Oral Steroids Should Be Avoided in Patients With RA and ILD

Written by Sara Freeman

Long-term use of oral glucocorticosteroids should be avoided in patients with rheumatoid arthritis (RA) who have concomitant interstitial lung disease (ILD), according to the findings of a British initiative.

Presenting author Clive Kelly, MD, Queen Elizabeth Hospital, Gateshead, Tyne and Wear, United Kingdom, explained that respiratory diseases, including pulmonary fibrosis and infection, are a leading cause of mortality in patients with RA, second only to cardiovascular disease [Young A et al. *Rheumatology (Oxford)* 2007].

ILD has been long been recognized as a complication of RA; ILD previously was associated with a high (40%) postmortem incidence, and this was confirmed in approximately 25% of patients using high-resolution computed tomography (HRCT) in the 1990s. Today, the clinical prevalence of ILD in RA is thought to be about 5%, with an estimated lifetime risk of 7.7% and estimated mean survival of just 2.6 years after diagnosis [Bongartz T et al. *Arthritis Rheum* 2010].

The British Rheumatoid Interstitial Lung (BRILL) Network is comprised of 16 UK centers that have contributed retrospective data to a central database of 260 proven cases of RA-ILD that occurred over a 25-year period since 1987. These data were used to examine trends in mortality and the effects of treatments on survival of patients with RA-ILD compared with a control group of RA patients without lung disease.

For RA-ILD patients in the database, ILD was diagnosed at a median age of 64 years, at a median of 9 years' RA duration and 4 years' ILD duration. RA was present before ILD in most cases (83%), with ILD seen first or occurring concurrently with RA in 10% and 7% of patients, respectively. The most common ILD subtype on HRCT was usual interstitial pneumonia (UIP; 65% of cases), which carries a worse prognosis in RA patients. Seropositive disease was more common in RA patients with ILD than in those without ILD.

Data from the BRILL Network showed that all-cause mortality was significantly higher for patients who had used oral steroids than for those who had not (p=0.0002). Respiratory mortality was also significantly increased in oral steroid versus nonsteroid users (p=0.0002; Table 1).

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Table 1. All-Cause and Respiratory Mortality in Patients With Rheumatoid Arthritis and Interstitial Lung Disease Who Received Oral Steroids versus Those Who Did Not

	Oral Steroid Users	Nonsteroid Users
RR of death from any cause	1.65 (95% CI, 1.2–2.3; p=0.002)	1.07 (95% CI, 0.7–1.6)
RR of death from respiratory causes	2.75 (95% CI, 1.6–4.7; p=0.0002)	2.06 (95% CI, 1.1–3.8; p=0.02)

RR=rate ratio.

Survival of patients with RA-ILD was shown to be improved in recent years (Table 2), but the effects of oral steroid use appear to have reduced this in some patients, Dr. Kelly observed.

Table 2. Trends in the Survival of Patients With Rheumatoid Arthritis and Concomitant Interstitial Lung Disease (RA-ILD)

Time of RA-ILD Diagnosis	Deaths From RA-ILD, % of Patients	Median Age at Death, years	Median Survival, months
1987–1993	67	63	33
1994–1999	42[a]	68	36
2000–2005	54	72[a]	50[a]
2006–2012	30[b]	76[b]	48[a]

[a]p<0.05; [b]p<0.01.

Patients with RA-ILD were more likely to have used steroids than were RA controls (59% vs 14%; p=0.01). Patients with RA-ILD were also more liked to have UIP (p=0.02). The excess of this ILD subtype may account for some of the increased mortality.

Conversely, the BRILL Network has recently reported that certain immunosuppressants and biologic therapies appear to carry a survival benefit.

Since all these data are retrospective, however, 2 prospective therapeutic trials are planned. The first will recruit RA patients with progressive ILD and compare the use of mycophenolate mofetil and azathioprine, allowing for the use of oral steroids. The second will recruit patients with active RA and ILD and compare the potential survival advantage of using rituximab over anti–tumor necrosis factor-a therapies.

