Complementary Therapies in Medicine (2007), in press, corrected proof, available online 12 July 2007

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The role of a homoeopathic preparation compared with conventional therapy in the treatment of injuries: An observational cohort study☆

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KEYWORDS
Traumeel;
Homoeopathy;
Primary care;
Observational cohort study;
Injury

Summary
Objectives: To assess the use, effectiveness and safety of a homoeopathic preparation (Traumeel) compared with conventional therapies in the treatment of trauma and injuries.
Methods: Multi-centre, prospective, comparative observational cohort study of patients with various musculoskeletal injuries. German physicians who were using homoeopathy in addition to conventional medicine included patients. Patients treated with Traumeel were compared with patients managed conventionally. The primary outcome measure was the rate of resolution of the principal symptoms (i.e. pain and inflammatory symptoms) at the end of therapy.
Results: Sixty-nine Traumeel treated and 64 conventionally treated patients fitted the selection criteria. The most common diagnoses were acute injuries (sprains, strains, contusions, etc.) of the ankles, knees and hands. There were no significant differences between demographic and anamnestic baseline characteristics of both groups. Complete resolution of the principal symptom at the end of therapy occurred in 41 (59.4%) patients in the homoeopathy group versus 37 (57.8%) patients in the conventional group. No adverse events were reported in the Traumeel group compared to six adverse events (6.3%) in the conventional group. Physician-assessed tolerability was significantly better in the Traumeel group ($P = 0.001$).
Conclusion: Traumeel is as effective as conventional medicines in the management of mild to moderate injuries in this population. Traumeel was safe in use and judged by physicians to be better tolerated than conventional medicines. This study contributes to the case for a broad clinical effectiveness of Traumeel in the treatment of acute injuries and trauma.

Introduction

Minor injuries such as sprains, contusions, bruises, etc., are common and associated with significant short-term disability. The most common acute trauma, sprain of the lateral

☆ This study was supported by a grant from Biologische Heilmittel Heel GmbH.
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0965-2299/$ – see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.ctim.2007.04.004

ligament of the ankle joint, leads for instance in the UK to an estimated 302,000 Accident and Emergency department attendances yearly,[1] corresponding to an incidence of 53 per 10,000 population per year. The true incidence is much higher and estimated to be about 365 per 10,000 population.[2] This is because many patients will be treated in the primary care setting, or not seek professional health advice at all. In the UK, for all sprains and strains of joints and adjacent muscles, an estimated 550 per 10,000 people consult their General Practitioner each year.[3]

For acute ankle sprains, functional treatments (an early mobilisation programme with the use of an external support such as elastic bandage, tape, semi-rigid ankle support, etc.) appear to be better than immobilisation.[4] However it is unclear what is the most effective functional treatment,[5] which contributes to the large variation seen in clinical practice. Non-steroidal anti-inflammatory drugs can be given for pain, but these drugs are not always tolerated.

There is an increasing trend among physicians in many countries, including Germany and the UK, towards the use of complementary and alternative medicine (CAM) in addition to, and in some cases instead of conventional medicines. A commonly used preparation in the treatment of minor injuries is Traumeel (Traumeel; Heel GmbH, Baden-Baden Germany), a fixed combination of highly diluted herbal and mineral extracts, which has been on the market in Germany since 1937 and is currently available in approximately 60 countries worldwide, including the UK. A recent survey of prescription patterns[6] indicated that Traumeel is one of the most commonly used homoeopathic products in Germany. It is prepared in accordance with the German Homoeopathic Pharmacopoeia (HAB), and can be used in the form of tablets, drops, injection solution or ointment. The constituents of Traumeel are used traditionally and in homoeopathy for the broad spectrum of symptoms associated with various traumas such as contusion, sprains, wounds, pain, inflammation, neuralgia, etc.[7] Anti-inflammatory activity has been demonstrated in various in vivo and in vitro models.[8–10] Placebo controlled trial data suggest efficacy of Traumeel in the treatment of sports injuries,[11] ankle sprains,[12] traumatic hemarthrosis of the knee,[13] corticosteroid-dependent asthma,[14] and chemotherapy induced stomatitis in children.[15] A number of studies in different settings indicate it is safe in use.[16–20]

The aim of this study was to assess the daily use, effectiveness and safety of Traumeel compared with conventional treatments in patients with trauma and injury as a basis for further, more focused research.

