

Fibromyalgia with severe forms of progression in a multidisciplinary therapy setting with emphasis on hyperthermia therapy – a prospective controlled study

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Introduction: Fibromyalgia syndrome (FMS) is a multi-factorial disease involving physiological as well as psychological factors. The aim of the study was to investigate a multidisciplinary inpatient treatment with emphasis on hyperthermia therapy by patients with widespread pain.

Materials and methods: The study involved 104 patients suffering from severely progressive FMS. A convenience sample and a prospective cohort design were used. The patients were treated in an acute hospital focusing on rheumatologic pain therapy and multidisciplinary complementary medicine. One patient group was treated with inclusion of hyperthermia therapy and the other group without. The therapy density (number of performed therapies per patient) was determined for every patient. Functional capacity measured by the Hannover functional status questionnaire (Funktionsfragebogen Hannover) and symptoms (von Zerssen complaint list) were analyzed for both groups on admission and on discharge.

Results: On admission, no significant difference could be established between control group (CG; multimodal without hyperthermia) and hyperthermia group (HG; multimodal with hyperthermia) (functional capacity, $P=0.936$). Functional capacity improved for the CG and the HG. On discharge, there was a significant difference between the two groups (functional capacity, $P=0.039$). There were no significant differences in fibromyalgia symptoms between CG (mean 41.8) and HG (mean 41.8) on their admission to hospital ($P=0.988$). On discharge, there was a significant difference ($P=0.024$) between the two groups (HG, mean 30.6; CG, mean 36.6). The inpatient therapy of patients with severely progressive fibromyalgia is characterized by a high frequency of therapy input.

Conclusion: FMS, especially with severe progression and a high degree of chronification, demands a multidisciplinary approach. In addition to the use of complementary medical procedures, integration of hyperthermia in the treatment process is a useful option.

Keywords: fibromyalgia, hyperthermia, pain, multidisciplinary approach

Background

Fibromyalgia syndrome (FMS) is a multi-factorial disease involving physiological as well as psychological factors. It is characterized by widespread pain and muscle tenderness accompanied by other comorbid symptoms.^{1,2} Those affected report chronic pain, which persists for at least 3 months in several regions of the body. The affected areas include the neck or upper or middle back, the small of the back, ribcage or abdomen, and at least one site of pain in both arms and both legs.

Patients can also have difficulty in falling asleep and sleeping through the night; in the morning, they feel that they have had too little sleep, and in many cases,

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feel mentally and physically exhausted. Numerous studies describe depression, anxiety, and panic disorders as comorbidities of FMS.³⁻⁵ Many sufferers report additional symptoms affecting the stomach, intestines, cardiovascular system, nervous system, or urinary passages.^{6,7}

The pathophysiology of FMS is still unknown. It is assumed that the levels of biogenic amines such as 5-hydroxytryptamine (5-HT) and norepinephrine are reduced in persons with FMS. A dysfunction of the 5-HT system may lead to panic disorders and depression.^{8,9}

Predictors of FMS are obesity, missing physical activity, high workload,^{10,11} increased physical discomfort, and permanent local pain for more than 6 years.¹² Prevalence of FMS is estimated to be 5%–6% of women in the USA and Europe.^{13,14} Individuals with FMS report frequent health care use¹⁵ concomitantly with lost productivity through higher absenteeism and unemployment.¹⁶ FMS places a significant economic burden on patients and health care systems.^{17,18}

The complexity of the FMS, its chronic progression, and the heavy burden of suffering present health care providers with an extensive set of problems.

There is no universally acceptable treatment for this condition.¹⁹ FMS leads to substantial limitations in physical functioning and activities of daily living. A higher absenteeism, unemployment, and disability lead to significant costs.

Multidisciplinary approaches are recommended for the treatment of fibromyalgia. These should include both psychotherapeutic methods (patient education and/or cognitive behavioral therapy) and exercise and activating therapeutic procedures.^{20,21}

These complementary methods do not exert their effects individually, but exert synergistic effects. Decisions to use a multidisciplinary approach to therapy should be determined based on a structured health care assessment of the individual.²²

Multidisciplinary approaches may include hydrotherapeutic and thermotherapeutic methods, hydrogalvanic baths (medical treatment [a type of electrotherapy] based on the simultaneous use of water and electric current), and acupuncture. Hydrotherapeutic methods are used by many individuals with FMS.²³ These methods include balneotherapeutic methods of hydrotherapy (part of naturopathy and physiotherapy, that involves the use of water for pain relief and treatment), such as herbal baths, mud baths, steam baths, and hot water whirlpool baths to soothe muscles and stimulate circulation.