Concluding, Dr. Kelly observed that patients with RA and concomitant ILD have increased mortality compared with controls and that more than half of these patients have been treated with oral steroids. This large, retrospective, multicenter study suggests that the long-term use of oral steroids should be reconsidered when possible in RA patients who also have ILD.

Long-Term Adalimumab Is Safe and Achieves Disease Control in Children With Advanced and Refractory JIA

Written by Jenny Powers

Long-term disease control was observed with adalimumab administered in routine clinical practice to patients with moderately to severely active juvenile idiopathic arthritis (JIA), according to Gerd Horneff, MD, Asklepios Klinik Sankt Augustin, Sankt Augustin, Germany.

Interim findings from an analysis done at 4 years were reported from an ongoing international registry of patients enrolled upon diagnosis of moderately to severely active JIA [NCT00783510]. The multicenter, noninterventional observational study aimed to evaluate long-term safety and effectiveness of adalimumab, which was recently approved for treating patients with severe and refractory JIA from the age of 2 years after failure or intolerance to methotrexate (MTX) treatment. Efficacy and safety were compared with MTX treatment administered in routine clinical practice. Patients aged 2 to 17 years were enrolled in the United States, European Union, and Australia. The planned follow-up was 10 years after enrollment in either treatment arm; crossover to the adalimumab group was allowed.

Patients in the adalimumab cohort had a more advanced disease course compared with those of the MTX cohort. Baseline values for mean disease duration were 1.3 years in the MTX arm and 3.8 years in the adalimumab arm. Patients in the adalimumab arm had a mean age of 12.2 years, a mean weight of 47.8 kg, and a mean height of 150.3 cm compared with patients receiving MTX, who had a mean age of 9.6 years, a mean weight of 37.9 kg, and a mean height of 137.2 cm. Mean baseline active joint count in both groups was 5.8, and disability index of Childhood Health Assessment Questionnaire scores was 0.6 in each arm.

At data cutoff, 306 patients received MTX monotherapy, and 459 received adalimumab with or without MTX. Clinical outcomes based on the 71-joint Juvenile Arthritis Disease Activity Score showed that mean scores improved from 13.1 at baseline to 11.2, 6.4, and 5.1 with MTX and from 12.1 at baseline to 8.5, 5.7, and 5.4 with adalimumab at Months 1, 3, and 6, respectively. In the MTX arm, 131 (42.8%) patients discontinued registry participation, compared with 81 (17.6%) in the adalimumab arm; 34 (25.9%) who discontinued MTX were switched to adalimumab.

Discontinuation due to treatment-related adverse events (AEs) occurred in 23 (7.5%) and 25 (5.4%) patients in the MTX and adalimumab cohorts, respectively. AEs determined by the investigators as possibly drug related were reported in 63 (20.6%) patients. Infectious AEs were reported for 64 (20.9%) and 80 (17.4%) of patients in the MTX and adalimumab arms, respectively. Of these, serious infectious AEs occurred in 7 (2.3%) MTX patients, compared with 12 (2.6%) adalimumab patients (Table 1).

Table 1. Overview of Observational Adverse Events, n (%)

Adverse Event	Methotrexate (n=306)	Adalimumab (n=459)
Any	125 (40.8)	142 (30.9)
At least "possibly drug related" per the investigator	63 (20.6)	71 (15.5)
Severe	12 (3.9)	22 (4.8)
Serious	16 (5.2)	30 (6.5)
Leading to discontinuation of study drug	23 (7.5)	25 (5.4)
Infectious	64 (20.9)	80 (17.4)
Serious infectious	7 (2.3)	12 (2.6)
Injection site related	3 (1.0)	20 (4.4)

In the adalimumab arm, 12 (2.6%) patients had a serious infectious AE: acute tonsillitis, cellulitis,