

Periarticular Therapy of Gonarthritits

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Abstract

This prospective study collected data on modes of application, efficacy, and tolerance of Zeel[®] administered via periarticular injection. In all, 48 established orthopedists took part in the study, treating a total of 643 patients with gonarthritits, arthritis of the knee. The majority of patients received twice-weekly periarticular injections of one ampule of Zeel[®] for a period of 4-6 weeks.

Results

Over the course of treatment, initial pain, pain after exercising, continuous pain, and joint stiffness decreased linearly in the majority of patients. Upon conclusion of treatment, 81% of patients achieved positive therapeutic results. Zeel[®] was well tolerated, even in combination with concomitant drug therapies.

Introduction

Because subjective experiences of pain and other symptoms vary greatly from person to person, patients suffering from degenerative rheumatic joint disorders (arthritis) first seek the help of orthopedists or family practitioners at widely differing stages in the development of symptoms. The first clinical signs of possible arthritis are fleeting pains in a joint or muscles after moderate exercise or exposure to damp cold. Symptoms that occur during movement, such as pain due to warm-up, fatigue, or exertion, are typical and are often combined with a feeling of stiffness.

As a general rule, orthopedic treatment of arthroses (and gonarthritits in

particular) tends to be conservative or minimally invasive. The choice of conservative forms of therapy for knee arthritis includes electrotherapy, topical treatments, hydrotherapy, and physical therapy. In addition, mechanical orthopedic aids can often be helpful. However, these forms of therapy alone do not always achieve the desired degree of success; frequently, intra-articular injections of medications to improve intra-articular tissue nourishment are implemented. Among physicians, however, there are different views on the relative risks and benefits of intra-articular injection. Many physicians hesitate to administer such injections because of the risks, especially the danger of infection.^{1,2}

The primary goal of the current prospective study was to answer the question of whether gonarthritits can be treated both reliably and with good tolerance by means of periarticular injections of Zeel[®]. Zeel[®] (manufactured by Biologische Heilmittel Heel GmbH, Baden-Baden) is a homeopathic combination preparation that improves joint function, relieves articular and muscular pain, and has a regenerative effect on

fibrous tissue. It also has an anti-inflammatory effect. A randomized clinical study has already confirmed the therapeutic efficacy of this homeopathic medication when administered to knee arthritis patients via intra-articular injection.³

Methods

Implementation

Because a prospective study is a monitoring study intended to gather information about the use of approved or registered drugs, and because such a study typically attempts to avoid influencing the individual physician-patient relationship any more than necessary, no more comprehensive criteria for inclusion or exclusion were defined. (For parameters of the study see Table 1). This way of proceeding was also intended to assure that the patient population was as unselected as possible.

The prospective study was structured to monitor the course of treatment - i.e., at each visit the physicians were to assess the severity of the primary clinical symptoms of gonarthritits (stiffness of the knee

• time period	February 1996-June 1996
• place	Germany
• physicians	48 orthopedists
• total number of questionnaires sent out	727
• total returned	643 (88.4%)
• structure	outcome study
• observation period per patient	maximum of 10 periarticular injections
• criteria for inclusion	confirmed diagnosis of arthritis, periarticular administration of Zeel [®]
• criteria for exclusion	none
• documentation	standardized questionnaire
• number of patients per physician	minimum 5, maximum 15

Tab. 1: Parameters of the prospective study

joint, pain during warm-up or exercise, continuous pain). (Scale: 0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe). The success of treatment was evaluated by the physicians on the basis of two criteria:

- the point in time when general improvement in symptoms occurred
- overall assessment of the therapeutic results achieved

(Scale: very good = complete freedom from symptoms; good = noticeable improvement; satisfactory = slight improvement; no success = symptoms remained the same or worsened.) In addition, patient tolerance of Zeel® was to be evaluated upon completion of treatment. (Scale: excellent, good, moderate, and poor.) Undesired incidents were to be reported on a separate questionnaire.

Processing and statistical evaluation of data

Although in individual cases certain information was missing (e.g., gender, age, or occupational degrees of physical activity), all 643 of the cases recorded were suitable for statistical analysis. With the help of the computer program REPORT (IDV/Gauting Co.), the recorded data were compiled and descriptively evaluated. The degrees of severity recorded at each office visit on a scale of 0-3 with regard to each symptom (stiffness of the knee joint, pain during warm-up and exercise, and continuous pain) were totaled and the resulting values divided by the number of patients to yield collective symptom scores per visit and per symptom. These score values were then analyzed for structure by means of regression analysis. The resulting correlation coefficient (r) is a measure of the relationship between two variables (in this case symptom severity and frequency of treatment). The closer the correlation coefficient is to 1, the more linear is the relationship between the two variables ($r = 0$ indicates no relationship).

