# Therapy of Osteoarthritis of the Knee with a Combined Zeel T/NSAID Treatment*

Olga J. Maiko

## Abstract

This study compares the efficacy of NSAID therapy and combined Zeel T/NSAID therapy of osteoarthritis of the knee. 80 patients with advanced osteoarthritis of the knee, often exacerbated by synovitis and/or periarthritis, received either the allopathic treatment or the combined allopathic-homeopathic treatment for four weeks. The maximum total monitoring period for each patient was 12 months. Ultrasound examinations and evaluation of osteoarthritis-specific symtoms and their severity were used to compare the efficacy of the two therapies. The combined allopathic-homeopathic treatment produced greater and longer lasting improvement in specific symptoms and proved especially effective in treating periarthritis and mild to moderate synovitis. Conclusions: Improvements in clinical data and ultrasound findings were more pronounced in patients receiving the combined Zeel T/NSAID therapy, persisting after conclusion of therapy and throughout the 12-month observation period.

**Keywords:** Antihomotoxic medicine, homeopathy, osteoarthritis, NSAID, Zeel T

## Introduction

Worldwide, osteoarthritis is the most common rheumatic disorder, causing enormous socioeconomic losses due to temporary or permanent disability (2, 4). Osteoarthritis strikes 10-12% of the population; its prevalence correlates with age and gender. Women are affected nearly twice as often as men, and the rate of new diagnoses is highest among 55 to 64-year-olds. The knee is the joint most frequently affected.

Conventional osteoarthritis therapy consists primarily of nonsteroidal anti-inflammatories (NSAIDs), chondroprotective agents, and medications that improve metabolic processes in cartilage. Physical therapy is also used. Drug treatment is controversial because medications such as NSAIDs are contraindicated in some cases and their use is known to entail a relatively high risk of side effects (2, 9, 12, 13, 21). The Rheumatology Institute of the Russian Academy of Medical Sciences recommends a maximum of two weeks of NSAID therapy, since longer-term use causes gastrointestinal complications and may also exacerbate degenerative changes in cartilage (6, 9, 12, 20, 24).

In treating degenerative disorders of the musculoskeletal system, physicians are once again turning to homeopathic medications such as the combination preparation Zeel T (manufactured by Biologische Heilmittel Heel of Baden-Baden, Germany). Numerous studies have confirmed the therapeutic potential of this medication (5, 8, 10, 19, 22, 23). Zeel T is presumed to work by inhibiting cartilage degeneration. Possible mechanisms

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include enhanced mitosis of cartilage cells and metabolic improvements in pathologically altered cartilage (3, 17, 23). Zeel T's chondroprotective effects develop only after long-term use (generally two to three months); its analgesic and anti-inflammatory potential is more prominent during shorter periods of treatment (four weeks in the case of the present study). No adverse effects of Zeel T have been documented (3, 8, 10, 19, 22).

The purpose of the present study was to ascertain whether combined allopathic-homeopathic treatment of osteoarthritis of the knee is superior to allopathic therapy alone.

## Methods

### Patients

80 patients suffering from various stages of osteoarthritis of the knee were examined and treated. (See Table 1 for demographic and medical history data). Most patients (n = 64) were female. The greatest concentration of cases (n = 39) fell in the 41 to 50 year age group, followed by the group of 51 to 60-year-olds (n = 24). The average age of the patients was 50.6+/- 1.2 years. Duration of the illness ranged from several months to more than 20 years but averaged 6.6 +/- 1.0 years.

### Diagnosis

Patients were diagnosed according to uniform osteoarthritis criteria used by the Russian Academy of Medical Sciences and based on those of Altman (1) (Table 2). X-ray and ultrasound were used to assess the extent of damage to the knee joints.

All patients admitted to the study underwent general medical examinations including sonography of internal organs, EKG, CBC, urinalysis, and tests for total protein and albumin as well as serum sialic acid and C-reactive protein.

