English Version of "Komplementäre und alternative Verfahren beim Fibromyalgiesyndrom. Systematische Übersicht, Metaanalyse und Leitlinie".
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Complementary and alternative therapies for fibromyalgia syndrome

Systematic review, meta-analysis and guidelines

In revising the guidelines, the task groups considered the following questions:

1. Are the complementary and alternative therapies for fibromyalgia syndrome (FMS) effective over short and long periods of time?
2. What are the risks of using complementary and alternative procedures to treat FMS?
3. Which complementary and alternative procedures should be refused in treating FMS?

Methodology

The procedures utilized for researching and analyzing the literature are presented in the article "Methodological fundamentals used in developing the guideline".

Results

The following findings apply to adults. Complementary and alternative procedures for chronic pain affecting multiple body regions in children and youths are discussed in the article entitled "Definition, diagnosis and therapy of chronic widespread pain and so-called fibromyalgia syndrome in children and adolescents". Key recommendations are italicized.

Highly recommended

Meditative movement therapies (tai chi, qigong, yoga)

Evidence-based recommendation

Meditative movement therapies (tai chi, qigong, yoga) should be considered.
EL1a, highly recommended, strong consensus

Comment. The meditative movement therapies analyzed included body-awareness therapy, qigong, tai chi, yoga, and Feldenkrais therapy.

A search of the literature identified 46 reports. One trial on Feldenkrais therapy was excluded because it was not randomized [39]. One randomized controlled trial (RCT) with yoga was available only as an abstract [31].

Nine RCTs with 420 patients in therapeutic trials lasting an average of 11 (6–20) weeks were analyzed. Seven of the trials included follow-up assessments performed on average 20 (6–78) weeks after the treatments had been completed (Evidence Report, Tab. 92; [4, 9, 11, 17, 28, 39, 42, 52, 59]).

The evidence was of moderate quality (moderate methodological quality, moderate external validity) (Evidence Report, Tab. 93), as was the efficacy. However, meditative movement therapies were superior to the control group therapies in reducing pain, fatigue, and sleep disorders as assessed at the completion of the respective trials (Evidence Report, Tab. 94 and Fig. 30). Acceptance in the treatment groups was moderate (dropout rate 19%) and did not differ significantly from that of the placebo groups (Evidence Report, Fig. 30).

Adverse effects were not reported in the analyzed trials. Availability is limited. Exercise therapies are not covered by health insurance in Germany. They are a part of multimodal therapeutic inpatient

programs at some hospitals and are offered by some adult education centers.

Recommendation open

Acupuncture

Evidence-based recommendation

Treatment with acupuncture for a limited period of time may be considered. EL 2a, degree of recommendation open, strong consensus

Comment. A search of the literature identified 340 reports. Three RCTs were excluded because the target variables did not fulfill the inclusion criteria [27] or because acupuncture was combined with other active therapeutic procedures [36, 54]. One review [10] included four Chinese trials: two compared acupuncture with amitriptyline and two compared acupuncture in combination (one with cupping and one with an antidepressant) with an antidepressant alone. These studies, which were not contained in the designated databanks and were only published in Chinese, were excluded from the analysis.

Thus, 9 RCTs with 414 patients treated for an average of 7 (2–15) weeks were analyzed. Three trials included follow-up assessments after a median of 17 (12–28) weeks (Evidence Report, Tab. 95; [2, 18, 29, 30, 34, 41, 43, 49, 53]).

The evidence was of moderate quality (poor methodological quality, moderate external validity) (Evidence Report, Tab. 96). The quality of evidence was downgraded due to the limited methodological quality.

Efficacy was limited. The standard mean deviation (SMD) (verum acupuncture vs. sham acupuncture) at the completion of therapy with regard to pain indicated a small effect size (Evidence Report, Tab. 97 and Fig. 31).

The dropout rate was 8.2%, which did not differ from that of the control group (Evidence Report, Tab. 31). Adverse effects were systematically reported in only one study. The frequency of severe adverse effects from acupuncture is controversial. However, severe complications such as bleeding or pneumothorax have been reported in the literature [16].

Acupuncture for comorbid back pain is covered by health insurance in Germany.

Because of its potential risks and limited availability, the strength of recommendation was downgraded one level.

