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Treatment of Osteoarthritis of the Knee with Zeel T

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Summary

In a drug monitoring study 100 patients were treated for osteoarthritis of the knee with the homeopathic remedy Zeel T (injection solution). The duration of treatment ranged from 2 to 8 weeks (97% of the patients) with a maximum for a 4–6 weeks treatment (58%). The majority of patients revealed fast improvement of the symptoms, with 76% reporting improvement after 6 injections. The clinical symptoms were reduced significantly and in a linear manner. Correlation coefficients showed a high correlation between the number of injections and the relief in symptoms. The general efficacy of the treatment was assessed by the investigators as 'very good' or 'good' in 70% the cases. The tolerability assessment of Zeel T by the investigators was 'excellent' or 'good' in 92% of the cases.

Key words: Osteoarthritis of the knee, drug monitoring study, Zeel T

Introduction

Besides cardiovascular diseases, rheumatic diseases are among the most frequent chronic illnesses nowadays with increasing incidence due to growing life expectancy, unhealthy life habits like lack of exercise, overstrain, imbalance of joint function and overweight. Numerous different types of such diseases exist, but they all include one predominant common symptom: pain.

Osteoarthritis of the knee (gonarthrosis) is a heterogeneous condition caused by degenerative processes and can lead to irreversible and progressive damage of the joint cartilage and bone. Therefore osteoarthritis of the knee is a leading cause of chronic disability in many countries with numerous consultations in the practice of general practitioners and orthopedists, particularly by elderly patients. The incidence and prevalence of osteoarthritis of the knee increases with age, with a strong increase beginning around age 50 (1). It is obvious, that the chronic character of the disease in combination with the intensity of the leading symptom "pain" significantly contributes to costs in public health and is a frequent reason for days off work.

According to the multifactorial causes for the degeneration processes, cure or significant alteration of the underlying disease is not possible in most cases (2). Therapy for osteoarthritis of the knee is therefore primarily directed at decreasing pain and increasing joint function (3). Pharmacological and physical interventions, as well as general measures (eg. weight reduction) are often combined in the medical management of osteoarthritis of the knee to relief at least modestly the pain symptoms (4).

Conventional pharmacological therapy is mainly based on the administration of nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, and corticosteroids. NSAIDs have demonstrated efficacy in clinical trials (5) but significant gastrointestinal complications have been observed in conjunction with the use with these compounds. Chronic NSAID use frequently leads to irritations of the mucosa of the gastro-intestinal tract. Lesions, ulceration and bleeding are serious side effects (6).

A safe and effective treatment of osteoarthritis of the knee has been achieved with the homeopathic remedy Zeel. This could be demonstrated by several drug monitoring studies and clinical studies according to GCP guidelines. Comparative trials versus Diclofenac and hyaluronic acid revealed equivalent efficacy of Zeel with the comparators and excellent safety results (7–11). Zeel is a homeopathic combination preparation (manufactured by Biologische Heilmittel Heel GmbH, Baden-Baden, Germany). Recently, a prospective drug monitoring study was conducted including 100 patients whose results are reported here. The intention was to ascertain further data on the therapeutic potential of Zeel T (injection solution) under conditions of daily routine treatment (Table 1).

Methods

According to the character of the study, the investigators were free to enter any patient suffering from osteoarthritis of the knee without any further inclusion or exclusion criteria, to reflect the real treatment situation of the patients. The respective study data was ascertained during a screening and a termination visit of the patient, and entered into a specific patient document form.

