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Patient-Centred Pain Management of Fibromyalgia Patient following a Holistic Approach and Mantra (Keep Calm and Forget the Pain)

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Abstract:Fibromyalgia is a musculoskeletal disease, which can result in chronic pain and it's an arthritis-related condition which impairs joints and soft tissues. The most common symptom is pain, which is severe and sharp sometimes and dull ache the other time in the form of constant and relentless aches all over the body. This study is based on a 45 years old male university professor who is diagnosed and suffering from fibromyalgia for the last 2.5 years (Appendix). Symptoms of fibromyalgia started gradually and in later stages, he use to feel chronic muscle pain, especially in the neck and back area. Other symptoms were muscle spasms, and moderate to severe fatigue, and he used to feel low ene rgy during his routine work. Due to fibromyalgia, his daily life, interaction with family and job is badly affected and this paper will discuss a bio-psychosocial approach for holistic management of his symptoms and improve his quality of life by employing a mantra i.e. Keep calm and forget the pain.

Keywords: (Bio-Psychosocial, Chronic Pain, Fibromyalgia, Holistic Management, And Physiotherapy.)

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Introduction

Pain is a disagreeable sensation that everybody recognizes and feels in life (Cervero 2012)[1]. It's an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (IASP 2012)[2]. Nay and Fetherstonhaugh (2012)[3] stated that pain is emotional, cognitive and physical and further classified it as somatic, visceral, neuropathic, centrally generated or peripherally generated and has a protective effect. According to Griensven, Strong and Unruh (2014)[4], many factors are considered in the perception of pain in an individual, such as age, gender, level of disability, and social and culture. Considering these statements about pain, it can be understood that pain is a complex phenomenon and its management need good knowledge and

Fibromyalgia is one of the diseases, which can result in chronic pain and it's an arthritis-related

outpatient

condition which impairs joints and soft tissues. The most common symptom is pain, which is severe and sharp sometimes and dull aches the other time in the form of constant and relentless aches all over the body (Chandler 2011)[5]. Other symptoms are dizziness, fatigue, morning stiffness, mood fluctuations, numbness or tingling in hands irritable bowe1 or feet. syndrome, temporomandibular joint disorder, and sleep disturbance which severely affects the quality of life and escalate stress level in fibromyalgia patients (Wallace and Wallace 2003)[6].

skills and implication of bio-psychosocial approach

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The etiology of fibromyalgia syndrome (FMS) is unknown, but research suggests that improper sleep, changes in muscles metabolism due to decreased blood flow and thus low oxygen flow to the muscles can be a reason, peripheral or central sensitization, hormonal and genetic influences and abnormalities in the autonomic nervous system could be the possible reasons (Ostalecki and Tamler 2009)[7].

There is no diagnostic test for fibromyalgia; however American College of Rheumatology proposed a classification criterion in 1990 based on widespread pain and tender points (ACR 2013)[8]. A revised version of this diagnostic criterion was published in 2010 which confirms the presence of FMS in a patient if he has 11 out of a total of 18 tender points and 2010 ACR criteria were found to be an effective diagnostic tool in most of the patients with FM (Hauser and Wolfe 2012)[9]. However, another study by Stahl (2009)[10] suggests that tender points are not an adequate tool to diagnose fibromyalgia.



Fig. 1: FM pain area

Pain Mechanism:

Persistent or intense nociception in FM patients can lead to transcriptional and translational changes in the spinal cord and brain resulting in central sensitization and pain (Staud and Rodriguez 2006)[12]. Woolf (2011)[13] explained

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that central sensitization is a state of CNS which is related to the evolution and preservation of chronic pain. Once central sensitization has been established, only minimal nociceptive input is required for the maintenance of the chronic pain state. Other factors, including pain-related negative affect, have been shown to significantly contribute to clinical fibromyalgia pain.

According to Staud (2006)[12], the mechanism behind this central sensitization in FM patients is due to the hyper-excitability of dorsal horn neurons (DHS) whose primary function is to transmit nociceptive stimulus to the brain. As a result, low-intensity input generates a high level of nociceptive stimulus to the brain and pain perception.