Negative recommendation

Mindfulness-based stress reduction as monotherapy

Evidence-based recommendation

Mindfulness-based stress reduction should not be used as monotherapy. EL 2a negative recommendation, consensus

Comment. A search of the literature identified 8 relevant reports. Four RCTs with 371 patients treated with mindfulness-based stress reduction (MBSR) for an average of 8 weeks were analyzed [4, 26, 50, 51]. In three of the trials patients of both arms of the studies were assessed at follow-up an average of 8 weeks after treatment. In one of the trials [26] follow-up evaluations of the MBSR, but not the control group, were carried out after 3 years in 26 of 39 patients (Evidence Report, Tab. 98).

The evidence was of moderate quality (poor methodological quality, moderate external validity; Evidence Report, Tab. 99). The secondary end points of one trial were not reported and not made available upon inquiry [51]. Since it is possible that negative results had not been published, the level of evidence was downgraded.

MBSR was not effective and was not superior to control treatments with respect to reducing pain or improving quality of life (Evidence Report, Tab. 100 and Fig. 32).

Acceptance was moderate (dropout rate 22%) and did not differ significantly from that of the controls (Evidence Report, Fig. 32). Adverse effects were not reported nor have any been mentioned in the literature.

Availability is limited. MBSR is not covered by health insurance in Germany. MBSR is offered as part of multimodal therapeutic inpatient programs in a few hospitals.

Homeopathy

Evidence-based recommendation

Homeopathy should not be considered. EL1a negative recommendation, consensus

Minority opinion (Complementary and Alternative Medicine Work Group: Langhorst J, Bernardy K, Lucius H, Settan M, Winkelmann A, Musial F): homeopathic therapy may be considered. EL 1a, recommendation open

Comment. A search of the literature identified 20 reports. The data of one trial were published twice [7, 8]. Five RCTs with 204 patients and an average trial length of 15 weeks were qualitatively analyzed (Evidence Report, Tab. 101; [7, 8, 23, 24, 46]).

The evidence was of moderate quality (moderate methodological quality, moderate external validity), and moderate external validity (Evidence Report, Tab. 102).

There was no consistent evidence that homeopathy was effective. Two trials could be quantitatively evaluated [8, 46]. The SMDs (homeopathy versus control at completion of therapy) showed that homeopathy tended to positively affect quality of life (Evidence Report, Tab. 103 and Fig. 33). In the two trials that could not be meta-analyzed, qualitative analysis revealed no consistent evidence that homeopathy was effective. In one trial there was no statistical difference in the reduction of pain and sleep disturbance. One subgroup analysis did show significantly reduced pain and sleep disturbance for those patients who presented at least more than three characteristic symptoms of the prescribed homeopathic medication [23]. One trial showed that a homeopathic treatment reduced pain and sleep disturbance better than a placebo [24]. A subsequent analysis of that trial with appropriate statistical methods did not confirm a significant difference between homeopathic and placebo treatments in the first crossover treatment phase [15].

Acceptance was moderate. The dropout rate, 13%, did not differ significantly from that of the placebo group (Evidence Report, Fig. 33). The risks are probably low: adverse effects were not determined. Relevant side effects are not known from the literature.

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Complementary and alternative therapies for fibromyalgia syndrome. Systematic review, meta-analysis and guidelines

Abstract

Background. The scheduled update to the German S3 guidelines on fibromyalgia syndrome (FMS) by the Association of the Scientific Medical Societies ("Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften", AWMF; registration number 041/004) was planned starting in March 2011.
Materials and methods. The development of the guidelines was coordinated by the German Interdisciplinary Association for Pain Therapy ("Deutsche Interdisziplinären Vereinigung für Schmerztherapie", DIVS), 9 scientific medical societies and 2 patient self-help organizations. Eight working groups with a total of 50 members were evenly balanced in terms of gender, medical field, potential conflicts of interest and hierarchical position in the medical and scientific fields.Literature searches were performed using the Medline, PsycInfo, Scopus and Cochrane Library databases (until December 2010). The grading of the strength of the evidence followed the scheme of the Oxford Centre for Evidence-Based Medicine. The recommendations were based on level of evidence, efficacy (meta-analysis of the outcomes pain, sleep, fatigue and health-related quality of life), acceptability (total dropout rate), risks (adverse events) and applicability of treatment modalities in the German health care system. The formulation and grading of recommendations was accomplished using a multistep, formal consensus process. The guidelines were reviewed by the boards of the participating scientific medical societies.
Results and conclusion. Meditative movement therapies (qigong, tai chi, yoga) are strongly recommended. Acupuncture can be considered. Mindfulness-based stress reduction as monotherapy and dance therapy as monotherapy are not recommended. Homeopathy is not recommended. In a minority vote, homeopathy was rated as "can be considered". Nutritional supplements and reiki are not recommended.The English full-text version of this article is available at SpringerLink (under "Supplemental").

