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Nutrient supplement enhances natural killer cell function in women with chronic fatigue syndrome and fibromyalgia: preliminary report

Rita R. Ellithorpe[a,b], Robert Settineri[a], Talon Ellithorpe[b] & Garth L. Nicolson[a]
[a]The Institute for Molecular Medicine, Huntington Beach, California
[b]Tustin Longevity Center, Tustin California

Abstract

Objectives: Chronic fatigue syndrome (CSF) and fibromyalgia (FM) share similarities in a sequela of symptoms, including post-exertional malaise, pain, sleep disturbances, neurological and cognitive manifestations and motor impairment along with reduced natural killer (NK) cell function. This brief clinical report examined the effects of a nutrient dietary supplement, Transfer Factor Multi-Immune™, on the functional activity of NK cells in a small number of women with a confirmed diagnosis of either CFS and/or FM. **Methods:** Subjects who met the inclusionary criteria and had reduced NK function were instructed to take two capsules of supplement per day. On Days 0 and 30 blood samples were taken to determine NK cell functional status. **Results:** After treatment, six out of the seven subjects had a statistically significant increase ($p=0.02$) in NK function ranging from 135% to 4,667% after treatment; one had a decrease of NK function of -61%. The median increase in NK cell function after treatment was 247%. **Conclusions:** This preliminary study suggests that the administration of a natural supplement can increase NK cell activity in women with CFS and FM with low NK activity.

Keywords: natural killer cells, fatigue, nutritional supplement, transfer factor

***Corresponding Author:** Prof. Emeritus Garth Nicolson, Department of Molecular Pathology, The Institute for Molecular Medicine, P.O. Box 9355, S. Laguna Beach, California 92652. Email: gnicolson@immed.org

Introduction

Chronic fatigue syndrome (CFS) is a condition characterized by a variety of signs and symptoms, with post-exertional malaise and/or chronic and persistent disabling fatigue being prevalent symptoms.[1-4] Other symptoms of CFS include pain, sleep disturbances, neurological and cognitive manifestations (impaired concentration, mental processing, short-term memory), motor impairments, and altered immune and autonomic responses.[1-4] It is difficult to estimate the prevalence of CFS because of the complexity of its case definition and its overlapping signs and symptoms with myalgic encephalomyelitis (ME).[4,5] The Center for Disease Control reported a prevalence for CFS of 0.3% with over 1,000,000 adults with this disorder in the U.S.[6], but the rate could be as high as 2.5% with the use of different case definitions.[7]

Fibromyalgia (FM) has overlapping symptoms with CFS and mostly affects adult women [8-10]. FM is a chronic, diffuse musculoskeletal pain syndrome of unknown etiology characterized by chronic widespread pain, abnormal pain processing/heightened pain sensitivity, chronic fatigue, sleep disorders, and emotional distress or depression.[9,10] FM decreases quality of life and productivity and is associated with varying degrees of functional disability, psychological distress, lost work time, and increased use of health care services when compared to unaffected individuals.[10-12] FM affects more than five million Americans [13] and is more prevalent in women compared to men (3.4% vs. 0.5%).[13,14] There appears to be more diagnostic variability in FM relative to other coexisting syndromes that have overlapping symptoms,[13] and it is often difficult to diagnose FM separately from CFS due to its overlapping symptom relationship.[15–19]

Immune responses are often impaired in CFS and FMS.[20-22] Impaired lymphocyte responses to mitogen and reduced natural killer (NK) cell cytotoxicity are the most consistent findings in a substantial proportion of patients with CFS.[23-26] Indeed, it has been suggested that NK cell measurement may be diagnostic in CFS.[26]

NK cells are cytotoxic lymphocytes of the innate immune system. They are potent effector cells that eliminate tumors and infected cells while providing signals that shape adaptive immune responses. NK cell counts in the high normal range are beneficial for long-term health.[27-29] Since NK cell deficiency is a consistent finding in CFS patients, [25,26] we measured NK function in a small group of women with CFS or FM and decreased NK function to see if a nutritional supplement could increase their NK function within one month.

Methods

Volunteers were recruited that ranged from 25 to 60 years of age. The criteria for acceptance encompassed a confirmed medical diagnosis of either FM or CFS, [3,9] and current symptoms involving severe fatigue and inability to perform normal activities without unusual exertion. Confirmation of a severe fatigue score utilized the Piper Fatigue Scale Survey (PFS) with a fatigue score of 6.5 or above [30].

