Consult Dr. A
anderson medical group

Consult Dr. A
anderson medical group

NUTRIENT INJECTION THERAPIES FOR CHRONIC FATIGUE & FIBROMYALGIA

Nutrient Injection Therapies for Chronic Fatigue and Fibromyalgia

Introduction:

The purpose of this review is to collate and summarize some of the available scientific data regarding potential causes, aggravations and therapies in the Fibromyalgia / Chronic Fatigue (FMS/CFS) and like syndromes. This review is not intended to be encyclopedic in its scope but rather to give some data driven rationale for common therapies clinically recognized as useful in these syndromes. Additionally, the data presented are limited to injection therapies (although if absorption is sufficient most of these compounds are known to help as oral supplements as well).

As injection therapies are a broad topic and the technical points of safe administration are numerous and beyond the scope of this paper limited discussion of technique oriented data (such as dose and administration) will be given. It is assumed that if a practitioner wishes to use this

information to treat patients they have the prerequisite training in the safe administration of any substances mentioned by injection therapies.

Additionally, it should be noted that non-injection therapies typically crucial to the treatment of FMS/CFS while not discussed in this review are assumed to be known and practiced concurrently. These include but are not limited to endocrine support, immune and infectious therapies, sleep hygiene and therapies, digestive support and diet therapy as well as many others. And finally any injectable nutrient mentioned below should be added to the oral repletion therapy of the FMS/CFS patient both between and after the injection therapy if the individual patient gastrointestinal function allows.

DISCLAIMER: This is a well referenced resource but nothing in this paper should be used as self-medication advice nor should practitioners untrained in parenteral therapies use this information to guide therapeutic decision making.

Basis of the disorders:

Much has been published regarding the potential causes of FMS/CFS. Most clinicians agree these conditions to be multifactorial and patient specific. Potential partial causes or aggravations of FMS/CFS include hippocampal dysfunction [1], neurotransmitter imbalance and autoimmune attack [2,4], lifestyle and physical activity deficits [3], oxidative stress and mitochondrial dysfunction [5,7,9-15,52], methyl cycle defects [6], seasonal affective disorder [8], anemia [36] and many others.

Given the broad base of data regarding potential cause and the logical conclusion that FMS/CFS are therefore multifactorial, anecdotal positive clinical experience in broad based therapies both oral and injection both match the available data and make logical clinical sense. The discussion below attempts to give scientific and clinical rationale to common injection therapies which address the above causal relationships in FMS/CFS. When the term “clinical experience” is used in this review it refers to the authors two decades experience in treating FMS/CFS with multiple therapies including over 50,000 IV and injection administrations.

As a small number of reviews or studies on injection therapies in FMS/CFS exist [18-20] this review will focus on updated information regarding potential biological indications for injection therapies commonly employed in the integrative medical setting.

Therapeutic targets for injection therapies:

Therapeutic targets for injection therapies are well suited to access some of the common potential causes of FMS/CFS. These include neurotransmitter imbalance and autoimmunity, oxidative stress and mitochondrial dysfunction, methyl cycle and other genomic defects, anemia, dehydration and like comorbidities.

Hydration:

Dehydration is known to aggravate many of the CNS manifestations of FMS/CFS such as “brain fog” [16] and is known to decrease quality of life in ill people [17]. Although many nutrient formulas are hypertonic and thus not hydrating our clinical experience shows that the desired IV formula can be made hydrating if the osmolarity is adjusted to isotonic or mildly hypotonic (170-310 mOsm/L) and that this adjustment can improve tolerance and outcome of the IV

therapy. While oral hydration is always a primary goal of therapy the addition of a hydrating type IV formula can additionally be beneficial in this population.

Vitamin C / Ascorbic acid (ASC):

The use of ASC in IV therapy is well known and reasonably well studied and reported on elsewhere in the literature and clinical experience. Limiting the discussion to symptoms related to FMS/CFS such as fatigue, pain and immune deficits ASC infusion can be a helpful addition. Use of ASC IV has been shown to improve pain in viral infections [21], improve fatigue [22] as well as improve oxidative / redox balance [7]. Doses in studies were moderate (5 to 15 grams) and are amenable to admixture in other water soluble nutrient infusions. In clinical practice the author has seen similar results with these relatively low dose strategies, as well as higher dose oxidative ASC infusions in treating infectious comorbidities of FMS/CFS.