Keywords

Fibromyalgia syndrome · Systematic review · Meta-analysis · Guidelines · Complementary therapies

Komplementäre und alternative Verfahren beim Fibromyalgiesyndrom. Systematische Übersicht, Metaanalyse und Leitlinie

Zusammenfassung

Hintergrund. Die planmäßige Aktualisierung der S3-Leitlinie zum Fibromyalgiesyndrom (FMS; AWMF-Registernummer 041/004) wurde ab März 2011 vorgenommen.
Material und Methoden. Die Leitlinie wurde unter Koordination der Deutschen Interdisziplinären Vereinigung für Schmerztherapie (DIVS) von 9 wissenschaftlichen Fachgesellschaften und 2 Patientenselbsthilfeorganisationen entwickelt. Acht Arbeitsgruppen mit insgesamt 50 Mitgliedern wurden ausgewogen in Bezug auf Geschlecht, medizinischen Versorgungsbereich, potenzielle Interessenkonflikte und hierarchische Position im medizinischen bzw. wissenschaftlichen System besetzt.Die Literaturrecherche erfolgte über die Datenbanken Medline, PsycInfo, Scopus und Cochrane Library (bis Dezember 2010). Die Graduierung der Evidenzstärke erfolgte nach dem Schema des Oxford Center for Evidence Based Medicine. Grundlage der Empfehlungen waren die Evidenzstärke, die Wirksamkeit (Metaanalyse der Zielvariablen Schmerz, Schlaf, Müdigkeit und gesundheitsbezogene Lebensqualität), die Akzeptanz (Abbruchrate in Studien), Risiken (Nebenwirkungen) und die Anwendbarkeit der Therapieverfahren im deutschen Gesundheitssystem. Die Formulierung und Graduierung der Empfehlungen erfolgte in einem mehrstufigen, formalisierten Konsensusverfahren. Die Leitlinie wurde von den Vorständen der beteiligten Fachgesellschaften begutachtet.
Ergebnisse und Schlussfolgerung. Meditative Bewegungstherapien (Qigong, Tai-Chi, Yoga) werden stark empfohlen. Die Therapie mit Akupunktur kann erwogen werden. Achtsamkeitsbasierte Stressreduktion als Monotherapie und Tanztherapie als Monotherapie werden nicht empfohlen. Homöopathie wird nicht empfohlen, wobei in einem Minderheitenvotum eine offene Empfehlung („kann erwogen werden") favorisiert wurde. Nahrungsmittelergänzungsprodukte und Reiki werden nicht empfohlen.

Schlüsselwörter

Fibromyalgiesyndrom · Systematische Übersicht · Metaanalyse · Leitlinie · Komplementäre Therapien

The availability is limited: the costs are covered by only a few of the health insurance funds.

Minority vote: In the trial reported by Fischer in 1989, homeopathic treatment reduced pain and improved sleep better than a placebo [24].

A subsequent analysis of this trial with modified statistical methods did not show that the homeopathic treatment was significantly better than the placebo in the initial crossover treatment phase. The author assumed that there is a carry-over effect, i.e., that the effects of the treatment period being observed are partly determined by the effects of the preceding treatment period [15]. However, this was not established by statistical analysis (p=0.07). Since the carry-over effect was not formally demonstrated, the homeopathic treatment would remain statistically superior.

Nutritional supplements

Evidence-based recommendation

Nutritional supplements (algae and malic acid/magnesium preparations; anthocyanins; carnitine; S-adenosyl methionine, SAM; soya oil; vitamin–dietary min-

eral preparations) should not be applied. EL3, negative recommendation, strong consensus

Comment. Anthocyanins are plant pigments. In the European Union, they are permitted in unlimited amounts as food additives under the number E163.

