FOREWORD

Special Focus Issue: Pain Management in Fibromyalgia

Pain Management

Pain management in fibromyalgia

Robert M Bennett*

“The multidimensionality of fibromyalgia stems from its amalgamation of diverse symptoms ... Furthermore, the majority of fibromyalgia patients have one or more comorbidities unrelated to fibromyalgia...”

First draft submitted: 20 June 2016; Accepted for publication: 20 June 2016; Published online: 13 July 2016

Fibromyalgia is a multidimensional pain syndrome that currently defies an exact definition [1]. Nevertheless, rheumatologists, pain specialists and increasingly primary care providers, are gaining confidence in making this diagnosis and initiating treatment [2]. The multidimensionality of fibromyalgia stems from its amalgamation of diverse symptoms: widespread pain, tenderness, fatigue, nonrefreshing sleep, musculoskeletal stiffness, cognitive dysfunction, environmental sensitivity, mood disorders, poor balance, muscle weakness, functional impairments and disability [3]. Moreover, there are the commonly associated issues of irritable bowel syndrome, restless leg syndrome, overactive bladder, pelvic pain, vulvodynia, dyspareunia, migraine headaches, paresthesia and suicidal ideation. Furthermore, the majority of fibromyalgia patients have one or more comorbidities unrelated to fibromyalgia, such as osteoarthritis, rheumatoid arthritis, obesity, low back pain, systemic lupus erythematosus, traumatic injuries and psychological traumas such as post-traumatic stress disorder [4]. Against this backdrop, it

is little wonder that clinical research studies, especially those involving medications, usually fail to deliver encouraging results. This is well exemplified by several of the papers in this issue of *Pain Management*.

The problem of multidimensionality in fibromyalgia patients is mentioned by several authors. This is well summed up in Dr Turk's review which noted “despite similarities in symptoms, patients with fibromyalgia are unique, and require individualized treatment based on their symptoms and experiences. Providers must avoid adopting the ‘patient-uniformity myth’, assuming that all patients with the same diagnosis are identical and thereby require the same treatment regimen.” This therapeutic mindset is helped by understanding fibromyalgia from a biopsychosocial perspective. While there is good evidence of central sensitization and defective pain modulation in fibromyalgia patients, it is increasingly apparent that subcortical nociceptive transmission is modified by psychosocial factors [5]. From this perspective, the patient's subjective experience of central sensitization is influenced

KEYWORDS

• fibromyalgia • opioids • pain

“Fibromyalgia is a multidimensional pain syndrome that currently defies an exact definition.”

*Professor of Medicine & Nursing, Oregon Health & Sciences University, Portland, OR 97239, USA; fbennetrob1@comcast.net

“The use of opioids nonmalignant states is currently a ‘hot potato.’”

by psychological variables such as mood states, sociocultural environment, past experiences, its expectancy beliefs, catastrophization and other behavioral factors.

Patient education is a key factor in developing a beneficial patient–doctor relationship [6]. Patients have to understand that there is currently no cure for fibromyalgia; searching endlessly for what is ‘medically wrong’ detracts from their engagement and self-management. As Dr Turk notes, “a blind focus on illness *per se* ignores the real ability of individuals with fibromyalgia to make meaningful gains, and further keeps them from enjoying life that they have before them despite symptoms.” Cognitive–behavioral therapy is currently the favored approach that focuses on thoughts, feelings and behaviors, and is thus ideally suited for treating fibromyalgia from a biopsychosocial perspective. Important components of cognitive–behavioral therapy are as follows [7]:

- Education reassurance;
- Focus on functional gains rather than fibromyalgia as a disease;
- Realistic goal setting;
- Lifelong self-management;
- Pacing and increasing activities;
- Managing sleep;
- Addressing cognitive dysfunction – use of daily planners, to do lists, attention techniques;
- Recognizing the role of stress in symptom development;
- Counteracting maladaptive thinking;
- Relapse and maintenance;
- Improved communication with others;
- Assertiveness training; and
- Use of medications.