Hydrotherapy can contribute in particular to reduce pain safely²⁴⁻²⁶ and offers beneficial treatment with no hidden side effects.²⁶ Hot baths^{27,28} are favored by many individuals

with FMS and can be a therapy option to reduce high pain intensity.²⁹ Acupuncture may be integrated into a multimodal therapy as an adjunctive treatment³⁰ and may help to reduce FMS symptoms^{31,32} and to increase the quality of life.³³

Conversations between health care providers during hospitalization should be client centered to improve and solidify the client–provider relationship.³⁴ The therapist is able to understand what the individuals are feeling and provide care that is more specific to their needs and therefore provide better care. Individuals are more likely to engage in treatment decisions, feel supported to make behavioral changes, and so feel empowered to self-manage.

Psychotherapy should include established methods of coping with pain and deflecting attention,³⁵ other problem-solving strategies,³⁶ and cognitive behavioral therapy.³⁷

Cognitive behavioral therapy is effective at helping you learn to manage your illness more effectively and it is based on the gate-control theory of pain and operant behavioral conditioning.³⁸

Physical therapies are found to be especially effective in the treatment of FMS³⁹ and also reflexology (physical act of applying pressure to the feet, hands, or ears with specific thumb, finger, and hand techniques).⁴⁰ Therefore, these therapies are integral components of the physiotherapy used in performing the study.

Hyperthermia

Different methods of hyperthermia exist.⁴¹ The mechanism of action of heat therapy in a wide range of different diseases is also the subject of numerous studies⁴²⁻⁴⁵ but the mechanisms are currently not completely understood and are in need of further scientific investigation (Figure 1). Infrared (IR)-A radiation may cause an immediate cellular effect, increasing nuclear DNA and RNA synthesis and ferritin levels.^{46,47}

Hyperthermia is usually incorporated with other complementary therapies.⁴⁸ Several studies also have demonstrated

- Acceleration of the biochemical metabolic processes
- Reduction of muscle tone
- Effect on cellular immune modulation
- Increase in nerve conduction velocity
- Inhibition of virus and growth of microorganisms
- Increasing the blood flow to tissues and organs

Figure 1 Assumed physiological effects of systemic whole-body hyperthermia.

that IR-A radiation accelerates healing of both chronic and postoperative wounds and reduces postoperative pain medication use.^{49,50} The use of hyperthermia has recently been studied, but is in its early stages.⁵¹ Pain in individuals with FMS was reduced for several months after discharge from the hospital.^{52,53}

Methods

Design

The study design was a convenience sample and a prospective cohort study. The authors chose an understudied area and reported a cohort study to highlight the additive effects of hyperthermia therapy as part of an in-hospital, multimodality program for the symptom management of FMS. The data in the study were collected according to the hypothesis formation, specifically for testing the hypothesis. Before starting the analysis, groups of patient were formed who were as similar as possible regarding relevant factors; the classification of the individuals was made according to the International Classification of Diseases.

All individuals approached by the investigator agreed to participate with a declaration of consent. Clinical patient number and all social data were deleted after the survey. Study participants always retained the right to withdraw at any time, for any reason. The study complies with the targets of the local ethical review committee and the targets of the privacy policy. The inclusion criterion for hospitalized individuals to participate in the study was a primary rheumatologic diagnosis of FMS by a specialist.

Exclusion criteria for study were severe epilepsy, chronic infections, acute infections, and claustrophobia.

