The Egyptian Rheumatologist (2016) 38, 117–122

HOSTED BY

Egyptian Society of Rheumatic Diseases

The Egyptian Rheumatologist

www.rheumatology.eg.net
www.elsevier.com/locate/ejr

ORIGINAL ARTICLE

Correlation between serum leptin, cytokines, cartilage degradation and functional impact in obese knee osteoarthritis patients

Naglaa A. Hussein [a,*], Gihan Sharara [b]

[a] Physical Medicine, Rheumatology and Rehabilitation Department, Alexandria University, Egypt
[b] Biochemistry Department, Alexandria University, Egypt

Received 17 May 2015; accepted 22 May 2015
Available online 22 June 2015

KEYWORDS

Leptin;
Matrix metalloproteinase-13 (MMP13);
Cytokines;
Nitric oxide (NO);
Obesity;
Knee osteoarthritis (KOA)

Abstract *Aim of the work:* The aim of the present work was to correlate between serum level of leptin, matrix metalloproteinase-13 (MMP13), interleukin-1β (IL1β), tumour necrosis factor (TNF-α), nitric oxide (NO) and functional impact in obese patients with knee osteoarthritis (KOA).

Patients and methods: The study included 84 obese patients suffering from primary KOA. The knees were examined; pain assessed by visual analogue scale (VAS) and Lequesne's index for functional impact calculated. Serum leptin, MMP13, IL1β, TNF-α and NO were assessed.

Results: The mean age of the patients was 54.64 ± 7.7 years. They were 72 females and 12 males (F:M = 6:1) with a mean BMI of 35.29 ± 4.8. Sixty patients had knee effusion which was bilateral in 54 (64.3%), unilateral in 6 (7.2%) while 24 (28.6%) did not have any effusion. Knee deformities were present in 60 (71.4%) patients. Female patients were only significantly higher than males regarding Lequesne's index (15.08 ± 4.4 vs 11 ± 3.4, $p = 0.003$). Patients with knee deformity had significantly higher VAS (9.12 ± 1.3 vs 6.96 ± 0.46, $p = 0.001$), IL1β (621.1 ± 98.8 vs 503.9 ± 74.6 pg/ml, $p = 0.001$), TNF-α (115.4 ± 29.1 vs 87.4 ± 4.4 pg/ml, $p = 0.001$), NO (67.32 ± 5.7 vs 59.2 ± 2.2 μmol/L, $p = 0.001$), MMP13 (33.98 ± 2.24 vs 30.1 ± 1.7 ng/ml, $p = 0.012$) and leptin (13.2 ± 1.6 vs 10.4 ± 0.6, $p = 0.004$) than those without. The VAS, Lequesne index, IL1β, TNF-α NO, MMP13 and leptin were significantly higher in patients with bilateral knee effusion ($p < 0.0001$ for all) compared to those with unilateral effusion or without. Leptin significantly correlated with BMI, VAS, Lequesne's index, IL1β, TNFα, NO and MMP13 ($p < 0.0001$ for all).

* Corresponding author at: Physical Medicine, Rheumatology and Rehabilitation Department, Alexandria University, Albert Einstein College of Medicine (2015–2016), Egypt. Tel.: +20 1003714793.
E-mail address: nagla_kashif@hotmail.com (N.A. Hussein).

Peer review under responsibility of Egyptian Society of Rheumatic Diseases.

http://dx.doi.org/10.1016/j.ejr.2015.05.003

Conclusion: Leptin plays a key role in obese patients with knee OA. It significantly correlates with knee pain, functional impairment, inflammatory cytokines and cartilage degradation.

1. Introduction

Knee osteoarthritis (KOA) is the most common type of arthritis leading to pain and disability in the elderly population [1,2]. Obesity is a significant risk factor for KOA and also increases the risk of osteoarthritis (OA) in non-weight bearing joints such as the hands [3]. This means that the mechanical factors alone do not explain the cause effect relationship between obesity and KOA [4]. In a previous study on Egyptian patients with KOA it was found that synovial vascular endothelial growth factor (VEGF) remarkably correlated with clinical manifestations, functional impact, as well as radiological changes [5]. In other studies, osteopontin served as a biochemical marker of disease severity in KOA [6] and obesity increased the risk of renal dysfunction [7] in Egyptian patients with KOA. It has furthermore been reported that the measurements of hyaluronic acid and serum cartilage oligomeric matrix protein may be of diagnostic and prognostic value in differentiating patients with early KOA. The combination with other biochemical markers as well as with clinical and radiographic data would most likely help to improve the clinical assessment of KOA patients [8].