Prolonged stimulus from A-δ and C fibers depolarize DHS which leads to the removal of magnesium ions from NMDA-gated ion channels followed by an influx of extracellular calcium ions and the production of nitric oxide resulting in the diffusion of DHS. According to Latremoliere and Woolf (2009)[14], nitric oxides facilitate the increased release of excitatory amino acids and substance P and make dorsal horn neurons hyperexcitable. Due to this reason, any physical activity done by FM patient gets amplified in the spinal cord and results in heightened pain perception. Evidence also suggests that stress, depression, poor sleep and interpersonal and environmental factors also contribute to and result in central sensitization in FM patients (Hansson 2014)[15].

In research by Gosselin et al. (2010)[16], they suggested that glial cells dorsal horn enhance hypersensitivity in chronic pain. In central sensitization, many factors like nitric oxide and substance-P result in the activation of glial cells. Once activated, these cells facilitate the release of inflammatory cytokines, substance-P, nitric oxide, L-1RA, IL-6 and IL-8, prostaglandins, excitatory amino acids, and ATP, which in response, further increase the discharge of excitatory amino acids and substance P from the A- δ and C afferents that synapse in the dorsal horn and also enhance the hyper-excitability of the dorsal horn neurons. It is affirmed by Gosselin et al. (2010)[16] that Proinflammatory levels of cytokines IL-1RA, IL-6 and IL-8 are increased in FM patients supporting the role of glial cells in central sensitization in FM patients. Furthermore, many types of muscle abnormalities like ragged red and moth-eaten fibres have been seen in FM patients which appear due to repeated micro-trauma and contribute to continuous muscle tension and pain and also lead to ischemia that results in central sensitization of pain (Staud 2011)[17].

According to Griensven, Strong and Unruh (2014)[4], continuous nociceptive stimulus from nociceptive specific neurons put an inhibitory impact on wide dynamic range neurons (receives stimulus from nociceptive specific neurons and Aß fibres) and alters the way $A\beta$ fibres transmit the information which results in low excitability by nociceptive stimulation. These all changes lead to low threshold stimulus, unable to pass through DHS and finally not being felt. Furthermore, prolonged stimulation from Aδ and C fibres depolarizes DHS and forces magnesium ions to leave N-methyl-D-aspartate (NMDA), leading to calcium influx. Calcium influx results in nitric oxide production which thus leads to irregular liberation of substance P. This increased amount of substance P not only results in more and more calcium intrusion but also keeps dorsal horn neurons (DHN) hyperactive. Due to continuous calcium intrusion and hyperactive DHN, lowintensity stimulation is presumed as high intensity and the body feels too much pain even when the stimulus is not painful. When this state is preserved for a long time, it changes into central sensitization. Glutamate and substance P also play role in preserving central sensitization by lowering down threshold of AMPA and NMDA receptors

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which leads to hyper-intrusion of calcium ions which keep gates open and keep DHN hyperactive.



Fig.2 : Central sensitization

Meeus and Nijs (2007)[18] confirm the presence of temporal summation or wind-up in FM patients. Wind-up is a central spinal mechanism in which repetitive noxious stimulation results in a slow temporal summation that is experienced in humans as increased pain. During this process, NMDA receptors are activated, which results in calcium intrusion which activates nitric oxide release. Nitric oxide in response escalates the release of sensory neuropeptides especially substance-P turn from presynaptic neurons, therefore contributing to the development of hyperalgesia and maintenance of central sensitization. They also confirmed that there is no evidence for peripheral sensitization as the cause of hyperalgesia as there is no real tissue damage in FM patients.