Methods

This was a multi-centre, prospective, parallel group, observational, pharmaco-epidemiological cohort study.

The 81 participating physicians were general practitioners and specialists from urban and rural areas throughout Germany, with and without additional formal qualification in CAM. Eleven percent of practitioners preferentially used CAM, 58% used CAM and conventional medicine to a similar extent, and 31% predominantly used conventional medicine.

The eligibility criteria were: new or recurring injuries and trauma, diagnosis in accordance with chapters "S" and "T" of the 10th revision of the International Classification of Diseases (ICD-10). The following exclusion criteria were applied: patients already undergoing treatment for their injury/trauma; patients receiving other homoeopathic medicines; patients without evaluable data after a maximum of 3 months; patients taking medicines that were not included in the 2003 German drug directory ("Rote Liste").

The Traumeel group consisted of patients treated with Traumeel as a monotherapy or in combination with other homoeopathic products. The control group consisted of patients treated with conventional medicines. Additional measures (e.g. functional treatment, compression, etc.) and the use of comedication were permitted and recorded in the case forms. Both conventional and homoeopathic treatments and prescriptions were usually paid for by the patients' health insurance.

The decision to include a patient in the study was taken at the point of prescription and based on informed verbal consent. The only guideline provided was to aim for inclusion of one patient treated with Traumeel for each patient with similar symptoms treated conventionally (case–control principle). Patients were treated in accordance with routine practice, the dosage and duration of treatment were therefore at the discretion of the physician. The observation period was maximally 3 months per patient.

Because it was an observational study of daily practice, obtaining approval from an ethical committee was not required. The study was conducted in accordance with Good Epidemiological Practice and the Declaration of Helsinki. Full confidentiality of patient data was ensured.

The primary outcome measure was the rate of resolution of the principal and second symptoms at the end of therapy. Secondary outcome measures were the time until symptomatic improvement and treatment outcome as assessed by the physician. The physician recorded the most important (principal) symptom as well as one second symptom and graded both for severity/intensity on a three point scale (mild, moderate, severe). The primary safety criterion was the number of patients with adverse drug reactions judged to be certainly or probably caused by Traumeel. Secondary safety criteria were the total number and type of adverse events certainly or probably caused by the study medication, and treatment compliance as assessed by the physician.

Data were analysed unadjusted as well as adjusted for relevant covariates, using Fisher's Exact Test, Wilcoxon–Mann–Whitney Test and Cox Proportional Hazard regression as appropriate. The principal and second symptoms were analysed separately, therefore Bonferroni correction of α took place. Statistical analyses were conducted using SPSS for Windows (V.11) and StatXact and LogXact (V.4) for Windows.

Results

In total 133 patients (69 Traumeel and 64 conventional) were included between 2002 and 2003. All patients received treatment as intended. Fifty-three (77%) patients in the Traumeel group and 50 (78%) in the control group completed therapy at the end of the (maximum 3 months) observation period. Treatment was still ongoing at the end of the observation period in 14 and 13 patients, respectively, in

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the Traumeel and control groups (20% in both groups). Two patients in the Traumeel group and 1 patient in the control group were lost to follow up.

The baseline demographic, clinical and other characteristics of the patients are given in Table 1.