This statistical evaluation was carried

Criteria	Number of Patients			
	w = 58.3%	m = 41.2%	n.r. = 0.5%	n.r. = 0.4%
Gender	w = 58.3%	m = 41.2%	n.r. = 0.5%	n.r. = 0.4%
Age (years)	<51 = 26.2%	51-70 = 53.2%	>70 = 20.2%	n.r. = 0.4%
Overweight	yes = 42.0%	no = 57.9%	n.r. = 0.1%	n.r. = 9.8%
Occupational activity	physically active = 42.3%	not physically active = 47.9%	n.r. = 0.2%	n.r. = 0.1%
Duration of illness (years)	<1 = 26.6%	1-5 = 40.9%	>5 = 32.3%	n.r. = 0.2%
Knee joint affected	right = 35.5%	left = 31.6%	both = 32.8%	n.r. = 0.1%
Severity of arthritis	mild-moderate = 64.9%	severe = 26.9%	very severe = 7.9%	n.r. = 0.3%
Local signs of inflammation	yes = 44.2%	no = 55.8%		
Previously treated	yes = 77.9%	no = 22.1%		

Tab. 2: Characteristics of the patient population ($n = 643$; n.r. = not reported)

out for the following samples:

- total group
- patients receiving this treatment as their only form of therapy
- patients receiving concomitant external therapies
- patients receiving both pharmaceutical and external concomitant therapies
- patients receiving concomitant pharmaceutical therapy

Results

Patient demographics

The patients admitted to the study were primarily women (58%) and people over 51 years old. Typically, their symptoms had persisted for more than a year before admission to the study. The majority of patients were suffering from moderate (46%) to severe (27%) gonarthrosis (Table 2). Stiffness of the knee joint was present in 63% of the patients, while pain during exercise was experienced by 95% of the patients, pain during warm-up by 80%, and continuous pain by 56%. Local signs of inflammation in the knee (warmth, pain, redness, joint exudate) were diagnosed in 4 out of 10 patients on initial examination. In 65% of the patients, degenerative damage (due to obesity, heavy physical labor, or sports, for example) was listed

as the primary cause of the arthritis. Other frequently listed causes were age-related changes and changes due to metabolic disorders, as were secondary joint deformations such as those resulting from inflammatory joint diseases.

A total of 78% of the patients had already received pharmaceutical and/or external therapy prior to admission to the study. Among the most frequently used pharmaceuticals were NSAIDs, corticosteroids, other antirheumatics, and Zeel® P. The dominant forms of conservative therapy were electrotherapy and treatment with cold packs.

Treatment with Zeel®

Sixty percent of the patients were given two periarticular injections per week, while 26% received one injection per week and 11% received three injections per week. In 67% of cases a single ampule (2 ml) of Zeel® was administered at each injection. In 46% of cases, the Zeel® was combined with a local anesthetic. Duration of therapy varied, ranging from <1 week to >12 weeks, with the largest number of patients (42%) being treated for a period of 4-6 weeks. The injections of Zeel® were the only therapeutic measure implemented for 49% of the patients. For the remaining 51%, concomitant pharmaceutical therapy (mainly NSAIDs, corticosteroids, other antirheumatics, Zeel® in tablet form or as

an ointment) and/or external therapies (mainly electrotherapy and treatment with cold packs) were implemented (Table 3). Concomitant therapies were most frequently implemented in the case of patients whose illness had been judged as severe to very severe.

The degrees of severity of clinical symptoms reported at the beginning of treatment (base values for visit 1) make it clear that for most patients, pain during exercise figured most prominently, followed by pain during warm-up, stiffness, and continuous pain (Figure 1). The linear decrease in symptoms presented in the Figure signifies that the degrees of severity of these four clinical symptoms declined as the duration or frequency of treatment increased. This linear relationship between change in symptoms and duration of treatment held good for all patients, with and without concomitant therapies (Table 4).

Results of therapy

Evaluating the criterion "point in time when global improvement of symptoms first occurred" revealed that global improvement occurred in 40% of the patients after only 1-4 injections and in an additional 42% after 5-8 injections. These estimates are confirmed by the overall assessment of the therapy provided by the physicians at the conclusion of treatment: freedom from symptoms in 15%, significant improvement in symptoms in 41%, and slight improvement in 25% of the patients (Table 5).