S-adenosyl methionine (SAM) is an essential amino acid. In the USA, SAM is sold as a nutritional supplement under the Dietary Supplement Health and Education Act of 1999. Under this law, nutritional supplements circumvent regulation by the Food and Drug Administration (FDA). SAM can be obtained over the internet.

Carnitine is a vitamin-like substance. It can be produced by the body but is usually provided by meat in the diet. In Germany it is permitted for treating the carnitine deficiency of renal insufficiency and special forms of muscular dystrophy. Carnitine can be obtained over the internet.

5-Hydroxytryptophan is an amino acid naturally occurring in bananas and the seeds of African black beans. The substance is not an authorized medication in Germany but can be obtained over the internet as a "natural mood-elevator".

A search of the literature identified 130 reports. Two trials with SAM were excluded from the analysis because the clinical endpoint [53] or the presentation thereof [54] was not suitable for analysis.

Eleven trials with 12 arms and 517 patients and an average length of treatment of 6 (1–12) weeks were analyzed. None of the trials included a follow-up [1, 12, 21, 22, 25, 35, 44, 47, 48, 57, 58]. Only one preparation (SAM) was the subject of more than one trial (3 trials, 121 patients) (Evidence Report, Tab. 104). The evidence was initially downgraded because so few trials were available. And since the quality of evidence was limited (limited methodological quality, limited external validity; Evidence Report, Tab. 105), it was further downgraded. The efficacy was limited. The SMDs (nutritional supplements versus controls) on pain, sleep, and fatigue at the completion of therapy were showed small effect sizes (Evidence Report, Tab. 106 and Fig. 34).

Acceptance was moderate (dropout rate 12%) and did not differ significantly from that of the placebo groups; Evidence Report, Fig. 34).

The risks were high: gastrointestinal adverse effects were 10% more frequent with SAM and 5-HT than in the control group.

The recommendation was downgraded a further level because of the high risks and low availability.

Reiki

Evidence-based recommendation

Reiki should not be applied. EL 2b, negative recommendation, strong consensus

Comment. A search of the literature identified 19 reports. One trial had no control group [19]. In one trial the 25 patients were treated for 8 weeks by either a reiki master or an actor, receiving either reiki (direct contact) or a "distance treatment". None of the treatments had a significant effect on pain, fatigue, sleep, or quality of life [3]. In spite of the limited data available, a statement on this treatment is included here because of the negative results of the trial.

Dance therapy

Evidence-based recommendation

Dance therapy should not be applied as monotherapy. EL 2b, negative recommendation, strong consensus

Comment. A search of the literature identified 9 reports. The data of one trial listed in the NIH databank as completed and evaluated could not be found in the other databanks [6]. In a Swedish RCT with 36 patients, dance therapy (once a week for 6 months) did not reduce pain in the therapy group when compared with controls neither at the completion of the trial nor at follow-up assessment 6 months later [32]. Although few data are available, a statement about this therapy is included here because of the negative results of the trials.

Neither positive nor negative recommendation possible

Dietary intervention (vegetarian diet, elimination diet, therapeutic fasting)

Evidence-based assessment

Due to the limited available data, neither a positive nor a negative recommendation is possible. Strong consensus

Comment. A search of the literature identified 27 reports. In one RTC, 37 patients were given a vegetarian diet, and 41 patients, amitriptyline (AMT; 10–100/day), depending on the severity of the patient's sleep disorder, for a period of 6 weeks. Both treatments resulted in pain reduction. At the completion of therapy, AMT was more effective than the vegetarian diet in reducing pain [5].

In a controlled trial, a 3-month low-salt uncooked vegetarian diet (18 patients) was superior to a normal diet in reducing pain and improving function [37].

In a controlled trial from the US, 40 patients received an exclusion diet (e.g., of wheat, nutritional supplements) based on immunological tests. They were compared with 11 patients who continued their normal diets. Patients of both groups participated in group discussions. At the end of the trial, the patients on exclusion diets reported a 50% reduction in pain, whereas the controls reported no changes [20].