Magnesium:

Long a staple of oral and injection therapies in FMS/CFS magnesium enjoys great clinical popularity in most clinicians' assessment. Some of the things injected magnesium can add to the therapy of FMS/CFS include NMDA / Glutamate receptor activity decrease causing lower nociception and CNS arousal and acetylcholine blockade causing skeletal muscle relaxation [23,24], cardiac muscle calcium channel down-regulation [27], as well as increased cell ATP [25] and glutathione activity [26]. An additional benefit of injected magnesium is a relatively long therapeutic window following injection. In a human study of IV magnesium Silver reported that tissue levels rose for 24 hours following infusion and distributed for another 24 hours giving a total post infusion therapeutic window of at least 48 hours following one infusion [27]. The authors clinical experience has been that IM doses of 0.5 to 2 grams Magnesium Sulfate 50% are tolerated as well as IV doses of between two and eight grams of magnesium. IV doses of this magnitude need to be appropriately diluted and started at lower doses and escalated to patient cardiac tolerance.

The amino structures Taurine and Carnitine:

While many amino acids are necessary in the therapy of FMS/CFS in the authors clinical experience tow amino structures found clinically to be exceptionally helpful are taurine and carnitine.

Carnitine (either in the "l" form or the more bioavailable "acetyl-l" form) is useful in varied targets affecting the FMS/CFS patient including decreasing neurotoxicity [28], decreasing lactic acid build up [29] as well as its more commonly known biochemical function of transporting fatty acids into the mitochondria for beta oxidation based energy production. The l-carnitine form in our clinic is administered IB at doses of 500 – 4000 mg and the acetyl-l-carnitine form at doses of 100 mg to 1000 mg in most cases.

Taurine is the master osmolyte in the human body and as such regulates distribution of the excitable ions (Na, K, Ca, Mg and Cl) to their appropriate sides of the cell membrane [30, 31]. In this role the authors clinical observation has been that the addition of taurine to IV formulas containing magnesium and other excitable tissue acting minerals causes a greater benefit as reported by patients. For example the addition of taurine to a formula with magnesium will be perceived by patients to have a more muscle relaxing effect in many cases. Taurine is used constantly at the cell membrane and thus depleted both in low dietary intake as well as by

oxidative stressors [31]. Taurine in our clinic is dosed between 200 and 1000 mg in most IV formulas.

Methyl Cycle and Genomic SNP support:

In a scientific presentation by the author [6] a trial was reported investigating the incidence of MTHFR defects in the general population versus a sample of race matched patients with known FMS/CFS (n=88). The incidence summarized in Table-1 was much higher for Homozygous C-677 defects as well as Compound Heterozygous defects in the FMS/CFS sample than the general population. Once this association was established an active comparator interventional trial was conducted to assess what if any help support of the damaged methyl pathways via nutrients would add to clinical outcomes. Addition of a balanced methyl support oral formula as well as methylated forms of injectable B-12 and Folate resulted in data summarized in Table-2. The intervention in the 88 patients already receiving treatment in an integrative medical clinic for their FMS/CFS already included all the comorbidity therapies mentioned in the introduction above. Prior therapy time frame was from one to five years and all patients were not progressing with respect to additional positive treatment or symptom outcome prior to the methyl support.

Well rounded support for methylation (MET) as well as cystathionine beta synthase (CBS) pathways appeared well tolerated in this study. This fact creates the need for more than simple injection of a methyl donor such as 5-MTHF or Methyl B-12 in these patients. A therapeutic injection strategy is listed below.

Care should be taken to titrate the doses of supportive parenterals up to patient tolerance. Some younger patients will tolerate a faster titration to full dose and some not. Most patients with higher grade defects (homozygous, compound heterozygous or heterozygous with CFS, FMS, chronic neuroinflammatory disease and any with elevated homocystiene) who are over 35-40 years of age will require a slower titration but ultimately higher dosing based on our observations. Additionally it should be mentioned that in some patients with numerous additional SNP defects a lower and more inclusive formula may be required in order to support the other SNP defects. In our clinical experience this is most common in patients with COMT/MAO and other like SNP defects.

