Pulmonary function profile in patients with benign goiters without symptoms of respiratory compromise and the early effect of thyroidectomy

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ABSTRACT

Background: A large number of patients in our country develop goiters which seem to be apparently asymptomatic. Conventional radiography does not address the abnormal air flow dynamics. Flow volume loop studies have shown characteristic dampening of both inspiratory and expiratory curves. Pulmonary function tests (PFT) can provide a simple noninvasive method of assessing airway compromise. Aim: To address the effect of longstanding asymptomatic, benign goiter by performing PFT on the preoperative airway dynamics and the early postoperative changes at six weeks. Setting and Design: Tertiary care center, Prospective study. Materials and Methods: Sixty-four patients with benign goiters were included after they satisfied the necessary exclusion and inclusion criteria. Pulmonary function tests were performed in the pre and postoperative period. Statistical Analysis Used: SPSS ver. 10 software, Pearson's Bivariate correlation and students T test. Results: The preoperative PFT showed significant reduction in the Vital capacity (VC), Forced Vital Capacity (FVC), Forced expiratory volume in one second (FEV1), mid expiratory flow (MEF 25) and MEF 50 in the females and VC, FVC and FEV1 in males. Postoperatively significant improvement was observed in the tidal volume (VT) and FEV1 in the females and airway resistance in males. Conclusions: Pulmonary function tests can demonstrate the unmanifested abnormal airflow dynamics in benign asymptomatic goiters, which would have otherwise taken years to manifest. This abnormality improved after thyroidectomy, especially the forced expiratory maneuvers. The duration and weight of the goiter correlated well with reduction in FEV1 and its subsequent improvement after surgery in females.

KEY WORDS: Goiter, pulmonary function tests

Airway compromise has been convincingly demonstrated in retrosternal goiters and goiters with tracheal invasion.[1] A significant fraction seems to be asymptomatic despite evident external pressure on the upper airway. Conventional radiography only provides a static measurement of the upper respiratory tract whereas lung function tests can provide a simple noninvasive method of assessing extra thoracic airway compromise.[2-4] The earlier studies using the flow volume loops have shown characteristic dampening of both inspiratory and expiratory curves in these patients. With fixed obstruction like large goiters both inspiratory and expiratory flow rates are blunted.[4] This effect on the inspiratory and expiratory airflow in patients with goiters and the duration of such compromise may affect the lungs downstream and changes may occur in measured lung parameters. The nature and degree of change in flow characteristics at different lung volumes, the lung volumes per se and the lower airway resistance with longstanding goiters is not known. We performed a prospective study aiming to address this issue and also to know how thyroidectomy results in changes in pulmonary functions in the early postoperative follow-up (at six weeks) in patients with apparently asymptomatic benign goiters.

Materials and Methods

This prospective study was conducted with the approval of the ethics committee of the institute during the period August 2005 to December 2006. All patients preoperatively diagnosed as having benign asymptomatic goiters and undergoing surgery were included in the study. The indications for surgery included cosmetic reasons, large goiter, toxic multinodular goiter (MNG), and Graves' disease. Asymptomatic goiters were defined as those patients who do not have symptoms like orthopnea, exertional dyspnea, sleep apnea, change in voice, dysphagia and were clinically asymptomatic. Written informed consent was taken for their inclusion in the study, apart from the consent for the surgical treatment. Patients with history of smoking, bronchial asthma, chronic obstructive pulmonary disease, ischemic heart disease, diabetes, collagen vascular diseases, elderly (>70 years), patients with clinical evidence of respiratory compromise and those with