The participants fulfilled the criteria of the American College of Rheumatology for the FMS diagnosis and showed severe disease progression as demonstrated by the disease activity, symptoms, and functional capacity. All patients had comorbid disease, over 700 diagnoses in total, which will not be presented due to their complexity and scope. It was

clearly evident that all the participants availed themselves of a wide variety of outpatient treatments (specialists, therapists, before hospitalization) on account of their FMS. For the measurement of chronic pain, the Mainz staging (Gerbershagen) was used.^{54,55} It was possible to blind outcome assessment by having this done by an independent person unaware of who received what. The investigators began enrolling subjects and collecting baseline exposure information; none of the subjects have developed any of the outcomes of interest.

During the entirety of their stay, all participants received interdisciplinary treatment from anesthesia specialist and internal medicine, rheumatology, and general medicine specialists. An integrative therapeutic approach in an acute setting is characterized by a high therapy density.^{56,57} If the application of hyperthermia is contraindicated, this is compensated by the use of other therapeutic procedures in order to ensure close-meshed, high-frequency therapy.

Nursing supervision was maintained. Process coordinators were in the middle of the workflow, deciding what information to share and when. The process coordinator was informed to collect all relevant parameters (disease activity, physical symptoms, functional capacity).

Complementary and alternative therapies were performed by a naturopathy specialist with the additional qualification, *Naturheilverfahren* (naturopathic methods), and with at least 3 years of experience in the field of “classical naturopathy”. In addition to specialist doctors, the team included specially trained nursing staff with at least 6 months of naturopathy experience.

The treatments applied were evidence based and best practice methods from hydro-/thermotherapy, physical therapy, phytotherapy, psychotherapy, lifestyle regulative therapy, and movement therapy. In addition, neural therapy, acupuncture, infiltrations, homeopathy, and dietary consultations were performed according to indication (Table 1).^{58–70} There was a standardized time of exposure to each therapy written into the protocol.

Table 1 Excerpt of evidence-based treatment regime in a multimodal setting

Hydrotherapeutic methods ^{65,66} : application of water through various methods (Kneipp treatments), eg, baths with added substances, mud baths, steam baths, water with whirlpool, bandages, or compresses
Thermotherapeutic methods ⁷⁰ : eg, infrared radiation only for hyperthermia group, heating pad, hot water bath
Psychotherapy ^{62,63} : eg, CBT, mind–body therapy
Practical therapies ⁶⁷ : eg, movement therapy, occupational therapy
Pain therapy ^{68,69} : eg, infiltration, cupping, cupping massage, acupuncture
Physiotherapy/physical therapy ⁶⁷ : eg, massage, transcutaneous electrical nerve stimulation, reflexology
Phytotherapy and dietary ^{58–61} : eg, use of herbal extracts in tea and medication, arnica pad, herbs, dietary consultations according to indication
Homeopathy ⁶⁴ : eg, substances that come from minerals, plants, or animals, such as arnica, or crushed whole bees

Abbreviation: CBT, cognitive behavioral therapy.

Every week, at least two extensive discussions were held with the patients, which focused especially on lifestyle regulative therapy.^{71,72}

The medication therapy for both groups was oriented on the requirements of the German S3 Guidelines.⁷³ Due to the psychological comorbidities, patients were additionally treated with tricyclic antidepressants.

The therapy progression and the therapy targets were evaluated in weekly, interdisciplinary team meetings and deviations were documented.⁷⁴

Hyperthermia therapy

In this study, the hyperthermia method used was whole-body hyperthermia with IR radiation (method according to Dr Heckel).⁷⁵ This contains a high fraction of wavelengths near the visible region (ie, short-wave IR, IR-A) and is emitted together with light. The total reflection scattering of the primary radiation produces an even surface irradiation tolerated by the skin. Fractions of this radiation penetrate through the outermost layers of skin and are absorbed in a depth of tissue at which the blood carries the released heat and distributes it throughout the body.

Heat losses are reduced by the individual lying in an insulated cubicle during the irradiation. A window opening in the roof of the cubicle allows air exchange. Pulse rate and temperature were monitored continuously by therapeutic staff. If required, pulse or electrocardiogram monitoring, oxygen administration, or an intravenous infusion could be implemented during treatment.

The hyperthermia treatment must not be used in the case of existing or threatening thrombosis, Marcumar medication (medication that may influence blood coagulation), or peripheral arterial occlusive disease. Figure 2 gives a summary overview of the indications and contraindications of systemic whole-body hyperthermia.