The presence of central sensitization and wind-up phenomena in FM patients is confirmed by various researchers like Griensven, Strong and Unruh (2014)[4], Woolf (2011)[19], Yunus (2007)[20], Staud, Robinson and Price (2007)[21]. Furthermore, a most recent systematic review by Cagnie et al. (2014)[22] also confirms decreased functional connectivity in the descending painmodulating system and increased activity in the pain matrix related to central sensitization in FM patients. Additionally, distress, depression, disturbed sleep and social and environmental factors could be converted into pain and central sensitization through forced hyperactivity of the sympathetic component of the stress response system (Lavin 2012)[23].

Management of Mr. B's Case

Managing pain, improving sleeping, reducing fatigue, increasing muscular strength, and giving patients confidence to deal with all psychological and social issues are the prime aims for my fibromyalgia-affected patient. Addressing these issues is critical to avoid further depression and permanent disability. The management plan will be pharmacological and non-pharmacological. Furthermore, a mantra i.e. "Keep calm and forget the pain" will be wielded in the management plan.

Pharmacological Management:

FM patients are advised with pain-killers, opioids, muscle relaxants, sleep medicines and antidepressants depending upon disease severity and present condition of the patient (NHS Choices 2014; Shipley 2014)[24,25]

Pain Killers:

Paracetamol is a commonly advised and used pain-killer in FM patients and found to be effective (Shipley 2014)[25]. NSAIDs are also advised for FM patients but current evidence suggests that NSAIDs are not useful in the long-term management of fibromyalgia as it's not an inflammatory disease (Slim, Villademoros and Calandre 2013)[26]. The most commonly prescribed opioid to FM patients is tramadol, however, long-term use of opioids is discouraged as it leads to physical dependence and can produce a chronic pain state (NIH 2014)[27]. Recent studies like Merchant et al. (2013)[28], Tripathi, Shah and Sharma (2012)[29], and Slim, Villademoros and Calandre (2013)[26] recommend that paracetamol with tramadol combination was found to be effective in FM patients.

Anti-depressants and sleep medicines:

Pregabalin is a well-tolerated drug that remarkably improves sleep for FM patients (Arnold et al. 2014) [30]. Patients who used Pregabalin reported less body pain as well (Roth et al. 2012)[31]. As mentioned above, stress and depression contribute to and result in central sensitization in FM patients so it should be addressed. Antidepressant treatment for fibromyalgia was effective in patients with and without major depression, but the functional response was greater in depressed patients (Marsa et al. 2011)[32].

Non-Pharmacological Management:

Fibromyalgia is a pathology, which can't be dealt with by medicines only. It needs a holistic approach by a multi-disciplinary team (Griffith and Zarrouf 2008)[33]. Below is the list of researchsuggested non-pharmacologic options which can be utilized in FM patients.

Physiotherapy, exercises and daily life activities:

Exercise interventions have excellent effects on fatigue and sleep dysfunction in FM patients (Russell et al. 2014)[34]. Exercise reduces depressive symptoms in FM patients. Patients doing proper exercise training achieve the largest antidepressant effects (Herring et al. 2012)[35]. Physiotherapy, aerobic and strength training to improve physical fitness and function, reduce fibromyalgia symptoms, and improve quality of life in FM patients (Busch et al. 2011)[36]. Furthermore, my patient can be encouraged to take part in his favorite sports activities as he will not be bored, and will forget his pain and depression for some time which will help in decreasing muscle stiffness and pain. Water-based exercises with intensity and duration on patient preferences also have good effects on pain, sleep and fatigue (Hauser et al. 2010)[37].

Cognitive behavioral therapy (CBT):

CBT has shown excellent results in managing psycho-social, emotional and behavioral issues in FM patients (Slim, Villademoros and Calandre 2013)[26]. Although CBT doesn't have direct effects on pain, fatigue and sleep disturbances, it improves depressed mood and helps FM patients to cope with the pain. CBT in individuals with FM improves insomnia which, in turn, lowers the intensity of pain (Edinger et al. 2013)[38].

