

SERUM ALPHA-1 ANTITRYPSIN LEVELS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE BEFORE AND AFTER CORTICOSTEROID TREATMENT

Orhan ÇILDAĞ, M.D.(x)
Ebubekir BAKAN, Ph.D.(xx)

SUMMARY

Serum alpha-1 antitrypsin levels and respiratory function parameter FEV were investigated in 30 patients with chronic obstructive pulmonary disease before and after corticosteroid treatment. Of 30 patients, 9 had subnormal alpha-1 antitrypsin levels before treatment (67-198 mg/dL; normal range 200-400 mg/dL). Following corticosteroid treatment, the improved alpha-1 antitrypsin and FEV values in all patients were seen. This shows that corticosteroid treatment, whatever the mechanism of action, gives rise to a healing process in these patients.

INTRODUCTION

Alpha-1 antitrypsin (AAT) has an antiprotease activity, whose deficiency associated with lung and liver diseases(1). The function of AAT is to neutralize lysosomal elastase released upon phagocytosis of particles by polymorphonuclear leucocytes AAT, being a relatively small molecule, can pass from capillaries into tissue fluid, bind protease, and pass back into the intravascular fluid(2). It is interesting that the inhibitory activity of AAT is maximal at the neutral to slightly alkaline pH of blood, being responsible for the lesser role AAT plays in the inhibition of intestinal enzymes and for the larger role it plays in the respiratory tract (2).

Many conditions are related to the functional and synthetic abnormality in AAT (3-5). On the other hand, it is well known (6-9) that treatment with some drugs may increase the inhibitory activity of AAT. However, little is known about

(x) : Assistant Professor, Pulmonary Division, Department of Internal Medicine, Faculty of Medicine, Atatürk University, Erzurum, Turkey

(xx) : Associate Professor, Department of Biochemistry, Faculty of Medicine, Atatürk University, Erzurum, Turkey

the mechanism of the effect of commonly described therapeutic agents on the inhibitory capacity of AAT(9).

This study presents the relationship between serum AAT levels and clinical and respiratory improvement of the patients with chronic obstructive plmonary disease (COPD) following corticosteroid treatment.

MATERIALS AND METHODS

Patients. Thirty patients with COPD were included in the study. The average age was 49.1, 12 patients were females. Smoking was not regarded because this situation exhibited no specificity for our cases with respect to serum AAT. For all patients, FEV₁ values were obtained before and after treatment with corticosteroid. The patients received 40 mg methylprednisolone daily for 10 days.

Experimental Procedures. Serum samples were obtained before and after treatment. In these sera, AAT was determined by radial immunodiffusion method (ICL Scientific, Calif. USA). Total protein (TP) and albumin (ALB) were measeured by Biuret and BCG methods, respectively. Electrophoretic pattern of serum pattern of serum proteins was obtained in cellulose acetate medium.

RESULTS AND DISCUSSION

Table 1 shows the results obtained and their statistical evaluation. Although serum AAT, TP, ALB, globulins, and alpha-1 fraction of protein electrophoresis and FEV values have increased after corticosteroid treatment when compared with those before treatment, the increase in AAT levels is of statistical significance (from 211 ± 78 to 420 ± 85 ; $P < 0.01$) for total 30 patients with COPD. On the other hand, of 30 patients, 21 had the AAT levels within normal range (200-400 mg/dL) and the remaining 9 patients had subnormal AAT values (ranging from 67 to 198 mg/dL) before corticosteroid treatment.

Several studies (10-15) have been conducted in order to explain the relationship between lung diseases and serum AAT levels. However, they have controversial results to each other. The present study showed a good correlation between rised AAT levels improved FEV₁ and descase procedure following corticosteoroid treatment. This was also confirmed by an increase in alpha-1 fraction of protein electrophoresis, since the majority of this band belongs to AAT.

It is certain that corticosteroids have many effects on body systems and they generally have anabolic effect on protein and RNA metabolsm in liver and catabolic effects on other sites(16). This may explain the increased AAT levels by means of corticosterod effect on hepatic synthetic capacity. Whatever the mechanism of action, it seems that corticosteroid treatment applied to the patients with COPD has a consistent effect on healing process, possibly by increased AAT levels.

