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Research Article

Assessment of Treatment Response in Collagen Vascular Disease Associated Interstitial Lung Disease with Combination of Prednisolone and Azathioprine

Dr. Hemalatha. V. S[1], Dr. K. Anitha Kumari[2]

[1]Assistant Professor, Dept. Of Pulmonary Medicine Sree Narayana Institute of Medical Sciences, Chalakka N. Kuthiathodu P.O, Ernakulam District

[2]professor and Hod Dept.Of Pulmonary Medicine, Govt.Medical College, Thiruvananthapuram

Abstract:

Background: Collagen vascular diseases are a heterogenous group of autoimmune disorders of unknown etiology of which ILD is the most common pulmonary complication. Treatment is usually aimed at slowing or preventing progression rather than in the hope of a striking short-term response.

Materials and Methods: The aim of the study is to assess response to treatment in patients with collagen vascular disease associated Interstitial lung disease who were started on combination of Azathioprine and Prednisolone.

Results: Majority of patients remained stable following 6 months of treatment.

Improvement in FVC in millilitres showed a trend towards significant difference between UIP and NSIP patterns of ILD.

Conclusion: Treatment response in collagen vascular disease associated ILD is largely dependent on the type of underlying lung disease.

Keywords: Collagen Vascular Disease,Interstitial Lung Disease, Prednisolone, Azathioprine, Treatment Response

Introduction

Abnormalities in blood vessel structure and function are typical, accounting for the term "collagen vascular diseases," which is often used interchangeably with connective tissue disorders. Collagen vascular diseases include SLE, Rheumatoid arthritis, Progressive systemic sclerosis / Scleroderma, Dermatomyositis & Polymyositis, Ankylosing spondylitis, Sjogren's syndrome & Mixed Connective Tissue Disease. [1,2]

The frequency & type of pulmonary involvement in collagen vascular diseases varies according to the type of underlying disease and the treatment response also varies accordingly. Approximately 10% of patients with a diagnosis of fibrosing alveolitis have an overt connective tissue disease, with rheumatoid arthritis (80%) much more frequent than scleroderma (14%) or polymyositis/ dermatomyositis (4%).[3] NSIP and UIP subgroups make up similar proportions of patients with rheumatoid lung. In the only large study of lung histology in Systemic Sclerosis there was a high prevalence of NSIP (62/80, 75%) and a very low prevalence of UIP (6/80, 8%).[4] UIP, lymphocytic interstitial pneumonitis, NSIP, and bronchiolitis obliterans organizing pneumonia have all been reported in SLE. The incidence of interstitial lung disease in mixed connective tissue disease is increased in comparison to other collagen vascular diseases.[5]

In general, the threshold for starting treatment in the hope of preventing progression of pulmonary fibrosis in CTD-associated ILD is reduced when disease is severe (as judged by HRCT or pulmonary function tests), recently progressive, or there is a short duration of systemic disease.[4] For the majority of CTDs, with the exception of Systemic Sclerosis, recommended initial treatment for ILD is oral prednisolone at an initial dose of 0.5–1 mg/kg with the aim of tapering to a maintenance dose of 10 mg/day or less, often in association with an immunosuppressive agent (usually oral or intravenous cyclophosphamide or oral azathioprine). In Systemic Sclerosis-associated ILD, recommended treatment, if required, is with low-dose oral steroids (10 mg/day) and/or cyclophosphamide (oral or intravenous). High-dose corticosteroid therapy (daily prednisolone dose >10 mg) should be avoided if at all possible because of the risk of renal crisis. [4]

The decision to treat must be largely based on the likelihood, in individual patients, that the risk of treatment (drug toxicity) will be outweighed by the benefit (protection against gression of disease).

Method

Objective:

To assess the outcome of 6 months of treatment with combination of oral Prednisolone and Azathioprine in patients with collagen vascular disease associated Interstitial lung disease.

Study Design:

Cohort study

Study Population:

All cases of collagen vascular disease associated ILD

attending the Respiratory Medicine OPD, Medical college, Thiruvananthapuram.

Study Setting:

Department of Pulmonary Medicine, Medical college, Thiruvananthapuram

Study Period:

February 2012 to November 2012

Inclusion Criteria:

Patients with collagen vascular disease associated Interstitial lung disease who are treated with combination of Prednisolone and Azathioprine.