A comprehensive, therapy-related, patient-related, survey was performed which recorded all the therapy methods used in both groups during the period of hospitalization and presents the intensity of the service provided by integrative multimodal therapy.

Outcome parameters

The parameters (Mainz Pain Staging System, disease activity, physical symptoms, functional capacity) were conducted by a coordinator, who coordinates clinical activities and shares information with everyone in the workflow. These parameters were controlled by physicians, therapists, and nurses.

For the measurement of chronic pain, the Mainz staging (Gerbershagen) was used. The Mainz Pain Staging System

A	<ul style="list-style-type: none"> ✓ Muscle dystonias ✓ Rheumatism ✓ Arthritis ✓ Additive application in oncology ✓ Treatment trial in refractory disease states, particularly in allergies and dermatoses ✓ Multimodal pain therapy ✓ Bronchial asthma, chronic respiratory disease
B	<ul style="list-style-type: none"> – Existing or impending thrombosis – Far advanced destructive inflammation of internal organs, such as progressive pulmonary tuberculosis, acute and progressive chronic hepatitis and nephritis, and liver cirrhosis – Cardiac insufficiency (>2nd degree), severe arrhythmia – Advanced coronary atherosclerosis – Pronounced dehydration with disorders of water–electrolyte

Figure 2 Hyperthermia indications and contraindications.

Notes: (A) Indications for systemic whole-body hyperthermia. (B) Contraindications for systemic whole-body hyperthermia.

is an instrument for the classification of chronic pain in three stages 1, 2, and 3 (ranging from acute =1 to chronic pain =3).⁷⁶ It is based on a questionnaire taking into account dimensions of pain patterns of occurrence, duration, change of intensity, medication usage, and the lifetime utilization of the health care system.⁷⁷

To measure the intensity of pain, the visual analog scale (VAS) was used. The VAS is a psychometric response scale to measure the intensity or frequency of various symptoms.⁷⁸ Respondents mark the location on the 10 cm line corresponding to the amount of pain they experienced (0= no pain, 10= worst pain ever). VAS has been widely used in diverse adult populations, including those with rheumatic diseases.⁷⁹

List of symptoms according to von Zerssen

The patients' physical symptoms were recorded in the study using this instrument. The procedure is used both in somatic medicine and in clinical psychology and psychiatry.^{80,81} Information can be gathered for all patients with chronified physical and mental diseases or disturbances. The use of the list of symptoms is suitable both for

an individual and for a group setting. The patients answer questions (Figure 3).

The items included general symptoms (eg, feeling of weakness, fatigue), localizable physical symptoms (eg, pain in the joints and limbs), and mental states (eg, inner restlessness, brooding). The degree of severity of the symptoms surveyed is classified according to a four-level Likert scale (strong–moderate–hardly–not at all).

The individual complaints can be evaluated on a scale with the response categories “not at all” (0 point), “hardly” (1 point), “moderate” (2 points), and “strong” (3 points). The addition of the score results in a sum value divided into three groups (“unremarkable”, “borderline”, and “conspicuous”).

The internal consistency (Cronbach’s alpha) is $\alpha=0.94$. The split half reliability is very highly pronounced at $r=0.93$. Criteria-related validity is 0.62.

Functional capacity

The functional capacity of all subjects was recorded using the Hannover Function Questionnaire (Funktionsfragebogen Hannover) (FFbH).⁸² This tool is a patient self-evaluation instrument for everyday recording of functional limitations resulting from diseases of the locomotor organs. Validity and reliability in repeated measurements are greater than 0.75. The FFbH can be used in a variety of rheumatic diseases and together with other assessment instruments.⁸³ The FFbH is sensitive to change, and appears to be of practical usefulness in clinical and epidemiological studies. The defined pool of items strives, on the one hand, to ensure the “everyday relevance” of the movement progressions recorded and the best possible representation of different areas of life and, on the other, to take account of rheumatological aspects. A total of 18 questions are provided for recording functional limitations of the activities of daily life. The grade of the

remaining functional capacity is expressed as a percentage of the maximum number of points achieved. A score of 0% indicates maximum limitation and 100% stands for an unlimited capability to perform the activities required in daily life. If more than two questions are not answered, the FFbH should not be evaluated. FFbH scores of 100% to approximately 80% correspond to a “normal” functional capacity; scores <70% are an indication of limited functional capacity.