The lower success rates shown in Table 5 for the group that received concomitant medication can be explained by the

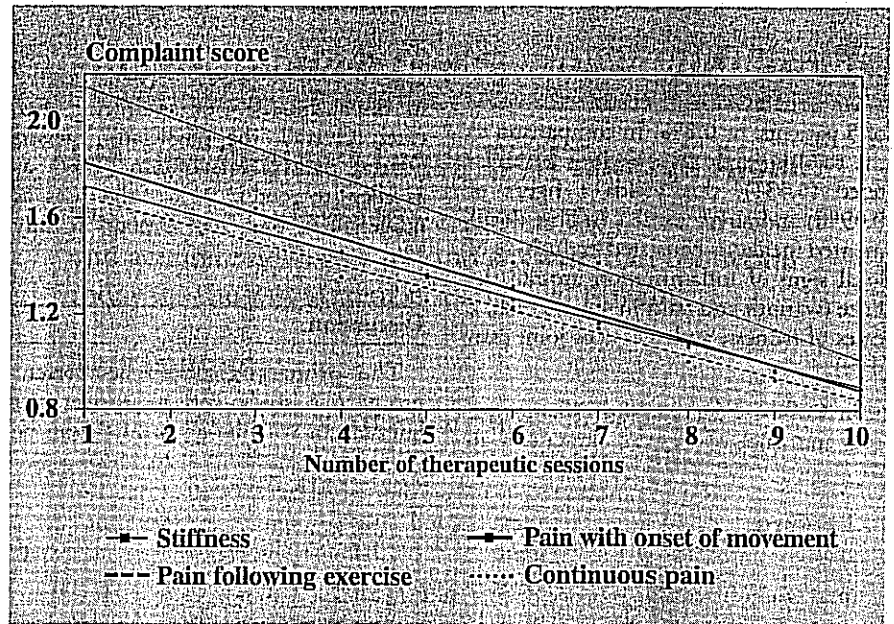


Fig. 1: Change in the symptom score for the entire patient population as a function of number of visits or frequency of treatment.

fact that patients with severe and very severe symptoms were the ones most likely to be treated with additional medications, and that the prognosis for this group was therefore worse from the start. This becomes evident when the therapeutic results achieved are sorted according to initial degree of severity of the patients' arthritis (Table 6).

Whereas in cases of mild to moderate arthritis, significant improvement or even complete freedom from symptoms was achieved in 60-70% of the patients, the corresponding success rates for patients with severe and very severe forms of the illness were strikingly lower, at 28-45%.

Treatment groups	Number of patients
Zeel® (as the only therapy)	314 (48.8%)
Zeel® + concomitant external therapy	187 (29.1%)
Zeel® + concomitant pharmaceutical and external therapies	110 (17.1%)
Zeel® + concomitant medication	32 (5.0%)

Tab. 3: Numerical breakdown of the different treatment groups (n = 643)

Criteria observed	Total group therapy (n = 643)	Patients w/ single therapy (n = 314)	Patients w/ external (n = 187)	Patients w/ pharm./external (n = 110)	Patients w/ pharmaceutical (n = 32)
stiffness (knee)	r = 0.997	r = 0.998	r = 0.993	r = 0.990	r = 0.991
pain (warm-up)	r = 0.992	r = 0.995	r = 0.986	r = 0.986	r = 0.959
pain (exercise)	r = 0.989	r = 0.992	r = 0.991	r = 0.993	r = 0.984
pain (continuous)	r = 0.991	r = 0.984	r = 0.972	r = 0.990	r = 0.943

Tab. 4: Relationship between change in symptoms (degree of severity) and frequency of application for the various treatment groups (r = correlation coefficient)

Tolerance

Undesired incidents occurred in a total of 5 patients, or 0.8%. In comparison to the total number of injections administered (5,531), this yields a figure of 0.09% undesired results. The documented incidents consisted exclusively of local signs of inflammation around the knee (warmth and pain in 4 cases each, 2 cases of redness, and 1 case of joint exudate).

In 4 of these 5 cases, anti-inflammatory and analgesics were prescribed in

addition to conservative treatment with ice. In all 5 cases, the undesired results were reversible. These incidents resulted in discontinuation of treatment in 2 cases. Overall, the physicians assessed general patient tolerance of Zeel® as excellent to good in 94% of the cases, as moderate in 5%, and as poor in only 1%.