Table 1 indicates there were no significant differences between the groups. Injuries of the ankle/foot were most common, and in the great majority of cases it involved an acute trauma. Traumeel was used in a single application form in 46 (67%) patients and in more than one application form (e.g. tablets, in conjunction with topical application ointment) in 23 (33%) patients. Conventional medicines prescribed in the control group were analgesics/antirheumatics (52%), anticoagulants (16%), anti-inflammatory (7%) and miscellaneous drugs (25%). Conventional medicines were prescribed as a monotherapy in 44 (69%) patients and in combination in 20 (31%) patients.

Pain was the most common principal symptom: 58% ($N=40$) in the Traumeel group compared to 56% ($N=36$) in the control group. Inflammation was the second most common principal symptom: 41% ($N=28$) of patients treated with Traumeel, compared to 36% ($N=23$) of patients treated conventionally.

Complete resolution of the principal symptom at the end of therapy occurred in 41 (59.4%) patients in the homoeopathy group versus 37 (57.8%) patients in the conventional group. The changes in the principal symptoms pain and inflammation are shown in Fig. 1. The number of reported patients cured of pain with Traumeel was 78, compared with 61 in the control group. The number of patients cured or with improved pain were similar in both groups, as were the numbers with cured or improved inflammatory symptoms. The changes in the principal symptom at the end of treatment were similar in both treatment groups ($P=0.962$).

Fig. 2 illustrates the time until improvement of the principal symptom. Most patients (49 in the Traumeel group compared with 31 in the control group) improved within 4 days of treatment. The rates of improvement were comparable in both treatment groups.

The most commonly reported second symptom was inflammation: 58% ($N=40$) in the Traumeel group compared to 55% ($N=35$) in the control group. The change in the second symptom at the end of treatment was similar in both groups ($P=0.487$).

The time until improvement was also analysed with Cox's Proportional Hazards regression (Fig. 3). The Hazard ratio of treatments indicates the influence of treatment on healing and improvement times. A Hazard ratio <1 indicates shorter, a ratio of 1 identical, and a ratio >1 longer healing and improvement times on Traumeel compared to conventional therapy. The unadjusted Hazard ratio was 0.95 (95% confidence interval 0.67–1.37). After adjustment for relevant covariates such as type of diagnosis, type of symptoms,

Table 1 Comparison demographic, clinical and other relevant characteristics

Characteristics	Traumeel group	control group	*P*-Value (statistical test)
Number of patients	69	64	
Age (S.D.)	32.6 (2.2)	31.6 (2.2)	(W–M–W[a]) = 0.815
Sex (men:women)	39:30	31:33	(Fisher[b]) = 0.388
Height in cm (S.D.)	168.8 (2.2)	165.8 (2.37)	(W–M–W) = 0.218
Weight in kgs (S.D.)	66.4 (2.2)	65.5 (2.4)	(W–M–W) = 0.952
ICD-10 S/T diagnostic categories			
S00–S89: injuries to sites from head down to knee	25 (36%)	31 (48%)	
S90–S99: injuries of the ankle/foot	21 (31%)	21 (33%)	
T08–T14: injuries, unspecified	18 (26%)	8 (13%)	
T66–T78: miscellaneous	0 (0%)	2 (3%)	
T79: early complications of traumas	2 (3%)	2 (3%)	
T90–T98: sequelae of injuries	3 (4%)	0 (0%)	
Type of condition (acute:chronic)	67:2	61:3	(Fisher) = 0.388
Duration of disease/condition; (<1 week:>1 week)	55:14	50:14	(Chi-Sq.[c]) = 0.965
Principal symptom			
Type of symptom (pain:inflammatory[d]:miscellaneous)	40:28:1	36:23:5	(Chi-Sq.[c]) = 0.345
Severity/intensity at baseline (mild:moderate:severe)	5:29:35	4:35:25	(W–M–W[a]) = 0.250
Co-morbidity (yes:no)	7:62	5:56	(Fisher) = 0.769
Sick leave due to injury (yes:no:not known)	21:47:1	26:38:0	(Fisher) = 0.278
Therapy decision (physician:patient wish:both:not known)	46:6:16:1	40:14:10:0	
Medicinal application(s) (internal:external:both:not known)	28:24:15:2	27:24:13:0	(Chi-Sq.[c]) = 0.577
Additional measures taken apart from main therapy (yes:no)	20:49	26:38	(Fisher[b]) = 0.202
Comedication (yes:no)	4:65	4:60	(Fisher[b]) = 1.000

