THE ROLE OF MTOR GENE EXPRESSION, APOPTOSIS AND INFLAMMATION IN OBESE PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Metabolic osteoarthritis (OA) has been identified in rheumatology as a specific phenotype due to the growing rates of obesity and other comorbidities, with meta-inflammation as the key factor in its pathogenesis. On the other hand, OA progression is associated with altered regulation of chondrocytes' metabolism, namely, with up-regulated expression of genes encoding inflammation, apoptosis, cartilage degeneration and inflammation.

Objectives: To measure the expression levels of genes encoding mTOR, apoptosis (caspase-3), cartilage destruction (cathepsin K), and inflammation (TNF-α) in patients with knee OA (KOA) and obesity.

Methods: 50 female patients (45–65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI >30 kg/m²) were randomised into 2 groups. Pts in Group 1 (n=25) were administered orlistat as a specific therapy for obesity for the period of 6 months, and lifestyle modifications including low caloric diet and physical exercises during 12 months. Peripheral blood samples were obtained at baseline and Mo 6, and life-style modifications including low caloric diet and physical exercises for 12 months. Pts in Group 2 were recommended to observe the diet and following orlistat therapy pts from Group 1 managed to reduce their body weight by 5,6% as compared to the values at Mo 6 during the second stage of the study, as compared to the expression values in pts from Group 2 (figure 1). The analysis demonstrated direct positive correlation (p<0.05) between expression of genes encoding inflammation, cartilage destruction and apoptosis and pain intensity in knee joints assessed by VAS and WOMAC scales.

Results: Following orlistat therapy pts from Group 1 managed to reduce their body weight by 10,07% at Mo 6 (p<0.05), while pts from Group 2 lost only 0,88% (p>0.05) of their body weight versus the baseline values. During the following 6 months pts from Group 2 on life-modifying regimen continued to lose their body weight, achieving 3,5% (p<0,05) weight reduction versus baseline values, while pts from Group 1 gained weight by 5,6% as compared to the values at Mo 6 during the study (figure 1). Expression of genes encoding inflammation, apoptosis and cell proliferation was assessed at Mo12 to evaluate possible correlation with the dynamics of body weight. Up-regulated expression (p<0.05) of genes encoding inflammation (mTOR), cartilage destruction (cathepsin K), apoptosis (caspase-3), and cell proliferation (m-TOR) was documented in KOA obese pts from Group 1, gaining body weight during the second stage of the study, as compared to the expression values in pts from Group 2 (figure 1). The analysis demonstrated direct positive correlation (p<0.05) between expression of genes encoding inflammation, cartilage destruction and apoptosis and pain intensity in knee joints assessed by VAS and WOMAC scales.

Conclusions: Therefore up-regulation of m-TOR, caspase-3, TNF-α and cathepsin K gene expression is observed in obese pts with KOA following weight gain and worsening of clinical parameters, which is suggestive of aggravated apoptotic, inflammation and cartilage destruction, providing further KOA progression.

Disclosure of Interest: None declared


PREGNANT WOMEN WITH HIP OSTEOARTHRITIS

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Objectives: The management of patients with severe pain caused by primary or secondary osteoarthritis (OA) of the hip joint (TBS) has not been developed. The aim of the present work was to evaluate the impact of NSAIDs, glucocorticoids (GCS), analgesics and non-drug treatment methods on pregnancy outcomes in patients with primary and secondary OA TBS.

Methods: The study included 99 pregnant women aged 35 to 49 with an intensive pain (≥4.0 points for VAS) due to primary or secondary OA TBS. Depending on the form of OA, the severity of the pain and the patient's opinion, the therapy was prescribed – ibuprofen up to 800 mg per day orally (n=31) or paracetamol up to 1000 mg per day orally (n=20) or methylprednisolone up to 12 mg per day orally (n=27) or non-pharmacological methods (n=21). The efficacy of the treatment was evaluated within a month from the start of the therapy, pregnancy outcomes for the mother and fetus and pathology of the child after 12 months after the birth. The factors, associated with low efficacy of treatment, were evaluated.

Results: In 50 (51%) women was established primary OA TBS, in 49 (49%) – secondary OA TBS. A decrease of pain in TBS in patients of all treatment groups (p>0.05 for comparison with baseline) was registered. Patients with secondary OA, who received Methylprednisolone, showed a statistically significant (p<0.05) improvement in pain compared to patients in other clinical groups. A correlation was found between the intensity of pain syndrome (VAS) and BMI. 85 (85%) patients had urgent deliveries, 14 (14%) had premature, natural delivery in 82 (82%) women, and a caesarean section was performed in 29 (29%) cases. The cases of ante- and perinatal fetal death were not recorded.

Pathological conditions were absent in 28 (84.85%) of newborns, whose mothers refused medical treatment, in 23 (85.19%), who were on methylprednisolone, showed a statistically significant (p<0.05) improvement in pain compared to patients in other clinical groups. A correlation was found between the intensity of pain syndrome (VAS) and BMI. 85 (85%) patients had urgent deliveries, 14 (14%) had premature, natural delivery in 82 (82%) women, and a caesarean section was performed in 29 (29%) cases. The cases of ante- and perinatal fetal death were not recorded.

Conclusions:

1. The use of non-medicamental and medicamental (non-selective NSAIDs or GCS in small doses or analgesics) treatment in pregnant woman with hip osteoarthritis has equal efficiency and safety for the health of the mother and fetus.

2. Children, born to mothers with primary or secondary hip osteoarthritis, treated with NSAIDs or analgesics or GCS by medical treatment in age of 12 months do not differ from children, born to mothers with osteoarthritis of hip joints, receiving non-medicamental therapy.

3. An increase of the body mass index of a pregnant woman with osteoarthritis of the hip joints is a predictor of refractoriness to any form of drug and non-drug therapy.

Disclosure of Interest: None declared