EFFICACY OF BUCILLAMINE THERAPY IN HYDROARTHROSIS ASSOCIATED WITH KNEE OSTEOARTHRITIS

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Introduction: In a series of cases of refractory hydroarthrosis associated with osteoarthritis (OA) of the knee who were markedly improved by bucillamine therapy, we compared changes in the levels of cytokines IL-6 and TNF-α in serum and synovial fluid with the treatment outcomes.

Materials and Methods: The subjects were 24 patients with 29 knees affected by OA and refractory hydroarthrosis. Their mean age was 68.2 (52-76). Blood and synovial fluid samples were taken prior to bucillamine therapy (200 mg/day), as well as at 2, 4, 6, 8, 10 and 12 weeks post administration. Samples were centrifuged at 3000 rpm for 10 minutes, and the supernatant was stored frozen. IL-6 and TNF-α levels in the samples were measured using the chemiluminescence (CL)-ELISA method, as developed by Tolleruds. This method combines chemiluminescence with ELISA techniques, and provides sensitivity some 100 to 1000 times greater than that possible with previous ELISA methods. Radiographic assessments were made using the Kellgren classification.

Results: The degree of improvement in knee hydroarthrosis with bucillamine therapy could be graded into 3 groups: group A, a marked decrease in the amount of fluid was seen within 3 months (9 knees, 31%); group B, a marked decrease in the amount of fluid was seen within 6 months (5 knees, 17%); and group C, the amount of fluid was unchanged (15 knees, 52%). Significant changes in serum levels of IL-6 and TNF-α before and after bucillamine therapy were seen only in group A (mean IL-6 concentration 7.8 x 10² pg/mL → 6.1 x 10² pg/mL, mean TNF-α concentration 1.1 x 10² pg/mL → 0.7 x 10² pg/mL). Significant changes in synovial fluid levels of IL-6 and TNF-α before and after bucillamine therapy were seen in group A (mean IL-6 concentration 2.8 x 10⁴ pg/mL → 0.4 x 10⁴ pg/mL, mean TNF-α concentration 2.6 x 10² pg/mL → 1.2 x 10² pg/mL) and group B (mean IL-6 concentration 1.7 x 10⁴ pg/mL → 0.9 x 10⁴ pg/mL, mean TNF-α concentration 1.9 x 10² pg/mL → 1.4 x 10² pg/mL), but not in group C (Figure 1). In other words, clinical response in knee hydroarthrosis to bucillamine therapy correlated with reductions in IL-6 and TNF-α levels. Significant differences were also seen in synovial fluid levels of IL-6 and TNF-α before and after bucillamine therapy in knees with Kellgren grades 1 and 2, but not in those of grades 3 or 4. Grades 1 and 2 were therefore common in groups A and B, whereas grades 3 and 4 were more common in group C.

Discussion: OA is a non-infectious chronic inflammatory joint disease, with some histological features extremely similar to those seen in early rheumatoid arthritis (RA). RA and OA share a number of common features, with inflammatory cells and activated lymphocytes infiltrating the synovial tissue and synovial fluid. More specifically, activated lymphocytes are present in the perivascular region of the synovial tissue and expansion of oligoclonal T cells is seen into the synovial membrane in OA, and amino acid analysis method reveals several common sequences in the CDR3 region in both OA and RA. These facts suggest that in some, but not all cases, OA is mediated by T cells. In this study, we observed improvement in hydroarthrosis associated with knee OA with bucillamine therapy, and also reduction of the production of cytokines in serum and in synovial fluid. These effects were thought to be due to the synovial anti-inflammatory activity of bucillamine.

Conclusions
Our results indicate that bucillamine is an effective treatment for hydroarthrosis associated with knee OA.