Smoking Lessens Response to TNF Blockers

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LIVERPOOL, ENGLAND — Patients with rheumatoid arthritis who have a history of cigarette smoking are more likely to have a poor response to anti–tumor necrosis factor therapy than are those who have never smoked.

Recent studies have provided strong evidence that cigarette smoking is a risk factor in susceptibility to rheumatoid arthritis (RA) and more severe disease. Smokers with RA appear to have increased production of cytokines like tumor necrosis factor, and autoantibodies such as rheumatoid factor. A recent study from the British Society for Rheumatology's biologics register found current smokers had a low response rate to infliximab (Rheumatology [Oxford] 2006;45:1558-65).

"To see if smoking affects the response to therapy in our patients and to determine if there is a relationship between response and pack-year history, we collected demographic data and smoking histories for all patients at our hospital who were started on anti-TNF drugs since 2002," said Dr. Derek L. Mattey of Staffordshire Rheumatology Centre, University Hospital of North Staffordshire, Stoke-on-Trent (England). A total of 154 patients whose mean age was 65 years were included. Infliximab was the agent used by 83 patients, etanercept by 55, and adalimumab by 16.

Two-thirds of the patients reported ever having smoked, but only 25% were still current smokers at the time they initiated treatment.

The extent of previous smoking was quantified, with one pack-year being equivalent to 20 cigarettes per day for 1 year, and intensity of smoking stratified as never (0 pack-years), light (1-15 pack-years), moderate (16-30 pack-years), and heavy (more than 30 pack-years).

At baseline, smokers were more likely to be rheumatoid factor positive and have nodular disease, but smokers and nonsmokers did not differ in baseline Disease Activity Score (DAS) 28, Health Assessment Questionnaire (HAQ) scores, pain scores, or C-reactive protein level, Dr. Mattey said.

Response was defined according to the EULAR (European League Against Rheumatism) improvement criteria, based on 3-month DAS28 and absolute change in DAS28 from baseline.

At 3 months, there were significant differences between the groups, with patients whose smoking history exceeded 30 pack-years having an odds ratio of 7.4 for nonresponse versus patients who never smoked. The odds ratios for those in the light and moderate groups were 1.9 and 1.8, respectively.

The association of smoking and nonresponse was significant at 3 months only for infliximab, but there was a trend for nonresponse by 12 months for etanercept, too.

Multivariate logistic regression analysis showed that the association of pack-year history with nonresponse was independent of age, sex, disease duration, baseline DAS28, and HAQ scores.

Moreover, the association was independent of smoking status at initiation of anti-TNF treatment.

Analysis also determined that the association of smoking and nonresponse was significant at 3 months only for infliximab, but there also was a trend for nonresponse by 12 months for etanercept.

On the DAS28, the subjective areas of patient global assessment and tender joint count were associated with increased pack-year history, unlike the objective areas of erythrocyte sedimentation rate and swollen joint count. "There also was an inverse relationship between pack-years smoked and change in pain scores," he said at the annual meeting of the British Society for Rheumatology.

Dr. Mattey also undertook an analysis of the cytokine and metalloproteinase profiles in a group of 80 patients with early RA, to identify the possible impact of smoking at this level. In a poster, they reported that on ELISA and multiplex analyses, elevated levels of interleukin-8, vascular endothelial growth factor, and metalloproteinases 1, 8, and 9 were associated with smoking, and vascular endothelial growth factor and metalloproteinases 8 and 9 showed significant associations with number of pack-years. ■