(kg/m2)	19.68 ± 4.76	20.41 ± 3.84	0.6	>0.05
Systolic BP (mm of Hg)	143.2 ± 4.9	119.72± 8.01	12.46	<0.0001**
Diastolic BP (mm of Hg)	92.84 ± 2.9	75.68 ± 4.68	15.15	<0.0001**
Heart Rate (bpm)	126.62 ± 5.02	81.26 ± 5.31	31	<0.0001**

Table 2: Shows mean values of QT Interval, corrected QT Interval, QT dispersion in COPD patients and control group.

Parameters	COPD	control	t value	p value
QT Interval (ms)	302.8 ± 8.18	322.72 ± 25.99	3.65	<0.001**
Qtc Interval (ms)	431.7 ± 26.6	384.24 ± 33.00	5.59	<0.0001**
QT dispersion (ms)	65.2 ± 4.5	37.34 ± 5.33	19.84	<0.0001**

Table 3 :Shows mean values of FEV1, FEV1/FVC & FEF(25-75), in COPD patients& control group.

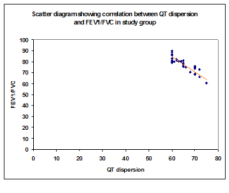
Parameters	COPD	control	t value	p value
FEV_1 (litres)	1.80 ± 0.69	2.63 ± 0.46	4.82	<0.0001**
FEV_1/FVC (%)	77.06 ± 6.97	88.18 ± 5.73	6.16	<0.0001**
FEF_{25-75} (l/sec)	2.78 ± 0.59	3.33 ± 0.90	2.53	<0.05*

Table 4: Shows correlation of QTdispersion with age, BMI, Heart Rate, Systolic and Diastolic Blood pressure in COPD patients andcontrol group.

Parameters	COPD		control	
	r value	p value	r value	p value
Age (Yrs)	-0.240	>0.05	-0.268	>0.05
BMI (Kg/m2)	0.201	>0.05	0.139	>0.05
Heart Rate (bpm)	0.888	<0.0001**	-0.169	>0.05
Systolic BP (mmHg)	0.670	<0.0001**	-0.264	>0.05
Diastolic BP (mmHg)	0.969	<0.0001**	-0.115	>0.05

Table 5: Shows correlation between QT dispersion and spirometric parameters in COPD patients and control group.

Parameters	COPD		Control	
	r Value	p Value	r value	p value
FEV1 (Litres)	-0.874	<0.0001**	-0.058	>0.05
FEV1/FVC (%)	-0.903	<0.0001**	-0.178	>0.05
FEF(25-75) (L/sec)	-0.715	<0.0001**	-0.066	>0.05



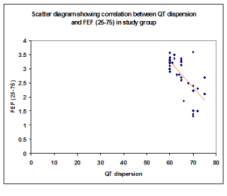


Table6: Comparison of age,BMI,Systolic BP,Diastolic BP, Heart Rate in Male and Female COPD Patients.

Parameter	Male (n=25)		Female (n=25)		t Value	P Value
	Mean	SD	Mean	SD		
Age (Yrs)	58.76	4.64	59.56	3.92	0.66	>0.05
BMI	19.29	5.31	20.06	4.25	0.57	>0.05
SBP (mmHg)	144.32	3.86	142.08	5.73	1.62	>0.05
DBP (mmHg)	92.16	2.7	93.52	3.02	1.68	>0.05
HR/min	127.04	5.73	126.2	4.29	0.59	>0.05

Significant at p < 0.05 * highly significant at p < 0.001**

Table 7: Comparison of QT interval, QTc interval, & QT dispersion(QTd)in Male and Female COPD group

Parameter	Male (n=25)		Female (n=25)		t Value	P Value
	Mean	SD	Mean	SD		
QT interval	300.4	8.87	305.2	6.78	2.15	<0.05

QTccorrected QT interval	432.68	26.74	430.72	27.12	0.26	>0.05
QTdispersion	64.12	4.16	66.28	4.77	1.71	>0.05

Table 8: Comparison of FEV1, FEV1/FVC, FEF (25-75) in Male and Female COPD group

Parameter	Male (n=25)		Female (n=25)		t Value	P Value
	Mean	SD	Mean	SD		
FEV1	1.89	0.65	1.76	0.75	0.65	>0.05
FEV1/FVC	79.08	4.29	75.06	8.52	2.11	<0.05
FEF(25-75)	2.92	0.76	2.66	0.31	1.58	>0.05

