ORIGINAL ARTICLE

Association Between Mobility Mode and C-Reactive Protein Levels in Men With Chronic Spinal Cord Injury

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ABSTRACT. Morse LR, Stolzmann K, Nguyen HP, Jain NB, Zayac C, Gagnon D, Tun CG, Garshick E. Association between mobility mode and C-reactive protein levels in men with chronic spinal cord injury. Arch Phys Med Rehabil 2008; 89:726-31.

Objective: To assess clinical determinants of systemic inflammation in persons with chronic spinal cord injury (SCI).

Design: Cross-sectional survey.

Setting: Veterans Affairs medical center.

Participants: As part of an epidemiologic study assessing SCI-related health conditions, 63 men with chronic SCI provided a blood sample and information regarding locomotive mode and personal habits.

Interventions: Not applicable.

Main Outcome Measure: Plasma high-sensitivity C-reactive protein (CRP).

Results: The mean ± standard deviation age was 56±14y, and participants were assessed 21±13y after injury. Adjusting for heart disease, hypertension, and body mass index (BMI), the mean CRP in 12 motorized wheelchair users (5.11mg/L) was not significantly greater than 23 participants who used a manual wheelchair (2.19mg/L) ($P=.085$) but was significantly greater than the 17 who walked with an assistive device (1.41mg/L) ($P=.005$) and the 12 who walked independently (1.63mg/L) ($P=.027$). CRP was significantly greater in participants with obesity but was not related to age, smoking, or SCI level and severity. CRP was elevated in participants reporting a urinary tract infection (UTI) or pressure ulcer within a year, but adjustment for this did not account for the elevated CRP in motorized wheelchair users.

Conclusions: These results suggest that CRP in chronic SCI is independently related to locomotive mode, BMI, and a history of pressure ulcers and UTI. It is suggested that future studies in SCI investigate whether modifying these factors influence systemic inflammation and cardiovascular health.

Key Words: Cardiovascular diseases; Inflammation; Rehabilitation; Spinal cord injuries.

SYSTEMIC INFLAMMATION IS implicated in the development of atherosclerosis and coronary heart disease and recently has been related to greater mortality from cancer and chronic respiratory disease. C-reactive protein (CRP) is a blood marker of systemic inflammation that is produced by the liver in response to the proinflammatory cytokine interleukin 6. Elevated CRP levels predict future coronary events and other manifestations of cardiovascular disease in the able-bodied[1-3] through mechanisms that are poorly understood. It is known that as an acute-phase reactant CRP facilitates the elimination of foreign pathogens and damaged cells by binding to phosphocholine and can also activate the complement system.[4] CRP may also increase levels of plasminogen activator inhibitor 1, a marker of impaired fibrinolysis and atherothrombosis.[5] CRP levels add predictive value to established cardiovascular risk factors. Relative risk categories have been established for tertile CRP values (low risk [<1mg/L], average risk [1–3mg/L], high risk [>3mg/L]).[6]

A recent study[7] reported cardiovascular disease to be a leading cause of mortality in persons with chronic spinal cord injury (SCI). It is possible that elevated CRP levels may contribute to the development of cardiovascular disease in this population. SCI results in increased fat mass, increased frequency of urinary tract infections (UTIs) and pressure ulcers, and in some instances loss of function of major muscle groups resulting in decreased levels of physical activity. All of these conditions may result in elevated CRP levels. In this study, we conducted a preliminary investigation of clinical predictors of CRP in persons with SCI and with varying levels of mobility. We hypothesize that insofar as mobility mode reflects the general activity level in persons with chronic SCI that it may be predictive of CRP levels independent of a history of infections and obesity.

METHODS

Participants

Participants were selected from a larger epidemiologic study assessing health in persons with chronic SCI conducted at the VA Boston Healthcare System.[7] Participants were recruited from veterans with SCI who had previously been treated at VA Boston and from participants in the community. Every 2 to 3 years, participants underwent pulmonary function testing, completed a health questionnaire, and, starting in October 2003,

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Presented to the American Spinal Cord Injury Association, June 28, 2006, Boston, MA.

Supported by the Research and Development Service, Department of Veterans Affairs, VA Boston Healthcare System Boston; National Institute of Child Health and Human Development, National Institutes of Health (grant no. RO1 HD42141), Massachusetts Veterans Epidemiology Research and Information Center, VA Cooperative Studies Program, and the Foundation for PM&R.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

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0003-9993/08/8904-00250$34.00/0
doi:10.1016/j.apmr.2007.09.046

were asked to provide a blood sample. Testing was conducted when participants are in their usual state of health and not clinically ill. Each person completed a health questionnaire and answered the question, "How do you usually get around (usually means more than half the time)?" Responses were recorded as motorized wheelchair, hand-propelled wheelchair, walk with aid (crutch, cane, or similar aid), or walk without assistance. Blood samples were collected from 82 white men between October 2003 and June 2005 who were 2 or more years post-SCI and who were not using statins. Because of financial constraints, for this preliminary investigation, we selected 64 participants based on the mobility mode. All participants using a motorized wheelchair (n=12), walking with an assistive device (n=17), and walking independently were included (n=12), and a random sample of the remaining participants who usually used a manual wheelchair (n=23) was selected. After subject selection, 1 person was found to be 1.6 years post-SCI and 1 was black. All subjects gave informed consent, and the study was approved by our institutional review boards.

