The Biological Treatment of Articular Affections

Results of a Study Conducted with 498 Patients

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Summary:

This prospective drug survey investigated the effectiveness of the homeopathic ointment preparation Zeel T, and tolerance to its application, among a total of 498 patients. The largest subset of the total patient population for whom this preparation was employed represented those suffering from monarthrosis, followed by those treated with the ointment for polyarthrosis, spondylarthrosis, periarthropathia humeroscapularis, and other degenerative articular disorders. The physicians participating in this survey administered medicamentous as well as non-medicamentous measures at their own discretion as adjuvant therapy, insofar as they felt such treatment was necessary for the respective symptom pictures. Throughout the course of therapy, the patients experienced rapid and definite relief from such complaints as pain experienced during the night, pain upon onset of motion, and pain during articular movement. The participating physicians assessed the overall results of therapy as either very good or good for 75.1% of the patients. The patients' tolerance to the preparation was good.

1. Introduction

Zeel T* ointment is a homeopathic ointment preparation which was introduced onto the market in 1992. As the successor preparation to Zeel ointment, which had already been commercially available, Zeel T ointment contains a number of active agents from various substance groups. In addition to botanical constituents (Toxicodendron quercifolium, Arnica montana, Solarium dulcamara, Symphytum, and Sanguinaria canadensis), Zeel T ointment also contains homeopathic attenuations of mineral substances (sulfur and acidum silicicum), as well as organ extracts in homeopathic form (Cartilago suis, Funiculus umbilicals suis, Embryo suis, and Placenta suis). Zeel T ointment further contains so-called biocatalyst (nicotinamide-adenindinucleotide, coenzyme A, acidum alpha-liponicum, and sodium diethyloxalaceticum), which in homeopathic concentrations are capable of activating cell and tissue functions.

With respect to the type and concentrations of the pharmaceutically active constituents which it contains, Zeel T ointment coincides to a highly extensive degree to its predecessor product Zeel ointment. The differences between the two preparations consist in the declaration of contents and the legal pharmaceutical status. As a result of changes in German pharmaceutical legislation, new stipulations have gone into effect for the declaration of medication which are also of import for Zeel T ointment as a registered homeopathic medication. New stipulations include the obligation of the manufacturer to declare the constituents in accordance with the official German Homeopathic Pharmacopoeia, and - in cases of registered preparations - the avoidance of listing specific indication information on the package insert.

A number of publications had earlier documented the therapeutic effectiveness of the predecessor preparation Zeel ointment, as used for various indications. [1 - 3] The objective of the present drug survey was to confirm the therapeutic effectiveness of the newly registered preparation Zeel T ointment under conditions of medical practice, for the primary indication areas for Zeel ointment - e.g., arthrosis, polyarthrosis, spondylarthrosis, and periarthropathia humeroscapularis - for a larger number of treated cases.

2. Methods employed

The present drug survey was conducted at a total of 7 centers, at which
between 28 and 200 patients per center underwent treatment with Zeel T ointment. The condition for acceptance in the study was the presence of a degenerative articular affection. No additional criteria of inclusion or exclusion were applied. The study ran from May to September of 1992 and included 498 patients.

Documentation of data on patients and therapy took place on a uniform data-collection form which allowed entry of all essential information for each individual case treated. The participating physicians used this questionnaire to record certain basic data before the beginning of therapy: these included age and sex, type of articular affection, location of the symptoms, as well as length of time the patient had suffered from the illness.

With respect to conduct of the treatment with Zeel T ointment, the participating physicians received no stipulations prescribing the manner and frequency of application. Physicians were allowed to conduct therapy with or without ointment dressing and with or without iontophoresis. The physicians were also free to determine the frequency of ointment application. The basic strategy of the drug survey likewise allowed the therapists complete freedom in the term of therapy: they determined the length of application entirely in accordance with the requirements of each individual case.

The drug survey similarly permitted complete freedom for the attending physician in administering accompanying therapy; the only stipulation was that he or she record the use of adjuvant measures. The data-collection form also expressly required the entry of specific information on the following: the simultaneous application of any other forms of administration of Zeel (Zeel P injection solution or Zeel tablets), any additional medication deemed necessary, and any non-medicamentous forms of therapy applied.