Statistical analysis

Statistical analyses were performed using SPSS for Windows, Version 20.0 (SPSS Inc, Chicago, IL, USA). For the comparison of two independent, normally distributed samples, the *t*-test was applied. Before that, the homogeneity of the variances was tested by means of the Levene test. When homogeneity of the variances was proven, Student’s *t*-test was carried out and when non-homogeneity of variances was tested, the Welch test was used. However, for non-normally distributed samples the Mann–Whitney *U*-test was applied as a nonparametric procedure. The metric variables were presented as means and medians, while the spreads were stated as standard deviations and interquartile ranges.

Normal distribution tests were used to check the distribution form of constant numbers of a sample. A significant deviation from the normal distribution exists at $P<0.05$. In such cases, nonparametric tests must be used for the variables concerned. The normal distribution tests in this study were performed using the Kolmogorov–Smirnov test. Comparison of two independent, normally distributed samples was done using the *t*-test. Comparison of two independent, non-normally distributed samples was done using the Mann–Whitney *U*-test.

The graphics were also produced using SPSS. Box-and-whisker plots were drawn to present the medians and quartiles. The median and 25th–75th quartiles are entered in the box, while the whiskers correspond to the smallest and largest value as long as these are neither extreme values nor outliers. Outliers are defined as values lying 1.5–3 box lengths outside the box and are shown as circles in the diagrams; extreme values, which measure more than 3 box lengths outside the box, are entered as crosses.

Findings

A total of 104 patients were studied; the average age of all fibromyalgia patients was 56.05 years (Table 2). A total of 272 hyperthermia treatments were performed in the hyperthermia group (HG). During their stay in hospital, the HG received on average 4.86 hyperthermia sessions (hs) (0–2 hs,

What symptoms do you have?	
– Globus sensation, tightness, or choking in the throat	– Profuse sweating
– Shortness of breath	– Cross or back pain
– Feeling of weakness	– Heaviness or fatigue in the legs
– Difficulty in swallowing	– Restlessness in the legs
– Stitches, pain, or pulling in the chest	– Hypersensitivity to heat
– Pressure or fullness in the abdomen	– Hypersensitivity to cold
– Fatigue	– Insomnia
– Nausea	– Dizziness
– Heartburn or acid regurgitation	– Trembling
– Irritability	– Neck or shoulder pain
– Brooding	– Weight loss

Figure 3 von Zerssen symptom list.

Table 2 Sociodemographic details of CG versus HG

	CG	HG
Female/male	47/1	55/1
Age (mean)	57	55.1
Age (median)	56.0	54.5
Age (range in years) 16–38	2	3
Age (range in years) 39–49	6	11
Age (range in years) 50–55	11	18
Age (range in years) 56–65	17	16
Age (range in years) 65 and older	12	8
Total (N)	48	56

Abbreviations: CG, control group; HG, hyperthermia group.

N=0; 3–4 hs, N=10; 5–6 hs, N=46) in the mildly warm temperature range between 37.5°C and 38.5°C.

All patients showed a polysymptomatic progression with lasting, persistent pain in muscles and joints, and with rare intervals with reduced symptoms. The overwhelming majority of the patients were subject to private and/or professional stressors with health-related anxieties. The disease activity was elevated significantly and all subjects suffered from considerable morning stiffness.

The great majority of the patients were in Stage 3 of the Mainz Pain Staging System according to Gerbershagen.

As part of the study, an analysis of secondary diagnoses was performed involving the comparison of several hundred secondary diagnoses. The basis of the analysis was allocation of the diagnoses in accordance with the International Statistical Classification of Diseases and Related Health Problems and the Major Diagnostic Category. Comparison of the secondary diagnoses revealed only a significant difference of Diagnostic Category “Circulatory system” in control group (CG) vs HG (Mann–Whitney *U*-test, asymptotic significance [two-tailed], $P=0.049$). This had no influence on results because this was no exclusion criterion for HG. There was no significant difference between the age of the two groups (*t*-test, $P=0.350$). The members of both groups were predominantly female (48 women in CG; 56 women in HG).