### Treatment

The patients admitted to the study (n = 80) were randomly divided into two treatment groups of 40 patients each. For a period of two weeks, patients in both groups received 25 mg of the NSAID diclofenac three times a day, nicotinic acid to stimulate blood circulation, a multivitamin, and electrophysiotherapy (Amplipulse therapy) to stimulate connective tissue and cartilage metabolism. In our clinic, the Amplipulse method is used routinely to treat degenerative and dystrophic diseases of the joints and spinal column. In this case, the Amplipulse therapy used sine-wave alternating current at a frequency of 5 kHz; the treatment cycle consisted of 10 daily sessions of 10 minutes each.

In addition to this standard therapy, the patients in the second group also received the homeopathic combination medication Zeel T (dosage: 1 tablet p.o. 3 times a day, to be taken 15 minutes before meals) for a total of four weeks.

The two treatment groups were equivalent in terms of gender and age distribution, average duration of the illness, average stage of the illness (based on radiological examinations), degree of functional impairment of the affected joints, and the type and frequency of concomitant illnesses (see Table 1).

### Diagnostic procedures

**Radiology:** The patients were assigned to three groups (stages I, II, and III; see Table 1) on the basis of x-ray images of their knee joints (frontal and lateral projections).

See Table 2 for the criteria used to assess functional joint impairment.

**Sonography:** Ultrasound examinations followed procedures outlined by Schastina. Eight periarticular images (four longitudinal and four transverse views) served to evaluate:

- the condition of the patient's soft periarticular tissue and articular capsules
- the quantity and consistency of articular fluid
- the synovial membrane
- the thickness of the joint cartilage of the kneecap, tibia, and fibula, and
- the outlines of the bones of the joint.

Ultrasound images were also used to assess:

- the extent of the bursae in front of and below the kneecap,
- the maximum thickness of synovial tissue
- the thickness of the cartilage of the central portion of the kneecap and the proximal tibiofibular syndesmosis
- the condition of the tendons of the sartorius, biceps, and semitendinosus muscles.

Corresponding data on 20 healthy individuals (16 female, 4 male) of varying sizes and weights and ranging in age from 22 to 30 years were used for purposes of comparison in assessing the ultrasound findings.

**Diagnosis of concomitant synovitis:**

Osteoarthritis patients with and without reactive synovitis were admitted to the study. Diagnosis of synovitis was based on the following criteria:

- pain that varies in intensity depending on activity level
- pain that disappears with continued movement
- slightly elevated skin temperature around the joint
- pain on palpation

Based on the severity of their synovitis, patients were assigned to one of four groups: subclinical (+/-), slight (+), moderate (++), and severe (+++). No subclinical cases of synovitis were found among the patients in this study.

Periarthritis and/or tendinitis were diagnosed by examination for local sensitivity to pressure and, in some cases, periarticular or peritendinous edema.

Since a patient's right and left knees may exhibit different degrees of inflammation and since some joints were asymptomatic, each knee was assigned separately to one or more of the following subgroups, according to its clinical characteristics:

- joints with synovitis
- joints with periarthritis
- joints with tendinitis
- asymptomatic joints.

**Statistical analysis:**

The success of treatment was analyzed upon conclusion of therapy and again three and six months later, and 20 patients from each group were also monitored after twelve months. Descriptive statistical methods were used to analyze data on patients and their treatments, and absolute and percentage frequency distributions were calculated. The Wilcoxon-U test was used to perform statistical comparisons.

## Results

### Patients

47 patients (58.8%) had Stage II osteoarthritis according to Kellgren's ranking system (11). Stage II functional impairment was evident in the joints of 46 patients (57.5%). On clinical examination, a total of 80 single joints in 64 patients exhibited symptoms of synovitis (see Table 1).

Mild cases of synovitis predominated in Group 1. In Group 2, all degrees of synovitis were more or less equally represented. Group 2 included more cases of moderate (n = 13 vs. n = 11) and severe (n = 12 vs. n = 5) synovitis than Group 1, and osteoarthritis symptoms were correspondingly more severe in Group 2.

Periarthritis was diagnosed with almost the same frequency in both groups, occurring in 34 patients (60 joints) in Group 1 and in 32 patients (56 joints) in Group 2.

### Symptoms

Upon conclusion of the four weeks of therapy, clinical symptoms had improved in both groups, but the improvement was more pronounced in the patients in Group 2 (Figure 1). Patients in both groups reported less pain as rated on a visual analog scale (Figure 1a), but the reduction in pain was more pronounced in Group 2. Functional tests (Figures 1b and c) yielded similar results.