Constituents	Pharmacological/clinical notes
Extr. (1:10) of <i>Cartilago suis</i>	Arthrosis deformans, coxitis, peri-arthritis humeroscapularis
Extr. (1:10) of <i>Funiculus umbilicalis suis</i>	Damage to connective tissues, circulatory disorders
Extr. (1:10) of <i>Embryo suis</i>	For revitalization in the cellular phases
Extr. (1:10) of <i>Placenta suis</i>	Circulatory disturbances, pernios
<i>Rhus toxicodendron</i>	Rheumatism and neuralgia, worse in cold, wet weather; polyarthritis, diseases of the mucosa and connective tissues
<i>Arnica</i>	To stimulate the healing of wounds, rheumatism, injuries arising from falls, blows or contusions; pains in the back and limbs
<i>Dulcamara</i>	Remedy to counteract the effects of wet weather sensation of having caught a chill, rheumatic disorders
<i>Symphytum</i>	Injuries to the tendons, ligaments and periosteum; acts on the joints in general, neuralgia of the knee
<i>Sanguinaria</i>	Neuralgic and rheumatoid pains of the joints and muscles
<i>Sulfur</i>	Reagent in all chronic diseases; cellular activity is influenced catalytically
<i>Nadidum</i>	Coenzyme, stimulation of the end oxidation in the respiratory chain
<i>Coenzyme A</i>	Coenzyme for transacetylation
<i>Acidum alpha-liponicum</i>	Coenzyme in the decomposition of pyruvic acid
<i>Natrium diethyloxalacetikum</i>	Active factor of the citric acid cycle and of redox systems; sensitivity to damp and wind

Tab. 1: Constituents and pharmacological/clinical notes of the single constituents of Zeel T (injection solution).

During the screening visit, the following data was compiled: demographic data, vital signs, risk factors, concomitant diseases, pre-duration of the examined disease, determination of the affected knee joint (in the case that both knee joints were affected, only the one which caused most pain was assessed), possible pre-treatment (medical/physical), and cause for the osteoarthritis.

To document baseline data for the assessment of efficacy, the intensity of the complaints (joint stiffness, starting pain (pain upon onset of movement), pain on exercise, and permanent pain) was assessed according to the following 4-point rating scale: none, slight, moderate, severe. During the course of the drug monitoring study the investigators continuously had to assess the intensity of the symptoms after each injection treatment.

Further data was ascertained with regard to the mode and planned number of injections per week, the planned number of ampoules per injection, possible concomi-

tant treatment (medical/physical), and occurrence of side effects.

For efficacy assessments the patients and the investigators assessed the efficacy of the treatment according to a 5-point rating scale: very good (no more complaints), good (significant improvement), moderate (slight improvement), without success (no change) or deterioration. For tolerability assessments by patients and investigators a 4-point rating scale was used: very good, good, moderate or bad.

Results

Patients

In total, 100 patients suffering from osteoarthritis of the knee took part in this study (78% females). According to the character of the disease, the majority (68%) of the patients was older than 60 years of age. For more than half of the patients, specific risk factors were identified (overweight for 55% of the patient population). Concomitant diseases occurred in 58%, in particular hypertension, osteo-

porosis, diabetes mellitus, and ischemic cardiopathy.

It became obvious from the documentation of the pre-duration of the disease, that in most cases the osteoarthritis of the knee was chronic and was lasting for several years (69% of the patients had such specific complaints for more than 2 years). Both knee joints were affected in 12% of the patients. When presenting to the investigator the intensity of the patients symptoms was moderate or severe in 68% of the patients treated. Very severe complaints still occurred in 19% (slight complaints: 9%, no data available: 4%). Multiple symptoms were reported from the patients concerning the osteoarthritis disease: pain on exercise (97%), starting pain (92%), stiffness (74%), and permanent pain (67%).

The investigators were asked to specify the reasons which presumably caused the complaints in conjunction with the disease. Wear and tear was documented most often (81%), followed by congenital dysplasia (22%), joint deformity (14%) and endogenous disorders (8%) (Table 2).

Only 9% of the patients did not have any pre-treatment before they entered the drug monitoring study. The majority of the patients was pre-treated either medical (16%), physical (7%), or both, medical and physical (68%). In the case of a medical treatment, NSAIDs, chondroprotectives and corticosteroids, and in the case of a physical treatment electrotherapy, balneotherapy and therapeutic exercise were prescribed most frequently.