Hospitalization for the HG was 16.2 days (minimum 12 days and maximum 17 days, standard deviation 1.1) and in the CG 15.7 days (minimum 10 days and maximum 19 days, standard deviation 2.2). Comparison of CG and HG showed no significant difference (Mann–Whitney *U*-test, asymptotic significance [two-tailed], $P=0.211$).

The mean level of pain (admission) was 6.8 (CG) on the VAS and 8.2 (HG). The mean level of pain (discharge) was 4.8 (CG) on the VAS and 4.0 (HG).

Functional capacity on admission and discharge

The functional capacity was measured for all the patients from both groups. All the patients in the two groups answered all the questions. On admission, no significant difference could be established between the two groups (*t*-test; $P=0.936$). The standard deviation in the CG was 20.1 (median 58.0, maximum 94.0) and in the HG it was 14.6 (median 58.0, maximum 91.0). On discharge, there was a significant difference (Mann–Whitney *U*-test; asymptotic significance, $P=0.039$) (Figure 4). The standard deviation in the HG was 19.1 (median 75.0, maximum 100.0) and in the CG it was 18.8 (median 62.0, maximum 97.0).

Symptoms according to von Zerssen on admission and discharge

All the members of both groups answered all the questions in the questionnaire. The survey of the list of symptoms according to von Zerssen revealed no significant differences between the two groups on their admission to hospital (*t*-test; $P=0.988$). The standard deviation for the HG was 9.4 (median 42.0) and for the CG 12.2 (median 41.0) on admission (Table 3). A significant difference was evident on discharge (*t*-test; $P=0.024$). The standard deviation for the CG was 14.6 (median 37.5) and for the HG it was 12.0 (median 29.0) (Figure 5 and Table 4).

Analysis of the therapy density of the therapy areas for both groups

Physical therapy (hydrotherapy)

Comparison of the amounts of physical therapy (hydrotherapy) received by the two groups showed no significant difference (Mann–Whitney *U*-test, asymptotic significance

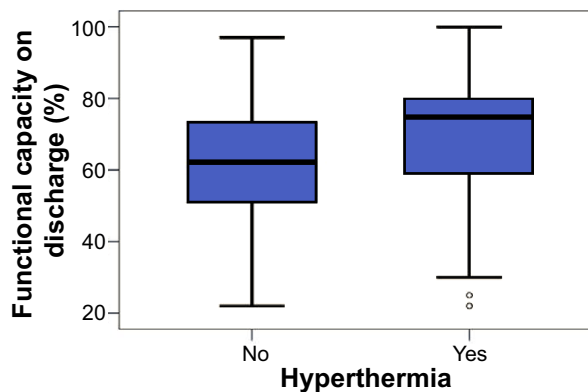


Figure 4 Functional capacity on discharge in patients with versus without hyperthermia.

Table 3 von Zerssen on admission with versus without hyperthermia

	von Zerssen on admission	
	Hyperthermia	
	CG	HG
Mean	41.8	41.8
Standard deviation	12.2	9.4
Standard error of mean	1.8	1.3
Percentile 25	34.0	35.5
Median	41.0	42.0
Percentile 75	48.5	48.0
Minimum	13	21
Maximum	67	60
Count	48	56
Total (N)	48	56

Abbreviations: CG, control group; HG, hyperthermia group.

[two-tailed], $P=0.979$). The standard deviation for the HG was 308.4 (median 97.5) and for the CG it was 105.9 (median 120.0).

Physical therapy (thermotherapy)

The difference measured in therapy minutes between the amounts of physical therapy (thermotherapy) was significant (Mann–Whitney U -test, asymptotic significance [two-tailed], $P=0.000$). The mean for the CG was 330.8 minutes and for the HG 693.7 minutes. The standard deviation for the HG was 321.5 (median 785.0) and for the CG it was 138.8 (median 340.0) (Table 5).