In Group 1, clinical symptoms began to worsen again as early as three months after conclusion of therapy. This trend became increasingly evident at the six and twelve-month follow-up examinations. In Group 2, recurrent symptoms affected fewer patients and appeared later than in Group 1 (Table 3).

Both therapies relieved pain and inflammation, but the effects were clearly greater in Group 2, especially among patients with periarthritis (Figure 2). Ultrasound examinations confirmed the superiority of the combined allopathic-homeopathic therapy.

Symptoms of tendinitis and synovitis decreased in both treatment groups, but in Group 2 the decrease was greater and remained evident six and twelve months after treatment (Table 4). Among patients with tendinitis, those in Group 2 experienced significantly better therapeutic results throughout the entire observation period. Twelve months after treatment, more patients were affected by tendinitis in Group 1 than in Group 2.

Ultrasound examinations confirmed that the number of most severe cases was met in Group 2. In these Group 2-cases, osteoarthritis was usually associated with severe synovitis and periarthritis. Both therapies reduced the size of knee-joint bursae, but this effect, which persisted throughout the entire observation period, was evident in more cases in Group 2 than in Group 1. In fact, ultrasound imaging revealed some cases of enlarged bursae in Group 1 after treatment.

## Conclusions

These findings confirm the beneficial effects of combined NSAID/Zeel T therapy for osteoarthritis. Several controlled multicenter studies have examined efficacy of the

antihomotoxic medication Zeel in treating osteoarthritis and specifically osteoarthritis of the knee (18, 19).

In addition to Zeel T's analgesic and anti-inflammatory effects (presumably due to inhibition of inflammatory cytokines), some of its individual components (e.g., Cartilago suis) are presumed to optimize binding of water in joint structures and to increase the elasticity of cartilaginous tissue. Similar effects are postulated for hyaluronic acid, which is presumed to activate proteoglycan synthesis (3, 16).

In one multicenter clinical study comparing Zeel to hyaluronic acid in treating osteoarthritis of the knee, the two medications had statistically equivalent therapeutic effects, and both significantly reduced the pain of osteoarthritis. According to the same study, adverse effects occurred only half as frequently among patients treated with Zeel (5.5%) as in those treated with hyaluronic acid (11%). In addition, Zeel therapy was significantly less expensive than treatment with hyaluronic acid (3).

Data from the current study indicate that therapy with Zeel T combined with NSAID achieves convincing success in patients with knee osteoarthritis accompanied by periarthritis and/or synovitis. Russian authors with years of experience in the use of Zeel T and Traumeel S also report decreased symptoms in 80% of patients with reactive synovitis (tendosynovitis and inflammation around the trochanter). According to the Russian study, these antihomotoxic medications produce strong anti-inflammatory, analgesic, and effusion-inhibiting effects, slow the rate of cartilage degeneration, and – unlike glucocorticoids – have low rates of side effects. Other authors also suggest that the synergistic effects of Zeel T, NSAIDs, and physiotherapy may make it possible to reduce patients' NSAID dosages (7, 14, 15, 22).

In the course of the current study, no adverse effects were observed during treatment with Zeel T. Tolerability of the medication was excellent. According to the literature, adverse effects occur in 0.45 to 5.5% of cases when the medication is administered parenterally and in less than 1% when other methods of administration are used. No authors have reported any cases of systemic adverse effects during therapy with Zeel T (3, 8, 18, 19, 22).

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Author’s address:
Olga Y. Maiko, M. D.
13-3, Ul. Koltcevaya
460023, Orenburg
Russia

