CARTILAGE DEGRADATION AND OXIDATIVE DAMAGE IN OA AND RA PATIENTS.

M Deberg¹, A Labasse¹, S Christgau², DB Henriksen², JY Reginster¹, Y Henrotin¹.

¹ Bone and Cartilage Research Unit, CHU Sart-Tilman, Liège, Belgium, ² Nordic Bioscience, Copenhagen, Denmark.

AIM

Protein nitration is a prominent feature of inflammation in joint. Our aim was to determine Coll 2-1 level, a peptide of type II collagen triple helix, and its nitrated form (Coll 2-1 NO₂) in serum of patients with early osteoarthritis (OA) and rheumatoid arthritis (RA).

MATERIALS AND METHODS

Coll 2-1 and Coll 2-1 NO₂ were measured in sera of 242 healthy subjects, 10 patients with early knee OA and 14 patients with early RA by two specific competitive immunoassays. These immunoassays are specific for amino acids sequence in the α triple helix of type II collagen, 108HRGYPGLDG116 (Coll 2-1), and its nitrated form (Coll 2-1 NO₂), respectively. The Coll 2-1 and Coll 2-1 NO₂ values were expressed as mean ± SEM. The non-parametric Mann-Whitney U-test was used to estimate the differences between each group of patients.

RESULTS

1. Reference values

Coll 2-1 and Coll 2-1 NO₂ concentrations during lifetime

In normal subjects (n=242), the mean concentrations of Coll 2-1 and Coll 2-1 NO₂ were 125.13 ± 3.71 nM and 0.16 ± 0.08 nM, respectively. When the population was stratified by 5 years brackets, Coll 2-1 and Coll 2-1 NO₂ serum levels did not significantly vary in the investigated age interval (Figures 1 A and B).

2. Coll 2-1 NO₂ concentration in premenopausal women versus postmenopausal women

When subjects aged from 46 to 55 years corresponding to the early postmenopausal were removed, Coll 2-1 NO₂ level was significantly higher in premenopausal women than in postmenopausal women. Further, before 45 years old, Coll 2-1 NO₂ level in serum was significantly higher in women than in men (0.22 ± 0.02 nM vs 0.16 ± 0.08 nM, p = 0.03), but decreased to men level after 55 years old (Figure 3).

3. Coll 2-1 and Coll 2-1 NO₂ concentrations in OA and RA patients

The Coll 2-1 level was higher (p<0.001) in serum of knee OA patients than in normal age-matched subjects (n= 80) (267.45 ± 26.42 nM vs 126.78 ± 6.61 nM), whereas Coll 2-1 NO₂ level was identical. In RA patients, the Coll 2-1 NO₂ concentration was 1.6 times higher (p<0.001) compared to the normal subjects (0.21 ± 0.02 nM vs 0.13 ± 0.03 nM), whereas Coll 2-1 concentration was not significantly different (158.35 ± 21.35 nM vs 126.78 ± 6.61 nM) (Figures 4 A and B).

CONCLUSIONS

These findings suggest that Coll 2-1 nitration is directly related with synovium inflammation and that Coll 2-1 NO₂ could be a promising marker of RA disease activity. In contrast, Coll 2-1 increase could be an interesting marker for detection of early structural changes in OA patients. Finally, these assays could be useful to elucidate type II collagen degradation and oxidative damages in inflammatory joint diseases.