Airway obstruction in heart disease

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ABSTRACT

Objective: To assess the airway function in 2 groups of patients suffering from heart disease of different etiology.

Methods: Preoperative flow volume curve was measured with pneumotachygraph and differential pressure transducer, and airway resistance (Rtot and Rex) was measured with the body plethysmograph in 79 patients with advanced mitral stenosis scheduled for valve replacement surgery (35 males and 44 females), and a 2nd group of 25 patients with atrial septal defect was scheduled for surgical repair (15 males and 10 females).

Results: Patients in both mitral valve replacement and atrial septal defect groups showed an obstructive ventilatory pattern, more prominent in the mitral valve replacement group for both males and females, reduced of forced expiratory volume in first second (FEV₁, 67% predicted), peak expiratory flow rate (77% predicted), flow rate of 50% of expiratory vital capacity (Vmax50 60% predicted) and increased Rtot and Rex more than 4cm H₂O/L/s. There was a statistically significant difference between the 2 males groups for FEV₁ as percentage of FVC (FEV₁/%FVC) (P<0.001), Rtot and Rex (P<0.05), and between the 2 female groups for FEV₁/%FVC, peak expiratory flow rate, Vmax50 (P<0.01), Rtot (P<0.05), and Rex (P<0.001).

Conclusion: The study revealed an obstructive ventilatory pattern in patients with mitral stenosis and in patients with atrial septal defect and concluded that the severity of airflow obstruction in patients with heart disease depends on the underlying cardiac pathology.

Keywords: Airway obstruction, bronchial hyperresponsiveness, rheumatic mitral stenosis, atrial septal defect.


Despite the frequent bronchial symptoms of coughing, wheezing and progressive nocturnal dyspnoea in patients with mitral stenosis and in patients with atrial septal defect (ASD), the obstructive airway disease pattern is not a well known feature, and very few investigators have studied the airway function and airway obstruction in these patients. Cosby et al¹ reported no evidence of obstructive airway in the 14 patients they studied with mitral stenosis and cardiac failure. Palmer et al² reported an increase in airway resistance in 12 out of the 30 patients with mitral stenosis. Singh et al³ reported reduction of the forced expiratory volume in first second, (FEV₁) and normal FEV₁/FVC ratio which indicated no evidence of airflow obstruction. Airway obstruction in mitral stenosis had been dismissed as an “unrelated condition”.⁴ There have been very few studies of airway function in patients with ASD. reduction of lung volumes and flow rates, an increased airway resistance with very high pulmonary artery pressure (PAP), progressive decrease in lung compliance with increasing pulmonary hypertension and increased pulmonary blood flow (PBF) were more recently described.⁵⁻⁷ De Troyer et al⁸ showed correlation between the PAP and FEV₁. Different factors have been suggested to produce airway obstruction in these patients, mainly patients with mitral stenosis; respiratory infection, pulmonary congestion, interstitial edema and edema of terminal bronchioles.⁹⁻¹⁰ Increased pulmonary

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Received 10 November 1998. Accepted for publication in final form 8 March 1999.

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vascular resistance and blood flow (pulmonary hyperemia) in ASD patients.

The aim of this study was to study and to correlate the airway function in 2 groups of cardiac patients with different etiology. The first group of patients with advanced rheumatic mitral stenosis who required mitral valve replacement (MVR) and the 2nd group of patients with congenital ASD who required septal repair.