Data regarding injection / parenteral support of methylation defect treatment in this setting covers a span of two decades but due to the lack of available active form nutrients for parenteral administration some interpretation is necessary. Older recommendations were generally safe but lacked the agents we have available currently such as parenteral 5-MTHF and Methyl B-12 [32,33,34]. Newer interventional trials used injection grade 5-MTHF and hydroxyl-B-12 with success and patient tolerance. [35]

Iron Status and Ferritin:

Ortancil et.al.[36] include a statement that significantly correlates with the authors clinical experience “Our study implicates a possible association between FM and decreased ferritin level, even for ferritin in normal ranges. We suggest that iron as a cofactor in serotonin and dopamine production may have a role in the etiology of FMS.” Most commonly oral repletion of iron stores via diet and supplement interventions is preferred. In the authors experience in those with the other mentioned comorbidities and low ferritin of over five years duration injectable iron may be required. Clinical experience and the study by Ortancil indicate that a ferritin level over

40 (and ideally 50-75) is required to replete the mitochondrial iron reserves as well as hematologic requirements. Both primary targets of iron stores (mitochondrial and hematologic) contribute significantly when iron stores are low.

Injectable iron is known to have a higher incidence of anaphylaxis and other high grade adverse events than most other nutrients. As such the clinician should have very specific and proper training before attempting injectable iron formulas, as well as available emergency medications and interventions should an adverse event occur.

Glutathione:

A favorite IV additive, glutathione is known by those who use it to have extremely positive effects in the treatment of a wide range of illnesses. In the FMS/CFS setting it also is known to be a helpful addition to most IV protocols. Although much has been written about the potential benefits of glutathione augmentation in medicine the FMS/CFS patient may have a greater need for glutathione augmentation due to higher oxidative stress loads [37] as well as a greater need for appropriate cell regulation [38]. In addition to these factors a connection between FMS/CFS and Multiple Chemical Sensitivity (MCS) is clinically noted in many patients. Glutathione is one factor in aiding repair of cell metabolism in MCS [45] as well as damaged redox states in FMS/CFS [51-52]. These and other likely reasons for inclusion are why the author includes glutathione IV in all FMS/CFS patient protocols. General doses are between one and three grams and may be as high as six to ten grams in some cases. Clinically the use of glutathione IV appears to be more efficient when support nutrients (such as are found in the general nutrient IV formulas) are given before the glutathione infusion. As some patients will have sulfation SNP defects and other reasons not to tolerate glutathione the author typically uses a lower test dose on the first IV infusion of glutathione ranging from 100-500 mg.

The Lipoic Acid based Thiols:

Alpha Lipoic Acid (ALA):

ALA is a thiol and as such is known in basic science to support levels of glutathione in the liver and other tissues. In experimental models [39,40] ALA has been shown to be helpful in pushing the redox balance in a positive direction via modulation of inflammatory cytokines such as Tumor Necrosis Factor and NF-kappa-b. Like glutathione the lipoic acid molecules hold a high level of respect for clinical efficacy in those who use them. Due to recent changes in pharmacologic compounds of ALA it is recommended that practitioners discuss dosing and potential reactions based on the available form of ALA from their individual compounding pharmacy before administration.

Lipoic Acid Mineral Complex (LAMC):

Known as the proprietary formula “Poly MVA” in North America, LAMC has shown to be helpful in cell repair, mitochondrial repair and radioprotection [41-44]. The author has found that low IV doses (5-15 mL) combined with low oral doses (5-10 mL BID) improve energy and other quality of life measures in FMS/CFS patients. Like ALA, LAMC does take time to work so most patients are advised that either therapy (like all others) may need to be continued for a number of months for a positive effect to be noted.

DMSO:

The sulfur containing molecules DMSO and MSM have been reported as potentially therapies in FMS/CFS [50] as well as useful in pain syndromes for palliation [46]. DMSO is also used to transport drugs and nutrients across membranes including the blood brain barrier [47-49]. Given these data as well as a long clinical history with both substances the author utilizes both in the therapy of those with FMS/CFS. IV MSM is water soluble and mixes with most any water soluble IV formula. DMSO is fat and water soluble and mixes well with most water soluble formulas as well. As DMSO is a solvent special handling and administration guidelines as taught in standard IV training should be observed. The author favors DMSO for acute and neuropathic pain syndromes and MSM for long term therapies in FMS/CFS.

Summary:

In summary it is clear that there exist many potential therapies both oral and parenteral for the patient suffering from FMS/CFS. Both the data presented and the authors experience would speak to the utility and improvement in outcomes when the above, and many other, interventions are used in a well planned comprehensive care plan for these patients. Basic training and understanding of the biochemistry and pharmacology of these agents allow for safe and effective use in the IV or IM setting.