Many fibromyalgia patients state that fatigue is their major problem [8]. Our understanding of the neurophysiology fatigue is still in its infancy. Dr Mannerkorpi’s special report concludes that fatigue and sleep disturbance are multifactorial, and partly related to hypersensitivity to unpleasant sensory stimuli. She recommends that the management of fatigue needs to incorporate regular physical exercise with appropriate pacing and improved sleep hygiene. However, many patients

find that exercise often aggravates their pain and fatigue, and they drop out before any benefits are realized. Keeping patients in an exercise program is the subject of Dr Jones’ editorial. She advises to avoid discussing an ‘exercise program’. Rather, the patient needs to focus on increasing physical activity, not necessarily going to the gym, among others. She provides a menu of ten talking points that providers can use to start a conversation about how to successfully increase their level of activity. Each talking point provides a different way of increasing activity. This is another example of learning a self-management skill that needs a paradigm shift from a passive patient role to an active role. Dr Ablin discusses medications, such as modafinil, that may benefit fibromyalgia-related fatigue [9].

Fibromyalgia patients often inquire about dietary interventions [10]. The Internet abounds with recommendations, usually focusing on foods that benefit fibromyalgia patients and foods that aggravate fibromyalgia. Most of these recommendations are anecdotal. However, a few well done research studies support the recommendation of avoiding glutamate and aspartate. Dr Holton’s special report notes that glutamate is the major excitatory neurotransmitter in the brain and that fibromyalgia patients have higher levels of glutamate in the cerebrospinal fluid. Aspartate activates NMDA receptors; a crucial first step on the road to central sensitization. Dr Holton discusses three studies that demonstrated benefits from the elimination of monosodium glutamate and aspartame.

Central sensitization is driven by peripheral pain generators. With this in mind, all fibromyalgia patients should be carefully evaluated for pain generators, which commonly include osteoarthritis, injuries, migraine headaches, temporomandibular joint dysfunction and myofascial pain. Dr Fernández de las Peñas reviews the role of myofascial trigger points as important pain generators in the development of central sensitization. He outlines various strategies for managing myofascial trigger points. This is apparently an underappreciated topic, as none of the other contributors mention myofascial pain.

Dr Goldenberg’s editorial starts by noting that systematic reviews of pharmacologic intervention in fibromyalgia have been somewhat discouraging. For instance, he reports that most reviews have found little evidence that selective serotonin reuptake inhibitors are efficacious in fibromyalgia, while most have found only modest efficacy for the dual-reuptake inhibitors [2,3]. Duloxetine

and milnacipran provided a small incremental benefit over placebo in reducing pain but not in reducing fatigue or improving sleep or quality of life. Most long-term studies have found little change in symptoms over time but significant individual patient variability.

He supports Dr Turk's notion that 'the patient uniformity myth' is a significant factor leading to poor results in clinical trials. Dr Goldenberg suggests that patients entering clinical trials should be stratified according to variables such as pre-existing mood disorders, catastrophizing, multiple somatic symptoms, stress levels, poor sleep, obesity, disability, unemployment and inactivity.

Dr Choy's Special Report provides an overview of sleep dysfunction in fibromyalgia patients. In the mid-1970s, Drs Moldofsky and Smythe provided polysomnographic evidence of disordered non-rapid eye movement sleep in fibromyalgia and also produced a transient fibromyalgia-like syndrome in healthy volunteers by disrupting their non-rapid eye movement sleep [11]. Since that time other sleep abnormalities have been described, and their role in modulating dysfunctional sensory processing is described by Dr Choy. He notes that epidemiological and experimental studies have indicated that sleep dysfunction may lead to the development of fibromyalgia, and in healthy individuals sleep disruption impairs pain processing with reduction in descending pain modulation [12]. Among currently available pharmacological treatments, he states that amitriptyline and pregabalin can improve sleep quality. Interestingly, there is one study that finds daytime napping is associated with increased severity.

Dr Okifuji's review echoes the views of most contributors in saying "fibromyalgia continues to be a very difficult condition to successfully treat. fibromyalgia is by nature a multi-symptom, possibly multimechanistic disorder; thus any single modality that does not cover relevant areas of fibromyalgia would likely fail. The importance of considering individual variations in developing a personalized approach cannot be overstated." Dr Okifuji is a strong proponent of using psychological/behavioral approaches in the management of fibromyalgia, and stresses the importance of a patient's active engagement in all therapies. Until

a patient becomes fully committed, the chances of success are considerably reduced. The use of motivational enhancement therapy is a relatively new technique that has the potential for improving the patient's active engagement in therapy [13].