advanced malignancies of thyroid invading the airway/recurrent laryngeal nerves were excluded. The preoperative investigations included - apart from routine laboratory tests - thyroid function tests, ultrasound neck, fine needle aspiration cytology (FNAC), indirect laryngoscopy (IDL), a plain X-ray of neck (PA and lateral views) and pulmonary function tests (PFT). As per the requirement of the study PFT were also performed in the postoperative follow-up after six weeks of thyroidectomy when the patients were euthyroid biochemically. Pulmonary function test was done on PowerCube computer-supported system (Ganshorn Medizin Electronic GmbH, Germany manufactured 2002). The LF8 software program (Ganshorn Medizin Electronic GmbH, Germany) supplements the PowerCube hardware. The PowerCube Body Plethysmography measures the values of spirometry and flow volume characteristics. It also very precisely measures the total lung volume, the airway resistance and the thoracic gas volume (TGV) via the pressure changes in the body plethysmograph cabin. A single technician performed the procedure thus removing the bias of the technique and standardization method adopted was as per the European Thoracic Society guidelines. The technician instructed the patient - once inside the PowerCube body cabin which is kept airtight so as to measure the smallest of change in volume - to breathe at normal tidal volume into the ultrasonic transducer through a filter attached to it. The data thus measured is streamed digitally into the LF8 software program. The airway was temporarily blocked by a shutter for a fraction of a second during this procedure by starting the TGV program. The TGV, residual volume (RV), total lung capacity (TLC) and airway resistance were thus calculated by the software. Subsequently, spirometry was performed. The best observed value after three respiratory maneuvers was used for analysis. Since the PowerCube system and its software are programmed for European patients, we have used 80% of prediction values for vital capacity (VC), forced vital capacity (FVC), forced expiratory volume 1st sec (FEV1), peak expiratory flow (PEF), mid expiratory flow (MEF25), MEF50 and 88% of prediction values for TLC and 93% of prediction value for RV for our Indian patients.[5] Pulmonary function test was repeated at six weeks post thyroidectomy and the data was collected and tabulated. Indirect laryngoscopy performed at six weeks postoperatively revealed no vocal cord palsy in any of the study patients. At SGPGIMS we perform total thyroidectomy if a patient presenting to us with solitary/ multiple nodules involving one lobe of the thyroid is found to have another nodule of more than 1 cm in the opposite lobe either in the preoperative ultrasound evaluation of the neck or if the nodule is detected intraoperatively. All other patients having toxic multinodular goiter (MNG), Graves' disease and non-toxic MNG involving both lobes of the thyroid underwent total thyroidectomy.

Statistics: The demographic data was presented in mean ± SD. The PFT parameters in the preoperative and postoperative period were tabulated as mean ± SD. Data for male and female patients were analyzed separately. In the preoperative period change in all lung parameters (VC, FVC, FEV1/FVC, PEFR, MEF25, MEF50, TLC, RV, RWTOT and RWEXP) was compared with the predicted value for that particular patient and presented as percentage change from predicted. Similarly, after thyroidectomy, the change in PFT parameters from measured was presented as percentage change from measured. Students paired T test was used to compare measured with predicted values. Similarly, the same test was used to compare the change in preoperative and postoperative PFT values. Significance was taken as $P < 0.05$ at 95% confidence interval. The parameters which showed significant change were further analyzed with Pearson's Bivariate correlation to see the effect of the duration and weight of the goiter on PFT parameters. The weight of the goiter was measured immediately after the surgery in the operating room and the duration of goiter was taken from the time the patient had first noted the neck swelling. All the analysis was done using software SPSS (vs10) (Chicago, Illinois, USA).

Results

A total number of 71 patients were enrolled in the study. The postoperative follow-up was available in 64 patients. Seven patients were lost to follow-up for unknown reasons. There were 44 females and 20 males. The mean age, tracheal diameter, duration of the goiter, height, weight, body mass index (BMI) of the patients and the mean gland weight in males and females are given in Table 1. Eighty-seven per cent (n = 56) patients had Grade 3 goiters (WHO grading). At presentation 34% (n = 22) were having thyrotoxicosis but well controlled on thionamides. The mean tracheal diameter was as shown in Table 1. This measurement was performed from the X-ray soft tissue neck PA and lateral views. The measurement of the tracheal dimension was done at the C6 vertebral body level. The preoperative FNAC diagnosis was colloid nodule in 42 cases (79%) and follicular neoplasm in eight cases (15%). Radiological evidence of tracheal angulation/deviation/compression in different combinations was seen in 46 patients. Indirect laryngoscopy was normal in all patients. Seventy-seven per cent (n = 49) underwent total thyroidectomy and 23% (n = 15) had hemithyroidectomy. None of the patients had recurrent laryngeal nerve palsy as evidenced by the postoperative indirect laryngoscopy. The goiter-related factors are given in Table 1. All patients were euthyroid in the postoperative period when they reported for PFT at six weeks as evidenced by normal T4/T3/TSH. Tables 2 and 3 show the mean predicted, pre and postoperative PFT values in male and female subjects. The preoperative PFT showed significant reduction in the VC, FVC, FEV1, MEF 25 and MEF 50 in the female subjects [Table 2]. Even though PEF did show reduction it did not reach significance (P = 0.053) whereas the total airway resistance was increased though expiratory resistance was within normal range. In males VC, FVC and FEV1 [Table 3] showed similar reduction from the predicted values. The PEF was reduced without attaining significance. The percentage change in the air flow, in the postoperative period was compared with that of the preoperative period [Tables 2 and 3]. In the female subjects the tidal volume (VT, P = 0.021) and the FEV1 (P = 0.018) improved whereas in male patients no such observation was made. However, in male patients the airway resistance showed significant improvement when compared to the preoperative resistance [Table 3]. Using the bivariate correlation taking Pearson's coefficient a further analysis of the duration and weight of goiter on the preoperative PFT was done. In the female subjects the duration of goiter significantly influenced