Table9: Correlation between QTd and age, BMI, HR, Blood pressure in non Smoker COPD male and female group

Qtd	Male COPD		Female COPD	
	r Value	P Value	r Value	P Value
Age (Yrs.)	-0.38	>0.05	-0.16	>0.05
BMI	0.32	>0.05	0.05	>0.05
HR	0.99	<0.0001	0.93	<0.0001
SBP	0.47	<0.0001	0.95	<0.0001
DBP	0.95	<0.0001	0.98	<0.0001

Table 10: Correlation between QTd and spirometric parameters inCOPD male and female group

Qtd	MaleCOPD		Female COPD	
	r Value	P Value	r Value	P Value
FEV1	-0.89	<0.0001	-0.87	<0.0001
FEV1/FVC	-0.78	<0.0001	-0.99	<0.0001
FEF(25-75)	-0.74	<0.0001	-0.87	<0.0001

DISCUSSION:

In the present study, we evaluated

1. Comparison of ECG derived indices like QT interval, corrected QT interval, QT dispersion between50 COPD patients and 50 age and sex matched Control group.
2. Comparison of QT interval, corrected QT interval, QT dispersion between 50 male &50 female COPD patients.
3. Correlation of QT dispersion with age,BMI, heart Rate, systolic blood pressure, diastolic blood pressure. &Spirometric parameters like FEV_1, FEV_1/FVC, $FEF_{(25-75)}$ in male & female COPD patients.

Increased QTd in COPD patients than control group:

Several explanations have been put forward to explain increase inQTdispersion in COPD patients.

1) Hypoxia in COPD patients cause increased myocardial O_2 demand and adversely effects left ventricular performance, which may alter QT dispersion.[11]
2) Hypoxia increases phase 4 depolarization of myocardial muscles and also increases rate of spontaneous depolarization in conducting tissues of heart leads to vulnerable development of tachyarrhythmias.[12]
3) Flick& Block found that cardiac arrhythmias were at their maximum when arterial oxygen saturation is at its lowest and oxygen therapy ameliorates these arrhythmias. [13]
4) Autonomic Nervous System directly affects QT interval. Autonomic tone may affect corrected QT interval and QT dispersion through depolarization and repolarization kinetics of myocardial cells. [14]
5) QT dispersion has been reported to be prolonged in patients with primary autonomic failure. [14]Prolonged QT dispersion is an indication of inhomogeneous ventricular repolarization phase responsible for developingtachyarrhythmia's& sudden cardiac death.[4] So, the present study shows that COPD patients are prone to develop tachyarrhythmias& sudden cardiac death due to prolonged QT dispersion compared to control group**.**

Positive correlation of QTd with various spirometricparameters FEV1, FEV_1/FVC and $FEF_{(25-75)}$

In COPD patients decreasein FEV1, FEV_1/FVC and $FEF_{(25-75)}$ is responsible for prolongation of QT dispersion suggesting that hypoxia, hypercapnia due to airway obstruction may influence ventricular repolarization which is responsible for prolongation of QT dispersion.[12,13]$FEF_{(25-75)}$ is a sensitive index of obstructive pathology.[15]
In COPD patients, chronic airway obstruction affect cardiovascular system leading to increase inheart Rate,systolic Blood pressure, diastolic blood pressure when compared to control group. It is due to increased myocardialoxygen demand and workload.[16] In due course it affects electrophysiological parameters like QT Interval, QT dispersion,leading to prolonged QT dispersionand ventricular arrhythmia.

All women in this study were chulha users from rural areas exposed tobiomass smoke since 10 to 15 years, which mainly contain firewood, woods, charcoal, crop residues & animal dung [17]& all male patients were smokers, tobacco chewers,and flour mill workers.

The ratio of FEV1/FVC is less in women in comparison to men indicates airflow limitations.FEV1 is influenced by age, sex,height while FVC indicates vital capacity which is also influenced by age,sex, height, BMI which might be the cause for reduced ratio in women.

There was no significant difference between men & women COPD patients as far as QT dispersion is concerned except increase inQT interval which is heart rate dependent parameter.Negative correlation of QT dispersion with spirometric parameters strongly indicate that in COPD patients decrease in FEV_1, FEV_1/FVC and $FEF_{(25-75)}$is responsible for prolongation of QT dispersion suggesting that hypoxia, hypercapnia due to airway obstruction may influence ventricular repolarization which is responsible for prolongation of QT dispersion.[12,13]Therefore it appears that prolonged QT dispersion in COPD patients lead to cardiovascular complications irrespective of etiology of airway obstruction. There is no influence of gender difference on lung parameters like FEV_1, FEV_1/FVC and $FEF_{(25-75)}$ as well as cardiovascular parameters like QT interval & QT dispersion.

