DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTEINASE-13 AND INTER LEUKIN-1 BETA DURING REMISSION AND FLARE-UPS OF PRIMARY OSTEOARTHRITIS OF THE KNEES.

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introduction:

The diagnosis of osteoarthritis is currently based on radiographic criteria (eg, joint space width) and clinical symptoms (eg, pain and loss of function)(1).The evaluation of new disease-modifying osteoarthritis drugs (DMOADs) is performed on the same basis, since the regulatory bodies currently require evidence for an impact on radiographic joint space narrowing (JSN) and an impact on symptoms.(2,3) However, the limitations of radiography have led to research into alternative

parameters for monitoring osteoarthritis that could serve as biomarkers in drug development.(4)

Aim of the work:

detect the serum level of MMP-13 and IL-1 β In OA of the knee during remission and exacerbation and if these Biomarkers can be validated as gold biomarkers in assessing OA progression and drug development in OA.

Methods:

This study was performed on 60 patients with knee osteoarthritis, 18 males (30%) and 42 females(70%), all diagnosed as osteoarthritis of one or both knees. Their ages ranged from (40 -65) years. The duration of their disease ranged from one to 15years. The control groups were 8 males(32%) and 17 females(68%). their ages ranged from(40-65)years

We have excluded

- 1.Significant conditions of the spine, hips, or feet that affect the ability to walk.
2. Significant medical conditions that affect the ability to walk and function.3
Inflammatory arthritis, such as rheumatoid or gouty arthritis.
- 4 .Degenerative arthritis secondary to other conditions, such as hemochromatosis, Wilson ' s
disease, or ochronosis.
5. Current significant soft tissue rheumatism such as fibromyalgia, or trochanteric bursitis.
6. significant trauma and surgery (including arthroscopy) or intra-articular corticosteroid injection

to the index knee within 6 months of enrollment.

The patients were allowed to continue on the medications that they have pro inflammatory cytokines (IL-1 β) and degradative enzymes (MMP-13) are measured.

Asssesing the flare-ups using Knee Osteoarthritis Flare Ups Score (KOFUS)

- Results

Table (1): comparisons between demographic data in the two groups

<i>Parameters</i>	<i>Patients (n=60)</i>	<i>Control (n=25)</i>	<i>P-value</i>
Age (Years)			
Mean $\pm$ SD	50.7 $\pm$ 6.7	48.2 $\pm$ 9.1	0.348
Gender (n, %)			
Male	18 (30)	8 (32)	0.855
Female	42 (70)	17 (68)	
BMI (Kg/m²)			
Mean $\pm$ SD	32.4 $\pm$ 2.9	31.2 $\pm$ 3.6	0.365
Disease duration (Years)			
Mean $\pm$ SD	5.8 $\pm$ 3.8		
Affected knees (n, %)			
Bilateral	43 (71.7)		
Unilateral	17 (28.3)		
KL			
Mean $\pm$ SD	2.6 $\pm$ 0.8		

Table (2): comparison between IL-1 β levels in the four groups

<i>IL-1β (Pg/ml)</i>	<i>No flare-up (n=10)</i>	<i>1 flare-up (n=26)</i>	<i>2 flare-ups (n=21)</i>	<i>3 flare-ups (n=3)</i>	<i>P-value</i>
Mean $\pm$ SD	70.7 $\pm$ 34 ^b	82.5 $\pm$ 46.6 ^b	86.3 $\pm$ 42.5 ^b	129 $\pm$ 8.2 ^a	<0.001*
Median	72	99	95	131	
Range	15 - 126	13 - 148	12 - 144	120 - 136	

Table (3): comparison between MMP13 levels in the four groups

<i>MMP13 (mg)</i>	<i>No flare-up (n=10)</i>	<i>1 flare-up (n=26)</i>	<i>2 flare-ups (n=21)</i>	<i>3 flare-ups (n=3)</i>	<i>P-value</i>
Mean ± SD	0.04 ± 0.06 ^c	0.08 ± 0.08 ^b	0.11 ± 0.10 ^b	0.18 ± 0.06 ^a	0.045*
Median	0	0.10	0.12	0.21	
Range	0 – 0.13	0 – 0.28	0 – 0.28	0.12 – 0.22	

Table (4): comparison between KOFUS in the three groups

<i>KOFUS</i>	<i>1 flare-up (n=26)</i>	<i>2 flare-ups (n=21)</i>	<i>3 flare-ups (n=3)</i>	<i>P-value</i>
Mean ± SD	9.9 ± 2.1 ^b	10.1 ± 1.7 ^b	11 ± 1.7 ^a	0.615
Median	10	10	12	
Range	7 – 13	7 – 13	9 – 12	

Table (6): comparison between different medications in the four groups

<i>Medications</i>	<i>No flare-up (n=10)</i>	<i>1 flare-up (n=26)</i>	<i>2 flare-ups (n=21)</i>	<i>3 flare-ups (n=3)</i>	<i>P-value</i>
<i>Analgesic + NSAID (n, %)</i>	0 (0)	0 (0)	2 (9.5)	0 (0)	<0.001*
<i>Analgesic (n, %)</i>	0 (0)	0 (0)	0 (0)	1 (33.3)	
<i>NSAID (n, %)</i>	1 (10)	13 (50)	13 (61.9)	1 (33.3)	
<i>Systemic (n, %)</i>	0 (0)	6 (23.1)	2 (9.5)	1 (33.3)	
<i>Systemic + Analgesic (n, %)</i>	2 (20)	4 (15.4)	2 (9.5)	0 (0)	
<i>Systemic+ NSAID (n, %)</i>	7 (70)	3 (11.5)	2 (9.5)	0 (0)

Figure (2): positive correlation between disease duration and IL-1 β level in patients with no flare-up

Figure (3): positive correlation between MMP13 and IL-1 β level in patients with no flare-up

Figure (4): positive correlation between disease duration and IL-1 β level in patients with flare-ups

Figure (5): positive correlation between KL and IL-1 β level in patients with flare-ups

Figure (6): mean IL-1 β levels with different medications

Table (7): correlation between MMP13 levels and different variables in patients with flare-ups

<i>Variables</i>	<i>Correlation coefficient</i>	<i>P-value</i>
MMP13 and duration	0.657	<0.001*
MMP13 and KL	0.668	<0.001*
MMP13 and VAS	0.572	<0.001*
MMP13 and Stiffness score	0.621	<0.001*
MMP13 and Pain score	0.571	<0.001*
MMP13 and Functional score	0.554	<0.001*
MMP13 and Total WOMAC	0.626	<0.001*
MMP13 and Lequen	0.326	0.021*
MMP13 and KOFUS	0.587	<0.001*

Figure (8): mean MMP13 levels with different medications

SUMMARY & CONCLUSION

The conclusion of our work was that there is a potential role for IL1 beta and MMP 13 biomarkers in assessing the development in osteoarthritis.

IL 1 b and MMP 13 were founded to be correlated positively in patients with knee OA this correlation sounded right as the expression of MMP 13 depends on the level of IL1 b .

Another important point in treatment is that although all medications groups failed to lower the level of IL 1 b and MMP 13, yet there was a numerical difference in favor of Diacerine and NSAID .

What is really important to be concluded from the study is that patients on both diacerine and NSAID had the lowerest rate of flare ups

It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups

Recommendations

For all the previous reasons, we recommend:

- *Undertaking further studies on a large scale with a large number of patients to confirm our promising results.

- * For further understanding of the whole issue, serum and synovial fluid should be drawn from patients at the same time.

- *Measuring these biomarkers at the risky patient groups and at the early phase of the disease to assess their role in the progression and destruction.

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