In order to acquire the necessary data on the effectiveness of Zeel T ointment, the participating physicians recorded scores for the following characteristic manifestations: night pain, pain upon onset of movement (starting pain), and pain during movement. The physicians graded their patients before the beginning of therapy, as well as later at intermediate points during the entire course of treatment, by respectively awarding one of the four following scores for each case, at each point in time: no pain, slight pain, moderately severe pain, and severe pain. The lengths of time between the individual grading procedures differed from patient to patient. In addition to the initial examination (before beginning of therapy), the drug survey provided for a maximum of three additional interim examinations. At the patient's last visit, the therapist also made an overall assessment of the results of therapy achieved, in accordance with one of the following four grading categories: very good, good, moderate, or poor.

At the patient's final appearance, the physician also evaluated his or her tolerance to Zeel T ointment by awarding a grade from the following four-point scale: very good, good, moderate, or poor. The therapist at this time also documented any adverse side effects which may have appeared during the course of treatment.

3. Patient profile

Among the 498 patients able to be included in the drug survey, males (56.0%) were somewhat more prevalent than females (44.0%). The average age of the entire patient population was 42.9 years (s = ±15.4 years).

Nearly half the cases (48.8%) consisted of patients suffering from monarthrosis, among whom the most frequent symptom was unilateral gonarthrosis: 129 of 243 cases. For 51 of the patients (10.2% of the entire population), the diagnosis was polyarthrosis; for 56 (11.2%), spondylarthrosis; and for 74 (14.9%), periarthropathia humeroscapularis. The patients with other degenerative articular disorders made up a total fraction of 14.9%.

Fig. 1 graphically depicts the number of cases attributed to each of the individual forms of disease diagnosed.

Among the monarthrosis patients, the knee was the most frequently afflicted joint, followed in order by the hip, the ankle, and the shoulder. In addition to these joints, polyarthrosis was also diagnosed in a relatively great number of cases in the finger joints. Spondylarthrosis occurred most frequently in the area of the lumbar spine, somewhat less frequently at the cervical spine, and for only a very
few patients at the thoracic vertebral column. In the category of disorders designated under "miscellaneous affections," the participating physicians relatively frequently recorded epicondylitis and conditions of irritation/inflammation of the Achilles tendon (achillodynia).

Referenced to the entire patient population, the average term of illness before beginning of therapy with Zeel T ointment was 18.8 months. The mean term of illness was longest for poly-arthritis: 42.1 months. For monarthritis and spondylarthrosis, the lengths of 20.4 and 20.6 months, respectively, were in the same approximate order of magnitude as the average term for the entire population. On the other hand, the patients suffering from periarthropathia humeroscapularis, as well as the group in "miscellaneous affections," had suffered for relatively short periods of time: an average of 8.1 months for periarthropathia humeroscapularis, and 6.7 months for "miscellaneous affections."

4. Manner and frequency of application of Zeel T ointment

Within the context of the present drug survey, the participating physicians were free to apply Zeel T ointment in a manner left to their own professional discretion. For 258 patients (51.8% of the entire population), the therapists applied the preparation without ointment dressing and without iontophoresis. In 38 cases (7.6%), application of Zeel T ointment took place only in the form of an ointment dressing. For 57 persons (11.4%), the ointment was applied exclusively by means of iontophoresis. In 80 cases (16.1%), administration of Zeel T ointment was conducted by ointment dressing and iontophoresis. Twenty-eight patients (5.6%) received Zeel T ointment for part of the treatment time with ointment dressing, and for part of the time without ointment dressing. In 36 cases (7.2%), patients who underwent treatment partly with and partly without ointment dressings, also underwent ointment administration with iontophoresis. For those patients partly with and partly without ointment dressings, Zeel T ointment was applied during the day without ointment dressing and during the night with ointment dressing. In one case, the attending physician did not provide details on the mode of ointment application. Table 1 provides further information on the number of patients as well as the percent breakdowns for the salient forms of application of the ointment preparation.

The frequency of prescribed application with Zeel T ointment varied for this drug survey between once and five times a day. For more than half the patients, the participating physicians advised three times a day. See Fig. 2 for a graphical representation of the number of patients and the daily frequency of administration.

5. Adjuvant medicamentous and non-medicamentous therapy

In addition to application of Zeel T ointment, the participating physicians administered additional (adjuvant) forms of accompanying therapy to a portion of the patient population as part of treatment for their degenerative articular diseases.

Of the various forms of administration of Zeel - i.e., Zeel T ointment, Zeel P injection solution, and Zeel tablets - the most frequent application was of the injection solution (in ampules) in combination with Zeel T ointment. For a smaller fraction of the patients, the therapists also prescribed Zeel tablets in conjunction with Zeel T ointment - or, all
three forms of administration were applied together. Table 2 depicts the number of cases as well as the percent fractions of the overall patient population which were treated with the various forms of administration of Zeel. A total of 120 patients (24.1% of the total population) obtained at least one additional form of Zeel.