Dr Ablin's review provides a thorough commentary of current medications and novel therapies that are currently being evaluated. He notes that "at the current point in time much of the art of treating fibromyalgia remains an exercise of trial and error." A recent review in *Expert Opinion in Pharmacotherapy* complements Dr Ablin's contribution: according to the available evidence, pregabalin, duloxetine and milnacipran should be the drugs of choice for the treatment of this disease, followed by amitriptyline and cyclobenzaprine. Other drugs with at least one positive clinical trial include some selective serotonin reuptake inhibitors, moclobemide, pirlindole, gabapentin, tramadol, tropisetron, sodium oxybate and nabilone. Combination therapy is an option that needs to be more thoroughly investigated in clinical trials [14].

The use of opioids nonmalignant states is currently a 'hot potato' [15]. Dr Littlejohn's review states that "there is no evidence that pure opioids, such as morphine or oxycodone have any benefit in fibromyalgia. Tramadol has moderate evidence for efficacy, but adverse events and drug cross-reactions limit its use. Low-dose naltrexone targets activated glial cells and has some evidence of benefit." Dr Littlejohn has found that buprenorphine, a partial μ -opioid agonist action, with κ - and δ -opioid receptor antagonist actions, is useful in selected fibromyalgia patients, particularly where there is comorbid painful osteoarthritis of the hip, knee and back.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

- Bennett R, Friend R, Marcus D *et al.* Criteria for the diagnosis of fibromyalgia: validation of the modified 2010 preliminary ACR criteria and the development of alternative criteria. *Arthritis Care Res.* 66(9), 1364–1373 (2014).
- Arnold LM, Clauw DJ, Dunegan LJ, Turk DC. A framework for fibromyalgia management for primary care providers. *Mayo Clin. Proc.* 87(5), 488–496 (2012).
- Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2,596

- people with fibromyalgia. *BMC Musculoskeletal Disord.* 8, 27 (2007).
- 4 Rehm SE, Koroschetz J, Gockel U *et al.* A cross-sectional survey of 3035 patients with fibromyalgia: subgroups of patients with typical comorbidities and sensory symptom profiles. *Rheumatology (Oxford)* 49(6), 1146–1152 (2010).
- 5 Fombergstein K, Qadri S, Ramani R. Functional MRI and pain. *Curr. Opin. Anaesthesiol.* 26(5), 588–593 (2013).
- 6 Faller H, Ehlebracht-König I, Reusch A. [Empowerment by patient education in rheumatology]. *Z. Rheumatol.* 74(7), 603–608 (2015).
- 7 Huppert JD. The building blocks of treatment in cognitive–behavioral therapy. *Isr. J. Psychiatry Relat. Sci.* 46(4), 245–250 (2009).
- 8 Crawford BK, Piault EC, Lai C, Bennett RM. Assessing fibromyalgia-related fatigue: content validity and psychometric performance of the Fatigue Visual Analog Scale in adult patients with fibromyalgia. *Clin. Exp. Rheumatol.* 29(6 Suppl. 69), S34–S43 (2011).
- 9 Schwartz TL, Rayancha S, Rashid A, Chlebowksi S, Chilton M, Morell M. Modafinil treatment for fatigue associated with fibromyalgia. *J. Clin. Rheumatol.* 13(1), 52 (2007).
- 10 Rossi A, Di Lollo AC, Guzzo MP *et al.* Fibromyalgia and nutrition: what news? *Clin. Exp. Rheumatol.* 33(1 Suppl. 88), S117–S125 (2015).
- 11 Moldofsky H, Scarsbrick P, England R, Smythe H. Musculoskeletal symptoms and non-REM sleep disturbance in patients with “fibrositis syndrome” and healthy subjects. *Psychosom. Med.* 37, 341–351 (1975).
- 12 Tiede W, Magerl W, Baumgartner U, Durrer B, Ehlert U, Treede RD. Sleep restriction attenuates amplitudes and attentional modulation of pain-related evoked potentials, but augments pain ratings in healthy volunteers. *Pain* 148(1), 36–42 (2010).
- 13 Polcin DL, Galloway GP, Palmer J, Mains W. The case for high-dose motivational enhancement therapy. *Subst. Use Misuse* 39(2), 331–343 (2004).
- 14 Calandre EP, Rico-Villademoros F, Slim M. An update on pharmacotherapy for the treatment of fibromyalgia. *Expert Opin. Pharmacother.* 16(9), 1347–1368 (2015).
- 15 Wilkerson RG, Kim HK, Windsor TA, Mareiniss DP. The opioid epidemic in the United States. *Emerg. Med. Clin. North Am.* 34(2), e1–e23 (2016).