CBT in FM patients includes educating and discussing with the patient about pain, pain mechanism, fibromyalgia itself, sleep, diet, exercises and necessary changes that the patient should bring into his lifestyle. He should be explained the process for which he is the victim i.e. central sensitization. This will help him to recognize that it's his perception that is causing more fatigue, pain and sleeplessness and will help him to cope with it. (Lee et al. 2014)[39]. CBT is talking with the patient about his problems, fears, psychosocial issues and giving confidence and knowledge to the patient and making him ready to fight with the thing which is more in his thoughts and exists to a very little extent in reality.

CBT can also be attributed to talking therapy which helps people identify and develop skills to change negative thoughts and behaviours and make them enough confident and strong to cope with pain; sleep disorder, stress and psycho-social issues. (Koffel, Koffel and Gehrmanc 2014)[40].

Mind-body therapy / Mindfulness-Based Stress Reduction (MBSR):

MBSR is an 8-week group program teaching mindfulness meditation and mindful yoga exercises and is developed by Jon Kabat-Zinn. (Cash et al. 2014)[41]. MSBR is found to be an effective treatment for a variety of psychological problems and is especially effective for reducing anxiety, depression, and stress. It improves the ability to cope with the symptoms of fibromyalgia, as well as improving quality of life and decreasing pain severity (Thiagarajah et al. 2014)[42].

Balneotherapy / Spa therapy:

Balneotherapy or SPA therapy is defined as the treatment of disease by bathing, usually at a SPA resort, using hot or cold water rich in minerals, and including also drinking, inhalation, massage through moving water, mud-baths, relaxation, or stimulation. (Gutenbrunner et al. 2010)[43]. In a systematic review by Terhorst and Schneider (2012)[44], it was concluded that balneotherapy provides beneficial effects in patients with fibromyalgia by increasing blood flow which dissolves and eliminates toxins from the body, bringing improved nourishment to stiff fibromyalgic muscles. It also encourages FM patients who can't do full weight-bearing exercises on land; can exercise vigorously and comfortably in water (Ablin, Häuser and Buskila 2013) [45].

Massage Therapy:

According to Sanchez et al. (2011)[46], massage and myofascial release techniques improve pain and quality of life in patients with fibromyalgia. It increases the number of sleep hours and decreases substance-P levels which have a significant role in contributing to the development of hyperalgesia and maintenance of central sensitization (Field et al. 2002)[47]. A recent systematic review by Li et al. (2014)[48] confirms that massage therapy with a duration of≥5 weeks has immediate beneficial effects on improving pain, anxiety, and depression in FM patients. High-quality evidence for the effectiveness of manual therapy in FM patients is concluded by Clar et al. (2014)[49].

Furthermore, deep oscillation vibration massage (Kraft, Kanter and Janik 2013)[50] and Shiatsu massage (Yuan, Berssaneti and Marques 2013)[51], Tai-Chi (Raman , Mudedla and Wang 2014)[52] are safe and well tolerated in FM patients and improve pain intensity, pressure pain threshold, sleep quality, and quality of life.

Ayurveda Treatment

Ayurveda therapy is non-inferior to conventional treatment in patients with severe FM and has significant improvements in the Fibromyalgia impact questionnaire (FIQ) (Kessler et al. 2013)[53].

Craniosacral Therapy (CST):

It's a gentle way of working with the body using light therapeutic touch, aiming to release restrictions around the spinal cord and brain and subsequently restore body function (Jakel and Hauenschild 2012)[54]. CST improves the quality of life of patients with fibromyalgia, reducing their perception of pain and fatigue and improving their night rest and mood, with an increase in physical function.

Role And Importance Of Mantra And Its Implication In The Current Case:

A mantra can be a word, a phrase or a verbal instrument to produce something in one's mind. When you hear something again and again or repeat a rumour, again and again, it can become a reality in your mind (Newman 2014)[55]. It's purely dependent on a mantra user whether to take benefit or damage from it as it's like a fire, which has both destructive and helpful qualities

As the evidence mentioned above suggests that pain in FM patients is centrally sensitized. Its presence is far less than being pictured in FM patients. CBT, educating the patient about FM and pain mechanisms along-with goal setting and following a mantra i.e. "Keep calm and forget the pain" will help the patient to understand the reality. As Newman (2014)[55] suggested, repeating a mantra, understanding it and implementing it can help to wipe out the fake picture of pain in mind, my patient has to understand it. I will have face-to-face sittings with him; will listen to his fears, problems, and psychosocial issues, and then make a short-term and long-term plan. However, following the mantra i.e. "Keep calm and forget the pain" exactly supports the pain mechanism behind his pathology. He should remain calm, try to forget the pain and busy himself with constructive activities.

