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Early decrease of serum biomarkers of type II collagen degradation (Coll2-1) and joint inflammation (Coll2-1NO$_2$) by hyaluronic acid intra-articular injections in patients with knee osteoarthritis

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OBJECTIVES

To investigate in knee OA patients the effect of viscosupplementation (VS) on type II collagen degradation using serum Coll2-1, a peptide located in triple helical part of type II collagen molecule, and its nitrated form, Coll2-1NO$_2$.

METHODS

Fifty one patients with unilateral symptomatic K-OA received an intra articular injection of 2 ml of HA (hylan GF-20 a high molecular weight cross-linked HA derivative) on days (D) 1, 7, 14 and were followed 3 months. At D-15, patients were examined and X-rays were performed. Walking pain (WP) on VAS was obtained at each visit. Clinical response was defined as a WP decrease $\geq$ 50% between D1 and D90. Serum samples were obtained 2 weeks before the first injection (D-15), then at D1 (1st injection), D30 and D90. Coll2-1 and Coll2-1NO2 were measured in the serum using specific immunoassays. Variations over time for each biomarker were studied using Wilcoxon rank sum test. Predictive factors of response were analyzed using univariate comparison and logistic regression. Correlations between variables were obtained using Spearman test.

RESULTS

Between D-15 and D1, there was no significant difference for sColl2-1 and sColl2-1NO2 biomarkers (all p>0.05), indicating a good reproducibility in serum measurements and the absence of spontaneous variation over time. At D1, sColl2-1 and sColl2-1NO2 were unrelated to age, sex, BMI, disease duration and WP. However, sColl2-1 and sColl2-1NO2 were significantly higher in KL III/IV OA group than in KL I/II group (p < 0.01). Variation of the biomarkers over time: Coll2-1 and Coll2-1NO2 decreased systematically and significantly over time (Coll2-1/D1-D30: p = 0.0002; D1-D90: p = 0.054; Coll2-1NO2/D1-D30: p = 0.04; D1-D90: p = 0.025). The effect of HA was observed only in patient with the most severe OA (KL III/IV) (Table). sColl2-1 at baseline was significantly lower in responders than in non responders [139.8(34.8) versus 167(45.1); p = 0.03] even after adjustment for age, BMI and KL grade (Figure).

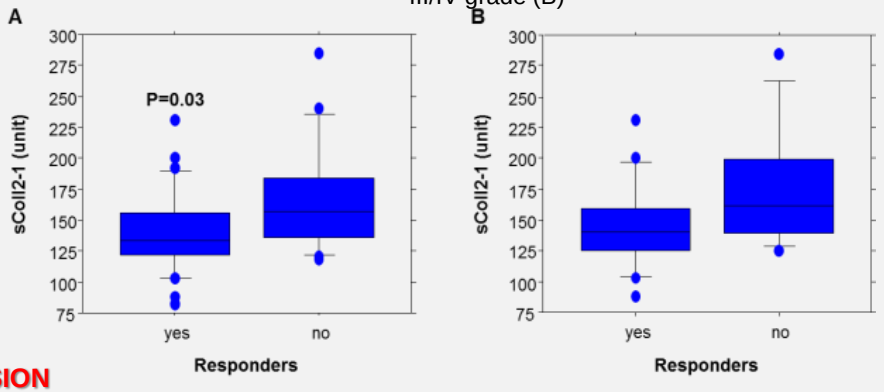
Table

Concentrations (nM) of sColl2-1 and sColl2-1 NO$_2$ over time ¨[mean (SD)] . * *p values versus D1 obtained with Wilcoxon signed rank test.*

	ALL PATIENTS		PATIENTS WITH KL III/IV	
	sCOLL2-1	**sCOLL2-1NO$_2$**	**sCOLL2-1**	**sCOLL2-1NO$_2$**
D-15	149.46 (37.10)	0.404 (0.196)	-	-
D1	149.15 (40.55)	0.442 (0.233)	156.43 (42.53)	0.469 (0.231)
D30	136.81 (42.36)	0.406 (0.180)	137.51 (45.66)	0.419 (0.184)
	*p=0.0002**	*p=0.066*	*p=0.0006*	*p=0.04*
D90	140.85 (33.50)	0.403 (0.172)	144.51 (32.67)	0.415 (0.158)
	p=0.054	*p= 0.025*	*p=0.004*	*p=0.026*

Figure

sColl2-1 concentrations (unit) at D1 of responders and non-responders in the whole population (A) and in the patients with KL III/IV grade (B)



CONCLUSION

This study suggests a rapid slowdown of type II collagen degradation and joint inflammation after viscosupplementation with hylan GF-20. Coll2-1 and Coll2-1NO2 serum levels significantly decrease compared to baseline especially in patients with advanced OA. Long term prospective trials are required to confirm this potential chondroprotective effect of HA.