**Method. Patients.** Seventy nine patients with severe mitral stenosis, 35 were males with age range of between 10 to 60 years and 44 females aged between 13 to 61 years. Twenty five patients with ASD, 15 males with age range between 14 to 50 years and 10 females aged between 15 to 42 years, diagnosed on the basis of clinical assessments, echocardiography and evidence of significant hemodynamic derangements obtained at catheterization and angiography, were assessed in the cardiac unit of the Chest Diseases Hospital in Kuwait. The first group were scheduled for MVR, the means ±SD for the males pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR) and cardiac index (CI) were 38.2 ± 13.2 mmHg, 372.4 ± 368.9 dyne/s/cm² and 2.4 ± 0.7 L/M² for the males and for the females were 35.5 ± 13.0 mmHg, 392.0 ± 362.7 dyne/s/cm², and 2.3 ± 0.6 L/M². The 2nd group were scheduled for ASD surgical repair, the mean ±SD for the males and for females L-R shunt % systemic blood flow (L-R BF) were 173.8 ± 85.2% and 181.4 ± 90.3. The means of age and height are shown in Table 1. None of the patients were smokers and none of them had a history of asthma or any primary lung disease. All patients were receiving digoxin and diuretics, and none of them were considered to be in cardiac failure.

**Calibration and standardization.** The pneumotachographs and pressure transducers were calibrated with standard flow rates, volumes and pressures. The ambient temperature, barometric pressure and the patients' weight, height, age and sex were entered, and the printout values for all pulmonary function data was obtained as actual values at saturated body temperature and ambient pressure (BTPS) and as a percentage of the predicted using prediction nomograms for VC, FEV₁, and flow-volume curve parameters.¹⁴

**Lung function tests.** Pulmonary function tests (PFT) were carried between 09.00 and 11.00 hours in the sitting position a few days preoperatively. Forced vital capacity maneuvers (FVC) were performed and flow volume curves were recorded with a computerized pulmonary function system (Jaeger, Wurzburg, West Germany). The values of flow measured with a pneumotachograph and differential pressure transducer were digitized and integrated to give FVC, FEV₁, FEV₁ as percentage of FVC (FEV₁, % FVC), peak expiratory flow rate (PEFR) and flow rate of 50% of expiratory vital capacity (Vmax50) corrected to standard pressure and BTPS. The individual flow volume curves were displayed online on an X-Y recorder. The best maneuver of 3 acceptable trials with the highest sum of FVC and FEV₁ was selected.¹⁵ Total airway resistance (Rtot) and expiratory airflow resistance (Rex) were measured according to the methods of Dubois and Associates,¹⁶ using the constant whole-body, plethysmograph as described by Schmidt and Chon.¹⁷ After temperature equilibration, 5 loops were made, the results were digitized and the best loop as visually determined on the X-Y recorder was selected for analysis, where the flow rate during shallow rapid breathing did not exceed ± 0.5L/s. The resistance values were automatically calculated.

**Statistical analysis.** Independent Student’s t-test was used to test the significant differences between 2 independent groups. Probabilities (P) value as statistically significant was indicated as (P<0.05), (P<0.01) and (P<0.001).

**Results.** Physical characteristic and lung function test values of the subjects who were designated for MVR and ASD surgical repair are described in Table 1. It can be noted that the ASD group were younger in age than the MVR group for both sexes, and there were significant differences between the 2 groups among the males (P<0.01). There were reduced values for the MVR group in both males and females for FVC and dynamic flow rates ranged between 66 and 77% of predicted with an increase of airway resistance of greater than 4 cmH₂O/L/s. There was less reduction of FVC, FEV₁, and Vmax50 for both males and females in the ASD group than those of the MVR group, ranging between 67 and 87% of predicted, with an increased Rex of more than 4 cmH₂O/L/s in the male group. The ASD male group had a significantly higher value for FEV₁, %FVC (P<0.001) and significantly less values for airway resistance than the MVR male group (P<0.05) for both Rtot and Rex. The male patients in the ASD group had a higher FVC, FEV₁, PEFR and Vmax50 than the males patients in the MVR groups, but the differences were not significant (P>0.05).

The ASD female group had significantly higher values than the MVR females group for PEFR, Vmax50, FEV₁, %FVC (P<0.01), and significantly less values for Rtot (P<0.05) and Rex (P<0.001). The female patients in the ASD group had a higher FVC and FEV₁ than those in the MVR group, but the differences were not significant (P>0.05).
Table 1 - Comparison of pre-operative lung function test values for mitral valve replacement and atrial septal defect surgery.