| | Group 1 ( n = 40) | Group 2 (n = 40) | Total (n = 80) |
|---|---|---|---|
| | **n (%)** | **n (%)** | **n (%)** |
| **Gender:** male | 7 (17.5) | 9 (22.5) | 16 (20.0) |
| female | 33 (82.5) | 31 (77.5) | 64 (80.0) |
| Total | 40 (100) | 40 (100) | 80 (100) |
| **Age [in years]** | | | |
| • < 40 | 3 (7.5) | 3 (7.5) | 6 (7.5) |
| • 41–50 | 18 (45.0) | 21 (52.5) | 39 (48.8) |
| • 51–60 | 12 (30.0) | 12 (30.0) | 24 (30.0) |
| • > 60 | 7 (17.5) | 4 (10.0) | 11 (13.8) |
| Average age (in years) | 51.4 ± 1.37 | 49.7 ± 0.95 | 50.55 ± 1.16 |
| **Duration of illness (years)** | | | |
| • less than 1 | 1 (2.5) | 4 (10.0) | 5 (6.3) |
| • 1–4 | 18 (45.0) | 14 (35.0) | 32 (40.0) |
| • 5–9 | 10 (25.0) | 10 (25.0) | 20 (25.0) |
| • 10–15 | 6 (15.0) | 8 (20.0) | 14 (17.5) |
| • 16–20 | 4 (10.0) | 2 (5.0) | 6 (7.5) |
| • more than 20 | 1 (2.5) | 2 (5.0) | 5 (6.3) |
| Average duration of illness (in years) | 6.6 ± 1.0 | 6.65 ± 1.05 | 6.62 ±1.02 |
| **Radiological assessment (Kellgren)** | | | |
| • Stage I | 11 (27.5) | 14 (35.0) | 25 (31.3) |
| • Stage II | 24 (60.0) | 23 (57.5) | 47 (58.8) |
| • Stage III | 5 (12.5) | 3 (7.5) | 8 (10.0) |
| **Functional joint impairment** | | | |
| • Stage I | 11 (27.5) | 10 (25.0) | 21 (26.3) |
| • Stage II | 21 (52.5) | 25 (62.5) | 46 (57.5) |
| • Stage III | 8 (20.0) | 5 (12.5) | 13 (16.3) |
| **Joints affected** | | | |
| • right | 5 (12.5) | 2 (5.0) | 7 (8.8) |
| • left | 6 (15.0) | 10 (25.0) | 16 (20.0) |
| • both | 29 (72.5) | 28 (70.0) | 57 (71.3) |
| **Synovitis (number of joints)** | (n = 80) | (n = 80) | (n = 160) |
| • subclinical | -- | -- | -- |
| • mild | 24 (30.0) | 15 (18.8) | 39 (24.6) |
| • moderate | 11 (13.8) | 13 (16.2) | 24 (15.1) |
| • severe | 5 (6.2) | 12 (15.0) | 17 (10.7) |
| **Total number of joints** | | | |
| • with synovitis | 40 (50) | 40 (50) | 80 |
| • with periarthritis | 60 (75) | 56 (70) | 116 |
| • with tendinitis | 29 (36.25) | 30 (37.5) | 59 |

Tab. 1: Patient demographic and medical history data

- Patient's rating of knee joint pain on a 100 mm visual analog scale (VAS): 0 mm = no pain, 100 mm = unbearable pain
- Knee joints painful to the touch: 0 = no pain, 1 = slight pain, 2 = severe pain
- (Morning) stiffness (duration in minutes)
- Circumference of the upper, central, and lower thirds of the knee joint (in cm)
- Range of motion of the knee joint (goniometry); normal: 35–45° bent, 180° extended
- Time it takes the patient to walk 30 m in a straight line (in seconds)
- Time it takes the patient to walk up and down a flight of 10 stairs (in seconds)