Entirely apart from additional administration of other forms of Zeel, the present drug survey also analyzed medicamentous accompanying therapy with other preparations. This analysis reveals that only a relatively small fraction of the entire patient population required accompanying medicamentous treatment, in the form of other-brand preparations, for therapy of their articular affections. Of the total of 32 patients who received adjuvant medication for therapy of the same affections, half underwent treatment exclusively with non-steroidal antiinflammatory medications. The remainder of the adjuvant other-brand medication can be assigned to one of the following classifications of therapeutic agents: antiinflammatory medicaments and corticosteroids, local anesthetics, vitamin preparations, and homeopathic remedies.

In comparison to the medicamentous adjuvant therapy just described-which involved only a relatively small fraction of the entire patient population - non-medicamentous therapy played an overall greater role as accompanying therapy. Of the 498 patients treated with Zeel T ointment, 390 (78.3%) underwent one or more of these forms of non-medicamentous therapy. The most frequent forms were as follows: kinesitherapy (247 cases = 49.6% of the entire population), followed by cryotherapy (36.7% of the entire number of patients), and electrotherapy (33.7% of the entire population).

Less frequent was administration of massage (19.7% of the patients) and balneo therapy (16.1% of cases). In addition, a total of 32.5% of the patients were treated with various other non-medicamentous measures which have been subsumed under the generic classification "miscellaneous forms of therapy."

6. Results of therapy

The criterion for effectiveness of Zeel T ointment was a comparison of pain intensity for each patient between the recorded data before beginning of therapy, and data obtained from a maximum of three additional examination dates during therapy. The participating physicians recorded scores for the following characteristic manifestations: night pain, pain upon onset of movement (starting pain), and pain during movement. The intervals between the individual examinations were not stipulated beforehand, and varied according to the individual patient. The therapists recorded the intensity of pain on the data-collection form by using a four-level grading scale (1 = no pain; 2 = slight pain; 3 = moderately severe pain; 4 = severe pain), in accordance with responses elicited from the patients.

From the scores for the various types of pain, a sum score was formed; the changes observed in this sum score may be considered to serve as an indicator for the effectiveness of the therapy. Due to the differences in the lengths of the intervals between the examinations, the progress in the patient's condition -as based on pain intensity measured at the respective dates of examination-cannot without reservation be compared among the individual patients. In order to ensure better comparability, the data gained at the individual examinations were arranged in such a manner that the chronological intervals from the beginning of treatment to the respective date of evaluation were all approximately of the same order of magnitude.

For representation of the progress in pain intensity, certain evaluation dates were established so as to lie within the following time ranges:

1st evaluation date: immediately before beginning of therapy.

2nd evaluation date: from day 1 to day 3 after beginning of therapy (day 1-3).

3rd evaluation date: from day 4 to day 10 after beginning of therapy (day 7 ±3).

4th evaluation date: from day 11 to day 17 after beginning of therapy (day 14 ±3).

5th evaluation date: from day 18 to day 24 after beginning of therapy (day 21 ±3).

6th evaluation date: from day 25 to day 31 after beginning of therapy (day 28 ±3).

7th evaluation date: period of time after day 31, as reckoned from the beginning of therapy.

All survey data which were able to be acquired for the individual patients during the time windows listed above were assigned to the respective evaluation dates, and have been represented in the following graphical and tabular representations of this survey in the form of average or percent values. Since, however, the conditions for this survey did not stipulate the intervals between the examinations of the patients and since, consequently, not all patients were examined on everyone of the post-facto-defined evaluation dates listed above, the average values as calculated in each case were based on patient populations which slightly differed from date to date.
Fig. 3: Decrease in the sum index for pain scores, for all patients treated

Fig. 4: Decrease in the sum index for pain scores, for patients suffering from monarthrosis and polyarthrosis

**Average sum score for pain**

**Polyarthrosis**  
**Monarthrosis**

Term of treatment (in days)

Fig. 3 shows a plot of the development in the total summation score for all types of pain, throughout the entire treatment time frame for all patients examined. This plot discloses that the pain index has already distinctly declined between the initial value and the second evaluation date. Beginning with the third evaluation date, the plot shows a virtually continuous decrease for the average pain scores: a development maintained until the end of the monitoring period.