<table>
<thead>
<tr>
<th>Observations (no.)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age (Year)</td>
<td>Height (cm)</td>
</tr>
<tr>
<td>MVR 35</td>
<td>32.7 ± 11.7</td>
<td>168.5 ± 9.5</td>
</tr>
<tr>
<td>ASD 15</td>
<td>22.5 ± 10.4</td>
<td>167.7 ± 7.9</td>
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<tr>
<td></td>
<td>P &lt; 0.01</td>
<td>P = NS</td>
</tr>
<tr>
<td>MVR 44</td>
<td>34.5 ± 11.4</td>
<td>157.0 ± 5.9</td>
</tr>
<tr>
<td>ASD 10</td>
<td>27.4 ± 8.3</td>
<td>160.5 ± 7.8</td>
</tr>
<tr>
<td></td>
<td>P = NS</td>
<td>P = NS</td>
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FVC, forced vital capacity; FEV₁, forced expiratory volume in 1s; FEV₁/FVC, FEV₁ as percentage of FVC; PEFR, peak expiratory flow rate; Vmax50, flow rate of 50% of expiratory vital capacity; Ritot and Rex, airway resistance. Values are mean of percent predicted ± SD, except for airway resistance, which is expressed in absolute units (cm H₂O/L/s). Probability values are for comparing the ASD group with the MVR group in both males and females.

Discussion. The ability to move air rapidly in and out of the lungs is essential for normal activity and any diminution of more than minimal extent will usually cause breathlessness on exertion and hence reduce the capacity for exercise. Dynamic lung volumes and flow rates are assessed during forced expiration when maximal effort is applied through the respiration maneuver. Changes in airway function were determined in patients with advanced mitral stenosis and in patients with ASD in an effort to find out whether recurrent respiratory infection, pulmonary congestion, interstitial edema of the terminal bronchioles, increased pulmonary vascular resistance and blood flow, as they occur in cardiac disease of different etiology, have different effects on airway function.

This study revealed a pattern of airflow obstruction in patients with advanced mitral stenosis (MVR) and in patients with ASD: decreased flow rates (PEFR, Vmax50), decreased FEV₁/FVC, increased airway resistance in both sexes, as shown in Table 1, but more prominent with the mitral stenosis patients. Few studies have carried out systematic investigation of airway function in mitral stenosis. Cosby and colleagues used the maximum breathing capacity timed vital capacity and residual volume as a percent of the predicted value in each case as an index of airway function and reported no evidence of airway obstruction. Palmer et al. reported a reduction of mean values for the maximal mid-expiratory flow rate and increased airway resistance. Singh et al. reported a reduction in FEV₁ and an increase in residual volume. The airflow obstruction in patients with mitral stenosis had been conventionally explained on the basis of pulmonary vascular congestion, interstitial edema and edema in the terminal bronchioles as a result of increased left atrial pressure and increase in the capillary hydrostatic pressure. In previous work, we showed a significant correlation between airway function parameters and the hemodynamic data, mainly PVR in patients scheduled for MVR preoperatively.

Changes in airway function were determined in patients with ASD in an effort to find out whether pulmonary congestion, increased pulmonary vascular resistance as they occur in cardiac disease of different etiology have different effects on airway function and whether these effects vary at different stages of the disease process. The findings in this study of mild reduction of FVC, FEV₁, PEFR, Vmax50 among patients with ASD in the preoperative period (Table 1) is in agreement with earlier studies. The study showed normal airway resistance (Table 1), this is in agreement with earlier studies of Wood et al. when they studied 3 patients with ASD, whom they showed to have vascular plethora that could produce loss of elastic recoil at low lung volumes, and disagreement with other studies in which they reported increased airway resistance. It has been postulated that competition for space between vessels and airways within bronchovascular sheaths increases the resistance of the small airways. In a recent study we showed a significantly lower FEV₁ in patients with ASD in the group that was considered to have a higher mean PAP (mean PAP 16-26 mmHg), and this was with the agreement of other studies. Earlier, Yoshioka and coworkers reported a reduction
of vital capacity in a group of patients with ASD with high PAP and increased PBF which could partly be explained by cardiomegaly.26