Treatment

The mode of application of Zeel T was almost uniform. In all of the cases the investigators injected Zeel T periarticularly. The planned regular interval of injections was 2 injections per week (86%). With regard to the number of ampoules which were injected per visit, 1 ampoule/injection (71%) was preferred. The duration of the treatment with Zeel T predominantly was 4–6 weeks (58%). Almost $\frac{3}{4}$ of the patients (72%) received Zeel T as monotherapy without any further concomitant medica-

tion. In the case, that a co-therapy was considered, this was a physical therapy (68%) rather than a medical (28%) or combined medical and physical (4%).

Efficacy parameters

At each visit of the patients, before injecting Zeel T, the investigators assessed the specific symptoms associated with the osteoarthritis disease: pain on exercise, starting pain, stiffness, and permanent pain. The intention was to continuously evaluate the intensity of the specific symptoms during the course of the treatment. Pain on exercise and starting pain were the most prominent symptoms at study start. The evaluation of the intensity of the symptoms revealed a linear reduction, depending on the frequency of application. After 10 injections, each of the parameters was significantly improved (Fig. 1). This was also documented by the calculation of correlation coefficients demonstrating a high and direct correlation between the frequency of application and the improvement in the intensity of symptoms (Table 3).

The time-point of first significant improvement of the symptoms was assessed as one of the further parameters to ascertain the therapeutical potential of Zeel T. According to the results mentioned above, the highest percentage of patients was obtained already after 2 to 5 injections (67%), with a maximum after 5 injections (22%). In total, for 89% of the patients significant improvements were reported during the course of the injection series.

The therapy was assessed (investigators/patients) as very good in 23% / 24%, good in 47% / 37%, and moderate in 19% / 24% of the cases. Therefore, it was stated by the investigators, that the therapy result was clinically relevant in 84% of the cases.

Tolerability

The patients compliance was excellent, considering the fact, that the therapy consisted of 10 successive injection applications. 96% of the patients terminated the treatment according to the treatment scheme. Side effects were reported for 2 patients, who complained about painful

Intensitiy of osteoarthritis of the knee					
	slight	moderate	severe	very severe	no data available
Total (%)	9	32	36	19	4
Cause of osteoarthritis of the knee					
	wear and tear	endogenous disorders	congenital dysplasia	joint deformity	others
Total (%)	81	8	22	14	11
Symptoms					
	stiffness	starting pain	pain on exercise	permanent pain	others
Total (%)	74	92	97	67	34

Tab. 2: Baseline parameters of patients entered into the drug monitoring study (N = 100)

injection procedures. The tolerability of Zeel T was assessed as very good by 79% and as good by 13% of the investigators (no data available: 8%). The results obtained from patients assessment were as follows: very good = 65%, good = 26%, moderate = 6%, bad = 1% (no data available: 2%).

Discussion

The incidence and prevalence of osteoarthritis of the knee increase with age. The disease is a leading cause of chronic disability and often associated with severe and progressive pain conditions. A causal therapy seems not to be possible up to now, therefore drug therapy and physical

treatment of osteoarthritis is primarily directed towards relief of pain and functional limitations. The most frequent medical approach is the use of analgetics and nonsteroidal anti-inflammatory drugs (NSAIDs) to provide short-term pain relief. Long-term treatment with currently used NSAIDs significantly increases the risk of severe gastrointestinal side effects like lesions, ulceration and bleeding due to the known gastrotoxic potential of these compounds. Better tolerability seems to be possible with specific COX-2 inhibitors, but experiences with long-term treatment are still lacking.