Recent studies suggest that systemic inflammatory mediators namely adipokines contribute to the increased risk of osteoarthritis with obesity [9–11]. These adipokines mediate synovial inflammation and up regulate cartilage matrix synthesis and degradation [9,10]. One of those adipokines is leptin which is a peptide hormone secreted primarily by adipocytes [12,13]. It regulates body weight by centrally inhibiting food intake and stimulating energy expenditure. Studies have shown high serum and synovial levels of leptin in obese patients which also correlated with percentage of body fat. This defect in leptin action suggests that obesity may be associated with central resistance to leptin [14,15]. Leptin modulates the degradative functions of the chondrocytes through up-regulation of matrix metalloproteases. Moreover, leptin was shown to enhance the synthesis of proinflammatory mediators in human OA cartilage [15]. Thus, leptin may be a metabolic link between obesity and OA [16].

The relationship between serum levels of leptin and the severity of KOA in obese patients as reflected by the functional impairment as well as laboratory parameters has to be more clarified. The aim of this study was to correlate between serum level of leptin, matrix metalloproteinase-13 (MMP13), interleukin-1β (IL1β), tumour necrosis factor-alpha (TNFα), nitric oxide (NO) and functional impact in obese patients with knee OA.

2. Patients and methods

This cross sectional study was conducted on 84 obese patients (Body mass index BMI $\geqslant 30\ kg/m^2$) [17] suffering primary knee OA according to the American College of Rheumatology (ACR) classification criteria [18]. Patients that did not receive any medication for treatment of the symptoms of knee OA at least 4 weeks prior to obtaining their blood test were enrolled in the study. Patients signed an informed consent and the ethical approval was obtained from the research committee of our institution before initiation of the study. The exclusion criteria were secondary OA due to any other causes as rheumatologic diseases such as rheumatoid arthritis, any clinical evidence of knee trauma or any orthopaedic diseases, medical diseases such as diabetes mellitus, hypercholesterolemia or cardiovascular diseases.

The following data were recorded for all patients; medical, occupational and drug history. The body mass index was calculated [19] and a detailed knee examination was performed including; alignment, presence of any deformity, bilaterality of disease, tenderness and effusion. Visual analogue scale (VAS) for knee pain was recorded [20]. Lequesne's algofunctional index was carried out [21].

Serum leptin was detected with enzyme-linked immunosorbent assay (ELISA) (DRG International Inc., DRG Leptin sandwich ELISA; EIA-2395); the following values were observed: males 3.84 ± 1.79 ng/mL, females 7.36 ± 3.73 ng/ml. The MMP13 (Human Matrix Metalloproteinase-13; MMP-13, ELISA Cat. No.: RBMS2022R Biovendor – Laboratorní, medicína a.s, Czech republic), IL1β (Abcam's Human Interleukin-1β ELISA kit ab100562) TNF-α (RayBio® Human TNF-alpha ELISA Kit Cat#: ELH-TNFα RayBiotech, Inc.) and NO (Kit for Quantitative Determination by Human Nitric oxide ELISA Kit, CK-E30290, Glory Science) were measured using ELISA. Normal serum Human MMP-13 levels ranged between 0 and 9.7 ng/ml. Normal serum IL1β: 5.4 ± 3.9 pg/ml, ranging between 0 and 13.6 pg/ml. Normal level of TNF-α was 11.2 ± 7.31 (0.0–32.5 pg/mL). Normal NO ranged from 10 to 20 μmol/L.

2.1. Statistical analysis

Data were analysed using statistical package for social science version 20(SPSS 20). Mean and standard deviation were used to describe data distribution. T test was used for comparison between 2 groups. Analysis of variance (ANOVA) was used for comparison between more than 2 groups. Pearson correlation was used to study the association between two parameters. The level of significance was 0.05.

3. Results

Eighty-four obese patients suffering from primary knee osteoarthritis were included in the study. Seventy-two (85.7%) were females and 12 (14.3%) males. The mean age was 54.6 ± 7.7 (41–72 years). The mean BMI was 35.3 ± 4.8 (30–50.2). Sixty patients (71.4%) had knee deformity.