SCI Classification

Motor level and completeness of injury were assessed by physical examination. The level of injury was classified according to strength preservation in key muscle groups in the upper and lower extremities and reported regionally as tetraplegia or paraplegia. Injury completeness was reported according to guidelines suggested by the American Spinal Injury Association (ASIA).[8] Participants were assigned as motor complete (equivalent to ASIA motor score of A or B, ie, no motor function below the neurologic level of injury), C (motor incomplete, motor function preserved below the neurologic level, and more than half the key muscles below the neurologic level are not strong enough to overcome gravity), or D (motor incomplete, preservation of motor function below the neurologic level, and more than half the key muscles below the neurologic level are strong enough to overcome gravity). The SCI level and the severity of injury were considered in 3 groups that included motor complete and ASIA grade C tetraplegia, motor complete and ASIA grade C paraplegia, and ASIA grade D tetraplegia or paraplegia. By using participants in each of these 3 impairment groups, we were able to examine the effect of SCI in participants ranging from profound neurologic impairment to minimal or no neurologic impairment.

Biochemical Analyses

Blood was drawn into an ethylenediaminetetracetic acid tube, stored with a cooler pack in an insulated container, and shipped overnight to the core blood laboratory. The samples were centrifuged for 15 minutes at 2600rpm (1459×g) at 4°C, and plasma was stored at −80°C until batch analysis. High-sensitivity CRP was determined by using a high-sensitivity immunoturbidimetric assay with a sensitivity of .03mg/L. The day-to-day variability of the assay at concentrations of .91, 3.07, and 13.38mg/L is 2.81%, 1.61%, and 1.1%, respectively (Clinical & Epidemiologic Research Laboratory, Children's Hospital Boston, MA). A quality-control specimen was analyzed every tenth sample. The 6 CRP results were within .04mg/L and had a standard deviation of .016mg/L.

Clinical Data

Participants completed a health questionnaire based on the American Thoracic Society adult respiratory disease questionnaire.[9] Smokers were defined as smoking 20 or more packs of cigarettes or using 336g (12oz) of tobacco or more in a lifetime or smoking 1 or more cigarettes a day for at least 1 year. Current smokers reported cigarette use within 1 month of testing. Hypertension and diabetes were defined if previously diagnosed by a doctor; heart disease was defined as receiving treatment for heart trouble in the 10 years prior to blood draw. These definitions of disease were validated in an earlier study.[7] Participants were asked about a history of urinary infections or a pressure ulcer in the past year and if they had a cold in the week before testing (available in 60 participants). As part of the study protocol, subject length was measured in 60 participants, was available by self-report in 2, and from SCI clinic notes in 2. In 57 participants, weight was measured, was available by self-report in 3, and was obtained from SCI clinic notes in 4 participants. Length and weight were used to calculate body mass index (BMI). For 3 participants whose health questionnaires were completed at a time other than the blood-draw date, SCI clinic progress notes were reviewed to confirm previously reported questionnaire responses.

Statistical Analysis

Because the distribution of CRP was skewed, natural log-transformation was used to normalize the distribution and stabilize variance. General linear models[a] were used to assess determinants of CRP. Variables in table 1 were assessed in univariate models and, if significant at the .1 level or less, were included in a multivariate model in participants with complete data available. The Tukey-Kramer test was used to adjust for multiple comparisons.

RESULTS

Participant Characteristics

One participant who walked with an assistive device had a CRP value of 217mg/L and was considered an outlier and excluded from analysis. Of the remaining 63 participants (see table 1), the average age at the time of blood draw was 56±14y with an average of 21±13y since injury. Twenty-five percent of participants had CRP values of 4.03mg/L or above, and 6 participants (16%) had values greater than 10mg/L (maximum, 33.6). Of note, one third of the participants were in the low cardiovascular risk category based on CRP levels, one third in the average category, and one third in the high-risk category in tertiles similar to that described in the general population. The distribution of natural log CRP was continuous and normally distributed (Shapiro-Wilks test W=.98, P=.379) (fig 1). Specifically, there was no evidence that higher or lower values represented outliers, and all values were included in subsequent analyses. Other participant characteristics are presented based on mobility level (motorized wheelchair, hand-propelled wheelchair, walks with aid, walks without aid). Boxplots of natural log CRP based on mobility level are presented in figure 2 and show no obvious outliers. The median CRP level was 1.63mg/L and was greatest in motorized wheelchair users (5.22mg/L).

Predictors of CRP

In univariate regression models, age, duration of injury, SCI level and completeness of injury, history of smoking, diabetes, UTI history, or a cold in the preceding week were not associated with CRP. Univariate predictors of CRP included locomotive mode (P=.013), BMI (P=.049), heart disease (P=.084), hypertension (P=.029), and pressure ulcer in the past year (P=.021) (table 2). In a multivariate model (table 3), locomotive mode, BMI (normal, overweight, obese), heart disease, and hypertension were significant predictors of CRP. CRP in motorized wheelchair users (5.11mg/L) was not sig-