Table 1: Goiter-related factors

Mean age (range in years)	40.4 ± 10.8 (18-62)	41.9 ± 10.7 (23-68)
Mean duration of the goiter (months)	104.3 ± 105.5 (range 3-480)	67.2 ± 90.8 (range 1-300)
Mean tracheal diameter (cm)	1.3 ± 0.2 (1-2.2)	1.5 ± 0.2 (range 1.2-2)
Height of the patient (cm)	152.3 ± 4.3 (range 144-163)	168.6 ± 5.6 (range 156-177)
Weight of the patient (kg)	57.7 ± 10.7 (range 39-84)	69.95 ± 12.6 (range 45-91)
Body mass index (range)	24.9 ± 4.4 (17-37)	24.4 ± 4.03 (17-30)
Gland weight (g)	126.4 ± 109.1 (range 26-500)	150.3 ± 127.1 (range 11-510)
Toxicity profile	Graves' (*n* = 7)	Graves' (*n* = 1)
Hyperthyroid 22 (34%)	Toxic MNG (*n* = 11)	Toxic MNG (*n* = 3)
Fine needle aspiration cytology (*n* = 50)	Colloid nodule (*n* = 28)	Colloid nodule (14)
	Follicular neoplasm (*n* = 4)	Follicular neoplasm (*n* = 4)
Procedure performed	Total thyroidectomy(*n* = 35)	Total thyroidectomy (*n* = 14)
	Hemithyroidectomy (*n* = 9)	Hemithyroidectomy (*n* = 6)
Radiological evidence of tracheal angulation/ deviation/compression *n* = 46 (72%)	*n* = 38	*n* = 08

Female (*n* = 44); Male (*n* = 20)

Table 2: Predicted and measured pre-thyroidectomy PFT, comparison of predicted vs. pre-thyroidectomy PFT and comparison of pre vs. post thyroidectomy PFT in females

Parameters	Predicted	Measured pre-thyroidectomy	Predicted vs. pre-thyroidectomy (Sig *P* = at 95% confidence interval {CI})	Post thyroidectomy	Pre vs. post thyroidectomy (Sig *P* = at 95% confidence interval {CI}
FVC (liters)	2.24 ± 0.27	2.08 ± 0.37	*P* = 0.00 (CI 0.62-0.82)	2.11 ± 0.32	*P* = 0.10 (CI -0.09-0.02)
FEV1 (liters)	1.92 ± 0.25	1.67 ± 0.36	*P* = 0.00 (CI 0.64-0.83)	1.72 ± 0.30	*P* = 0.02 (CI -0.1- -0.01)
FEV1/VC Max (%)	81.3 ± 2.1	77.5 ± 8.1	*P* = 0.16 (CI 1.26-6.18)	78.7 ± 7.0	*P* = 0.07 (CI-3.2-.007)
MEF25 (liters/sec)	1.35 ± 0.29	0.97 ± 0.40	*P* = 0.00 (CI 0.61-0.82)	0.99 ± 0.42	*P* = 0.33 (CI -0.12-0.06)
MEF50 (liters/sec)	3.10 ± 0.23	2.3 ± 0.84	*P* = 0.01 (CI 1.31-1.79)	2.42 ± 0.99	*P* = 0.09 (CI 0.29-0.05)
PEF (liters/sec)	4.85 ± 0.32	3.05 ± 1.12	*P* = 0.09 (CI 2.67-3.34)	3.3 ± 1.18	*P* = 0.05 (CI -0.60-0.03)
Raw-tot (kPas/l)	0.35	0.42 ± 0.26	*P* = 0.06 (CI -0.16-0.03)	0.39 ± 0.28	*P* = 0.56 (CI -0.06-0.10)
Raw-ex (kPas/l)	0.35	0.35 ± 0.2	*P* = 0.13 (CI -0.08-0.07)	0.33 ± 0.30	*P* = 0.61 (CI -0.07-0.12)
TLC (liters)	3.76 ± 0.23	4.16 ± 0.74	*P* = 0.02 (CI -0.13-0.33)	4.05 ± 0.93	*P* = 0.50 (CI -0.22-0.44)
RV (liters)	1.29 ± 0.18	2.04 ± 0.57	*P* = 0.69 (CI -0.87-0.44)	1.8 ± 0.83	*P* = 0.27 (CI -0.16-0.45)