[a] Wilcoxon–Mann–Whitney *U*-test (two-tailed).
[b] Fisher exact test (two-tailed).
[c] Pearson chi-square test (two-tailed).
[d] Includes: inflammation, swelling, oedema and functional disturbance.

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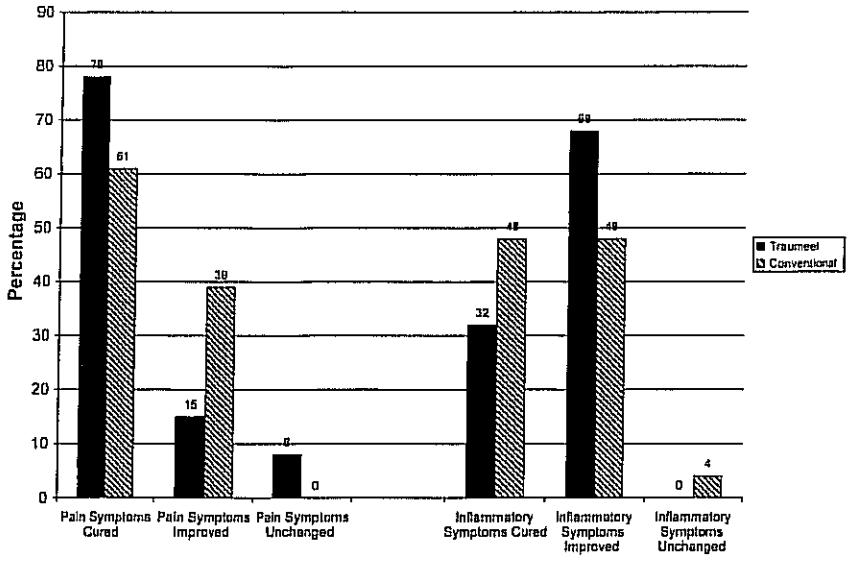

Figure 1 Changes in the principal symptoms, pain and inflammation, at the end of the treatment period in both groups.

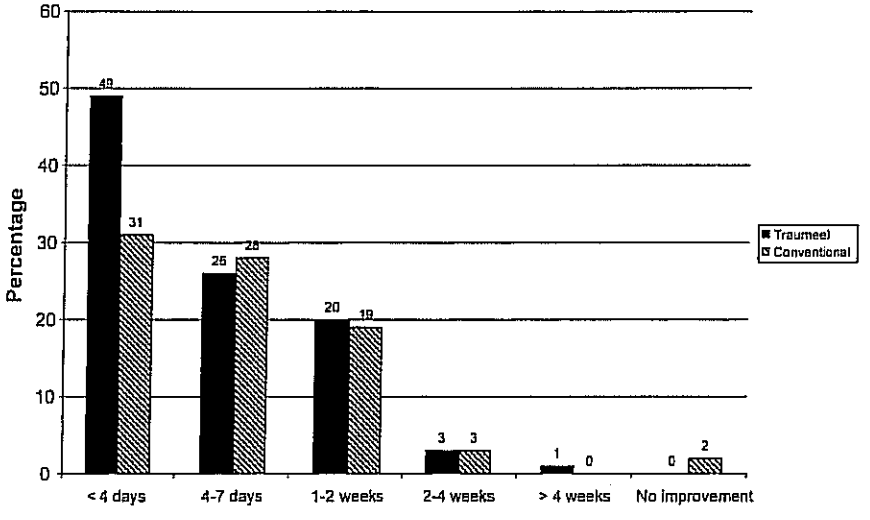

Figure 2 Time until improvement of principal symptoms in both treatment groups.

