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Biochemical Defects in the 2-5A Synthetase/RNase L Antiviral Pathway in Chronic Fatigue Syndrome (CFS). R.J. Suhadolnik[1], N.L. Reichenbach[1], P.M. Hitzges[1], D.H. Gillespie[2], D.R. Strayer[2], and W.A. Carter[3]. Temple University[1], Hahnemann University[2], HEM Pharmaceuticals Corp.[3], Philadelphia, PA USA.

The 2', 5'-oligoadenylate (2-5A) synthetase/RNase L system, an antiviral cellular defense mechanism, has been shown to be a promising target for study in CFS. Based on the possible role of virus reactivation in CFS, mismatched dsRNA (Ampligen®), a biological response modifier with antiviral activity, was studied in 92 individuals who met the CDC definition for CFS in a multicenter, randomized, double-blind, placebo-controlled clinical trial. Pretherapy in CFS, latent 2-5A synthetase was increased; bioactive 2-5A level and RNase L activity were significantly upregulated. Therapy with mismatched dsRNA restored these activities towards normal. Decreases in RNase L correlated significantly with improvements in clinical response in terms of Activities of Daily Living (ADL) and cognitive and symptom tests within the SCL-90-R. Mismatched dsRNA therapy resulted in improvements in Karnofsky Performance score, and Activities of Daily Living. Viral reactivation was significantly decreased after therapy with mismatched dsRNA compared to placebo. Use of the 2-5A synthetase/RNase L pathway shows promise as a molecular marker of disease activity in CFS.

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Treatment of Chronic Fatigue Syndrome (CFS) with Ampligen®. D. Strayer, D. Gillespie, D. Peterson, P. Cheney, P. Salvato, M. Loveless, R. Suhadolnik, D. Walters and W. Carter. HEM Pharmaceuticals Corp., Hahnemann and Temple Univ., Phila., PA, Univ. of Oregon, Portland, OR, Charlotte, NC, Incline Village, NV, Houston, TX.

A multicenter, double-blind, randomized trial of Ampligen®, 400 mg twice weekly vs. placebo was performed with 92 patients with severely debilitating symptoms meeting the CDC case definition of CFS. All patients had baseline Karnofsky Performance Scores (KPS) between 20 and 60. 45 patients received Ampligen® up to 24 weeks and showed a median KPS improvement of over 8 points; while 47 patients receiving placebo showed 0 KPS change. The difference in KPS improvement between the two groups was significant ($p<0.01$). KPS improvement was unrelated to prior psychological illness as determined with the Diagnostic Interview Schedule. KPS increases correlated with symptom reduction as determined by the SCL-90-R, improvements in ability to perform work during treadmill testing, and increases in Activities of Daily Living (ADL). In addition, significant improvement ($p<0.05$) was also observed in ADL. The Ampligen® treated group utilized significantly less CNS and pain medications, and had fewer hospitalizations. Reductions in virus reactivation were significantly greater in those receiving Ampligen®. There were no significant differences in the total number of adverse events (AEs) reported or in the number of dropouts between the two study arms. Several patients in the Ampligen® group reported severe AEs not seen in the placebo arm; however, these AEs appeared to be related to the patient's underlying medical condition. No patients were discontinued because of toxicity. These results indicate that Ampligen® is generally well tolerated and active in CFS.