P = < 0.05 (At 95% confidence intervals); FCV = forced vital capacity, FEV1 = forced expiratory volume in 1st second, MEF (mid expiratory flow), MEF 25: mid expiratory flow 25; MEF 50: mid expiratory flow 50; PEF = peak expiratory flow, Raw tot = total resistance, Raw ex = expiratory resistance, TLC = total lung capacity, RV = residual volume, VT = tidal volume

Table 3: Predicted and measured pre-thyroidectomy PFT, comparison of predicted vs. pre-thyroidectomy PFT and comparison of pre vs. post thyroidectomy PFT in males

Parameters	Predicted	Measured pre- thyroidectomy	Predicted vs. pre-thyroidectomy (Sig *P* = at 95% confidence interval {CI})	post thyroidectomy	Pre vs. post thyroidectomy (Sig *P* = at 95% confidence interval {CI})
FVC (liters)	3.41 ± 0.31	3.23 ± 0.5	*P* = 0.00 (CI.86-1.22)	3.26 ± 0.46	*P* = 0.27 (CI -0.25-0.17)
FEV1 (liters)	2.83 ± 0.29	2.65 ± 0.44	*P* = 0.00 (CI.75-1.04)	2.64 ± 0.38	*P* = 0.38 (CI -0.12-0.14)
FEV1/VC Max (%)	79.65 ± 1.95	78.21 ± 5.28	*P* = 0.79 (CI -1.31-4.25)	78.5 ± 5.92	*P* = 0.34 (CI -2.1-1.9)
MEF 25 (liters/sec)	1.57 ± 0.23	1.45 ± 0.57	*P* = 0.09 (CI 0.26-0.76)	1.43 ± 0.53	*P* = 0.58 (CI -0.13-0.19)
MEF 50 (liters/sec)	3.79 ± 0.29	3.5 ± 0.87	*P* = 0.31 (CI 0.83-1.66)	3.56 ± 1.11	*P* = 0.44 (CI -0.15-0.24)
PEF (liters/sec)	6.97 ± 0.42	4.77 ± 1.43	*P* = 0.59 (CI 3.23-4.65)	5.43 ± 1.76	*P* = 0.07 (CI -1.04-0.06)
Raw-tot (kPas/l)	0.30	0.29 ± 0.16	*P* = 0.20 (CI -0.07-0.08)	0.23 ± 0.11	*P* = 0.03 (CI.004-0.12)
Raw-ex (kPas/l)	0.30	0.25 ± 0.15	*P* = 0.09 (CI -0.03-0.12)	0.20 ± 0.13	*P* = 0.03 (CI.007-0.11)
TLC (liters)	5.63 ± 0.39	5.69 ± 1.43	*P* = 0.36 (CI -0.04-1.39)	5.84 ± 1.03	*P* = 0.09 (CI -0.76-0.55)
RV (liters)	1.76 ± 0.23	2.36 ± 1.1	*P* = 0.95 (CI -1.02-0.11)	2.5 ± 0.88	*P* = 0.36 (CI -0.67-0.53)

P = < 0.05 (At 95% confidence intervals); FCV = forced vital capacity, FEV1 = forced expiratory volume in 1st second, MEF (mid expiratory flow), MEF 25: mid expiratory flow 25; MEF 50: mid expiratory flow 50; PEF = peak expiratory flow, Raw tot = total resistance, Raw ex = expiratory resistance, TLC = total lung capacity, RV = residual volume, VT = tidal volume

the FEV1 ($P = 0.018$) and MEF 25 ($P = 0.027$), even though MEF 50 also decreased it did not reach statistical significance. The gland weight influenced FEV1 ($P = 0.017$) in the female subjects, however, in the males the duration and weight of goiter did not show any effect on the lung parameters. No other PFT parameter showed such correlation.

