The role of biomarkers of joint damage in monitoring the efficacy of different prophylaxis regimens regimens for severe haemophilia

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OBJECTIVES

The aims of this study were to detect correlations between serum and urine concentrations of biomarkers of joint cartilage degradation and the radiological score for haemophilic arthropathy, as well as to estimate whether measurement of these biomarkers could be useful in monitoring the efficacy of different (secondary) prophylaxis regimens for severe haemophilia A.

METHODS

This single-center study included 20 adult males with severe haemophilia A manifested by plasma FVIII < 1% of normal, without inhibitor. The first group involved five patients treated with full-dose prophylaxis: 20 U/kg three times per week. The second group included five patients given intermediate-dose prophylaxis: 10-15 U/kg three times per week. The third group consisted of 10 patients treated on demand (i.e. only in acute bleeding episodes). The following joint cartilage degradation products were measured: serum cartilage oligomeric matrix protein (COMP) and urinary C-terminal telopeptide of type II collagen (CTX-II). Blood and urine samples were collected initially, before the start of treatment (marked as COMP-1 and CTX-II-1) and after 3 months follow-up (marked as COMP-2 and CTX-II-2). Radiological evaluation of haemophilic arthropathy was estimated initially according to the Pettersson score. Approval from the local Ethics Committee and informed written consent were obtained from each subject.

Figure 1: Correlation between levels of COMP at the start and after 3 months of treatment with different prophylaxis regimen

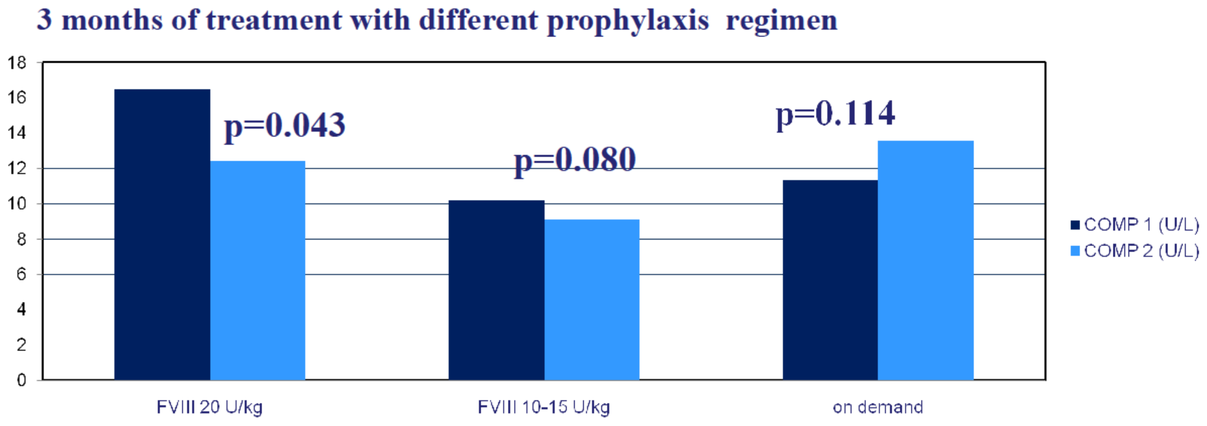
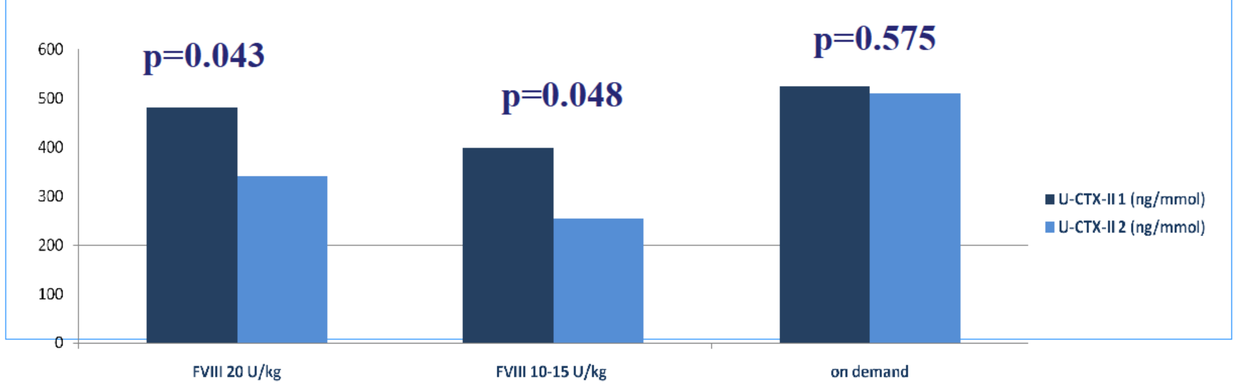


Figure 2: Correlation between levels of U-CTX-II at the start and after 3 months of treatment with different prophylaxis regimen



RESULTS

The mean age of the patients was 32 years (range 19-55). In the group of patients given full-dose prophylaxis, the mean value for COMP-2 was significantly lower than that for COMP-1 (p = 0.043), while in the group of patients receiving intermediate-dose prophylaxis and in those treated on demand the mean values of COMP-2 were not significantly changed when compared to those for COMP-1 (Figure 1). Likewise, in the group of patients treated with full-dose prophylaxis, the mean value for CTX-II-2 was significantly lower than that for CTX-II-1 (p = 0.014). Moreover, the mean value of CTX-II-2 was also significantly decreased compared to that for CTX-II-1 (p = 0.028) in the group receiving intermediate-dose prophylaxis. The mean values of CTX-II in the group of patients treated on demand showed no change. (Figure 2) The results showed significant positive correlations between the number of points in the Pettersson score and both COMP level (r = 0.602, p = 0.006), and CTX-II level (r = 0.580, p = 0.009,.

CONCLUSIONS

Joint cartilage degradation products, such as the biomarkers: serum COMP and urinary CTX-II, can provide an estimation of the amount of joint damage in patients with haemophilia A. Measurement of serum/urinary biomarker levels is useful for monitoring the efficacy of the applied doses of FVIII in different treatment approaches towards these patients.

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