Exclusion Criteria:

Collagen vascular disease patients who are not willing to participate in the study.

Methodology:

Response to treatment assessed in those patients with collagen vascular disease associated Interstitial lung disease who were started on combination of azathioprine and prednisolone based on worsening of dyspnoea score or poor lung function. This was done in those patients who had already completed six months of treatment with these drugs at the time of interview, based on their treatment records. Patients undergoing treatment during the study period were also included. The recruitment of patients for assessing treatment response was stopped six months prior to completion of the study. The aim was to assess treatment response to low dose prednisolone started at a dose of 0.5 – 1 mg/kg/day (lower dose in systemic sclerosis) and gradually tapered biweekly over 6 months and azathioprine at 2.5mg/kg/day for 6 months. Spirometry was the tool used for assessing treatment outcome. Treatment response classified as improved if the % predicted FVC increased more than 10% from baseline and at least 200ml, and stable if it remained within 200 ml or 10% of baseline. Serial dyspnea scores were recorded. Six minute walk test was performed before and after treatment with these drugs and improvement in distance walked and oxygen saturation recorded. Statistical analysis done with chi square and anova tests.

Results

In this study, response to treatment with the combination of Prednisolone and Azathioprine was assessed in 16 patients with Rheumatoid arthritis, 20 patients with systemic sclerosis and 6 patients with Mixed connective tissue disease. These patients were followed up for a period of six months.

Assessment of treatment response in interstitial lung disease with combination of Prednisolone and Azathioprine showed that majority of patients remained stable following 6 months of treatment, in all the three groups. One patient with UIP pattern in rheumatoid arthritis and 2 patients with UIP pattern in systemic sclerosis worsened after treatment. Only one patient in the Systemic sclerosis group with NSIP pattern in HRCT however showed improvement in pulmonary function. (Table 1)

Diagnosis			Treatment response			Total
			Worsened	Stable	Improved	
RHEUMATOID ARTHRITIS	PATTERN	UIP	1	7	0	8
		NSIP	0	6	2	8
	Total		1	13	2	16
SYSTEMIC SCLEROSIS	PATTERN	UIP	2	8	0	10
		NSIP	1	8	1	10
	Total		3	16	1	20
MCTD	PATTERN	UIP		3		3
		NSIP		3		3
	Total			6		6

Assessment of change in six min walk distance was done. In Rheumatoid arthritis, majority of patients with both UIP and NSIP patterns showed up to 50 metre improvement. In systemic sclerosis and MCTD also majority of patients with both patterns showed up to 50 metre improvement. (Table 2)

Diagnosis			Change in 6 min. Walk distance		
			Worsened	Improvement up to 50 m	More than 50m improvement
RHEUMATOID ARTHRITIS	**PATTERN**	**UIP**	1	6	1
		NSIP	1	5	2
	Total		2	11	3

SYSTEMIC SCLEROSIS	**PATTERN**	**UIP**	2	8	0
		NSIP	1	6	3
	Total		3	14	3
MCTD	**PATTERN**	**UIP**		3	
		NSIP		3	
	Total			6	

On comparison between treatment response in UIP and NSIP patterns in the three groups of collagen vascular diseases, improvement in FVC in millilitres showed a trend towards significance between UIP and NSIP patterns of ILD. Mean improvement in FVC (mL) in UIP 76.6 and in NSIP 130.5 (p value 0.074). But comparison between improvement in six minute walk distance did not show significant difference. Mean improvement in 6 min walk distance in UIP 20.1metre and NSIP 32 metre (p value 0.108)

Discussion

The histological entities of the ATS/ERS classification for Idiopathic Interstitial Pneumonias (IIPs) can all be associated with the collagen vascular diseases. [6]As in IIP, fibrotic disease predominates. Outcome differs little between UIP and NSIP in Systemic Sclerosis, even after adjustment for baseline disease severity.[7] Thus, the range of HRCT appearances in Systemic Sclerosis from ground glass to reticular does not translate into corresponding differences in outcome.[8] Furthermore, UIP in Systemic Sclerosis has a better outcome than IPF, perhaps reflecting a lower profusion of fibroblastic foci in UIP in CTD in general [9] or earlier diagnosis of the lung disease. Comparisons between outcome in UIP and NSIP in RA have not been sufficiently powered to provide robust conclusions. As with SSc, however, UIP associated with RA appears to have a better outcome than the idiopathic form of the disease.

