Association Between Oxidative Stress and Fatty Acid Metabolism in The Synovial Fluid in Knee Osteoarthritis

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Introduction: Omega-3 polyunsaturated fatty acids (PUFA) such as eicosapentaenoic acid (EPA) are believed to prevent the progression of osteoarthritis (OA), since they act as an antioxidant and possess anti-inflammatory effect to suppress protein catabolism in cartilage and synovial cells. However, association between oxidative stress and fatty acid (FA)-related markers in synovial fluid of knee OA have not been fully understood. Therefore, the aim of this study is to investigate the relationships between oxidative stress and FA-related markers in the patients with knee OA.

Methods: We examined the oxidative stress- and FA-related markers both in the serum and synovial fluid taken from the patients with knee OA (male/female: 4/6). The Kellgren-Lawrence classification of knee OA in these patients were II-IV. The average age was 60.7 years old. The levels of biological antioxidant potential (BAP) and reactive oxygen metabolites (d-ROMs) were measured using free radical analytical system (FRAS4, Wismer Co. Ltd., Tokyo Japan). Omega-6 PUFA (arachidonic acid: AA), omega-3 PUFA (EPA), and eicosanoid (Leukotriene C4: LTC4, Thromboxane B2: TXB2, hydroxyeicosatetraenoic acid: HETE) were investigated as FA-related markers using LC/ MS/MS method. In statistics, Spearman’s rank correlation coefficient (r) and statistical significance (p) were calculated using GraphPad Prism version 6.0 (GraphPad Software). The values of p < 0.05 were considered to be statistically significant.

Results: The serum level of BAP/d-ROMs ratio (antioxidant capacity) was lower than that of synovial fluid; 5.8 (95%CI: 4.9-6.6) in serum and 18.9 (13.2-24.7) in synovial fluid (p < 0.01, paired t-test), the ratio of serum/synovial fluid was 0.31, suggesting that antioxidant capacity within joint is higher than that in serum. The ratio of serum/synovial fluid of FA were as follow: EPA: 3.8 (1.5-6.1), DHA: 0.4 (0.2-0.6), AA: 0.7 (0.5-0.9). The serum/synovial fluid ratio of EPA/AA (indicator of the anti-inflammatory capacity) was 4.3 (1.3-7.3). These data indicates that the levels of FA in synovial fluid depend on the types of FA, and FA-related anti-inflammatory capacity is low in the synovial fluid of knee OA. There were significant negative correlation between the levels of BAP/d-ROMs and AA, LTC4, 15HETE, 12HETE (r = -0.72, -0.79, -0.85, -0.68, respectively, p < 0.05) in synovial fluid, whereas no correlation in serum, suggesting that oxidative stress within knee joint are related to the activation of AA cascade.

Discussion: We examined the relationships between oxidative stress and FA metabolism both in serum and synovial fluid of knee OA and found that oxidative stress in synovial fluid was involved in the AA cascade. Since omega-3 PUFA such as EPA and DHA poses anti-inflammatory effect, administration of these FA would be helpful to relief the inflammation of knee OA via suppression of oxidative stress within knee joint. Furthermore, our data suggest that the improvement of systematic methabolic conditions such as hyperlipidemia can loose their body weights in obesity individuals as well as supress inflammation within the knee joint. Therefore, it’s important to evaluate general health conditions when we manage the patients with OA.

Key words: knee OA, fatty acid, oxidative stress, synovial fluid

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