Bahrain Medical Bulletin, Vol.24, No.1, March 2002

Predictive Factors of Poor Lung Function in Cured Tuberculosis Patients

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Objective: To evaluate clinical factors that can influence the results of spirometry in cured tuberculosis patients.

Design: Measurement of spirometry in treated tuberculosis patients with review of patient's records for duration of symptoms, chest radiography and residual changes within five years of completion of anti-tuberculosis therapy.

Setting: Sahary Chest Hospital, Riyadh, Saudi Arabia

Results: Forty-six patients were studied (23 males, 23 females). Forced Vital Capacity (FVC), Forced Expiratory Volume at end /1 Sec (FEV_1) and ratio of FEV_1/FVC were abnormal in 13 cases, and oxygen saturation was less than 90% in three cases. Significantly higher rate of abnormal spirometry was observed in patients with poor compliance (poor 58.3% Vs good 17.6%), patients with duration of treatment less than 6 months (<6m 53.3% Vs ≥6m 16.1%), and patients with advanced lung damage (advanced 38.5% Vs mild 10%).

Conclusion: Poor compliance with the prescribed drug regimen, and significant lung damage seen on radiography were found to adversely affect the degree of loss of lung function. Furthermore, lung functions appear to improve with time, and the longer the duration of recovery from tuberculosis.

Bahrain Med Bull 2002;24(1):19-22.

Pulmonary tuberculosis is endemic in Saudi Arabia with estimated annual prevalence of 30 cases per 100,000 population[1]. Despite major improvement in health care and particularly in the treatment of tuberculosis, sequelae of the pulmonary disease continue to be frequently encountered in clinical practice[2]. Post tuberculous lung diseases including bronchiectasis, fibrosis and pleural disease are some of the well known complications of the disease[3,4]. Patients with history of tuberculosis frequently present

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with impaired lung function and a clinical picture similar to chronic obstructive pulmonary disease (COPD)[5,6]. Although treated pulmonary tuberculosis is a recognised cause of COPD, the medical literature is scant regarding the extent of impaired lung function[7]. This study is designed to assess lung function and correlate it with medical or personal factors that could change the outcome of the treatment of pulmonary tuberculosis with respect to respiratory function.

METHODS

Over a period of 6 months (from January - June 1999), 46 patients with pulmonary tuberculosis who were declared cured by their treating physician were enrolled in a pulmonary out-patient clinic of Sahary Chest Hospital, Riyadh.

Fifty patients were initially registered for the study, however 4 patients were excluded because of lack of cooperation in performing spirometry tests. All these patients had pulmonary tuberculosis diagnosed by positive smear and/or culture of sputum. They were treated by standard therapy of 4 drugs (rifampicin, isoniazid, pyrazinamide or ethambutol for a minimum duration of 6 months). Because of the possible development of unrelated chest disease, five years post-treatment limit was chosen. Only patients seen within these five years were considered for the study.

Patients were subjected to spirometry (FEV_1, FVC, FEV_1/FVC), oxygen saturation by pulse oximetry and a posterior-anterior chest radiography. Spirometry was performed according to instructions (Schiller spirometer, Germany). Predicted values were selected appropriately for the population studied according to the current international guidelines[8].

Oxygen saturation was measured by Omeda Oximeter, USA using the thumb of either hand while the patient was in the sitting position[9,10]. The chest radiographs were interpreted by an experienced chest physician and was compared with the previous radiographs. For a uniform computing of findings of chest x-rays a code system was developed. The interpreter of the radiographs decided which category a chest radiograph belonged to with regards to residual changes; none or mild, moderate and advanced. Mild: linear/stellate streaks, limited pleural thickening or limited scattered nodular densities; moderate: nodular dense changes, persistent cavitation, or gross pleural thickening; advanced: wide fibrotic changes, bullae or destroyed lung. Good compliance was defined as attending 90% or more of clinic appointments with drug interruption of no more than one week duration, otherwise, the patient was regarded as having poor compliance. Biodata and results of measurements were processed and coded. Analysis was done using Epi-Info and SPSS computer software and P value of < 0.05 was considered significant.