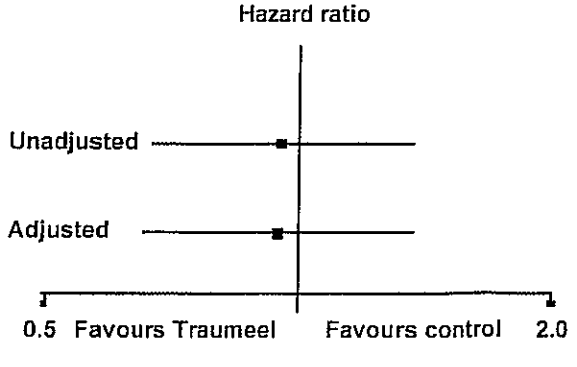

Figure 3 Unadjusted and adjusted Hazard ratios with 95% confidence intervals for time until improvement on Traumeel compared to conventional therapy.

age, etc., the Hazard ratio was similar: 0.94 (95% confidence interval 0.65–1.37).

The therapeutic result and treatment compliance as assessed by the physician are given in Table 2.

Treatment compliance was judged by the physicians to be very good in both groups, but appeared to be better in patients receiving Traumeel than in the group receiving conventional treatments.

In the Traumeel group 21 patients took sick leave, compared to 25 patients in the control group. The median number (minimum/maximum) of days sick leave was 5 (2/28) in the Traumeel group versus 4 (2/56) in the control group.

There were no patients with adverse drug reactions deemed to be probably or certainly related to any of the treatments. No adverse events were reported with Traumeel. In the control group 6 patients reported mild to moderate adverse events which did not lead to further complications. Physicians judged the tolerability to be "very good" in 62 (90%) patients in the homoeopathy group versus

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Table 2 Therapeutic result and treatment compliance as assessed by physician

	Traumeel group	Control group	*P*-Value (statistical test)
Therapeutic result			(W–M–W[a]) = 0.236
Cured/resolved	41 (60%)	32 (50%)	
Significantly improved	26 (38%)	28 (44%)	
Moderately improved	1 (2%)	3 (5%)	
Unchanged	0 (0%)	1 (1%)	
Worse	0 (0%)	0 (0%)	
Treatment compliance			(Chi-Sq.[b]) = 0.024
Very good	49 (72%)	31 (49%)	
Good	18 (27%)	29 (46%)	
Moderate	1 (1%)	3 (5%)	

[a] Wilcoxon–Mann–Whitney *U*-test (two-tailed).
[b] Pearson chi-square test (two-tailed).

25 (50%) patients in the control group. This difference was statistically significant (*P*-value Wilcoxon–Mann–Whitney test = 0.001).

Discussion

This study shows that Traumeel is as effective as commonly used conventional therapies in the treatment of mild to moderate injuries/trauma. Traumeel was safe in use and appeared to be better tolerated than conventional treatments.

The findings of this study are consistent with the available data on Traumeel. Placebo-controlled trials in patients with conditions such as acute sprains of the ankle, sports injuries and traumatic hemarthrosis of the knee indicate relevant analgesic as well as anti-inflammatory effects on ankle mobility, pain and a number of objective criteria such as the resolution/resorption of hemarthrosis.[11–13]. The anti-inflammatory effect of Traumeel is further supported by an increasing number of in vitro and in vivo studies that indicate that Traumeel inhibits the acute inflammatory process at the local level.[8] A recent study[21] reports that Traumeel inhibits the secretion of the pro-inflammatory cytokines IL-1β, TNF-α and the chemokine IL-8, from (mobile) human leukocytes and (resident) gut epithelial cells in vitro. These results suggest an immunomodulary effect at specific low doses of Traumeel. Traumeel may contain substances in the right quantities to stimulate macrophages to produce antigen motifs, which in turn stimulate the formation of regulatory lymphocytes as part of the 'immunological bystander reaction'.[22] Although further research is required, these studies offer a possible mechanism for the anti-inflammatory effects of Traumeel observed clinically.

