

FIBROMYALGIA: ABSTRACTS 2009 FROM ARTICLES IN MEDICAL JOURNALS

The abstracts in this collection are intended to provide doctors and other health professionals with a convenient overview of trends in research on fibromyalgia published in medical journals in the year 2009. The studies were selected from the extensive literature on fibromyalgia so as to cover a wide range of subjects in limited space.

The following studies were published in the period January through March, 2009, and others will be added to this selection at intervals during the year. Similar collections of abstracts produced annually from 1999 on can be found on the website of the National Fibromyalgia Partnership: www.fmpartnership.org.

The abstracts are arranged in alphabetical order by lead author.

Bazzichi L, Palego L, Giannaccini G, Rossi A, De Feo F, Giacomelli C, Betti L, Giusti L, Mascia G, Bombardieri S, Lucacchini A

Altered amino acid homeostasis in subjects affected by fibromyalgia

OBJECTIVES: To evaluate plasma amino acid (AA) concentrations in patients affected by fibromyalgia (FM) and to study the relationships between their levels and FM clinical parameters. **DESIGN AND METHODS:** 20 AAs were assessed in 34 FM patients and in 18 healthy volunteers by means of a modified version of the Waters picotag method. **RESULTS:** Significant lower plasma taurine, alanine, tyrosine (Tyr), valine, methionine, phenylalanine and threonine concentrations, and the sum of essential AAs were observed in FM patients vs healthy controls ($P < 0.05$). Tyr CAA' ratio and the sum of AAs competing with tryptophan for brain uptake were significantly reduced in FM ($P < 0.05$). A significant correlation was found between FM clinical parameters and certain AAs. **CONCLUSIONS: Our results suggest probable defects of gut malabsorption of certain AAs in FM patients. Moreover, given the reduced Tyr CAA' ratio in FM patients, a possible impairment of the catecholaminergic system in the FM syndrome may be suggested.**

Clin Biochem. 2009 Mar 10. [Epub ahead of print]

Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, Spaeth M, Saraiva F, Nacci F, Thomas E, Caubère JP, Le Lay K, Taieb C, Matucci-Cerinic M

Prevalence of fibromyalgia: A survey in five European countries

OBJECTIVE: A survey was performed in 5 European countries (France, Germany, Italy, Portugal, and Spain) to estimate the prevalence of fibromyalgia (FM) in the general population. **METHODS:** In each country, the London Fibromyalgia Epidemiological Study Screening Questionnaire (LFESSQ) was administered by telephone to a representative sample of the community over 15 years of age. A positive screen was defined as the following: (1) meeting the 4-pain criteria alone (LFESSQ-4), or (2) meeting both the 4-pain and the 2-fatigue criteria (LFESSQ-6). The questionnaire was also submitted to all outpatients referred to the 8 participating rheumatology clinics for 1 month. These patients were examined by a rheumatologist to confirm or exclude the FM diagnosis according to the 1990 American College of Rheumatology classification criteria. The prevalence of FM in the general population was estimated by applying the positive-predictive values to eligible community subjects (ie, positive screens). **RESULTS:** Among rheumatology outpatients, 46% screened positive for chronic widespread pain (LFESSQ-4), 32% for pain and fatigue (LFESSQ-6), and 14% were confirmed FM cases. In the whole general population, 13% and 6.7% screened positive for LFESSQ-4 and LFESSQ-6, respectively. The estimated overall prevalence of FM was 4.7% (95% CI: 4.0 to 5.3) and 2.9% (95% CI: 2.4 to 3.4), respectively, in the general population. The prevalence of FM was age- and sex-related and varied among countries. **CONCLUSION: FM appears to be a common condition in these 5 European countries, even if data derived from the most specific criteria set (LFESSQ-6) are considered.**

Semin Arthritis Rheum. 2009 Feb 26. [Epub ahead of print]

Häuser W, Bernardy K, Arnold B, Offenbächer M, Schiltenswolf M

Efficacy of multicomponent treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials

OBJECTIVE: To systematically review the efficacy of multicomponent treatment of fibromyalgia syndrome (FMS). **METHODS:** We screened Medline, PsychINFO, Scopus, and the Cochrane Library (through December 2007), as well as reference sections of original studies, reviews, and evidence-based guidelines. Randomized controlled trials (RCTs) on the multicomponent treatment (at least 1 educational or other psychological therapy with at least 1 exercise therapy) of FMS were analyzed. **RESULTS:** We included 9 (of 14) RCTs with 1,119 subjects (median treatment time 24 hours) in the meta-analysis. Effects were summarized using

standardized mean differences (SMDs) or weighted mean differences (WMDs). There was strong evidence that multicomponent treatment reduces pain (SMD -0.37; 95% confidence interval [95% CI] -0.62, -0.13), fatigue (WMD -0.85; 95% CI -1.50, -0.20), depressive symptoms (SMD -0.67; 95% CI -1.08, -0.26), and limitations to health-related quality of life (HRQOL) (SMD -0.59; 95% CI -0.90, -0.27) and improves self-efficacy pain (SMD 0.54; 95% CI 0.26, 0.82) and physical fitness (SMD 0.30; 95% CI 0.02, 0.57) at post-treatment. **There was no evidence of its efficacy on pain, fatigue, sleep disturbances, depressive symptoms, HRQOL, or self-efficacy pain in the long term.** There was strong evidence that positive effects on physical fitness (SMD 0.30; 95% CI 0.09, 0.51) can be maintained in the long term (median followup 7 months). **CONCLUSIONS:** There is strong evidence that **multicomponent treatment has beneficial short-term effects** on the key symptoms of FMS. Strategies to maintain the benefits of multicomponent treatment in the long term need to be developed.

Arthritis Rheum. 2009 Feb 15; 61(2):216–24

Häuser W, Bernardy K, Uçeyler N, Sommer C

Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis

CONTEXT: Fibromyalgia syndrome (FMS) is a chronic pain disorder associated with multiple debilitating symptoms and high disease-related costs. Effective treatment options are needed. **OBJECTIVES:** To determine the efficacy of antidepressants in the treatment of FMS by performing a meta-analysis of randomized controlled clinical trials. **DATA SOURCES:** MEDLINE, PsycINFO, Scopus, and the Cochrane Library databases were searched through August 2008. Reference sections of original studies, meta-analyses, and reviews on antidepressants in FMS were reviewed. **STUDY SELECTION:** Randomized placebo-controlled trials with tricyclic and tetracyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs) were analyzed. **DATA EXTRACTION AND DATA SYNTHESIS:** Two authors independently extracted data. Effects were summarized using standardized mean differences (SMDs) by a random-effects model. **RESULTS:** Eighteen randomized controlled trials (median duration, 8 weeks; range, 4–28 weeks) involving 1427 participants were included. Overall, there was strong evidence for an association of antidepressants with reduction in pain (SMD, -0.43; 95% confidence interval [CI], -0.55 to -0.30), fatigue (SMD, -0.13; 95% CI, -0.26 to -0.01), depressed mood (SMD, -0.26; 95% CI, -0.39 to -0.12), and sleep disturbances (SMD, -0.32; 95% CI, -0.46 to -0.18). There was strong evidence for an association of antidepressants with improved health-related quality of life (SMD, -0.31; 95% CI, -0.42 to -0.20). Effect sizes for pain reduction were large for TCAs (SMD, -1.64; 95% CI, -2.57 to -0.71), medium for MAOIs (SMD, -0.54; 95% CI, -1.02 to -0.07), and small for SSRIs (SMD, -0.39; 95% CI, -0.77 to -0.01) and SNRIs (SMD, -0.36; 95% CI, -0.46 to -0.25). **CONCLUSION:** **Antidepressant medications are associated with improvements in pain,**

depression, fatigue, sleep disturbances, and health-related quality of life in patients with FMS.

JAMA. 2009 Jan 14; 301(2):198–209

Jones KD, Horak FB, Winters-Stone K, Irvine JM, Bennett RM

Fibromyalgia is associated with impaired balance and falls

BACKGROUND/OBJECTIVE: The purpose of this study was to determine whether fibromyalgia (FM) patients differ from matched healthy controls in clinical tests of balance ability and fall frequency. **METHODS:** Thirty-four FM patients and 32 age-matched controls were administered the Balance Evaluation-Systems Test (BESTest), rated their balance confidence with the Activities-Specific Balance Confidence (ABC) Scale, and reported the number of falls in the last 6 months. The Fibromyalgia Impact Questionnaire was used to assess FM severity. **RESULTS:** FM patients had significantly impaired balance in all components of the BESTest compared with controls. They also scored more poorly on balance confidence. Overall FM severity (Fibromyalgia Impact Questionnaire) correlated significantly with the BESTest and the ABC scale. The BESTest and ABC correlated significantly with 6 commonly reported FM symptoms (excluding pain). FM patients reported a total of 37 falls over the last 6-months compared with 6 falls in healthy controls. **CONCLUSION: FM is associated with balance problems and increased fall frequency.** Patients were aware of their balance problems. These results suggest that FM may affect peripheral and/or central mechanisms of postural control. Further objective study is needed to identify the relative contributions of various neural and musculoskeletal and other impairments to postural stability in FM to provide clinicians with methods to maximize postural stability and help fall prevention.