Holistic Management:

Dealing with FM patient is not a responsibility of a GP or a therapist alone and need a systematic biopsychosocial approach and team effort of the interdisciplinary team comprising a medical consultant, occupational therapist, physiotherapist and psychologist (Dubin 2014)[56]. The patient is already in much stressful condition and needs confidentiality, respect and polite behavior This will encourage him to share his fear and personal problems and social issues with the service provider. Without winning patient confidence, every therapy will fail so patient empowerment and patient-centered care are critical to be employed in FM patients. Furthermore, a discussion session should be done with the patient's employer to reduce the number of hours they work and cooperate with them to adapt to their current job. Employers can be asked to make necessary changes in their office furniture

to make patients comfortable and services of the occupational therapist should be acquired to design a more comfortable workstation.

How to measure progress in FM patients?

The Fibromyalgia Impact Questionnaire (FIQ) is an assessment and evaluation instrument developed to measure FM patient status, progress and outcomes. It let service providers assess the clinical effectiveness of interventions being given. It is a self-administered instrument that takes approximately 5 minutes to complete and is a valid and reliable scale (Bennett 2005)[57]

Fibromyalgia Assessment Status (FAS) index is a valid three-item instrument (pain, fatigue and sleep disturbances) that performs at least as well as the FIQ in FM patients, and is simpler to administer and score (Iannuccelli et al. 2011)[58]. Furthermore, Fatigue VAS can be utilized as an assessment tool to measure improvements in fatigue in FM patients (Crawford et al. 2011)[59].

Conclusion:

This study has increased the researcher's clinical reasoning, knowledge and skills and will be more confident in the management of his patient as a physiotherapist. Generally, the treatment plan for fibromyalgia could be combined with a lot of options otherwise the most important point is psychosocial factors and Evidence cited above clearly suggests that the management of FM needs a holistic approach, team effort, patient centered care. These steps along with patient empowerment and educating him clearly and thoroughly about the pathology and convincing him to implement the mantra i.e. "Keep calm and forget the pain" will help to decrease pain, and disability and improve quality of life.

Appendix/Case Study

Mr. B is 45 years old, male university professor, diagnosed with and suffering from fibromyalgia for the last 2.5 years. Being a university professor, he had many sleepless nights and long working days during his career. Symptoms of fibromyalgia started gradually and in later stages, he use to feel chronic muscle pain, especially in the neck and back areas. Other symptoms were muscle spasms, and moderate to severe fatigue, and he used to feel low energy during his routine work. His sleep is also disturbed and he feels stiffness during his gym work and normal walking and in conditions in which he used to be in the same position for longer times i.e. standing during giving lectures and sitting for self-study before lectures etc. His pain becomes worse in the winter season and due to increased pain, fatigue, morning stiffness and stress, he took many leaves from university in the last 2 years.

He uses anti-depressants and tramadol for pain relief. He is under immense stress due to his body pains which have disturbed his daily routine i.e. job, gym workout, hang-out with family, shopping etc. Sleep disturbance notices from the head of the department due to many off days and less interaction with family members and staying away from leisure activities are increasing his stress factor day by day.

Keeping this case study in mind, a pain management strategy will be devised for Mr X in this study, focusing on mantra: (Keep calm and forget the pain).