Discussion

The primary goal of the present prospective study was to answer the question of whether gonarthrosis can be

treated reliably and with good tolerance using periarticular injections of Zeel®. To answer this question, data on the treatment of a total of 643 gonarthrosis patients were compiled and analyzed. The age (73% more than 50 years old) and gender distribution (58% women) in this patient population confirm the experience that older persons and especially women tend to suffer from degenerative joint symptoms. The main causes of arthritis named by this study (degeneration, aging, metabolic disorders) are typical of this illness. The data confirm that the patients taking part in this prospective study constituted a representative sample with regard to both etiology and age/gender distribution.

To permit us to judge the success of the treatment, degree of severity of each of the four most important clinical symptoms of arthritis (stiffness in the knee joint, pain during warm-up, pain during exercise, continuous pain) was assessed individually and on an ongoing basis by the physicians at each office visit. The numerical results of their observations confirm that scores for all four symptoms declined noticeably and in a linear fashion over the course of treatment. As a rule, the clear symptomatic improvement that was observed was achieved at an average treatment frequency of two injections per week (one ampule per injection) for a period of 4-6 weeks. In this context, it is worth noting that 49% of the patients received Zeel® as their only therapy. As a result, we can give an affirmative answer to the question of whether it is possible to treat gonarthrosis reliably with periarticular Zeel®. This is especially true in mild to moderate cases of the illness. Incidentally, this prospective study confirms the results of Potrafki's study inves-

Treatment group	Results of therapy					
	very good	good	satisfactory	no success	worse	not reported
total group (n = 643)	15.3	40.8	25.3	16.6	1.1	0.9
single therapy (n = 314)	15.9	41.4	22.9	17.5	1.0	1.3
patients w/concomitant external therapy (n = 187)	19.8	40.1	25.7	13.3		1.1
patients w/concomitant pharm./external therapy (n = 110)	7.3	41.8	32.7	14.6	3.6	
patients w/concomitant pharmaceutical therapy (n = 32)	9.4	34.4	21.8	34.4		

Tab. 5: Overall results of therapy as a function of the type of treatment (figures in percent)

Severity of the arthritis	Results of therapy					
	very good	good	satisfactory	no success	worse	not reported
mild (n = 124)	37.1	33.9	15.3	11.3	2.4	
moderate (n = 293)	12.3	49.5	25.6	11.6	0.7	0.3
severe (n = 173)	8.7	35.8	29.5	22.5	0.6	2.9
very severe (n = 51)	2.0	25.5	31.3	39.2	2.0	

Tab. 6: Overall assessment of therapy as a function of the degree of severity of the knee arthritis (figures in percent)

Preparation	Indication/mode of administration	Number of patients	Clinical Symptoms			
			Stiffness (knee joint)	Pain (warm-up)	Pain (exercise)	Pain (continuous)
Zeel® ¹⁾	arthritis/i.a.	1845	r = 0.988	r = 0.990	r = 0.990	r = 0.985
Zeel® ²⁾	arthritis/i.a.	446	r = 0.995	r = 0.996	r = 0.988	r = 0.988
Zeel® ³⁾	arthritis/p.a.	643	r = 0.997	r = 0.992	r = 0.989	r = 0.991

Tab. 7: Relationship between change in symptoms (degree of severity) and frequency of application in arthritis (r = correlation coefficient); a comparison of the results of three prospective studies (¹see reference 5; ²see reference 6; ³see the present study)

tigating the possibility of using Zeel® P for periarticular therapy of arthritis.⁴

Comparing the correlation coefficients resulting from this study with correlations derived from equivalent prospective studies on Zeel® P⁵ and Zeel® confirms that periarticular and intra-articular administration are of equal therapeutic value (Table 7). Thus periarticular treatment of arthritis with Zeel® can be implemented as an alternative to intra-articular administration.

The results of the present prospective study are also of interest in view of the criticism that has been leveled at intra-articular administration. For years, the risk/benefit ratio of this mode of application has been seen as unfavorable from various points of view. This criticism is not justified, however, as empirical studies by Anders⁷ and Bernau^{8,9} demonstrate. Both authors come to the conclusion that the probability of articular empyema resulting from intra-articular administration amounts to only 0.034-0.035% (1: 34,000 to 1:35,000). Absolute prerequisites for the implementation of intra-articular application, however, are absolute certainty that the treatment is indicated and observing strict standards of hygiene.¹⁰ These standards were published as early as 1988 by the German Society for Orthopedics and

Traumatology and by the Professional Association of Orthopedic Physicians.¹¹

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