RESULTS

A total of 46 patients (23 males and 23 females) were studied Table 1. The duration of the treatment regimen was 6 months in 15 patients, 9 months in 27 patients and 12 months in only 4 patients. Compliance with treatment was rated by the treating physician

to be good in 34 patients (73.9%) and fair or poor in 12 patients (26.1%). History of asthma or COPD was present in 4 patients (8.7%). Six patients gave history of present or past smoking (13.1%). The post treatment duration ranged between 1-60 months with a mean duration of 19.43 month (SD = 17.61). Fifteen patients (32.6%) had duration of less than 6 months and 31 patients (67.4%) had a duration of 6 months or more, up to 5 years.

Table 1**. Patients data**

Total number of patients	46
Gender: Male/Female	23/23
Age in years	33.6 (13-77)*
Duration:Drug treatment regimen	No. of patients
6 month	15 (32.6%)
9 month	27 (58.7%)
12 month	4 (8.7%)
Compliance with treatment	No. of patients
poor	12 (26.1%)
good	34 (73.9%)
Duration after treatment	
mean in months	19.43 (1-60)*
	No. of patients
< 6 month	15 (32.6%)
≥ 6 month	31 (67.4%)
History of:	No. of patients
Asthma/COPD	4 (8.7%)
Smoking	6 (13%)
Tuberculosis	4 (8.7%)

Chest radiography: The plain PA chest x-rays was clear in only 7 patients (15.2%). According to the criteria provided in "methods" the following categories for residual changes were found. Mild residual changes (or none) were seen in 20 patients (43.5%), moderate residual changes were seen in 13 patients (28.3), and advanced changes were seen in 13 patients (28.3%).

Table 2. **Results of chest radiography findings, spirometry and oxygen saturation**

Spirometric	Data

Parameters		
Residual changes	Mild / none	20 (43.5%)
	Moderate	13 (28.3%)
	Advanced	13 (28.3%)
FEV_1	Mean ± SD	83.59 ± 17.95
	Abnormal (<80%)	13 cases (28.3%)
FVC	Mean ± SD	86.02 ± 14.98
	Abnormal (<80%)	13 cases (28.3%)
Ratio FEV_1/FVC	< 75%	11 cases (23.9%)
	>95%	2 cases (4.3%)
O_2 saturation	< 90%	3 cases (6.5%)

SD = standard deviation, FEV_1 = Forced expiratory flow in one second
FVC = Forced expiratory flow, O_2 Sat = Oxygen saturation

Spirometry: (Table 2) The mean percentage of the predicted value for Forced Vital Capacity (FVC) was 86.02 (SD = 14.98). Using published criteria for assessment of airway obstruction with a cut-off value of 80% as the lower limit of normal, 13 patients (28.3%) were found to have abnormal FVC[8]. The mean percentage of the predicted value for Forced expiratory volume in one second (FEV_1) was 83.59 (SD = 17.95). Using the cut-off value as above 13 patients (28.3%) were found to have abnormal results. The ratio of FEV_1/FVC was calculated and any results below 75% or above 95% was regarded as abnormal. Eleven patients were found to have reduced FEV_1/FVC (23.9%) indicating an obstructive pattern and only 2 patients had ratio above 95% indicating a restrictive pattern. All but 3 patients (6.5%) had oxygen saturation of 90% or above as measured by finger pulse oximeter, a result that is too small for a meaningful statistical correlation.

Table 3. **Effect of compliance and duration after treatment on lung function**

Parameters		FEV_1 No.	(%)	FVC No.	(%)	Ratio No.	(%)
Compliance	Poor	7/12	(58.3)*	6/12	(50)**	5/12	(41.7%)†
	Good	6/34	(17.6)	7/34	(20.6)	6/34	(17.6%)
Duration after treatment	< 6 months	8/15	(53.3)*	4/15	(26.7)†	7/15	(46.7)**
	≥ 6	5/31	(16.1)	9/31	(29)	6/31	(19.4)

	months			

**P = < 0.05 **P = 0.05 † = P is not significant*
denominator = cases with abnormal spirometry.
numerator = all cases in the corresponding category.