Each volunteer was given a general physical exam and asked to fill out a medical intake form. Excluded subjects were those who had been on any immunostimulatory pharmaceuticals or nutraceutical products, especially those containing transfer factor, for 60 days prior to start of the study. As part of acceptance for inclusion in the study, a 20ml blood sample was taken from volunteers and analyzed for NK activity. A minimum cutoff of a NK blood level activity of 35 Lytic Units (LU) was set as a requirement for entry into the study. This was based on a mid-range stratification of NK functional determination (average LU) of CFS individuals.[31]

Volunteers who met the inclusionary criteria were given a 30-day supply of Transfer Factor Multi-Immune™ (TFMI), a polyvalent transfer factor preparation supplied by Researched Nutritionals, Los Olivos, CA. TFMI contains a proprietary combination of natural ingredients formulated to support beneficial immune and cellular functions.[32] Subjects were instructed to take two capsules per day on an empty stomach, either two hours after or one hour before eating, during the 30-day trial period. On Day 30, a final blood sample was taken to determine NK functional cell analysis. During the trial, volunteers received weekly dosage and frequency reminders via email to help maintain compliance.

For assessment of NK cell function, 20ml of blood was collected on Day 0 and Day 30, and then expressed mailed (overnight delivery) [with cold packs to Viracor-IBT Laboratories, Lee's Summit, MO]. Peripheral blood monocyte cells (PBMC) were isolated from whole blood and mixed at various ratios with fluorescently labeled K562 target cells. Following incubation, the percent of lysed K562 cells were determined by flow cytometry.[33-35]

Results

Seven out of 18 volunteers were able to meet the inclusionary criteria for this study. The eleven volunteers were excluded, either because they did not have a PFS score $\geq$ 6.5 or their NK functional score was above 35 LU. The qualifying enrollees were all female, with ages ranging from 30 to 60 years old (mean age=49.9 years). Their average PFS score was 8.0, indicating severe fatigue on the PFS rating scale.

At day 30 one of the seven women had a 61% decrease in NK LU functional value, while six out of the seven individuals ranged from a 135% to 4667% increase in NK LU functional values. Using the actual data values, the pre-treatment baseline mean was 13.2 ± 4.2, and this increased to 24.2 ± 3.2 in NK functional LUs post treatment. The increase was statistically significant ($p=0.02$) utilizing a T-test determination. However, there were two outliers, the lowest and highest responders, -61% and +4667% difference over baseline, respectively. Reporting the mean alone could be altered by the influence of the extreme outliers; therefore, using the median (midpoint value of the percent difference) compensates for skewed data resulting from outliers. The median percent increase of NK cell LU within the entire group treated after 30 days of TFMI was 247% (Table. 1). The magnitude of the individual percent differences are shown in Figure 1.

Discussion

There are some overlapping symptom and immunological relationships between CFS and FM. Impaired lymphocyte responses to mitogens and reduced NK cell cytotoxicity are the most consistent findings in a substantial proportion of patients with CFS, and a decline in NK cell functionality/activity have also been observed in FM.[25,26] Here we used a natural dietary supplement (TFMI) to increase NK functional activity and found that in five of six women the product significantly increased NK activity. Although this was a small patient group, the patients with the lowest NK function appeared to be the best responders to the TFMI supplement.

Previously a human herpesvirus-6 (HHV-6) transfer factor preparation was administered to two CFS patients with an active HHV-6 infection, and the treatment inhibited the infection and reduced some of the clinical manifestations of CFS in one patient but had no effect in the other.[36] Using an oral polyvalent transfer factor preparation against Herpes viruses De Vinci et al. [37] found that 12 out of 20 CFS patients responded within 3-6 weeks with reduced symptom scores but correlation with virus serology was not evident. This exploratory clinical pilot study provides an indication that a nutrient combination containing polyvalent transfer factor (TFMI) can increase NK cell functional activity after 30 days of administration in individuals with CFS and FM who have depressed NK function. NK function is related to infection control, and individuals with reduced NK function should benefit from the TFMI supplement. CFS and MF patients are known to have ongoing chronic viral and bacterial infections [8,38], and the number of such infections correlates significantly with symptom severity.[39] Thus TFMI should benefit patients with CFS and FM by increasing NK function.

