AB0083

LOCAL ICE CRYOTHERAPY DECREASES PROSTAGLANDIN-E2, NF-KB AND IL-6 SYNOVIAL LEVELS IN ARTHRITIC KNEES COMPARED TO CONTRALATERAL NON-TREATED JOINTS

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Background: Cryotherapy is widely used in rheumatic diseases, with a low level of evidence. Tissue mild hypothermia was reported to inhibit pivotal pro-inflammatory enzyme pathways such as COX-2/PG-E2¹ and NF-kB.²

Objectives: We hypothesised that local cryotherapy (LC) might reduce joint inflammation through PG-E2 and NF-kB repression.

Methods: 47 patients suffering from non-septic knee arthritis were included (17 gout, 11 calcium pyrophosphate dehydrate crystal deposition diseases, 6 spondyloarthritis, 13 rheumatoid arthritis), taking no concurrent anti-inflammatory drug/DMARD. They were first randomised to receive local ice (30 min-N=16) or cold pulsed CO2 (2 min – Cryo+ Cryonic-N=16) at 9 A.M and 5 P.M. Synovial fluid was collected just before the first cold application then 24 hours later (9 A.M). Synovial fluid IL-6, IL-1 β , TNF- α , IL-17A, VEGF (Multiplex flow cytometry), NF-kB P65 (total/phosphorylated) and PG-E2 (ELISA) were measured and compared before and after 2 LC applications. Contralateral non-treated knees were then used as paired controls (in 16 other ice-treated patients).

Results: Synovial IL-6 significantly decreased after 2 LC applications (n=43 paired Wilcoxon:p=0.00015). This decrease was also significant in ice-treated subgroup (n=16 p<0.005) but not in CO2-treated patients (n=14;p=0.1). IL-1 β and VEGF levels also decreased after treatment (n=44-p=0.02 and n=47-p=0.03) but not significantly in treatment subgroups. By contrast, IL-6 (n=13), IL-1 β (n=15) and VEGF (n=15) didn't change in contralateral non-treated knees. LC had no significant effect on IL-17A nor TNF- α synovial levels. LC significantly reduced synovial NF-kB (n=38-p=0.04) and NF-kB-P levels (n=38-p=0.004). These levels were also significantly decreased in ice-treated patients (n=26-p=0.03 and 0.003) but not in CO2-treated patients (n=13). We observed no effect on the NF-kB levels in contralateral non-treated knees (n=12). NF-kB variations correlated significantly with IL-6 (Pearson's r=0.48-N=32 p<0.01) and VEGF (r=0.34-N=36-p=0.038) variations, and with the maximal skin temperature drop induced by LC (r=0.32-N=36-p=0.047). LC significantly reduced synovial PG-E2 (n=38-p=0.04), which was also significantly decreased in ice-treated patients (n=26-p=0.02) but not in CO2-treated patients (n=13). Conversely, we observed a significant increase in PG-E2 levels in contralateral non-treated knees (n=12-p=0.04), with a significant inter-class effect-size (weighted mean difference –1329 [–2232;–426] pg/mL in 12 bi-arthritic patients).

Conclusions: Local ice cryotherapy applied twice during one day showed superior anti-inflammatory effects compared to local CO2, notably by reducing synovial IL-6 levels in arthritic knees. We also showed for the first time that this inhibitory effect on cytokine levels might be PG-E2 and NF-kB dependent, notably through significant inhibitory effects on the PG-E2 and (to a lesser extent) NF-kB pathways.

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AB0084

ELEVATED LEVELS OF IL-37 ARE ASSOCIATED WITH TOPHUS AND SUPPRESSED THE PRODUCTION OF INFLAMMATORY CYTOKINES IN PATIENTS WITH GOUT

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Background: IL-37 has been identified as a natural inhibitor of innate immunity. Although increasing evidence shows elevated IL-37 expression in various autoimmune diseases, its correlation with clinical symptoms in gout is still unclear.

Objectives: This study aims to determine the correlation between the levels of IL-37 and clinical indexes in gout patients, and to examine the inhibitory effect of IL-37 on pro-inflammatory cytokine including IL-1 β , IL-6 and IL-18 from peripheral blood mononuclear cells (PBMC) of gout patients in culture.

Methods: Levels of serum IL-37 and concentrations of IL-1 β , IL-6, IL-18 in cell culture from 42 patients with gout and 40 healthy controls (HCs) were measured by enzyme-linked immunoassay (ELISA). Moreover, the relative mRNA

expression of these cytokines in PBMCs was detected by real-time PCR (RT-PCR). The correlations between serum IL-37 levels and clinical values in gout patients were analysed by Spearman correlation test.

Results: Both protein and mRNA levels of IL-37 were higher in gout patients than healthy controls, especially in patients with tophus. Serum IL-37 levels of gout patients were positively correlated with C-reactive protein and uric acid. Furthermore, the expression of IL-1 β , IL-6 and IL-18 in PBMCs from gout patients was significantly increased, which were markedly suppressed by IL-37 in culture.

Abstract AB0084 – Figure 1. IL-37 suppresses the expression of pro-inflammatory cytokines in PBMCs from gout patients

Conclusions: Serum levels of IL-37 are closely associated with clinical symptoms in gout patients and may represent a potential biomarker for the disease activity.

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AB0085

THE MECHANISM OF TOTAL GLUCOSIDE OF PAEONY AND SINOMENINE ON THE PREVENTION OF ACUTE GOUT FLARES

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Background: The compliance of drug prevention for acute gout flares (GFs) during urate-lowering treatment (ULT) is very low. New preventive drugs of GFs during ULT is required. Our previous study found that the total glucoside of paeony (TGP), a traditional Chinese drug's extracts, has a good effect on the prevention and treatment for urate induced acute gouty arthritis (AGA) in rat.

Objectives: To explore the possible mechanism of TGP and Sinomenine (SIN) in the prevention and treatment of acute gouty arthritis.

Methods: Logarithmic growth phase of RAW264.7 cells were seeded into 96 well plate at a density of 5×10^4 /mL. Cultured overnight in a humidified atmosphere of 5% CO₂ at 37°C. Then, the medium was changed to serum-free DMEM. Then divided into Control group (DMEM), Model group (DMEM +50 mg/L MSU), Colchicine group (DMEM +50 mg/L MSU +1 μmol/L Colchicine), TGP group (DMEM +50 mg/L MSU +40 mg/L TGP), SIN group (DMEM +300 mmol/L SIN), SIN +TGP group (DMEM +40 mg/L TGP +300 mmol/L SIN). The final volume of solution was 2 ml in each well, and each group had 3 wells, culturing for 24 hour in a humidified atmosphere of 5% CO₂ at 37°C. Then, culture supernatant was collected. NO level were detected by method of nitrate reductase, the level of IL-1 β ,