Figs. 4 to 6 separately depict the plots of the average pain scores for the various types of degenerative articular affections. With the monarthrosis patients, these plots reveal a distinct decrease in the pain index, especially between the first and second, and between the third and fourth evaluation dates (Fig. 4). The development in pain levels for polyarthrosis patients is greatly similar to that of monarthrosis patients: for the polyarthrosis cases, however, the decrease in scores is somewhat slower than for monarthrosis over the initial days of treatment, whereas it drops off more rapidly than monarthrosis toward the end of therapy.

For the patients with spondylarthrosis, plotted data likewise disclose a noteworthy reduction in average pain intensity, starting already during the first days of treatment (Fig. 5). For this symptom picture, however, the development in pain was able to be monitored only up to the fifth evaluation date, since no further patient data were available for the following periods of time.

Similarly with cases treated for periarthropathia humeroscapularis, the reduction in pain scores is impressive over the term of therapy with Zeel T ointment (see Fig. 6). The slight rise in the pain score at the end of the monitoring period can be explained by the fact that numerous patients with good therapy results had already left the study between the fifth and sixth evaluation dates. As a result, only a few patients with less positive results remained behind and must be considered, so to speak, as a type of “negative subset” - which therefore negatively influenced the average value for pain intensity by the sixth evaluation date.

The change in the number of patients who served as basis for the calculated average pain scores at the successive evaluation dates is likewise responsible for the unusual plot of the pain curve for the group of patients suffering from the “miscellaneous degenerative affections” depicted in Fig. 6. For these patients, we observe an initial, surprisingly steep fall in the pain index from the beginning of treatment until the second evaluation date, followed by an increase up to the third evaluation date, at which time the average pain score is only slightly below the level at the beginning of therapy. This apparent rise in pain values, how-
ever, may be explained by the fact that only the data from a few patients who may be considered as the "positive subset" conspicuously influence the plot of the curve during the very early phase during the first to third days of treatment. During the further course of treatment (beginning with the third evaluation date), the results for this patient group then demonstrate a practically continuous decrease in recorded pain intensity.

In addition to the plots of pain scores each of which was based on changes in the total summation score for all qualities of documented pain-separate analysis also took place to demonstrate the improvement in the individual types of pain: i.e., night pain, pain upon onset of movement (starting pain), and pain during movement. Table 3 lists, for each of the above-listed types of pain, the percent of the patients who suffered from severe or moderately severe pain at the consecutive evaluation dates. The percent data given in this table were calculated with reference to the number of cases for which specific values were available on the respective dates.

Table 3 discloses that the proportion of patients with severe or moderately severe pain significantly decreased during the course of treatment from the levels at the beginning of the survey for all documented types of pain. The diminution in pain intensity demonstrates an extensively similar course for the individual qualities of pain. The proportion of patients with severe or moderately severe pain for all qualities of pain had by the fourth evaluation date fallen to smaller than half of the original share. By the fifth evaluation date, the percent of cases with severe or moderately severe pain had been reduced to approximately a quarter of the original level for each of the documented types of pain.

An exact analysis of the development in plotted pain data for the different patient groups with various adjuvant medication has demonstrated that there was no significant difference with respect to therapy results between those patients with accompanying other forms of administration of Zeel P or Zeel, and those who received Zeel T ointment alone. The drug survey also revealed that the administration of adjuvant medication of other types did not significantly influence the decrease in the pain index. The average reduction in this index was practically the same for patients with adjuvant medication and for patients without adjuvant medication. A comparison of the development in pain levels for patients with and without accompanying physical therapy disclosed that the pain index in the group with physical therapy decreased somewhat faster than in the group without physiotherapy. Ad-
juvant physical therapy, however, showed an influence on the decrease in the pain index only beginning with the third evaluation date.

Comparison of the plots of pain levels for the group of those patients who, in addition to Zeel T ointment, also received either another form of administration of Zeel, or other accompanying medication as treatment for the same affection, or physical therapy - with the plots for pain in the group of those patients who received Zeel T ointment as the only form of therapy, reveals the following: that the average decrease in the pain index was approximately the same for both patient groups. It was only at the date of the final evaluation that slight advantages for the patient group with accompanying therapy became evident. The outcome as "moderate" for an additional 17.5%, and as "poor" for only 7.2%. These data allow the conclusion that treatment resulted in therapeutic success for a total of 92.6% of the patients. Fig. 7 depicts the percent share of the various therapy results within the total patient population.