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Table 1. NK Levels after Treatment with TFMI in CFS and FM Subjects

Initials	Age	Sex	Pre Tx NK LU	Post Tx NK LU	% Difference NK LU	PFS Score
LF	44	Female	31.80	19.60	-62%	8.57
SW	30	Female	20.90	28.30	135%	8.38
CP	56	Female	15.30	23.90	156%	7.52
DA	54	Female	13.70	33.90	247%	8.43
DS	59	Female	7.60	21.00	276%	8.48
SN	60	Female	1.80	9.90	550%	8.48
LD	46	Female	0.70	32.60	4667%	6.76
SW	30	Female	20.90	28.30	135%	8.38
Mean ± SE	**49.9 ± 4.0**		**13.1 ± 4.2**	**24.2 ± 3.2***	**852.7 ± 639.5**	**8.0 ± 0.03**

*p=0.02

Figure 1. Percent Difference of Pre- and Post-Treatment with TFMI

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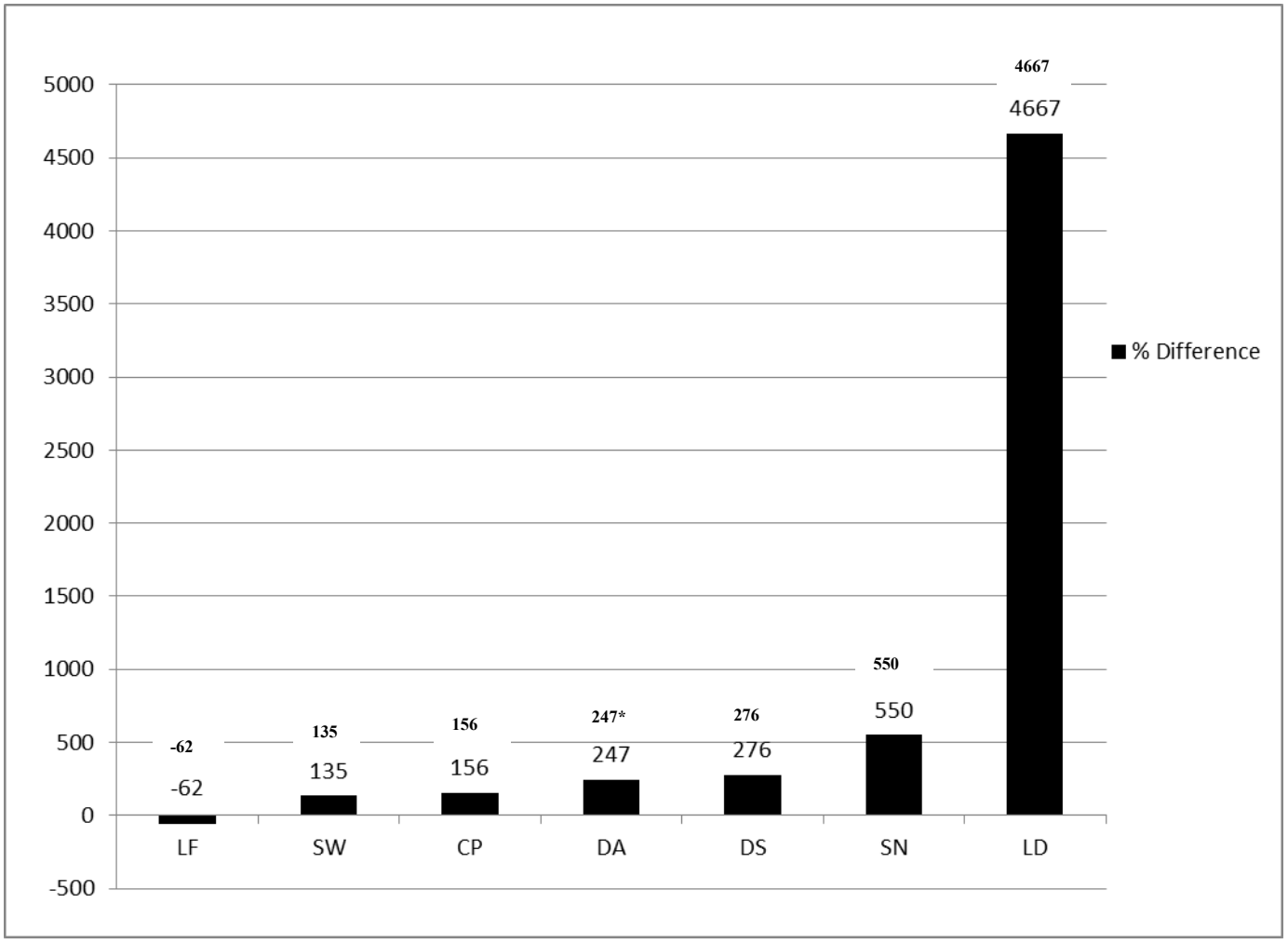

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