Discussion

In benign goiters the indications for surgery include large goiter size, retrosternal extension, suspicion of malignancy, symptoms of airway obstruction and cosmetic reasons. However, in the majority of the patients there seems to be no overt

airway compromise on clinical assessment. Up to 50-70% of tracheal occlusion is well tolerated by many patients, without any major obstructive symptoms[6] and hence even the X-rays and computerized tomography (CT) scan are deceptive in predicting the degree of airway compromise. These tests do not demonstrate the abnormal airflow dynamics within the larger airways as a consequence of the tracheal deviation, partial compression and angulation. A few studies have used the flow volume loops to predict the early and asymptomatic airway obstruction and had shown them to be superior to plain neck X-ray in predicting airway obstruction.[2,7] On studying the flow volume loops, Thusoo *et al.*,[3] observed a 100% improvement in the upper airway obstruction in their patients undergoing thyroidectomy. They also observed that the presence of normal tracheal radiology did not rule out abnormal upper airway dynamics. Empey *et al.*,[8] observed that flow volume curves can be helpful but they are not easy to construct and their interpretation is not always clear. Geraghty *et al.*,[2] in their study based on 51 patients with goiter, observed that the maximum inspiratory flow rate improved significantly in patients who had evidence of tracheal narrowing on plain X-ray (n = 21). However, Melissant *et al.*, [9] observed that the correlation of lung function indices and radiological measurements are weak.

The major observations in our study were that female patients had significantly low VC, FVC, FEV1, MEF 25, MEF 50 and TLC before thyroidectomy. In male patients VC, FVC and FEV1 showed significant reduction preoperatively. After the thyroidectomy, in the sixth postoperative week a significant improvement in the FEV1 and VT was seen in female patients and in males, only total and expiratory airway resistance (raw tot and raw exp) showed significant reduction. The FEV1, MEF 50, MEF 25 and PEFR are flow-related parameters. In benign goiters with no clinical signs of airway obstruction the reduction in these parameters reflects the change in the airflow profile with forceful expiration. Trachea being surrounded with unyielding goiter probably results in building up of pressure gradient downstream and this results in reduction in flow velocity thus decreasing FEV1 and MEF 50 and probably MEF 25. Once the goiter is removed the change in the alignment of the trachea, expansibility of the trachea and the change in the architecture, produced significant increase in FEV1. Even a small increment in the diameter of the trachea from the removal of fixed upper airway obstruction increases the expansibility of the trachea and results in tremendous improvement in the airflow capacity. Increase in TLC in males further proves this explanation. The TLC is measured by body plethysmography which is the most sensitive test for lung capacities available at present. Increase in the TLC in the preoperative period shows gas retention for longer time in the lung, thus producing increased expansion, due to extra-thoracic dynamic obstruction. The TLC came down to normal once this dynamic obstruction was relieved. In our study this phenomenon affected females more than males. The duration and weight of goiter correlated with reduction in FEV1 and it improved after surgery in females; however, no such correlation was observed in males. The duration was very long in females whereas weight of the gland was more in males. This suggests that persistence of tracheal rigidity due to the presence of goiter affects the inflow and outflow of air more in females. This could also be due to the structural difference of the trachea in females and males.

The total number of patients in the male group was less as compared to female patients and that could affect the significance pattern. The other shortcoming of the study was that we did not use any objective radiological parameter and therefore could not compare those with the PFT. We think reliable radiological parameters to define upper airway obstruction does not exist,[10] therefore routine PFT becomes mandatory to assess the flow restrictions and airway obstruction.

We conclude that benign goiters do show covert respiratory compromise, which can be properly evaluated by PFT. However, to assess this compromise, no single parameter exists among the battery of lung function tests but the evaluation with many parameters provides enough and accurate information. We have seen that after surgery, the PFT show improvement. In females the duration and weight of the goiter correlated with the reduction in the preoperative FEV1, which improved later after thyroidectomy. Hence these patients with longstanding goiters have to be subjected to early thyroidectomy.

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