Change in FVC has emerged as the serial lung function measurement in interstitial lung disease most consistently predictive of mortality. The prognostic value of serial change in pulmonary function indices was first evaluated by Hanson et al in a study of 58 patients, with change defined as a 10% alteration in FVC and a 20% alteration in TLCO. [10] The mortality of patients with a decline in FVC (24% of the total) was significantly higher than in the remaining patients, and the same outcome differences were seen when a decline in TLCO (22% of patients) was evaluated. For the majority of CTDs, with the exception of Systemic Sclerosis recommended initial treatment for ILD is oral prednisolone at an initial dose of 0.5–1 mg/kg with the aim of tapering to a maintenance dose of 10 mg/day or less, often in association with an immunosuppressive agent (usually oral or intravenous cyclophosphamide or oral azathioprine).[4]

In this study, response to treatment with the combination of Prednisolone and Azathioprine was assessed in 16 patients with Rheumatoid arthritis, 20 patients with systemic sclerosis and 6 patients with Mixed connective tissue disease. These patients were followed up for a period of six months. Spirometry was the tool used for assessing treatment outcome. Response was classified as improved if the % predicted FVC increased more than 10% from baseline and at least 200ml, and Stable if it remained within 200ml or 10% of baseline.

For assessment of response to treatment, a total of 42 patients with collagen vascular disease who were started on combination of Prednisolone and Azathioprine were selected. Of the 16 patients with RA 13 patients remained stable of which 7 were UIP and 6 were NSIP. One patient with UIP pattern worsened following six months of treatment. Two patients with NSIP showed improvement. Of the 20 patients with SS 8 patients each with UIP and NSIP respectively remained stable.2 patients with UIP pattern and 1 patient with NSIP worsened after treatment. One patient with NSIP showed improvement. All the six patients with Mixed connective tissue disease, of which three were UIP pattern and three were NSIP remained stable.

Conclusions

Assessment of treatment response in interstitial lung disease with combination of prednisolone and Azathioprine showed that majority of patients remained stable following 6 months of treatment, in all the 3 groups. One patient with UIP pattern in rheumatoid arthritis and 2 patients with UIP pattern in systemic sclerosis worsened after treatment. Only one patient in the systemic sclerosis group with NSIP pattern in HRCT however showed improvement in pulmonary function.

References

1.Hunninghake GW, Fauci AS. Pulmonary involvement in the collagen vascular diseases. Am Rev Respir Dis 1979; 119:471-503.

2.Eisenberg H. The interstitial lung diseases associated with the collagen vascular disorders. Clin Chest Med 1982;3:565–578

3. Hubbard R, Venn A. The impact of coexisting connective tissue disease on survival in patients with fibrosing alveolitis. Rheumatology (Oxford) 2002;41:676–9

4. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society A U Wells,1 N Hirani;Thorax 2008;63;v1-v58

5.Saito Y, Terada M, Takada T, et al. Pulmonary involvement in mixed connective tissue disease: comparison with other collagen vascular diseases using high resolution CT. J Comput Assist Tomogr 2002;26(3): 349– 57.

6. Nicholson AG, Colby TV, Wells AU. Histopathological approach to patterns of interstitial pneumonia in patient with connective tissue disorders. Sarcoidosis Vasc Diffuse Lung

Dis 2002;19:10–7.

7.Bouros D, Wells AU, Nicholson AG, et al. Histopathologic subsets of fibrosing alveolitis in patients with systemic sclerosis and their relationship to outcome.Am J Respir Crit Care Med 2002;165:1581–6.

8.Wells AU, Hansell DM, Rubens MB, et al. The predictive value of appearances on thin-section computed tomography in fibrosing alveolitis. Am Rev Respir Dis 1993;148:1076–82.

9. Flaherty KR, Colby TV, Travis WD, et al. Fibroblastic foci in usual interstitial pneumonia: idiopathic versus collagen vascular disease. Am J RespirCrit Care Med 2003;167:1410–5.

10.Hanson D, Winterbauer RH, Kirtland SH, et al. Changes in pulmonary function test results after 1 year of therapy as predictors of survival in patients with idiopathic pulmonary fibrosis. Chest 1995;108:305–10.