Some caution is justified in considering the findings of the current study. There may be a potential selection bias present in non-randomised studies, e.g., physicians participating in this study might more likely to have a positive attitude regarding CAM, influencing the physician towards selecting patients with a better capacity to respond (e.g. milder cases) in the Traumeel group, or inversely, more severe cases for conventional management. However, the absence of significant differences between both cohorts in the various demographic, clinical and other relevant variables recorded at baseline suggests that a significant selection bias is unlikely. In this patient population, 81 physicians included, on average, two patients each. Since physicians were asked to include one patient treated with Traumeel for each conventionally treated patient with similar symptoms (case–control principle), it is unlikely that the physician would have been in a position to selectively allocate patients.

It is often claimed that observational studies exaggerate treatment effects compared with randomised clinical trials. The available data suggest however that although treatment effects obtained from randomised and non-randomised studies may differ, one method does not give a consistently greater effect than the other.[23] Reviews indicate that in particular for prospective studies there is often a good correlation between randomised and non-randomised studies.[24] Despite an ongoing debate on the latter issue, observational studies can add valuable data to our knowledge.[25]

The overwhelming majority of mild to moderate injuries are self-limiting. Whether or not patients are better at the end of treatment may therefore have been a rather crude instrument. Future studies should focus more closely at the speed of the healing process. The Cox regression analysis, which made fuller use of the available data on the improvement of symptoms in the course of time, proved to be useful, and may be a more sensitive analytical tool to assess the speed of recovery in future studies.

The interpretation of data is complicated by the heterogeneity of conventional treatments. This reflects the current state of therapy for mild-to-moderate injuries, but a better understanding of the appropriateness of these medicines as well as other aspects of conventional management would be desirable. This would need a larger population than that included in this pilot study.

The current lack of evidence-based conventional treatments for the treatment of pain and inflammation associated with trauma/injuries further underlines the relevance of establishing if homoeopathic medicines can be an effective and possibly safer alternative. The effectiveness and tolerability findings in the current study provide some evidence to this effect for Traumeel.

The traumatic disorders investigated in this study are common and generally have a good prognosis, therefore tolerability and cost are very important considerations. While

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the former is addressed in this study, the latter is not. If, as this study suggests, Traumeel is as effective as conventional approaches, cost will become an important factor informing usage.

Therefore, further pragmatic, randomised trials in specified indications, such as for instance ankle sprains, are desirable. Such studies should preferably be publicly funded to allow for independent reproduction of findings, and include a detailed assessment of cost-effectiveness.

The results of observational cohort studies such as this one, supported by insights from basic science research and randomised clinical trials, inform physicians about the effectiveness and safety of therapies for patients treated in routine daily practice.[26] Traumeel is one of the few homoeopathic products for which all of the above sources of information can be combined. This study contributes to the case for a broad clinical effectiveness of Traumeel in the treatment of acute injuries and trauma.

Acknowledgements

We thank Dr. Menachem Oberbaum, The Center for Integrative Complementary Medicine, Shaare Zedek Medical Center, Jerusalem, Israel, for discussion of core ideas and advice on the manuscript.

Contributors: Dr. Christian Schneider was the principal investigator. Prof. Berthold Schneider advised on the design of the protocol, and participated in data collection. Dr. Juergen Hanisch and Michael Weiser managed the project, discussed core ideas, co-ordinated writing of the protocol, participated in the analysis and interpretation of data and in the writing of the manuscript. Dr. Robbert van Haselen provided advice on the analysis and interpretation of data, conducted background literature research and was closely involved in writing of the manuscript.

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