Physiotherapy

Comparison of the amounts of physiotherapeutic intervention showed a significant difference between the groups (Mann–Whitney U -test, asymptotic significance [two-tailed], $P=0.000$). The mean for physiotherapeutic interventions in the CG was 492.4 minutes compared with 284.2 minutes in the HG. The standard deviation for the HG was 222.8

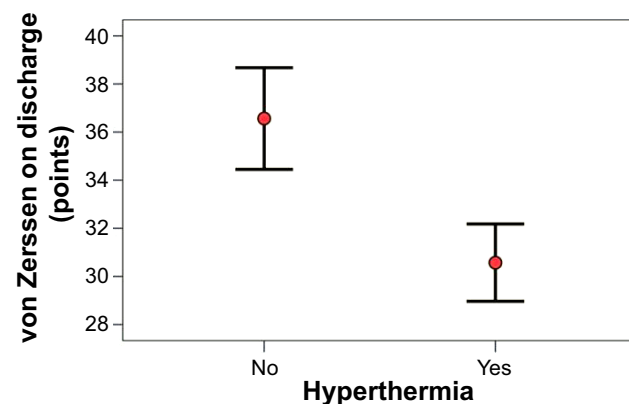


Figure 5 von Zerssen on discharge in patients with versus without hyperthermia.

Table 4 von Zerssen on discharge with versus without hyperthermia

	von Zerssen on discharge	
	Hyperthermia	
	CG	HG
Mean	36.6	30.6
Standard deviation	14.6	12.0
Standard error of mean	2.1	1.6
Percentile 25	28.0	21.5
Median	37.5	29.0
Percentile 75	45.5	39.5
Minimum	5	9
Maximum	65	55
Count	48	56
Total (N)	48	56

Abbreviations: CG, control group; HG, hyperthermia group.

(median 222.5) and for the CG it was 239.6 (median 437.5) (Table 5).

Phytotherapy

The mean time taken up by phytotherapeutic interventions was 154 minutes for the CG and 176.4 minutes for the HG. There was no significant difference (Mann–Whitney U -test, asymptotic significance, $P=0.506$).

Psychotherapy/mind body medicine

Comparison of the two groups revealed no significant difference (Welch test, $P=0.199$). The standard deviation for the HG was 134.6 (median 507.5) and for the CG it was 207.0 (median 605.0).

Movement therapy

The mean amount of movement therapy for the CG was 476.4 minutes (standard deviation 229.2, median 320.0) and for the HG 307.0 minutes (standard deviation 202.3, median 167.5) (Table 5). Comparison of the two groups revealed a significant difference in the therapeutic effort (t -test, $P<0.001$).

Detoxifying process

There was no significant difference for the detoxifying process in patients receiving and not receiving hyperthermia (Mann–Whitney U -test, asymptotic significance, $P=0.452$). The standard deviation for the HG was 44.8 (median 100.0) and for the CG it was 32.5 (median 90.0).

Neural therapy/infiltration/acupuncture

Regarding the amount of therapy in the procedures of neural therapy/infiltration/acupuncture, no significant difference was observed between patients receiving and not receiving

Table 5 Physical therapy/thermotherapy, physiotherapy, movement therapy, and homeopathy in patients with versus without hyperthermia (intervention in minutes)

	Physical therapy/ thermotherapy		Physiotherapy		Movement therapy		Homeopathy	
	Hyperthermia		Hyperthermia		Hyperthermia		Hyperthermia	
	CG	HG	CG	HG	CG	HG	CG	HG
Mean	330.8	693.7	492.4	284.2	476.4	307.0	46.9	31.6
Standard deviation	138.8	321.5	239.6	222.8	229.2	202.3	62.5	55.6
Percentile 25	267.5	397.5	335.0	115.0	33.1	27.0	0.0	0.0
Median	340.0	785.0	437.5	222.5	320.0	167.5	0.0	0.0
Percentile 75	412.5	917.5	640.0	352.5	470.0	315.0	120.0	30.0
Minimum	0	30	120	0	40	0	0	0
Maximum	695	1,240	1,080	840	950	850	180	150
Count	48	56	48	56	48	56	48	56
Total (N)	48	56	48	56	48	56	48	56

Abbreviations: CG, control group; HG, hyperthermia group.

hyperthermia (Mann–Whitney *U*-test, asymptotic significance, $P=0.157$). The standard deviation for the HG was 103.4 (median 60.0) and for the CG it was 87.7 (median 75.0).