J Clin Rheumatol. 2009 Feb; 15(1):16–21

Russell IJ, Perkins AT, Michalek JE;
Oxybate SXB-26 Fibromyalgia Syndrome Study Group

Collaborators (43): Bennett RM, Price M, Barron A, Evans T, Diab I, Lacombe J, Habros JS, Yatabe H, Holman AJ, Meyers R, Kivitz A, Morrisson D, Kopp E, Downs J, Mease P, Granner D, Neiman A, Fanguy D, Nordstrom D, Sturgeon RB, Pappas J, Wilkinson J, Patkar A, Tarter K, Russell J, Haynes W, Seiden D, Rosen F, Sheldon EA, Alabaci M, Silverman SL, Joseph C, Smith NL, Francisco T, Wallace D, Arnold I, Willis LG, Craddock A, Winfield JB, Bradshaw P, Daughtridge A, Wood P, Warren L

Sodium oxybate relieves pain and improves function in fibromyalgia syndrome: a randomized, double-blind, placebo-controlled, multicenter clinical trial

OBJECTIVE: To evaluate the safety and efficacy of sodium oxybate for management of the symptoms of fibromyalgia syndrome (FMS). **METHODS:** Patients with FMS (according to the American College of Rheumatology 1990 criteria) were randomized, after discontinuing their prestudy medications for FMS, to receive 4.5 gm or 6 gm of sodium oxybate or matching placebo once per night for 8 weeks. The primary outcome variable (POV) was a composite score for changes from baseline in 3 coprimary self-report measures: patient's pain rating (in daily electronic diaries) on a visual analog scale (PVAS), the Fibromyalgia Impact Questionnaire (FIQ) score, and the Patient Global Impression of Change (PGI-C). A beneficial response rate for the POV composite score was defined as $\geq 20\%$ improvement in the PVAS and FIQ scores plus a rating of "much better" or "very much better" on the PGI-C. Secondary measures included subjective sleep outcomes (on the Jenkins Scale for Sleep) and quality-of-life measures. The analyses were based on an intent-to-treat (ITT) population. **RESULTS:** The ITT population included 188 patients with FMS, 78% of whom completed the trial. Significant benefit was observed with both dosages of sodium oxybate, according to changes in the POV and subjective sleep quality. Improvements in the PVAS score were significantly correlated with sleep outcomes. Sodium oxybate was well tolerated overall; dose-related nausea ($\leq 28\%$ of patients) and dizziness ($\leq 18\%$ of patients) tended to resolve with continued therapy. **CONCLUSION:** **Sodium oxybate therapy was well tolerated and significantly improved the symptoms of FMS.** Further study of sodium oxybate as a novel therapeutic option for FMS is warranted.

Arthritis Rheum. 2009 Jan; 60(1):299–309

Schafranski MD, Malucelli T, Machado F, Takeshi H, Kaiber F, Schmidt C, Harth F

Intravenous lidocaine for fibromyalgia syndrome: an open trial

Fibromyalgia is a disorder characterized by chronic widespread pain. In this study, we investigated the effect of intravenous infusions of lidocaine in pain and quality of life of patients with fibromyalgia. Twenty-three consecutive patients were included in the study, which consisted on five sequential intravenous 2% lidocaine infusions with rising dosages (2–5 mg/kg, days 1–5). Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire, and a visual analog scale (VAS) for pain were applied before the first lidocaine infusion, immediately after the fifth infusion and 30 days after the fifth infusion. A significant improvement was observed in the FIQ scores after the fifth infusion (73.52 \pm 16.56 vs 63.29 \pm 21.21, $p = 0.02$), which was maintained after 30 days (73.52 \pm 16.56 vs 63.85 \pm 24.59, $p = 0.04$). Similar results were seen concerning the VAS: 8.19 \pm 1.76 vs 6.84 \pm 2.44, $p = 0.01$ and 8.19 \pm 1.76 vs 7.17 \pm 2.35, $p = 0.05$,

respectively. **Intravenous lidocaine infusions are safe and effective in the management of fibromyalgia.**