Melatonin

Evidence-based assessment

Due to the limited data available, neither a positive nor a negative recommendation is possible. Strong consensus

Comment. A search of the literature identified 34 reports. In a non-controlled Argentinean trial with 19 patients, 3 mg melatonin/day for 4 weeks improved sleep and decreased the tender-point score [14]. In a RTC, 24 patients received 5 mg melatonin/day, 24 patients 20 mg fluoxetine/day, 27 patients 20 mg fluoxetine/day plus 3 mg melatonin/day, and 23 patients 20 mg fluoxetine/day plus 5 mg melatonin/day. A placebo control was not carried out. Pain was significantly reduced

Tab. 1 Changes from the first edition of the guidelines in the degree of recommendation for complementary and alternative therapies

Therapeutic procedure	Recommendation 2008	Recommendation 2012
Mindfulness-based stress reduction as sole treatment	No statement possible	Strongly negative
Acupuncture	Strongly negative	Open
	Minority opinion: open	
Breathing therapy	Open	Not considered
Elimination diet	Open	No statement possible
Foot reflexology massage therapy	Open	No statement
Homeopathy	Open	Negative
		Minority vote: open
Meditative Movement Therapies	Open	Strongly positive
Reiki	No statement	Negative
Vegetarian diet/therapeutic fasting	Open	No statement possible

in all arms of the trial, but sleep was significantly improved only in the melatonin groups [33]. Melatonin is approved for the short-term treatment of primary insomnia in patients older than 55 years.

Music therapy

Evidence-based assessment

Due to the limited data available, neither a positive nor a negative recommendation is possible. Strong consensus

Comment. In a US RCT with 26 patients and passive musical therapy, musically fluctuating vibrations (60–300 Hz) were not superior to sinusoidal vibrations in reducing the intensity of pain [13]. In a German controlled trial, a program of active music therapy in a group of 12 patients with various pain syndromes including FMS patients was superior to control therapy in reducing pain and pain-related disability at the completion of therapy [45].

Discussion

As pointed out in the first edition of the guidelines [40], complementary and alternative medicine (CAM) is widely used by patients with FMS (87–91%). However, these various therapies remain to be satisfactorily evaluated and their effectiveness established, since few good controlled trials on CAM therapies for fibromyalgia are available. Further research in this area is desirable and necessary.

In the first edition of the guidelines [40], the recommendations were designated "open" for breathing therapy, elimination/vegetarian diets, and foot massage therapy. In this update, they again cannot be either positively or negatively recommended because of the absence of satisfactory trials. The open recommendation for homeopathy has been changed to a negative recommendation due to the results of a quantitative data synthesis. However, the relatively sparse data can be interpreted in different ways (see Minority opinion). The recommendation for acupuncture was changed from negative to open as a result of new trials and quantitative data synthesis (Tab. 1).

As a rule, complementary procedures are applied in an interdisciplinary and integrative medical setting. Frequently they constitute a useful supplement within the framework of a multimodal therapeutic concept. One advantage of some complementary therapeutic procedures (e.g., qigong or tai chi) is that patients can apply the procedures themselves and are not dependent on a therapist.

Especially needed are randomized clinical trials on the effectiveness of music and dance therapies, homeopathy, and dietary intervention.

Many basic therapeutic approaches of complementary medicine, e.g., acupuncture, are thought to activate intrinsic physiological mechanisms. Frequently the exact mediators of potential therapeutic effects are still not understood. Thus, not only clinical trials to evaluate the complementary therapies are needed, but also trials in the realm of basic research. In addition, more information about how frequently FMS patients in Germany utilize complementary procedures and what motivates them to do so is needed.

Conclusion with regard to practice

FMS patients frequently utilize complementary and alternative medicine therapies. Complementary procedures as a rule are applied in an interdisciplinary and integrative medicine setting. They can be a useful supplement within the framework of a multimodal therapeutic concept. The use of meditative exercise therapies (tai chi, qigong, yoga) is strongly recommended. Acupuncture can be applied for a limited period of time. Dietary supplements and Reiki should not be utilized, nor should mindfulness-based stress reduction or dance therapy be utilized as the sole treatments.

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Conflict of interest. See Tab. 5 in "Methodological fundamentals used in developing the guideline" by W. Häuser, K. Bernardy, H. Wang, and I. Kopp in this issue.

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