References:

1. Yasser E. et.al. Hippocampus Dysfunction May Explain Symptoms of Fibromyalgia Syndrome. A Study with Single-Voxel Magnetic Resonance Spectroscopy. J Rheumatol 2008;35:1371-1377.

2. Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis. JAMA. 2009; 301(2):198-209 (ISSN: 1538-3598) PreMedline Identifier: 19141768

3. Fibromyalgia Symptoms Eased by "Lifestyle Physical Activity" Arthritis Res Ther. Published online March 29, 2010.

4. Klein R, Berg PA. High incidence of antibodies to 5-hydroxytryptamine, gangliosides and phospholipids in patients with chronic fatigue and fibromyalgia syndrome and their relatives: evidence for a clinical entity of both disorders. Eur J Med Res. 1995 Oct 16;1(1):21-6. PMID: 9392689

5. Nazıroğlu M, Akkuş S, Soyupek F, Yalman K, Çelik Ö, Eriş S, Uslusoy GA. Vitamins C and E treatment combined with exercise modulates oxidative stress markers in blood of patients with fibromyalgia: a controlled clinical pilot study. Stress. 2010 Nov;13(6):498-505. doi: 10.3109/10253890.2010.486064. Epub 2010 Jul 28. PMID: 20666654

6. Anderson, PS (2012, August). Active comparator trial of addition of MTHFR specific support versus standard integrative naturopathic therapy for treating patients with diagnosed Fibromyalgia (FMS) and Chronic Fatigue Syndrome (CFS). Poster Presentation, presented at the American Association of Naturopathic Physicians annual convention, Bellevue, WA.

7. Nazıroğlu M, Akkuş S, Soyupek F, Yalman K, Çelik Ö, Eriş S, Uslusoy GA. Vitamins C and E treatment combined with exercise modulates oxidative stress markers in blood of patients with

fibromyalgia: a controlled clinical pilot study. Stress. 2010 Nov;13(6):498-505. doi: 10.3109/10253890.2010.486064. Epub 2010 Jul 28. PMID: 20666654

8. Michael Terman, PhD, Susan M Levine, MD, Jiuan S Terman, PhD, Sean Doherty. Chronic fatigue syndrome and seasonal affective disorder: comorbidity, diagnostic overlap, and implications for treatment. The American Journal of Medicine Volume 105, Issue 3, Supplement 1 , Pages 115S-124S, 28 September 1998. published online 16 August 2004.

9. Sarah Myhill, Norman E. Booth, John McLaren-Howard. Chronic fatigue syndrome and mitochondrial dysfunction. Int J Clin Exp Med (2009) 2, 1-16. www.ijcem.com/IJCEM812001

10. Bell DS. Cellular Hypoxia and Neuro-Immune Fatigue. Livermore: WingSpan Press, 2007.

11. Pall ML. Elevated, sustained peroxynitrite levels as the cause of chronic fatigue syndrome. Med Hypotheses 2000; 54: 115-125.

12. Richards RS, Roberts TK, McGregor NR, Dunstan RH and Butt HL. Blood parameters indicative of oxidative stress are associated with symptom expression in chronic fatigue syndrome. Redox Report 2000; 5: 35-41.

13. Zeevalk GD, Bernard LP, Song C, Gluck M and Ehrhart J. Mitochondrial inhibition and oxidative stress: Reciprocating players in neurodegeneration. Antioxid Redox Signal 2005; 7: 1117-1139.

14. Kennedy G, Spence VA, McLaren M, Hill A, Underwood C and Belch JJF. Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms. Free Radic Biol Med 2005; 39: 584-589.

15. Pall ML. Explaining "Unexplained Illnesses". New York: Harrington Park Press, 2007.

16. Ross AJ, Medow MS, Rowe PC, Stewart JM. What is brain fog? An evaluation of the symptom in postural tachycardia syndrome. Clin Auton Res. 2013 Dec;23(6):305-11. doi: 10.1007/s10286-013-0212-z. Epub 2013 Sep 3. PMID: 23999934

17. A BegumMN, Johnson CS. A review of the literature on dehydration in the institutionalized elderly. e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 5 (2010) e47–e53

18. Ali A, Njike VY, Northrup V, Sabina AB, Williams AL, Liberti LS, Perlman AI, Adelson H, Katz DL. Intravenous micronutrient therapy (Myers' Cocktail) for fibromyalgia: a placebo-controlled pilot study. J Altern Complement Med. 2009 Mar;15(3):247-57. PMID: 19250003

19. Brinkman K, Vrouenraets S, Kauffmann R, Weigel H, Frissen J. Treatment of nucleoside reverse transcriptase inhibitor-induced lactic acidosis. AIDS 2000;14 (17):2801-2803. PMID: 11125906

20. Osborne V, White C. Fibromyalgia and Chronic Fatigue Syndrome: Benefits of IV Micronutrient Therapy. NDNR: 3-8;August 2007

21. Schencking M, Vollbracht C, et al, Intravenous Vitamin C in the treatment of shingles: Results of a multicenter prospective cohort study. Med Sci Monit, 2012 Apr 1; 18(4):CR215-224.