Clin Rheumatol. 2009 Mar 5. [Epub ahead of print]

Schneider M, Vernon H, Ko G, Lawson G, Perera J

Chiropractic management of fibromyalgia syndrome: a systematic review of the literature

OBJECTIVE: Fibromyalgia syndrome (FMS) is one of the most commonly diagnosed nonarticular soft tissue conditions in all fields of musculoskeletal medicine, including chiropractic. The purpose of this study was to perform a comprehensive review of the literature for the most commonly used treatment procedures in chiropractic for FMS and to provide evidence ratings for these procedures. The emphasis of this literature review was on conservative and nonpharmaceutical therapies. **METHODS:** The Scientific Commission of the Council on Chiropractic Guidelines and Practice Parameters (CCGPP) was charged with developing literature syntheses, organized by anatomical region, to evaluate and report on the evidence base for chiropractic care. This article is the outcome of this charge. As part of the CCGPP process, preliminary drafts of these articles were posted on the CCGPP Web site www.ccgpp.org (2006–8) to allow for an open process and the broadest possible mechanism for stakeholder input. Online comprehensive literature searches were performed of the following databases: Cochrane Database of Systematic Reviews; National Guidelines Clearinghouse; Cochrane Central Register of Controlled Trials; Manual, Alternative, and Natural Therapy Index System; Index to Chiropractic Literature, Cumulative Index to Nursing and Allied Health Literature; Allied and Complementary Medicine; and PubMed up to June 2006. **RESULTS:** Our search yielded the following results: 8 systematic reviews, 3 meta-analyses, 5 published guidelines, and 1 consensus document. Our direct search of the databases for additional randomized trials did not find any chiropractic randomized clinical trials that were not already included in one or more of the systematic reviews/guidelines. The review of the Manual, Alternative, and Natural Therapy Index System and Index to Chiropractic Literature databases yielded an additional 38 articles regarding various nonpharmacologic therapies such as chiropractic, acupuncture, nutritional/herbal supplements, massage, etc. Review of these articles resulted in the following recommendations regarding nonpharmaceutical treatments of FMS. **Strong evidence supports aerobic exercise and cognitive behavioral therapy. Moderate evidence supports massage, muscle strength training, acupuncture, and spa therapy (balneotherapy). Limited evidence supports spinal manipulation, movement/body awareness, vitamins, herbs, and dietary modification.** **CONCLUSIONS:** Several non-pharmacologic treatments and manual-type therapies have acceptable evidentiary support in the treatment of FMS.

J Manipulative Physiol Ther. 2009 Jan; 32(1):25–40

Togo F, Natelson BH, Adler GK, Ottenweller JE, Goldenberg DL, Struzik ZR, Yamamoto Y

Plasma cytokine fluctuations over time in healthy controls and patients with fibromyalgia

We examined the pattern of cytokine secretion across the 24-hr day for women with widespread pain and tenderness having the diagnosis of fibromyalgia (FM) and matched healthy controls. Subjects were given time to habituate to being in a clinical research laboratory environment and then were sampled for cytokines without their being disturbed for a 24-hr period including an 8-hr sleep period. Cytokine levels were uniformly low but characterized by bursts of secretion. Bursting occurred either in singlets or in doublets with a range from 88 to 131 mins between doublet bursts. There was an element of synchronization of these bursts with most occurring at the beginning of sampling. FM patients showed a shift to increased IL-10 in the nighttime compared to controls. The relation between this anti-inflammatory cytokine to the pro-inflammatory cytokines studied also differed between groups: FM patients showed an increased ratio of IL-10 burst amplitude to that of pro-inflammatory cytokines IL-1beta, IL-8, and TNF-alpha. We interpret this to indicate a skew away from the normal balance favoring pro-inflammatory cytokines in controls toward one favoring an anti-inflammatory response in FM. **These changes toward anti-inflammatory predominance in FM may explain the common complaint of disturbed sleep because these cytokines are known to disrupt sleep.**

Exp Biol Med (Maywood). 2009 Feb; 234(2):232–40. Epub 2008 Dec 8