Pulmonary function tests in patients with primary hyperparathyroidism

Sanjay Kumar Bhadada, Ahutosh Agrawal¹, Viral N. Shah, Anil Bhansali, Arnanshu Behera², Anish Bhattacharya³, Uma Nahar⁴

Departments of Endocrinology, ¹Pulmonary Medicine, ²Surgery, ³Gastroenterology and ⁴Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh (UT), India

ABSTRACT

Context: There is limited information on respiratory muscle functions in patients with primary hyperparathyroidism (PHPT). AIM: To assess respiratory muscle dysfunction in patients with PHPT. Setting and Design: This prospective study was carried between January 2005 and December 2006 by the Department of Endocrinology at the Postgraduate Institute of Medical Education and Research, Chandigarh. Materials and Methods: PHPT was defined as elevated parathyroid hormone in the presence of hypercalcemia. Spirometry was performed using a dry rolling seal spirometer and spirometric indices like forced vital capacity (FVC), forced expiratory volume in first second (FEV₁), and FEV₁/FVC ratio were measured using standard guidelines. Results: Thirty patients were studied with a mean age of 37.1 ± 2.4 years and 18 were women. The most common presenting symptoms were fatigue (75.0%) and bone pain (60.7%). The mean (±SD) of percentage predicted FVE₁, FVC, FEV₁/FVC ratio, PEF, and FEF were 98.7 ± 16.1, 93.9 ± 14.7, 84.5 ± 3.4, 89.3 ± 22.5, and 99.7 ± 33.6, respectively. Two had obstructive lung disease and two had restrictive lung disease. We did not find correlation with preoperative serum calcium, phosphate, and PTH with FVE₁, FVC, FEV₁/FVC ratio, PEF, and FEF.

Conclusion: Elevated calcium, low phosphate, and elevated PTH levels in patients with moderate to severe PHPT do not significantly affect respiratory muscle functions.

Key words: Primary hyperparathyroidism, pulmonary function test, restrictive lung disease

INTRODUCTION

Primary hyperparathyroidism (PHPT) is characterized by elevated corrected calcium with elevated intact parathyroid hormone (PTH). After the advent of multichannel biochemical screening, presentation of PHPT changed from symptomatic to asymptomatic PHPT in the West.[1] However, the presentation of PHPT in the developing countries like India is still symptomatic. The common presentation of PHPT in India is bone pain, muscle pain, and/or fatigue.[2] This aches and pains are possibly due to associated hypercalcemia, hypophosphatemia, and anemia. Calcium is important for muscle contraction while phosphate for generation of adenosine triphosphate, the energy substance. Therefore, imbalance in calcium and phosphate homeostasis may result in muscle contraction abnormalities and fatigue. Studies have reported reduced muscle strength in PHPT, which improves after parathyroidectomy.[3-4] Taking into account aforementioned fact, we hypothesized that respiratory muscle should also have similar effects like skeletal muscle and hence, patients with PHPT should have respiratory muscle dysfunction resulting in restrictive pulmonary disease.

MATERIALS AND METHODS

This prospective study was carried out at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, between January 2005 and December 2006. PHPT was defined as elevated PTH in the presence of hypercalcemia.
Patients with secondary or tertiary hyperparathyroidism
and existing pulmonary disease or any other comorbidity
(fracture, kyphosis, scoliosis, pancreatitis, etc.) that can
affect respiration were excluded. The written informed
consent was obtained from all the cases and the Institute’s
ethics committee approved the study protocol.

Pulmonary function testing
Spirometry was performed using a dry rolling seal
spirometer (Spiro RS232; P K Morgan Ltd, Kent, UK).
Spirometric indices such as forced vital capacity (FVC),
forced expiratory volume in first second (FEV$_1$), and
FEV$_1$/FVC ratio were measured by experienced technicians
for all subjects using standard guidelines.$^{[1]}$ The highest
measurements from among three technically acceptable
and reproducible maneuvers were expressed at body
temperature and pressure saturated with water vapor. The
predicted value for each of these measured parameters
was calculated using reference equations for healthy north
Indian adults, previously derived at our center.$^{[2]}$ Lower
limit of normal (LLN) for each parameter was calculated
as the difference between the predicted value and 1.645
times the standard error of estimate of the relevant
regression equation. This value represented the lower
90% confidence limit, and any observed value below the
corresponding LLN was considered abnormal.$^{[3]}$ FEV$_1$,
FVC, and FEV$_1$/FVC ratio were used as basic parameters
to interpret spirometry data.$^{[3]}$ Presence of FEV$_1$/FVC ratio
less than the LLN for that subject was categorized as an
obstructive pattern. Presence of FVC less than the LLN,
associated with a normal FEV$_1$/VC ratio, was categorized
as a restrictive pattern.

