Exercise in frail elderly men decreases natural killer cell activity

H.G. Rincón1, G.F. Solomon2, D. Benton3, and L.Z. Rubenstein4

1Department of Psychiatry and Behavioral Sciences, Valle del Lili Foundation, Cali, Colombia, 2Norman Cousins Program in Psychoneuroimmunology, UCLA School of Medicine, Los Angeles, California, 3Department of Gerontology, University of Southern California, University Park, Los Angeles, California, 4Geriatric Research Education and Clinical Center, Veterans Affairs Medical Center, Sepulveda, California, U.S.A.

ABSTRACT. Six frail male outpatients 70 years and older deemed at risk for fall, but not suffering from serious medical problems nor receiving immune-altering drugs, received an exercise intervention of increasing strenuousness for 60 minutes 3 times a week for 3 months in comparison with 7 controls having no intervention. Psychosocial and immunologic assessments were made at baseline (Time 1), and after 6 (Time 2) and 12 (Time 3) weeks of physical conditioning. Cytotoxic activity of natural killer (NK) cells significantly decreased during the course of the study, in spite of transient exercise-induced increases at times 2 and 3. Despite the many known benefits of exercise, this report suggests its possible adverse effects on NK cell cytotoxicity in the very frail elderly. Mild overexertion in frail old people may be clinically significant in view of the now recognized role of NK cells in the prevention of metastasis.

EXERCISE AND IMMUNITY IN FRAIL OLD MEN

Age-related changes in immunity appear to involve a general decline in function (1); however, these changes are characterized by high inter-individual variability (2). Decline in cell-mediated immunity is greater than that in humoral immunity. The mediators of decline in immune competence with age are myriad, and not fully understood. It remains unclear how much of the commonly reported age-related “decline” in immune competency is inevitable and irrevocable. A correlation appears to exist among immune competence, physical health, and psychological well-being in the elderly (3). Natural killer (NK) cell cytotoxicity is a non specific immunologic function that remains intact in healthy vigorous elderly persons. Several studies have shown that exercise programs for the elderly can improve endurance (4-6). Disease states common in old age that may be modified by exercise include cardiovascular disease, diabetes, and osteoporosis (7-9). Studies of the effects of exercise on immunity in younger adults suggest that acute exercise is associated with increases in total leukocyte count (10, 11), cytotoxic lymphocytes (12), plasma interferon levels (13), interleukin-1 levels (14) and natural killer cell activity (15). Two studies have found that acute exercise in older adults is related to a significant immediate increase in NK cell cytotoxic activity and numbers (16, 17). This increase in exercise-induced NK activity (NKA) was found to be opioid mediated (18). In contrast, immunologic dysfunction [decreased NK numbers, increased catabolism of immunoglobulin G (IgG)] has been described in older patients who have been subjected to physical inactivity, such as bed rest (19, 20). The effects of a long-term exercise program on immunologic function have not been reported. It is unclear whether short-term increases in immunologic function, particularly NK activity, if regularly induced by a physical conditioning program, increase basal or “steady-state” immune function.

PURPOSE AND HYPOTHESES

The purpose of this pilot research was to assess the effect of exercise on immunologic functions in a group of frail older men at risk for falling. We hypothesized that baseline levels of NK cell numbers and activity would be significantly increased with repeated up-
regulation induced by brief physical exercise over a three-month period. In addition, we hypothesized that changes may occur in the acute alteration in NK activity and numbers as a result of short-term exercise from pre- to post-exercise on each of three assessments.

METHODS

Subjects

Thirteen ambulatory male outpatients 70 years and older (mean age, 75.3; range, 71.6-81.2), who had volunteered for participation in the exercise research project at the Veterans Administration Medical Center, Sepulveda, CA were screened from a larger group deemed at risk for falling by virtue of a history of having fallen in the past year, noticeable muscle weakness, or a measureable gait and/or balance impairment. Patients with the following conditions were excluded from participating in the study: 1) active cardiac or pulmonary disease; 2) use of more than two prescription medications; 3) use of any drug known to affect immune function; 4) hypertension (≥160/90 mmHg at rest); 5) malnutrition or obesity (weight more than 20% above or below the average weight for height; 6) severe joint pain; 7) moderate to severe dementia, depression or psychosis; 8) history of cancer or cancer treatment in past five years (except non-invasive skin cancer).

Assessment, immune testing, and randomization

The initial assessment of the 13 eligible subjects included: 1) a questionnaire concerning demographic factors, medical history, and functional abilities; 2) a multi-dimensional geriatric assessment; 3) measures of muscle strength, gait and balance. The non-exercise controls were selected via a random number generator, and were comparable to experimental subjects (N=6) in: age, medical history, neurologic and musculoskeletal assessment, blood pressure (reclining and standing), anthropometric measurements, immunologically relevant medications, cognitive function, depression and activities of daily living. The initial and subsequent immune status testing herein reported comprised: 1) NK cell cytotoxicity as assessed on the day of blood collection, according to the methodology previously described (18). Flow cytometry on lymphocyte subsets with NK activity (CD16 and CD56) was performed on fresh blood. Subjects were told not to smoke, drink or take aspirin within 24 hours of testing, and to have a low fat breakfast on that morning. The initial and subsequent psychosocial questionnaire administered to each subject included: 1) Life Satisfaction Scale; 2) Physical Activity Index; 3) A measure of psychological hardiness (21). Subjects randomized to the intervention group received the graded exercise program, immune testing, and psychosocial interviews. The controls did not participate in the exercise program. All immune testing was done at the same time of day for each subject in both groups (8-10 a.m.). The psychosocial interview was given 1/2 hour prior to the blood sample and exercise session. Subjects’ immune testing was done one minute prior to starting the session, and a second time within one minute of stopping post-exercise cool down. Controls’ immune testing was done at the same intervals, but only on one occasion at each.

Exercise intervention

Each intervention subject attended 3 exercise classes per week for 3 months. The daily regimen included a 5-minute warm-up on a bicycle ergometer, about 45 minutes of strength and balance exercises, 20 minutes of walking practice, and 10 minutes of stretching. Subjects were oriented gradually to the program and slowly advanced, so that by weeks 8-12 they were able to perform the exercise protocol for the duration. At the end of three months, subjects were reassessed for muscle strength, gait and balance. All subjects attended and completed all intervention sessions; all controls completed evaluations.

Data analysis

Several types of data analysis were used. The epidemiologic data were analyzed with descriptive statistics as mean, proportions, and standard deviation. Analysis of the pre- and post-immune scores was conducted using t-statistics to test changes between basal and post-exercise levels. Analysis of variance was used to treat the differences between the means in each group (control vs exercise), and look at the effect of time. Correlation statistics were used to look at immune and psychosocial relationships.