Tab. 2: Criteria for assessing severity of knee osteoarthritis

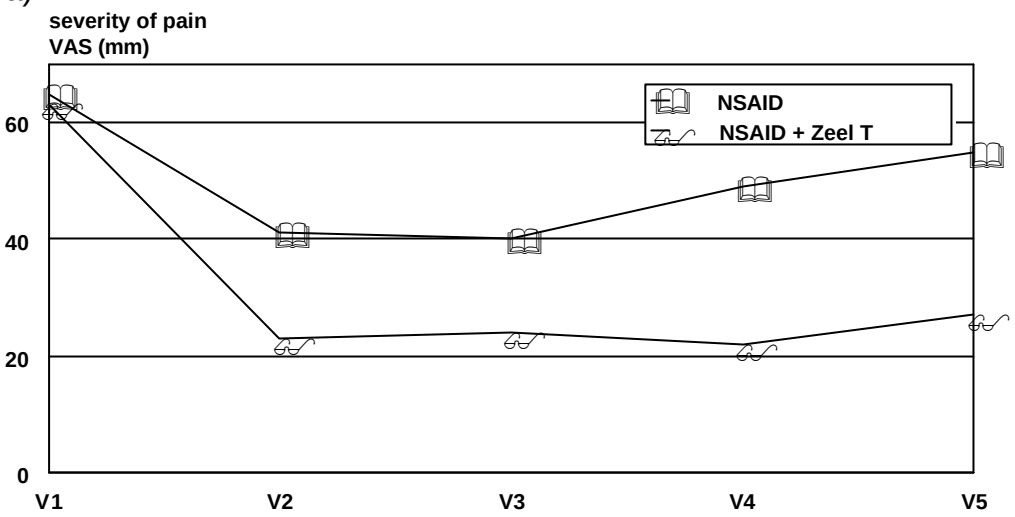
| | **Observation Period** | | | |
|---|---|---|---|---|
| | **on conclusion of therapy** | **3 months after therapy** | **6 months after therapy** | **12 months after therapy** |
| **Group 1 (NSAID)** | | | | |
| • Joints with synovitis | n = 40: 1 (2.5%) | n = 40: 6 (15.0%) • | n = 40: 7 (17.5%) • | n = 18: 9 (50.0%) • |
| • Joints with periarthritis | n = 29: – | n = 29: 4 (13.8%) • | n = 29: 6 (20.7%) • | n = 16: 7 (43.8%) • |
| **Group 2 (NSAID +Zeel T)** | | | | |
| • Joints with synovitis | n = 40: – | n = 40: 3 (7.5%) | n = 40: 5 (12.5%) | n = 20: 4 (20.0%) + |
| • Joints with periarthritis | n = 30: – | n = 30: 1 (3.3%) | n = 30: 3 (10.0%) | n = 15: 2 (13.3%) + |

Tab. 3: Change in symptoms over the entire observation period. For each subgroup, n (= total number of treated joints) is followed by the number and percentage of joints with the respective symptoms after therapy. + = differs significantly from Group 1; • = differs significantly from figures for the same group on conclusion of therapy ($p < 0,05$ Wilcoxon-U test)

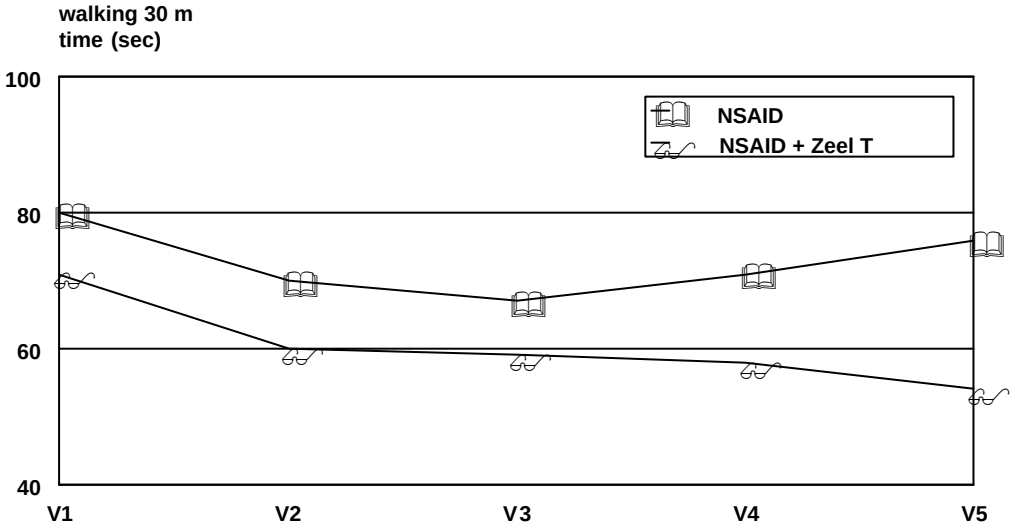
| Groups | Observation Period | | | | |
|---|---|---|---|---|---|
| | **before therapy** | **after therapy** | **3 months after therapy** | **6 months after therapy** | **12 months after therapy** |
| Group 1, joints predominantly with synovitis | n = 40: 32 (80%) | n = 40: 27 (67.5%) | n = 40: 28 (70.0%) | n = 40: 25 (62.5%) | n = 18: 12 (66.7%) |
| Group 2, joints predominantly with synovitis | n = 40: 32 (80%) | n = 40: 18 (45.0%) + / * | n = 40: 16 (40.0%) + / * | n = 40: 17 (42.5%) + / * | n = 20: 10 (50%) + / * |
| Group 1, joints predominantly with tendinitis | n = 29: 11 (38%) | n = 29: 12 (41.4%) | n = 29: 10 (34.5%) | n = 29: 10 (34.5%) | n = 16: 9 (56.2%) |
| Group 2, joints predominantly with tendinitis | n = 30: 15 (50%) | n = 30: 6 (20.0%) * | n = 30: 4 (13.3%) * | n = 30: 4 (13.3%) * | n = 15: 4 (26.7%) + |

