

Brief communications

Abnormal liver-function tests associated with long-term systemic corticosteroid use in subjects with asthma

Jeffrey A. Wald, MD, and Richard S. Farr, MD* *Denver, Colo.*

Oral glucocorticoids are used to treat a number of serious diseases, including asthma. Corticosteroids have been used in asthma therapy since 1950,¹ but their use remains limited by the high incidence of serious adverse effects including osteoporosis, cataracts, hypertension, myopathy, glucose intolerance, and hypothalamic-pituitary-adrenal axis suppression.²

In a study on troleandomycin in the management of steroid-requiring subjects with asthma,³ eight of 15 patients had two or more abnormal LFTs before receiving troleandomycin. These patients had no diseases known to effect the liver and were not receiving any medications with commonly recognized hepatotoxic side effects. Since asthma, in the absence of respiratory failure, has no known effects of LFTs, the possibility exists that systemic corticosteroids or other medications used in asthma may be responsible for the increased incidence of abnormal LFTs. In an attempt to answer this question, serum enzymes of subjects with asthma taking daily corticosteroids were compared to enzymes of a group of subjects with asthma who were taking similar medications with the exception of oral glucocorticoids.

MATERIAL AND METHODS

The charts of 500 consecutive referrals observed in the adult outpatient clinic at the National Jewish Center for Immunology and Respiratory Medicine were retrospectively reviewed. Patients were included for analysis only if all preselected criteria were met. These included demonstration of reversible airway obstruction evidenced by a 20% change in FEV₁, complete biochemistry panels performed by a Hitachi 705 (Hitachi Densi, Ltd., Woodside, N.Y.), complete

Abbreviations used

Alk phos:	Alkaline phosphatase
ALT:	Alanine transaminase
AST:	Aspartate transaminase
LDH:	Lactic dehydrogenase
LFT:	Liver function test
T Bili:	Total bilirubin

history of medications available, a history negative for ethanol abuse, hepatitis, compression fractures, or systemic illnesses, and no recent use of medications that commonly affect the liver. Of the 500 cases reviewed, biochemistry panels were available on 96 patients, of which 80 cases met all the above criteria.

Patients were divided into three groups based on the amount of corticosteroids used in the previous 4 months. Group 1 included 42 patients who received no systemic corticosteroids, whereas group 2 consisted of 13 patients who were taking a "low dose" of oral corticosteroids (<10 mg of prednisone every 24 hours) or who had received no more than four short steroid-tapered courses or injections during the previous 4 months. Group 3 included 25 patients maintained on "high-dose" corticosteroids (≥ 10 mg of prednisone every 24 hours). Five patients receiving oral steroid preparations other than prednisone were treated as if they had been receiving an equivalent dose of prednisone in terms of glucocorticoid potency.

RESULTS

Biochemistry panels included LDH, AST, ALT, Alk phos, and T Bili, and data for each of five tests are summarized in Table I. Although mean values were generally within the normal range, multiple comparison analysis demonstrated a statistically significant difference in AST ($p < 0.05$), ALT ($p < 0.001$), and LDH ($p < 0.001$) between patients receiving "high dose" (group 3) and both of the other two groups. Alk phos was significantly elevated in group 3 compared to patients with asthma not receiving corticosteroids ($p < 0.01$) but not compared to group 2, patients receiving "low-dose" corticosteroids. There was no significant difference in T Bili levels among groups.

Multiple regression analysis demonstrated a posi-

From the Department of Medicine, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colo.

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Reprint requests: Jeffrey A. Wald, MD, 4601 West 109th St., Suite 318, Overland Park, KS 66211.

*Present address: Department of Molecular Biology MB-8, Research Institute of Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, CA 92037.

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TABLE I. Biochemistry tests as a function of steroid dose

	Group 1 (no steroids)	Group 2 (low dose)	Group 3 (high dose)	Significance (p value)
T Bili				
Mean $\pm$ std error	0.56 $\pm$ 0.11	0.55 $\pm$ 0.11	0.54 $\pm$ 0.06	>0.25
Abnormal tests*	0/42	1/13	1/25	>0.25
AST				
Mean $\pm$ std error	19.4 $\pm$ 0.8	17.2 $\pm$ 1.0	25.7 $\pm$ 2.8	<0.05*
Abnormal tests*	0/42	0/13	7/25	<0.001*
ALT				
Mean $\pm$ std error	19.4 $\pm$ 1.1	14.4 $\pm$ 0.8	36.6 $\pm$ 5.7	<0.001*
Abnormal tests*	0/42	0/13	6/25	<0.001*
LDH				
Mean $\pm$ std error	166.6 $\pm$ 4.8	162.4 $\pm$ 7.3	229.3 $\pm$ 12.7	<0.001*
Abnormal tests*	1/42	0/13	10/25	<0.001*
Alk phos				
Mean $\pm$ std error	163.8 $\pm$ 5.8	169.7 $\pm$ 7.3	203.6 $\pm$ 10.9	<0.01†
Abnormal tests*	1/42	2/13	7/25	<0.01*

Std, Standard.

*Group 3 significantly different from both group 1 and group 2.

†Group 3 significantly different from group 1 only.

tive correlation between the steroid dosage in a given patient and the value of LDH ($r = 0.593$; $p < 0.001$), ALT ($r = 0.374$; $p < 0.001$), Alk phos ($r = 0.369$; $p < 0.001$), and AST ($r = 0.305$; $p = < 0.01$). Overall, 20 of the 25 patients (80%) in group 3 had one or more abnormal LFTs versus 23% of group 2 and 5% of group 1 ($p < 0.001$). Other parameters (including age, sex, weight, spirometry findings, number of emergency room visits, theophylline dosage and/or level, use of oral β -agonists, and number of doses of inhalers) failed to correlate with any biochemistry test result, and all parameters, except weight, failed to differ among groups.

DISCUSSION

Mild, but statistically significant, elevations in four serum enzymes (AST, ALT, LDH, and Alk phos) were observed in 80% of patients receiving systemic corticosteroids in doses ≥ 10 mg of prednisone per day. In comparison, these abnormalities were observed in only 5% of nonsteroid-treated patients. Changes in LDH and transaminases were more notable than in Alk Phos with respect to both incidence and magnitude of abnormalities. Other variables, including age, sex, weight, severity of asthma, and use of other medications, failed to correlate with either the absolute values of the tests or the prevalence of abnormal tests.

Although patients with compression fractures and systemic illnesses were excluded from this retrospective analysis, it is unclear whether rises in the serum enzymes were secondary to mild hepatocellular injury or whether they reflect injury to other organ system(s). It is also unclear whether shorter courses of corticosteroids produce similar changes and if larger doses of prednisone (≥ 1 mg/kg/day) would result in additional increases in the four enzymes studied. Our observations and these unresolved issues indicate a need for prospective studies on the effect of corticosteroids on LFTs in asthma and other chronic diseases. However, corticosteroid use should be considered as a possible pathogenic factor in steroid-treated patients with abnormal enzyme tests.

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