Table 1 The effect of corticosteroid treatment on AAT levels and other parameters (n=30)

	before treatment ($\bar{X} \pm SD$)	after treatment ($\bar{X} \pm SD$)
AAT (mg/dL)	211 \pm 87	420 \pm 85 ^x
TP(g/dL)	6.9 \pm 1.3	7.2 \pm 1.5
ALB (g/dL).	3.9 \pm 1.1	4.1 \pm 1.2
Globulins (g/dL)	3.0 \pm 0.9	3.1 \pm 1.0
Alpha-1 fraction(%)	5.3 \pm 1.5	7.1 \pm 1.2
FEV ₁	53.8 \pm 19	64.4 \pm 26

(x) P<0.01

ÖZET

Serum alfa-1 antitripsin düzeyleri ve solunum fonksiyon parametresi FEV₁ kronik obstrüktif akciğer hastalıklı 30 hastada kortikosteroid tedavisinden önce ve sonra araştırıldı. Toplam 30 hastanın 9, unda tedaviden önce normalin altında alfa-1-antitripsin düzeyleri gözlemlendi (67-198 mg/dL; normali 200-400mg/dL). Günde 40 mg 10 gün süreyle kortikosteroid tedavisinden sonra, tedaviden öncekinden daha yüksek alfa-1 antitripsin seviyeleri belirlendi. Ayrıca bütün hastalarda FEV₁ değerleri yükseldi. Bu durum, kortikosteroid tedavisinin, etki mekanizması ne olursa olsun, bu hastalarda iyileşmeye neden olduğunu gösterdi.

REFERENCES

1. Laurell CB and Jeppsson J.C.: Protease inhibitors in plasma. In: *The Plasma Proteins* Vol 1, 2nde ed. F. Bautman Ed. New York Academic Press p 229, 1975.
2. Silverman LM, Chirstenson RH, and Grant GH: Amino acids and protein In *Textbook of Clinical Chemistry*, NW Tietz Ed. Philadelphia, WB Saunders pp 590-591, 1986.
3. Eriksson S. Studies in alpha-1 antitripsin defficiency. *Acta Med Scand* 4, 32, 1-85, 1965.
4. Stockley RA and Burnett D. Serum derived protease inhibitors and leucocyte elastase and the effect of infection. *Bull Eur Physiopathol Respir* 12, 261-271, 1980.
5. Blue ML and Janoff A. Possible mechanism of emphysema in cigarette smokers: Release of elastase from human polymorphonuclear leucocytes by cigarette smoke condensate in vitro. *Am Rev Respir Dis* 115, 317-325, 1978.

6. Gadek J, Fulmer JD, Gelfand SA, Frank MM, Petty TM, and Crystal RG. Danazol-induced augmentation serum alpha-1 antitrypsin levels in individuals with marked deficiency of this antiprotease. *J Clin Invest* 66, 82-87, 1980.
7. Morrison HM, Afford SC, and Stockley RA. Inhibitory capacity of alpha-1 antitrypsin in lung secretions: variability and the effect of drugs. *Thorax*, 39, 510-516, 1984.
8. Morrison HM and Stockley RA. Anti elastase activity of lung secretions and the effect of corticosteroids. *Am Rev Respir Dis*. 129, 4, Part 2: A301, 1984.
9. Stockley RA, Morrison HM, Kramps JA, Djikman JH, and Burnett D. Elastase inhibitors of sputum sol phase: variability, relationship to neutrophil elastase inhibition, and effect of corticosteroid treatment. *Thorax* 41, 442-447, 1986.
10. Billinksley GD and Cox DW. Functional assay of alpha-1 antitrypsin in obstructive lung disease. *Am Rev Respir Dis* 121, 161-164, 1980.
11. Kueppers F and Black LF. Alpha-1 antitrypsin deficiency. *Am Rev Respir Dis* 110, 176-194, 1974.
12. Lieberman J, Winter B, and Sastre A. Alpha-1 antitrypsin P₁ types in 965 COPD patients. *Chest* 89, 3, 370-373, 1986.
13. Yavuzer S, Akkaynak S, Saygun N, Timlioğlu Ö, Erişkin astımlılarda serum alpha-1 antitrypsin (α AT) ve alpha-2-M (α_1 -M) değerleri : Astım-alpha-1 eksikliği ilişkisi, *Solunum* 8: 121 - 127, 1983
14. Beder S, Kömür madeni işçilerinde pnömokonyoz oluşumunda anti-proteolitik enzim (AAT) ve immunoglobulinlerin etkisi. *Tüberküloz ve Toraks* 1 (33): 59 - 63. 1985
15. Çobanlı B, Demirel YS, Tozlu ortamın ve Sıgaranın serum alpha-1 antitrypsin düzeyine etkisi. *Tüberküloz ve Toraks* 4 (34); 271 - 276, 1986
16. Baxter JD, and Forsham PH. Tissue effects of glucocorticoids. *Am J Med* 53, 573, 1972.