Reduction in Parasympathetic Autonomic Nervous System Function in Fibromyalgia Patients

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PURPOSE

Fibromyalgia syndrome (FMS) is characterized by chronic, widespread pain, fatigue and difficulty with sleep. Fibromyalgia patients often experience cognitive impairment, irritable bowel symptoms and posturally-mediated hypotension. The lack of restorative sleep in fibromyalgia patients is a particularly troubling symptom and may help to explain the daytime fatigue and many of the other symptoms described. Studies have indicated that autonomic nervous system (ANS) function is altered in fibromyalgia patients as revealed by objective ANS testing.

The ANS is intimately involved in maintenance of blood pressure, heart rate, bowel function, pain perception as well as initiation and maintenance of sleep. These abnormalities may help to explain the symptoms patients have with fibromyalgia. Heart rate variability (HRV) measures temporal differences between consecutive heart beats. One can determine the relative function of the ANS using Holter monitor to look at patterns of ANS function, particularly circadian rhythms.

In the frequency domain, High Frequency (HF) activity is known to be associated with parasympathetic nervous system activity, which is significantly active in normal subjects from midnight to 5am and slows down the body's system functions for restoration during sleep. Low Frequency (LF) is associated with sympathetic nervous system activity. We employed this methodology in order to understand parasympathetic and sympathetic nervous system function in this population while looking for a consistent pattern that might objectively separate FMS patients from patients with similar complaints who do not have FMS.

METHODS

58 control patients and 329 FMS patients from a single medical practice (DS) were tested using a Holter Monitor (ECG). FMS patients were defined as meeting the 1990 American College of Rheumatology criteria, were diagnosed as mild to severe and were consecutive patients presented at the medical practice.

Control patients were randomly selected from a cohort of patients in a larger database and were characterized as having the majority of their circadian index above the normal range and having an increase over 1500% during the hours of midnight to 5:00 am, which represents the 5th percentile.

Subjects wore holter monitors for a period of 24 hours and went about their daily routines. HRV data was performed by Laboratory Industry Services. HRV, sympathetic (LF) and parasympathetic (HF) data points analyzed were: SDNN, LF (0.04 to <0.15 Hz), HF (0.15 to <0.40 Hz), Total Power, Normal LF, Normal HF, LF/HF ratio and Circadian increase between the hours of 0:00 (midnight) to 5:00am. The means of these points were compared between the control and active groups using a Two-Sample t-Test, Assuming Equal Variances. Hypothesized Mean Difference was 0. QRS complexes were reviewed on a Pathfinder 710 (Reynolds Medical) by a specialized technician who censored aberrant complexes and artifacts using an algorithm based on the Lomb-Scargle method of spectral analysis to produce the standard measures of high frequency, low frequency and very low frequency (VLF, 0.003 to <0.04 Hz) spectral power, expressed in msec2.

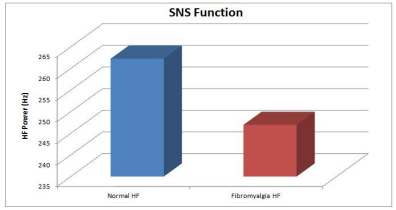

Figure 2: Mean high frequency corresponding to sympathetic function measured in Hertz

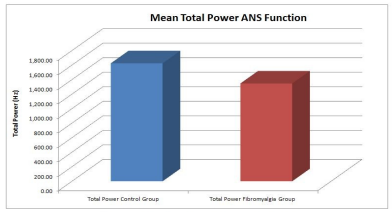

Figure 3: The mean total power of ANS function measured in Hz ($p < 0.02$)

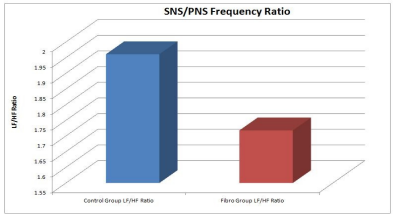

Figure 4: LF to HF ratio reflecting relative sympathetic hyper-reactivity ($p < 0.001$)

RESULTS

The FMS patients demonstrated decreased total power and parasympathetic ANS function, specifically reduction in parasympathetic nervous system function at night. The mean LF, corresponding to sympathetic function, of the 329 fibromyalgia patients was 388.99 Hz and the mean of the 58 normal patients was 470.0 Hz. ($p < 0.03$) The mean HF, corresponding to parasympathetic function, of the 329 fibromyalgia patients was 246.95 Hz and the mean of the 58 normal patients was 262.25 Hz ($p > 0.3$) The mean Total Power of ANS function for fibromyalgia patients was 1347.53 Hz and the mean of the 58 normal patients was 1625.13 Hz. ($p < 0.02$) The mean LF to HF ratio of the FMS patients of 1.718 and the mean of the normal patients was 1.961 ($p < 0.001$), which indicated relative sympathetic hyperreactivity compared to normals in the fibromyalgia population. The mean Circadian increase for the 320 fibromyalgia patients was 998% while the mean Circadian increase for the 58 normal patients was 7454% ($p < 0.001$), demonstrating lack of parasympathetic activation at night in the fibromyalgia patients.

CONCLUSIONS

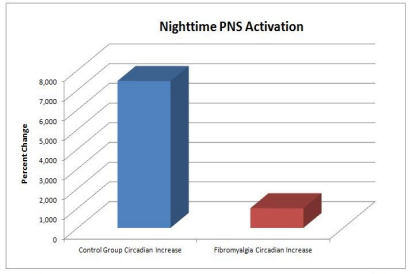

Figure 5: Mean circadian increase demonstrating lack of nighttime parasympathetic activation ($p < 0.001$)

Patients with fibromyalgia have persistently reduced parasympathetic ANS activity, specifically at night. The role of parasympathetic ANS function in initiation and maintenance of sleep may help to explain the sleep disturbance and daytime somnolence patients report. The ANS is closely tied to many physiologic functions that are involved in symptoms FMS patients including irritable bowel syndrome, posturally-mediated hypotension, sleep disturbance, widespread pain and anxiety, which can be explained by the relative sympathetic hyperreactivity. Holter monitor may represent an objective diagnostic tool for FMS and therapies that target abnormalities in ANS function may represent a new therapeutic option for FMS patients.