Tab. 4: Change in the symptoms “synovitis” and “tendinitis” over the entire observation period. For each subgroup, n = total number of treated joints is followed by the number and percentage (in parentheses) of joints with the respective symptom as confirmed by ultrasound examinations. Group 1 = NSAID; Group 2 = NSAID + Zeel T; + = differs significantly from Group 1, * = differs significantly from figures for the same group on conclusion of therapy, $p < 0,05$ Wilcoxon-U test)

a)


severity of pain
VAS (mm)
NSAID
NSAID + Zeel T
60
40
20
0
V1
V2
V3
V4
V5

b)


walking 30 m
time (sec)
NSAID
NSAID + Zeel T
100
80
60
40
V1
V2
V3
V4
V5

c)

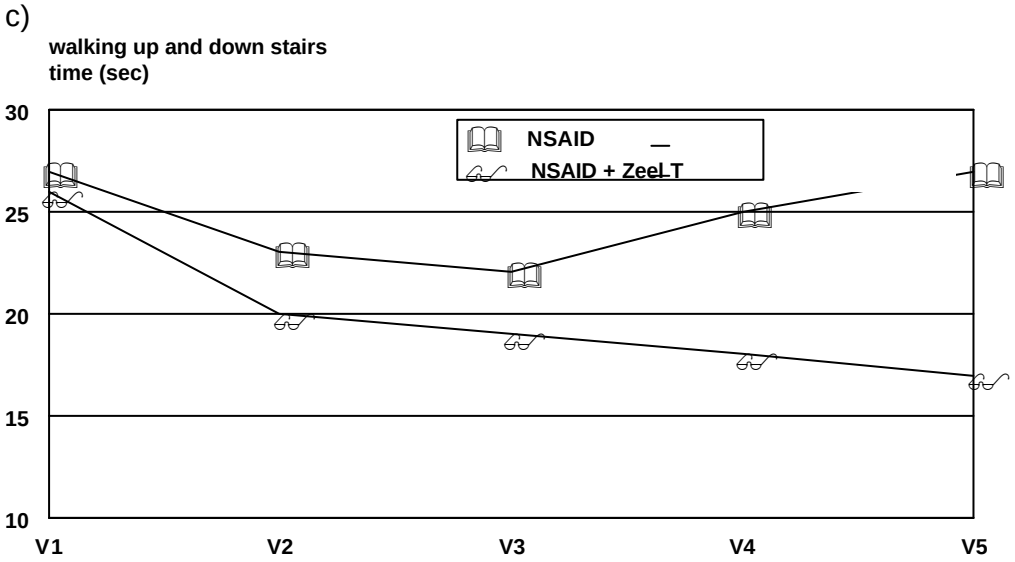
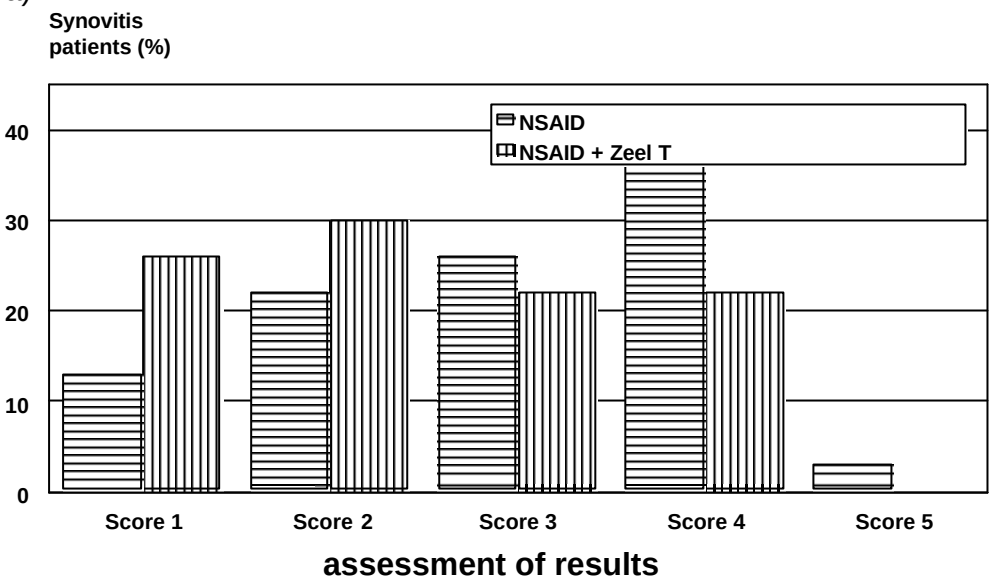