Table 3 showed the effect of compliance with drug therapy and the effect of the post-treatment duration on the results of spirometric measurements. More than 58% of patients with poor compliance had abnormal FEV_1, less than 80% of predicted value compared to 17.6% of patients who complied with their drug regimen instructions. FVC was also reduced in poorly compliant patients but results did not reach statistical significance. A duration of 6 months or less after completion of drug regimen for tuberculosis is associated with more cases having abnormal FEV_1 compared to a duration of 6 months or more (53.3% vs 16.1%). Furthermore, the ratio (FEV_1/FVC) was found to be abnormal in 46.7% of cases who finished their treatment less than 6 months compared to only 19.4% for cases who finished treatment more than 6 month prior to testing, (P = 0.05). Forced vital capacity (FVC) was not statistically different between these two groups.

Table 4. **Effect of residual chest x-ray changes on lung function**.

Residual Changes	FEV_1		FVC		Ratio	
	No.	(%)	No.	(%)	No.	(%)
Mild / none	2/20	(10)*	1/20	(50)*	4/20	(20%)**
Moderate	6/13	(46.2)	5/13	(38.5)	4/13	(30.8)
Advanced	5/13	(38.5)	7/13	(53.8)	5/13	(38.5)

** P = < 0.05 ** P = is not significant*
denominator = cases with abnormal spirometry
numerator = all cases in the corresponding category

The effect of the post-tuberculosis residual changes on lung function is shown in Table 4. With normal or only mild residual changes, abnormal FEV_1, FVC were seen only in 10% and 5% respectively compared to 46.2% and 38.5% for moderate changes and 38.5% and 53.8% for advanced changes. The distribution of abnormal ratio (FEV_1 /FVC) among the three categories was not found to be statistically significant.

DISCUSSION

This study revealed three main factors that may affect the ventilatory function of treated tuberculosis patients: compliance with drug therapy, residual radiological changes following treatment and the length of the post-treatment period. About 26% of our patients were not fully cooperative. Compliance is a very important determinant of success of tuberculosis treatment and this study showed yet an additional reason to consolidate effort to ensure full compliance of patients with anti-tuberculosis therapy[11].

It is possible that irregular use or interruption of drug therapy hampers complete healing of tuberculous infection which subsequently leads to permanent parenchymal changes that reflect on lung function tests[12].

Residual radiological changes in the form of pleural thickening or fibronodular changes may have been brought about by delay in diagnosis, advanced disease at the time of diagnosis or improper drug regimen[13]. Radiological changes seen on chest x-ray reflect parenchymal disease that gives variable impairment in lung function depending on the extent of these changes[14-15]. Rode and Shephard studied lung function in Canadian Innit and observed the accelerated loss of lung function in elderly patients with advanced tuberculosis[16]. In our study, over 56% of the cases were found to have moderate to advanced residual damage to the lungs. If future deterioration of lung function is to be avoided, much more efforts have to be directed to a good treatment program of tuberculosis management[17].

Lung function seems to be affected by the duration of the period of post therapy. The longer is the duration, the better is the lung function. This phenomena could be explained by the possibility that healing does continue even after stopping all anti-tuberculosis therapy leading to further improvement of lung parenchymal structure and better lung function measurements[18-20]. However, in the long term follow up of tuberculosis patients, Vargha reported a decline of FVC of 27.7 - 54.3 ml/year and FEV_1 of 28.8-35.3 ml/year over a period of 15 years[21]. It is possible that the improvement observed in our study occured only in the first few years (5 years or less) following treatment. Thereafter, depending on the extent of the lung residual damage, patients may follow the pattern described by Vargha as in their study no serial measurements were done especially in the first few years following treatment for tuberculosis.

It is possible to improve the post-treatment lung function by early diagnosis, better treatment and follow up. It is unclear whether extending the course of drug therapy from 6 to 9 or 12 months selectively for patients presenting with an advanced parenchymal disease would improve lung function. Further studies on this issue are needed.

CONCLUSION

Poor compliance with the prescribed drug regimen, and significant lung damage seen on radiography were found to adversely affect the degree of loss of lung function. Furthermore, lung functions appear to improve with time, and the longer the duration of recovery from tuberculosis.

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