22. Suh et al. Intravenous Vitamin C administration reduces fatigue in office workers: a double-blind randomized controlled trial. Nutrition Journal 2012, 11:7. http://www.nutritionj.com/content/11/1/7

23. Dubé L, Granry JC. The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine: a review. Can J Anaesth. 2003 Aug-Sep;50(7):732-46. PMID: 12944451

24. Soave PM, Conti G, Costa R. Arcangeli A. Magnesium and anaesthesia. Curr Drug Targets. 2009 Aug;10(8):734-43. PMID: 19702521

25. Nagai N1, Fukuhata T, Ito Y. Effect of magnesium deficiency on intracellular ATP levels in human lens epithelial cells. Biol Pharm Bull. 2007 Jan;30(1):6-10. PMID: 17202650

26. A Barbagallo M, et.al. Effects of Glutathione on Red Blood Cell Intracellular Magnesium : Relation to Glucose Metabolism. Hypertension. 1999;34:76-82. doi: 10.1161/01.HYP.34.1.76

27. Silver BR. Development of Cellular Magnesium Nano-Analysis in Treatment of Clinical Magnesium Deficiency. Journal of the American College of Nutrition, Vol. 23, No. 6, 732S-737S (2004). PMID: 15637223

28. Virmani A, Gaetani F, Binienda Z. Effects of metabolic modifiers such as carnitines, coenzyme Q10, and PUFAs against different forms of neurotoxic insults: metabolic inhibitors, MPTP, and methamphetamine. Ann N Y Acad Sci. 2005 Aug;1053:183-91. PMID: 16179522

29. Claessens YE, Cariou A, Chiche JD, Dauriat G, Dhainaut JF. L-Carnitine as a treatment of life-threatening lactic acidosis induced by nucleoside analogues. AIDS. 2000 Mar 10;14(4):472-3. PMID: 10770558

30. Lambert IH. Regulation of the cellular content of the organic osmolyte taurine in mammalian cells. Neurochem Res. 2004 Jan;29(1):27-63. PMID: 14992263

31. Stevens MJ, Lattimer SA, Kamijo M, Van Huysen C, Sima AA, Greene DA. Osmotically-induced nerve taurine depletion and the compatible osmolyte hypothesis in experimental diabetic neuropathy in the rat. Diabetologia. 1993 Jul;36(7):608-14. PMID: 8359577

32. Guenther, B.D. , C.A. Sheppard, P. Tran, R. Rozen, R.G. Matthews, and M.L. Ludwig. The structure and properties of methylenetetrahydrofolate reductase from Escherichia coli suggest how folate ameliorates human hyperhomcyseinmia. Nature Structural Biology 6, 359-365 (1999).

33. Rosenblatt, D. S. Inherited disorders of folate transport and metabolism. In The Metabolic Basis of Inherited Disease (eds Scriver, C.R., Beaudet, A.L., Sly, W. S., & Valle, D.) 2049-2063 (McGraw-Hill, New York, 1989).

34. Ogier de Baulny H, Gérard M, Saudubray JM, Zittoun J. Remethylation defects: guidelines for clinical diagnosis and treatment. Eur J Pediatr. 1998 Apr;157 Suppl 2:S77-83.