If the results of therapy are broken down into the individual diagnosis groups, the drug survey reveals that therapy with Zeel T ointment resulted in "very good" or "good results for 76.170 of monarthrosis cases, for 75.7% of periarthropathia humeroscapularis cases, and for 77.0% of cases classified as "miscellaneous degenerative disorders." The proportion of "very good or "good results was therefore higher for these patient groups than for the overall patient population. For the syndromes of polyarthrosis and spondylarthrosis, on the other hand - disorders traditionally very difficult to therapeutically influence - the success rates were, to be sure, below the average for the entire patient population. The proportion of 70.6% "very good" or "good results for polyarthrosis, and the share of 71.4% "very good or "good results for spondylarthrosis, at any rate, can doubtlessly be characterized as commendable success levels.

7. Patients' tolerance to the preparation

Of the entire survey population of 498 patients treated with Zeel T ointment, the data-collection forms for 20 of these persons indicated that they had suffered
from adverse side effects. The existence of a connection between these adverse side effects and the application of the medication may be considered probable in 8 cases, questionable in 11 cases, and highly improbable in 1 case. The phenomena observed involved local skin irritations and allergic reactions to the preparation which were associated with symptoms such as redness of the skin, itching, burning, and in some cases the formation of vesicles or pustules. For two patients, there was also report of burning during iontophoresis. No therapeutic measures of any kind were required for 8 of the patients; for the other cases, the side effects were effectively handled with systemic measures, or local administration of antihistamines and/or cooling. The intensity of the side effects was characterized in 10 cases as slight, in 7 cases as moderately severe, and in only 3 cases as severe.

Overall assessment of patients’ tolerance to Zeel T ointment took place as stipulated at the last examination of the patients by the attending physaiaans. The results were as follows: in 372 cases (74.7% of the overall patient population), patients’ tolerance was rated as very good; in 104 cases (20.9%), as good; in 10 cases (2.0%), as moderately good; and in 5 cases, as poor. In 7 cases, the physician made no indication of the patient’s tolerance to the preparation. Fig. 8 provides an additional, graphic representation of the results of tolerance assessment.

It is noteworthy in this connection that in five cases the participating physicians assessed the patients’ tolerance to Zeel T ointment as “good,” although they also indicated that adverse side effects had in fact occurred. Another finding worthy of notice is the fact that the therapists had classified therapeutic results as “very good” or “good” for a total of 10 patients for whom they had nevertheless documented adverse side effects.

Table 4 compares therapeutic results and tolerance assessment for those patients for whom the question on the data-collection form concerning adverse side effects had been answered with “yes.” This table discloses that, even in cases in which undesirable side effects occurred, a not inconsiderable share of the patients still enjoyed a favorable relation between the benefits of the medication and the negative effects of its therapy.

8. Interpretation of results

Drug surveys conducted with a large number of patients - as was the case for the present study - are particularly well suited for obtaining a realistic impression of the therapeutic application of a medicinal product under conditions of actual medical practice. The possibilities inherent in such a survey allow pinpointing and detailed study of the particular application potentials of a preparation. Such studies further reveal the frequency and the type of adverse side effects, as well as the therapeutic results obtained under conditions of medical practice.

The drug survey conducted with Zeel T ointment has revealed that this preparation in fact makes a positive contribution within the context of therapy of degenerative arthritic affections. Both for the syndrome treated in the greatest number of cases - monarthrosis - as well as for the remaining degenerative affections, the application of Zeel T ointment was associated for the great majority of patients with appreciable alleviation of the pain symptom complex. These results are especially worthy of note by virtue of the fact that Zeel T ointment contains no directly anesthetic or analgesic active constituents: which evidences that the positive effects which it exerts on pain maybe explained only by the direct action of the ointment preparation on the basic degenerative affection. The overall assessment of therapeutic success - i.e., 75.1 % “good” or “very good” - results - likewise confirms the therapeutic effectiveness of the homeopathic ointment preparation being investigated.

Within the context of risk-benefit considerations for the application of medication, patients’ tolerance to a particular preparation is in all cases one of the most essential therapeutic aspects. It is especially in this respect that homeopathic preparations such as Zeel T ointment
being investigated here distinguish themselves positively in comparison with other types of medication. Although this drug survey in fact reported a small number of cases of adverse side effects in conjunction with the application of Zeel T ointment, the conclusion is justified that patients' tolerance to this preparation is good to very good by virtue of the following: that the participating therapists made just such an evaluation in more than 95% of cases treated, and that the frequency of pronounced side effects was considerably less than 1%.

The present drug survey allows the following conclusion: that the homeopathic ointment preparation Zeel T doubtlessly represents an additional valuable therapeutic possibility for the treatment of degenerative articular affections.

References

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