Patients with ASD usually have a left-to-right shunt and pulmonary blood flow increases as a matter of course. It is likely that increased pulmonary blood flow would have an effect on airway function in ASD. Dyspnea occurred almost exclusively in patients with high PAP irrespective of whether this was due to high PBF or high pulmonary vascular resistance (PVR).27 We showed in an earlier study the effect of ASD surgical repair on airway function that showed a deterioration at 2 months postoperatively and generally recovered and improved at one year postoperatively and those patients in the group with high PAP had low FEV₁ and low FVC, which did not return to normal one year after surgery.24 This was explained in terms of irreversible change in the small airways and lung parenchyma as a consequence of long standing increased pulmonary blood flow. We also showed that those patients who survived MVR surgery showed a deteriorated pulmonary function in the early postoperative period, which recovered by 6 months postoperatively and progressively improved at 2 years postoperatively.22

Several factors known to contribute to the pathogenesis of airflow obstruction in asthma may be operative in mitral stenosis patients. Hypertrophied and hyperplastic airway smooth muscle with hypertrophy of submucosal glands and increased wall thickness are important causes of hyper-reactivity with unknown mechanism.28,29 It is suggested that pulmonary congestion and epithelial inflammation secondary to infection, with or without antigenic stimulation are important causes of bronchial hyper-reactivity in mitral stenosis. Activation of sensory nerve endings in the lower airways with edema or congestion causes bronchoconstriction by increasing vagal efferent activity.30 Chronic congestion and repeated respiratory tract infection in mitral stenosis may activate these receptors.31 Mediators released from mast cells, formed blood elements, complement fragments, could also stimulate sensory nerve endings and results in reflex sensitization of bronchomotor tone.32,33 Epithelial damage of the airways, due to respiratory tract infection and inflammatory changes, potentiate the effects of sensory stimuli and various inflammatory mediators, and lung congestion due to the mitral stenosis.10,34 Nadel and Sheppard postulated that airway epithelial damage activates arachidonic acid metabolism, releasing leukotrienes B₄ (LT B₄) and mediators from mast cells such as 5-hydroxyicosatetraenoic acid (5-HPETE), that directly produce bronchospasm.33

It has been suggested that stimulation of platelets by the platelets activating factor (PAF Acether) may release inflammatory mediators that directly cause bronchial smooth muscle to contract.35,36 The pool of all blood elements in long-standing mitral stenosis is evidently large. Rheumatic fever is a consequence of an immunological response or hypersensitivity reaction, or both to streptococcal antigens. Patients have a higher anti-streptolysin O response which suggests that the pathogenesis is autoimmune.37 The immune response may affect the bronchial system, although its main affection is on the heart.40 It remains to be seen whether one or more of the factors discussed leads to bronchial hyper-reactivity in rheumatic mitral stenosis. Chronic congestive heart failure (CHF) is characterized by mixed restrictive and obstructive ventilatory pattern and abnormalities of airway function.40,42 Kindman et al41 have shown that ipratropium bromide, an inhaled anticholinergic bronchodilator, improves FEV₁, FEV₂/FVC in patients with severe CHF. Most recently we have shown a reversible effect of salbutamol inhalation, B₂ agonist bronchodilator on obstructive impairment in patients with MVR pre and 6 months postoperatively.45

In conclusion, this study confirmed that the obstructive ventilatory pattern was more prominent in patients with rheumatic mitral stenosis than in patients with congenital atrial septal defect. Our findings indicate enhanced bronchomotor tone and hyper-responsiveness or both in these patients. Further studies are needed to investigate hyper-reactivity as a contributory factor in pathophysiology of airflow obstruction in patients with heart disease of different etiology.

Acknowledgments. The author would like to thank Dr. H. Shaibar, Senior Consultant Cardiothoracic Surgeon and Professor A. M. Yousof, Professor of Cardiology and Medicine, Chest Diseases Hospital, Kuwait for their support and help in the completion of this study.

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