Smoking cigarettes is a predictor of RA and may negatively impact on efficacy of anti-TNFs

EurekAlert

Rome, Italy, Thursday 17 June 2010: Smoking cigarettes is a significant risk factor for developing rheumatoid arthritis (RA) and may have a negative impact on the effectiveness of anti-tumour necrosis factor (anti-TNF) inhibitors in RA patients taking these treatments, according to results of two studies presented today at EULAR 2010, the Annual Congress of the European League Against Rheumatism in Rome, Italy. A further study has shown that smoking interferes with the expression of several genes which, when over-expressed can contribute to processes which exacerbate disease activity.

Results of a Swedish study1 showed that for both men and women, smoking at the time of study initiation was shown to be a predictor for future diagnosis with RA (Odds Ratio (OR) 1.55 95% CI 1.20-2.01). Socio-economic status also had an impact on the risk of developing RA with "Blue-collar workers" (those who do manual labour and earn an hourly wage) having an increased risk compared with white-collar workers (salaried professionals or educated workers) (OR 1.41: CI 1.02-1.94).

"The results of our study have confirmed that whether or not an individual smokes cigarettes, and the type of job that they do are surprisingly robust predictors of developing RA," said Dr Ulf BergstrÃ¶m, Department of Rheumatology, SkÃ¥ne University Hospital, MalmÃ¶, Sweden, and lead author of the first study. "Investigating the impact of socio-economic factors on the development of RA could help us to understand disease mechanisms and identify preventative strategies in the future."

Results of a second Swedish study2 showed that smoking predicted a poor response to anti-TNFs, as measured by two indices of disease activity: ?A 'poor' EULAR response (based on the assessment of disease activity) at 3 months (OR 0.53, (95% CI 0.32-0.87), p=0.012) ?A poor Simplified Disease Activity Index (SDAI) response at 6 months (OR 0.45 (CI 0.27-0.77), p=0.0003) and at 6 months (OR 0.47, (CI 0.25-0.88), p=0.02). Results of one further study undertaken in Switzerland3 showed that in experimental mice, the presence of smoke in the air induced the expression of the following genes: ?A 2.3 fold (p=0.02) induction of the expression of vascular endothelial growth factor (VEGF) was seen. VEGF is a growth signal that, when over-expressed, can stimulate the over-production of new blood vessels which can contribute to disease progression. ?A 2.7 fold (p=0.03) induction of the heat-shock protein DNAJC6 was seen. Heat shock proteins are induced in response to environmental stress and help to maintain cell function, but can also lead to activation of the immune system.

"The results of our study show that smoking (or the presence of smoke in the air) has an effect on the expression of the same genes and causes modifications in the

same proteins in both mouse models and in human beings," said Dr. Caroline Ospelt, Centre of Experimental Rheumatology, University Hospital Zurich, Switzerland. "We hypothesise that this is because smoking alters the ability of certain proteins to elicit an immune response in those with a genetic pre-disposition to rheumatic conditions. This could be a contributing factor to the symptoms experienced and an individual's disease progression."

Study designs and key statistics The first Swedish study1 (OP0045) assessed a total of 33,346 individuals who were included in the Swedish Preventive Medicine Program (PMP) between 1974 and 1992 (male n=22,444, female n=10,902; incident RA cases n=296). The median time from inclusion to RA diagnosis was 12 years with a mean age of RA diagnosis at 60 years. In the second Swedish study2 (OP0014) 934 RA patients from the South Swedish Arthritis Treatment Group responded to a questionnaire sent out in 2005 that covered smoking habits.

In the Swiss study3 (OP0081) investigators compared tissues samples from mice exposed to room air (n=8) compared with cigarette smoke (n=6) with samples from the joints from smoking (n=3) and non smoking (n=5) RA patients undergoing joint replacement surgery. Changes in gene expression were measured using whole genome microarrays and verified using real time Polymerase Chain Reaction (PCR, a DNA amplifying technique), and two assays to determine levels of protein presence - immunoblotting and ELISA (Enzyme-Linked Immuno Sorbent Assay).

SOURCE [1]

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