Homeopathy

No significant difference was observed between the homeopathy inputs for the two groups (Mann–Whitney *U*-test, asymptotic significance [two-tailed], $P=0.085$). The standard deviation for the HG was 55.6 and for the CG it was 62.5 (Table 5).

Diet advice

The outlay for diet advice was not significantly different between the two groups (Mann–Whitney *U*-test, asymptotic significance [two-tailed], $P=0.866$). The standard deviation for the HG was 21.3 (median 0) and for the CG it was 25.8 (median 0).

Discussion and conclusion

The participants were predominantly female, as also reported by other studies.^{84,85} The longer hospitalization time of these integratively treated patients also agrees with the findings of previous large-scale scientific studies.⁵⁶

The mean age of the patients in this study corresponds with the analysis of ages ascertained at the German national level. Out of 6.452 inpatients in Germany whose main diagnosis was FMS, >55% of patients in 2008 were between 40 years and 59 years of age. Software: G-DRG-Browser G-DRG-Version 2011, Daten 2010 gem; §21 KHEntG.

For 2011, data were available for 1,929 cases receiving inpatient treatment, of whom the majority also fell within this age range.⁸⁶

This study shows that interdisciplinary therapeutic approaches are worthwhile in the treatment of FMS.

Despite the severity of the disease with a pain-supporting mental-accompanying disease, a significant improvement in the symptoms was evident on discharge from hospital ($P=0.024$; Tables 3 and 4). The complex somatic and mental symptoms that were recorded with the von Zerssen score could also be alleviated by means of the complementary use of hyperthermia. The use of hyperthermia improved the outcome still further. The superior outcome for the HG was manifested in a significant improvement in the patient's functional capacity. A greater therapeutic density of both physiotherapeutic interventions and methods of movement therapy in the CG proved unable to equal the added benefit of hyperthermia. Whole-body hyperthermia is a part of a multidisciplinary approach.^{48,53} Previous studies with hyperthermia were performed in a rehabilitative setting.^{52,53,87,88} Hyperthermia has been carried out for several weeks. A sustained pain reduction was observed in a 6-month follow-up after intervention ended in patients with FMS.⁵² There were no specifications for other therapy methods, and their density and the form of progression were not described accurately.

Acute care is a care setting where an individual is treated for a brief but severe episode of illness. Acute programs in Germany have increased numbers of sessions and a larger care team. Acute care settings have full-time physicians and hospital staff who are available 24 hours a day. The aim of acute inpatient treatment is to improve the patients' condition sufficiently that they are once again capable of rehabilitation.⁸⁹ Continual acute diagnosis (in the case of an emergency situation or diagnosis aggravation) and therapy, and continual medical and nursing care are guaranteed during the entire period of hospitalization. Proven applications are summarized in Figure 6.

In future studies for the evaluation of the therapy of FMS, economic parameters must also be analyzed in order to perform diagnosis-related group (system to classify hospital

- Active patient participation
- Refer to specialists (rheumatologist, pain specialist, physiatrist, or psychiatrist)
- Specially trained nursing staff with experience of naturopathy, staff including physiotherapists, ergonomic therapists, psychologists
- Multicomponent therapy with: balneotherapy, strength training, acupuncture, exercise training, cognitive behavioral therapy
- Hyperthermia should be considered as a part of a multidisciplinary approach

Figure 6 Applications for clinical practice (fibromyalgia syndrome).

cases into groups) cost calculations (in addition to clinical effects), especially regarding the costs associated with claims for outpatient and inpatient therapy for FMS. In doing so, the question should be addressed as to whether the use of innovative, integrative therapeutic methods can generate the potential for long-term savings.

In addition, observational studies are needed of mildly warm whole-body hyperthermia treatment of further diseases and disturbances of the musculoskeletal system and connective tissues in acute inpatient therapy of pain and rheumatic diseases with the inclusion of complementary medical procedures. The development of further improved therapies for treating FMS, as well as analysis of delivery methods of each modality and how they potentially influence one another and also the recidivism in different hospital settings, is necessary.

Acknowledgment

The authors would like to thank the anonymous reviewers for reviewing the paper.

Disclosure

The authors have no conflict of interest.

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