The drug monitoring study reported here

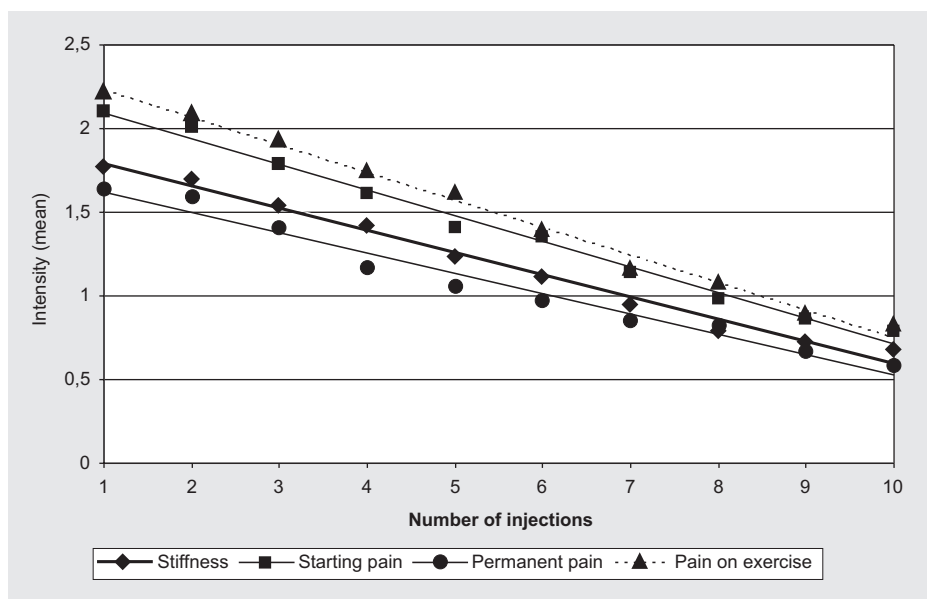


Figure 1: Change in the assessment of symptoms during treatment (no. of injections). No symptom = 0, slight symptom = 1, moderate symptom = 2, severe symptom = 3

Clinical symptoms	Correlation coefficients
Stiffness	$r = 0.994$
Starting pain	$r = 0.995$
Pain on exercise	$r = 0.996$
Permanent pain	$r = 0.987$

Tab. 3: Correlation between the change in the assessment of the clinical symptoms and the frequency of injections (improvement by 10 injections during the study course, r = correlation coefficient)

was performed to obtain additional data on the efficacy and tolerability of the homeopathic remedy Zeel T in the treatment of osteoarthritis of the knee under the conditions of daily routine practice. Several studies have already been performed with Zeel P and Zeel comp., preparations with similar compositions to Zeel T. Very recently, a clinical randomised multicenter-study according to GCP guidelines was performed, which revealed that the clinical efficacy capacity (evaluation of the WOMAC osteoarthritis index) of Zeel comp. was equivalent to Diclofenac (7). Another randomised clinical study (8) compared Zeel comp. and hyaluronic acid. Also in this study, equivalence was obtained with regard to pain relief between the homeopathic remedy and the standard drug. In addition to the randomised clinical studies, several drug monitoring studies were performed and demonstrated the excellent therapeutic effects of Zeel in the treatment of patients with osteoarthritis of the knee (9–11).

The results of the earlier investigations could be confirmed in this drug monitoring study. As expected, the majority of patients in this study was female, older than 60 years of age and suffered from chronic osteoarthritis with a pre-duration of several years and marked pain conditions. To characterise the efficacy potential of Zeel T injection solution, the most

relevant clinical symptoms were used: pain on exercise, starting pain, permanent pain and stiffness. A series of 10 injections resulted in clinically meaningful improvements. It was demonstrated that the symptoms were reduced significantly and in a linear manner. Correlation coefficients showed a high correlation between the number of injections and the relief in symptoms.

The data also revealed that a therapy with Zeel T resulted in a considerable fast improvement of the symptoms, with 76% of the patients reporting improvement already after 6 injections. Considering the fact, that a frequency of 2 injections per week was preferred, a 3 weeks therapy with the homeopathic remedy leads to remarkable improvements in the patients conditions. The benefits of a treatment with Zeel T was also reflected by the investigators and patients positive general assessment of efficacy. Besides the satisfactory efficacy results, the tolerability of the remedy was assessed as very good or good in more than 90% of the cases with excellent compliance of the patients.

Zeel T (injection solution) therefore can be considered as a valuable remedy for the treatment and disease control of osteoarthritis of the knee based on many years of medical experience.

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