35. Buccianti G, et.al. 5-methyltetrahydrofolate restores endothelial function in uraemic patients on convective haemodyalisis. Nephrol Dial Transplant (2002) 17: 857-864

36. Ortancil O, Sanli A, Eryuksel R, Basaran A, Ankarali H. Association between serum ferritin level and fibromyalgia syndrome. Eur J Clin Nutr. 2010 Mar;64(3):308-12. doi: 10.1038/ejcn.2009.149. Epub 2010 Jan 20. PMID: 20087382

37. La Rubia M, Rus A, Molina F, Del Moral ML. Is fibromyalgia-related oxidative stress implicated in the decline of physical and mental health status? Clin Exp Rheumatol. 2013 Nov-Dec;31(6 Suppl 79):S121-7. Epub 2013 Dec 16. PMID: 24373370

38. Ashtiani HR et.al. Glutathione, cell proliferation and differentiation African Journal of Biotechnology Vol. 10(34), pp. 6348-6363, 11 July, 2011. Available online at http://www.academicjournals.org/AJB. DOI: 10.5897/AJB10.044

39. Maes M, Mihaylova I, Bosmans E. Not in the mind of neurasthenic lazybones but in the cell nucleus: patients with chronic fatigue syndrome have increased production of nuclear factor kappa beta. Neuro Endocrinol Lett. 2007 Aug;28(4):456-62. PMID: 17693979

40. Moore RM et.al. Alpha-Lipoic Acid Inhibits Tumor Necrosis Factor-Induced Remodeling and Weakening of Human Fetal Membranes. Biol Reprod. Apr 2009; 80(4): 781–787. Prepublished online Dec 23, 2008. doi: 10.1095/biolreprod.108.073205. PMCID: PMC2673805

41. Menon, A., and Nair, C.K.K. (2011) Poly MVA – a dietary supplement containing alpha-Lipoic Acid Mineral Complex , enhances cellular DNA repair. Int. J. Low Radiation, in print.

42. Ramachandran, L., Krishnan, C.V., Nair, C.K.K. (2010) Radioprotection by α-Lipoic Acid Mineral Complex formulation, (POLY-MVA) in mice, Cancer Biotherapy and Radiopharmaceuticals, Vol. 25, No.4, 395-399.

43. Menon, A., Krishnan, C.V., Nair, C.K.K. (2009) Protection from gamma-radiation insult to antioxidant defense and cellular DNA by POLY-MVA, a dietary supplement containing palladium lipoic acid formulation. Int. J. Low Radiation, Vol. 6, No.3, 248-262.

44. Menon, A., Krishnan, C.V., Nair, C.K.K. (2008) Antioxidant and radioprotective activity of POLY-MVA against radiation induced damages, Amala Cancer Bulletin, Vol 28, 167-173

45. De Luca C. et.al. Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolizing enzymes. Toxicology and Applied Pharmacology 248 (2010) 285–292

46. Hoang BX, et.al. Dimethyl Sulfoxide–Sodium Bicarbonate Infusion for Palliative Care and Pain Relief in Patients With Metastatic Prostate Cancer. Journal of Pain & Palliative Care Pharmacotherapy. 2011;25:350–355. DOI: 10.3109/15360288.2011.606294

47. Brasnjevic I. Et.al. Delivery of peptide and protein drugs over the blood–brain barrier. Progress in Neurobiology 87 (2009) 212–251. doi:10.1016

48. RD Broadwell, M Salcman, and RS Kaplan. Morphologic effect of dimethyl sulfoxide on the blood-brain barrier. Science 9 July 1982:Vol. 217. no. 4555, pp. 164 – 166

49. Walker M. Profile of the holistic cancer therapist W. Douglas Brodie, MD, HMD. (Medical Journalist Report of Innovative Biologics). Townsend Letter for Doctors and Patients. 2/1/2002

50. Parcell S. Sulfur in human nutrition and applications in medicine. Altern Med Rev. 2002 Feb;7(1):22-44. PMID: 11896744

51. Sarah Myhill, Norman E. Booth, John McLaren-Howard. Chronic fatigue syndrome and mitochondrial dysfunction. Int J Clin Exp Med (2009) 2, 1-16. www.ijcem.com/IJCEM812001

52. Russell L. Blaylock and Joseph Maroon. Natural plant products and extracts that reduce immunoexcitotoxicity-associated neurodegeneration and promote repair within the central nervous system. Surg Neurol Int. 2012; 3: 19

Tables

Table-1

Incidence Data:	Hetero A1298C	Hetero C677T	Compound Hetero	Homo A1298C	Homo C677T
Study n = 88	23	12	19	9	22
% CFS/FMS Participants	26	13	23	10	25
% Normal population	43	43	15	11	11
% Incidence Difference	- 40	- 70	+ 53	- 1	+ 44

Table-2

Result of treatment – Active comparator :	Hetero A1298C	Hetero C677T	Compound Hetero	Homo A1298C	Homo C677T
Intervention % (of n)	22	25	47	50	27
% outcome improvement	+ 55%	+ 75%	+ 56%	+ 56%	+ 71%