CONCLUSION

1) QT dispersionis a non invasive marker of arrhythmogenicity so analysisof routine ECG is an important, non invasive, inexpensive, bedside, diagnostic tool to detect early arrhythmias in COPD patients.
2) Etiological factors like exposure to biomass smoke, cigarette, bidismoking, tobacco chewing all equally affect airway obstructive changes.
3) There is no difference in QT dispersion in male & female COPD patients even though the causes for COPD are different.
4) There is Intriguing relationship between the QT dispersion and functional respiratory parameters.
5) Greater the severity of COPD, greater will be the prolongation of QT dispersion. So, we recommend that all COPD patients should undergo ECG recordings forearly diagnosis as well as prevention of cardiac arrhythmia.

These findings suggest theneed for a global and multidisciplinaryrisk assessment in COPD patients. Therefore, special attention in the diagnostic work-up of these patients is needed, coming to a more integrated pulmonary and cardiovascular care.

REFERENCES:

1) Reilly JJ, Jr, Silverman E K, Shapiro S D. Chronic obstructive pulmonary disease. Harrison's, Principles of Internal Medicine.18th Edition. McGraw Hill; Volume I, 2012; Pg 2151-59.
2) Salvi S S, Barne P J. Chronic obstructive pulmonary disease in non-smokers. Lancet. 2009 ;663 (374): 733–43.
3) Warnier MJ, Rutten FH, Numans ME, Kors JA, Tan HL, Anthonius de B.et al.Electrocardiographic Characteristics of Patientswith ChronicObstructive PulmonaryDisease.COPD 2013; 10:62-71.
4) Yildiz P, Tu¨kek T, Akkaya V, So¨zen AB, Yildiz A, Korkut F et al Ventricular arrhythmiasin patients with COPD are associated with QT dispersion Chest2002;122(6):2055–61.
5) Barret KE, Barman SM, Boitano S, Brooks HL.Origin Of The Heart Beat And The Electrical Activity Of The Heart. Ganong's Review of Medical Physiology.23rdedition, Tata McgrawHill 2010; p.310-11.
6) Bazett HC. An analysis of the time relations of electrocardiograms. Heart1920; 7:353-70.
7) Malik M, Batchvarov VN. Measurement, interpretation and clinical potential of Q dispersion. J Am CollCardiol 2000; 36:1749.
8) ATS/ERS task force: Standardization of lung function testing. General consideration of lung function testing. EurRespirJ 2005;26: 151-61.
9) Park K. Park's textbook of preventive and social medicine. 20th ed. Jabalpur: M/S Banarsidas Bhanot 2009; 345-49.
10) Cosio M, Ghezzo H, Hogg JC, Corbin R, Loveland M, Dosman J et al. The Relations between Structural Changes in Small Airways and Pulmonary-Function Tests N Engl J Med 1978; 298:1277-81.
11) Singh K. Effect of smoking on QT interval, QT dispersion and rate pressure product.Indian Heart Journal2004; 56(2):140-42.
12) Tirlapur V G, Mir. Nocturnal Hypoxemia and Associated Electrocardiographic Changes in Patients with Chronic Obstructive Airways Disease.N Engl J Med 1982; 306:125-130.
13) Flick MR, Block AJ. Nocturnal vs diurnal cardiac arrhythmias in patients with chronic obstructive pulmonary disease. Chest1979;(75) :8-11.
14) Lo SS Mathias, C J Sutton, M S. QT interval and dispersion in primary autonomic failure.Heart (British Cardiac Society).May 1996; 75 (5): 498– 501.
15) Sreenivas S B, Sunitha M S, Nataraj S M, andMuraliDhar. A Study Of Deterioration Of Pulmonary Function Parameters Among Smokers And Recovery Among Ex-

Smokers In Bus Depot Workers. Indian J PhysiolPharmacol. 2012; 56(2) 154–160
16) Padrid PJ, Fuchs T, Candinas R. Role of sympathetic nervous system in the genesis of ventricular arrhythmia. Circulation.1990; 82: 103-13.
17) Zelikoff, JT, Chen, LC, Cohen, MD, and Schlesinger, RB. The toxicology of inhaled woodsmoke. J Toxicol Environ Health B Crit Rev. 2002; 5: 269–282