References

- 1. CERVERO, Fernando (2012). Understanding Pain: Exploring the Perception of Pain. 1st ed., USA, MIT Press.
- IASP (2012). IASP TAXONOMY. [online]. Last accessed 15 DECEMBER 2014 at: http://www.iasppain.org/Taxonomy?navItemNumber=576
- 3. NAY, R. and FETHERSTONHAUGH, D. (2012). What is pain? A phenomenological

approach to understanding. International Journal of Older People Nursing , 7 (3), 233-239.

- 4. GRIENSVEN, Hubert van, STRONG, Jenny and UNRUH, Anita (2014). Pain: A Textbook for Health Professionals. 2nd ed., China, Elsevier Health Sciences.
- CHANDLER, Pati (2011). Fibromyalgia Basics: A Beginner's Guide. 1st ed., Oklahoma, Tate Publishing.
- WALLACE, Daniel J. and WALLACE, J.B. (2003). Fibromyalgia : An Essential Guide for Patients and Their Families: An Essential Guide for Patients and Their Families. New York, Oxford University Press.
- OSTALECKI, Sharon and TAMLER, Martin S. (2009). 100 Questions & Answers About Fibromyalgia. 1st ed., Sudbury, Jones & Bartlett Learning.
- ACR (2013). Fibromyalgia. [online]. Last accessed 14th December 2014 at: http://www.rheumatology.org/Practice/Clini cal/Patients/Diseases_And_Conditions/Fibro myalgia/
- 9. HAUSER, W. and WOLFE, F. (2012). Diagnosis and diagnostic tests for fibromyalgia (syndrome). Reumatismo, 64 (4), 194-205
- STAHL, Stephen M. (2009). Fibromyalgia pathways and neurotransmitters. Human Psychopharmacology: Clinical and Experimental, 24 (S1), 11-17.
- 11. QUEIROZ, Luiz Paulo (2013). Worldwide Epidemiology of Fibromyalgia. Current Pain and Headache Reports, 17 (8),.
- 12. STAUD, Roland and RODRIGUEZ, Miguel E (2006). Mechanisms of disease: pain in fibromyalgia syndrome. Nature Reviews Rheumatology, 2 (2), 90-98.
- 13. WOOLF, Clifford J (2011). Central sensitization: Implications for the diagnosis and treatment of pain. Pain, 153 (2),.
- LATREMOLIERE, Alban and WOOLF, Clifford J. (2009). Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity. The Journal of Pain, 10 (9), 895-226.
- 15. HANSSON, Per (2014). Translational aspects of central sensitization induced by primary afferent activity: What it is and what it is not. PAIN, 155 (10), 1932–1934.
- GOSSELIN, Romain-Daniel, et al. (2010). Glial Cells and Chronic Pain. The Neuroscientist, 16 (5), 519-531.
- 17. STAUD, Roland (2011). Peripheral Pain Mechanisms in Chronic Widespread Pain.

Best Practice & Research Clinical Rheumatology, 25 (2), 155–164.

- MEEUS, Mira and NIJS, Jo (2007). Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. Clinical Rheumatology, 26 (4), 465-473.
- 19. WOOLF, Clifford J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. PAIN, 152 (3), 2-15.
- YUNUS, Muhammad B. (2007). Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. Seminars in Arthritis and Rheumatism, 36 (6), 339-356.
- STAUD, Roland, ROBINSON, Michael E. and PRICE, Donald D. (2007). Temporal Summation of Second Pain and Its Maintenance Are Useful for Characterizing Widespread Central Sensitization of Fibromyalgia Patients. The Journal of Pain, 8 (11), 893–901.
- 22. CAGNIE, Barbara , et al. (2014). Central sensitization in fibromyalgia? A systematic review on structural and functional brain MRI. Seminars in Arthritis and Rheumatism, 44 (1), 68-75.
- 23. LAVIN, Manuel Martinez (2012). Fibromyalgia: When Distress Becomes (Un)sympathetic Pain. Pain Research and Treatment, 2012, 1-6.
- 24. NHS CHOICES (2014). Fibromyalgia -Treatment - NHS Choices. [online]. Last accessed 14 December 2014 at: http://www.nhs.uk/Conditions/Fibromyalgia /Pages/Treatment.aspx
- 25. SHIPLEY, Michael (2014). Chronic widespread pain and fibromyalgia syndrome. Medicine, 42 (5), 271-274.
- SLIM, Mahmoud , VILLADEMOROS, Fernando Rico- and CALANDRE, Elena P. (2013). Current concepts in the treatment of fibromyalgia. JOURNAL OF SYMPTOMS AND SIGNS, 2 (4).
- 27. NIH (2014). Role of opioids in the treatment of chronic pain. [online]. Last accessed 14th December 2014 at: https://prevention.nih.gov/programsevents/pathways-toprevention/workshops/opioids-chronic-pain
- 28. MERCHANTE, Ignacio Morón, et al. (2013). Tramadol/Paracetamol Fixed-Dose Combination for Chronic Pain Management in Family Practice: A Clinical Review. ISRN Family Medicine, 2013,.
- 29. TRIPATHI, Sachidanand , SHAH, Rima and SHARMA, D C (2012). Analgesic activity of fixed dose combinations of paracetamol with diclofenac sodium and paracetamol with