Laboratory methods
Serum intact PTH [reference range (RR), 15–65 pg/ml]
and 25-hydroxyvitamin D (25-OH D; RR 11.1–41.9 ng/
ml) were measured by chemiluminescence assay using
commercially available kits (DiaSorin Inc., Stillwater,
MN). Other biochemical parameters [corrected serum
calculus (RR) 8.6–10.2 mg/dl, inorganic phosphate (RR)
2.7–4.5 mg/dl, serum albumin (RR) 3.4–4.8 mg/dl, and
alkaline phosphatase (RR) 40–129 IU/L] were measured
by autoanalyzer (Roche Diagnostics, Modular P 800).

Statistical analysis
The statistical analysis was carried out using SPSS.
Continuous variables were described as mean ± SD and
categorical variables were described as frequencies and
proportions. Pearson product moment correlation was used
to correlate the serum calcium, phosphate, and iPTH with
the parameters of pulmonary function test. All statistical
tests were two-sided and performed at a significance level
of $P < 0.05$.

RESULTS
Thirty patients were studied with a mean age of 37.1 ±
2.4 years (32.1–42.03; 95% CI) and women:men ratio of
18:12. The most common presenting symptoms were
fatigue (75.0%) and bone pain (60.70%). Mean (±SD)
of serum calcium, phosphate, alkaline phosphatase, PTH,
and 25 (OH) D levels were 10.61 mg/dl (±1.17), 3.19
(±0.47) mg/dl, 45.87 (±50.3) IU, 967.44 (±744.0) pg/ml,
and 25 (27.65) ng/ml, respectively. The mean (±SD) of
percentage predicted FVE1, FVC, FEV1/FVC ratio, PEF,
and FEF were 98.7 ± 16.1, 93.9 ± 14.7, 84.5 ± 3.4, 89.3 22.5,
and 99.7 ± 33.6, respectively. Two patients were identified
to have obstructive lung disease and two had restrictive lung
disease as per the criteria described in methodology. Using
multivariate analysis, we did not find any correlation with
preoperative serum calcium and predicted FVE1 (P = 0.9),
FVC (P = 0.8), FEV1/FVC ratio (P = 0.6), PEF (P = 0.5),
and FEF (P = 0.7). Similarly, we did not find correlation
between preoperative phosphate and PTH levels with any
of pulmonary function test parameters.

DISCUSSION
We investigated the effect of elevated calcium, low
phosphate, and high PTH levels with respiratory muscle
function using pulmonary function test. We did not find
any significant abnormalities in pulmonary function test
in PHPT patients and these parameters did not correlate
with calcium, phosphate, or PTH levels.

Not all but few studies on muscle function and strength
showed improvement in muscle function after curative
parathyroidectomy. This difference in results may be due to
difference in sample size, preoperative calcium levels, and
methods used to test muscle function.$^{[3-5]}$ We did not find
any significant alteration in respiratory muscle functions in
patients with moderate to severe PHPT and this result is in
consonance with other studies.$^{[6]}$ Negative findings of our
study may be due to small sample size and mildly reduced
serum phosphate level which may not be sufficiently low
to cause respiratory muscle dysfunction.

Limitations of the study are (1) we did not evaluate
parameters of pulmonary function tests after parathyroid
surgery in same subjects, (2) small sample size, (3) we did
not use body plethysmography for estimation of pulmonary
function test, and (4) we did not carry out bone scan to
look for thoracic cage involvement. However, prospective
study design and first Indian study to document respiratory
muscle functions in moderate to severe hyperparathyroidism
are major strengths.
In conclusion, elevated calcium, low phosphate, and elevated PTH levels in patients with moderate to severe PHPT do not significantly affect respiratory muscle functions. However, these findings should be confirmed in a large prospective study.

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