walking up and down stairs
time (sec)
NSAID
NSAID + Zeel T
30
25
20
15
10
V1
V2
V3
V4
V5

Fig. 1: Changes in clinical findings. a) severity of pain as rated by the patients on a 100 mm visual analog scale (VAS); b) time required for patient to walk 30 m; c) time required to walk up and down stairs (10 steps). V1 = first visit, before beginning therapy; V2 = on conclusion of therapy; V3 = 3 months after therapy; V4 = 6 months after therapy; V5 = 12 months after therapy.

a)




b)

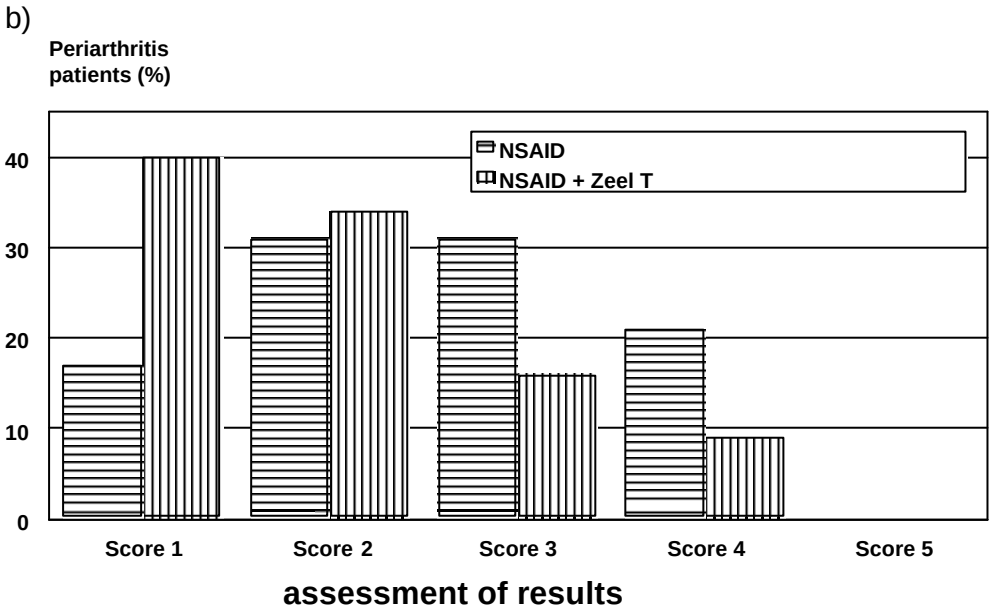



Fig. 2: Results of therapy within the patient subgroups with synovitis (a) and periarthritis (b). Score: 1 = very good improvement, 2 = good improvement, 3 = slight improvement, 4 = no change in symptoms, 5 = symptoms worsened