tramadol on different pain models in healthy volunteers - A randomized double blind crossover study. Journal of Anaesthesiology Clinical Pharmacology, 28 (4), 465-469.

- ARNOLD, L., et al. (2014). Pregabalin is effective irrespective of antidepressant class in fibromyalgia patients currently receiving antidepressant medication for comorbid depression. The Journal of Pain, 15 (4),.
- ROTH, Thomas, et al. (2012). Effect of pregabalin on sleep in patients with fibromyalgia and sleep maintenance disturbance: A randomized, placebocontrolled, 2-way crossover polysomnography study[†]. Arthritis Care & Research, 64 (4), 597–606.
- 32. MARSA, Marina Díaz-, et al. (2011). Psychological Factors Affecting Response to Antidepressant Drugs in Fibromyalgia. Psychosomatics, 52 (3), 237–244.
- GRIFFITH, James P. and ZARROUF, Fahd A. (2008). A Systematic Review of Chronic Fatigue Syndrome: Don't Assume It's Depression. The Primary Care Companion -Journal of Clinical Psychiatry, 10 (2), 120-128.
- RUSSELL, D, et al. (2014). The effectiveness of exercise in the management of fatigue and sleep dysfunction in fibromyalgia syndrome: A systematic review. Rheumatology , 53 (1),.
- 35. HERRING, Matthew P., et al. (2012). Effect of Exercise Training on Depressive Symptoms Among Patients With a Chronic Illness. A Systematic Review and Meta-analysis of Randomized Controlled Trials. Archives of Internal Medicine, 172 (2), 101-111.
- BUSCH, Angela J., et al. (2011). Exercise Therapy for Fibromyalgia. Current Pain and Headache Reports, 15 (5), 358-367.
- 37. HAUSER, Winfried, et al. (2010). Research article Efficacy of different types of aerobic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomised controlled trials. Arthritis Research & Therapy, 12 (79)
- 38. EDINGER, J., et al. (2013). Can CBT for insomnia also improve pain sensitivity in fibromyalgia patients?: results from a randomized clinical trial. Sleep Medicine, 14 (1),.
- LEE, J., et al. (2014). Chronic widespread pain, including fibromyalgia: a pathway for care developed by the British Pain Society. British Journal of Anaesthesia, 112 (1),.
- 40. KOFFEL, Erin A., KOFFEL, Jonathan B. and GEHRMANC, Philip R. (2014). A metaanalysis of group cognitive behavioral therapy for insomnia. Sleep Medicine Reviews,.

- 41. CASH, Elizabeth , et al. (2014). Mindfulness Meditation Alleviates Fibromyalgia Symptoms in Women: Results of a Randomized Clinical Trial. Annals of Behavioral Medicine,.
- 42. THIAGARAJAH, Angeline S, et al. (2014). The relationship between fibromyalgia, stress and depression. International Journal of Clinical Rheumatology, 9 (4), 371–384.
- 43. GUTENBRUNNER, Christoph, et al. (2010). A proposal for a worldwide definition of health resort medicine, balneology, medical hydrology and climatology. International Journal of Biometeorology, 54 (5), 495-507.
- 44. TERHORST, L and SCHNEIDER, M (2012). Complementary and alternative medicine in the treatment of pain in fibromyalgia: a systematic review of randomized controlled trials. BMC Complementary and Alternative Medicine, 12 (1),.
- 45. ABLIN, Jacob N., HÄUSER, Winfried and BUSKILA, Dan (2013). Spa Treatment (Balneotherapy) for Fibromyalgia—A Qualitative-Narrative Review and a Historical Perspective. Evidence-Based Complementary and Alternative Medicine, 2013,.
- 46. SANCHEZ, Adelaida María Castro-, et al. (2011). Benefits of Massage-Myofascial Release Therapy on Pain, Anxiety, Quality of Sleep, Depression, and Quality of Life in Patients with Fibromyalgia. Evidence-Based Complementary and Alternative Medicine, 2011,.
- FIELD, Tiffany, et al. (2002). Fibromyalgia Pain and Substance P Decrease and Sleep Improves After Massage Therapy. Journal of Clinical Rheumatology, 8 (2), 72-76.
- LI, Yan-hui, et al. (2014). Massage Therapy for Fibromyalgia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Plos One, 9 (2),.
- 49. CLAR, Christine, et al. (2014). Clinical effectiveness of manual therapy for the management of musculoskeletal and nonmusculoskeletal conditions: systematic review and update of UK evidence report. Chiropractic & Manual Therapies, 22 (14),.
- 50. KRAFT, Karin , KANTER, Susanne and JANIK, Hubert (2013). Safety and Effectiveness of Vibration Massage by Deep Oscillations: A Prospective Observational Study. Evidence-Based Complementary and Alternative Medicine, 2013,.
- 51. YUAN, Susan L.K., BERSSANETI, Ana A. and MARQUES, Amelia P. (2013). Effects of Shiatsu in the Management of Fibromyalgia Symptoms: A Controlled Pilot Study. Journal of Manipulative and Physiological Therapeutics, 36 (7), 436–443.
- 52. RAMAN , Gowri , MUDEDLA , Sreenuvasu and WANG, Chenchen (2014). How Effective

Is Tai Chi Mind-Body Therapy for Fibromyalgia: A Systematic Review and Meta-Analysis. The Journal of Alternative and Complementary Medicine, 20 (5),.

- 53. KESSLER, Christian S., et al. (2013). Additive Complex Ayurvedic Treatment in Patients with Fibromyalgia Syndrome Compared to Conventional Standard Care Alone: A Nonrandomized Controlled Clinical Pilot Study (KAFA Trial). Evidence Based Complementary Alternative Medicine, 2013,.
- JAKEL, Anne and HAUENSCHILD, Philip von (2012). A systematic review to evaluate the clinical benefits of craniosacral therapy. Complementary therapies in medicine, 20 (6), 456–465.
- 55. NEWMAN, Pam (2014). The Magic Of Mantra. 1st ed., USA, Raphael Walrond.
- 56. DUBIN, Ruth (2014). Keep it simple: Easing the care burden of fibromyalgia. Canadian Family Physician, 60 (7), 599-601.
- 57. BENNETT, R. (2005). The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. Clinical and Experimental Rheumatology, 5 (39), 154-62.
- IANNUCCELLI, C. , et al. (2011). Psychometric properties of the Fibromyalgia Assessment Status (FAS) index: a national web-based study of fibromyalgia. Clinical and Experimental Rheumatology, 6 (69), 49-54.
- 59. ,CRAWFORD, B., et al. (2011). Assessing fibromyalgia-related fatigue: content validity and psychometric performance of the Fatigue Visual Analog Scale in adult patients with fibromyalgia. Clinical and Experimental Rheumatology, 29 (6), 34-43.