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Current cigarette smoking is a reversible cause of elevated white blood cell count: Cross-sectional and longitudinal studies

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ABSTRACT

While cigarette smoking is a well-recognized cause of elevated white blood cell (WBC) count, studies on longitudinal effect of smoking cessation on WBC count are limited. We attempted to determine causal relationships between smoking and elevated WBC count by retrospective cross-sectional study consisting of 37,972 healthy Japanese adults who had a health check-up between April 1, 2008 and March 31, 2009 and longitudinal study involving 1730 current smokers who had more than four consecutive annual health check-ups between April 1, 2007 and March 31, 2012.

In the cross-sectional study, younger age, male gender, increased body mass index, no alcohol habit, current smoking, and elevated C-reactive protein level were associated with elevated WBC count. Among these factors, current smoking had the most significant association with elevated WBC count. In subgroup analyses by WBC differentials, smoking was significantly associated with elevated counts of neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Ex-smoking was not associated with elevated WBC count. In the longitudinal study, both WBC and neutrophil counts decreased significantly in one year after smoking cessation and remained down-regulated for longer than next two years. There was no significant change in either WBC or neutrophil count in those who continued smoking.

These findings clearly demonstrated that current smoking is strongly associated with elevated WBC count and smoking cessation leads to recovery of WBC count in one year, which is maintained for longer than subsequent two years. Thus, current smoking is a significant and reversible cause of elevated WBC count in healthy adults.

1. Introduction

It is not uncommon to find leukocytosis in otherwise healthy individuals. Epidemiological data indicate that cigarette smoking is associated with elevated white blood cell (WBC) count (Petitti and Kipp, 1986; Yarnell et al., 1987; Schwartz and Weiss, 1991; Schwarz and Weiss, 1994; Freedman et al., 1996; Sunyer et al., 1996; Van Tiel et al., 2002; Fröhlich et al., 2003; Smith et al., 2003; Lao et al., 2009). In addition, a variety of factors such as younger age (Schwartz and Weiss, 1991; Nagasawa et al., 2004), male gender (Schwartz and Weiss, 1991; Brown et al., 2001), increased body mass index (BMI) (Schwartz and Weiss, 1991; Nagasawa et al., 2004; Herishanu et al., 2006; Jee et al., 2005; Imano et al., 2007), high blood pressure (HBP) (Nagasawa et al., 2004; Brown et al., 2001; Jee et al., 2005; Imano et al., 2007; Lee et al., 2009), hyperlipidemia (Nagasawa et al., 2004; Jee et al., 2005), diabetes (Nagasawa et al., 2004; Jee et al., 2005), and decreased alcohol consumption (Schwartz and Weiss, 1991; Nakanishi et al., 2003) have been reported to be associated with elevated WBC count. On the other hand, elevated WBC count has been reported to be an independent predictor of coronary heart disease (CHD) and cardiovascular disease (CVD) (Brown et al., 2001; Madjid et al., 2004) and reduction in the WBC counts may be related to the reduction in the CHD and CVD risks.

A number of studies have reported that smoking cessation leads to a decrease in WBC count which appears to be associated with the duration of the smoking abstinent (Petitti and Kipp, 1986; Yarnell et al., 1987; Schwartz and Weiss, 1991; Schwarz and Weiss, 1994; Van Tiel et al., 2002; Fröhlich et al., 2003; Smith et al., 2003; Lao et al., 2009; Kawada, 2004; Ishizaka et al., 2007; Parry et al., 1997). However, most of these studies are based on cross-sectional studies. Although some prospective studies have shown that smoking cessation with nicotine replacement therapy (Jensen et al., 1998; Eliasson et al., 2001) or bupropion (Abel et al., 2005) or without pharmaceutical support

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(Sunyer et al., 1996; Green and Harari, 1995) led to a time-dependent decrease in WBC count which was apparent as early as eight weeks after cessation, there have been few reports on longitudinal effects of smoking cessation on WBC count. Especially, there is only one cross-sectional study which investigated the association of smoking cessation and WBC count in Japanese cohort but longitudinal effect of smoking cessation on WBC count in Asian population has not been studied (Kawada, 2004).

The aim of this study was to determine causal relationship between smoking and elevated WBC count in a large cohort of healthy Japanese adults. Our results adds to the literature further evidence of the causal relationship between smoking and WBC count and demonstrate that the effect of smoking on WBC count is reversible within one year after smoking cessation.

2. Patients and methods

This study is a retrospective observational study approved by The Ethics Committee of St. Luke's International Hospital and all the individuals had approved the use of their data.

2.1. Cross-sectional study

A total of 40,279 healthy adults (≥20 years old) had a general health check-up from April 1, 2008 to March 31, 2009 in the department of preventive medicine affiliated with a tertiary referral hospital in Tokyo Japan. Subjects who had known hematological and/or solid tumors and 50 subjects with incomplete questionnaire were excluded, leaving 37,972 individuals who comprised the subjects of the retrospective cross-sectional study (Fig. 1A). Age, gender, height, body weight, complete blood cell count with differentials of WBC, and C-reactive protein (CRP) level were collected from medical records. BMI was categorized into three categories; <22 kg/m^2, ≤22 kg/m^2 and <25 kg/m^2, and 25 kg/m^2 ≤. BMI < 22 kg/m^2 was used as reference in logistic regression analysis. Smoking history including number of cigarettes per day, years of smoking, and alcoholic consumption history were collected from self-administered questionnaire for the general health check-up. Smoking factors were categorized into current, past, and non-smoker. WBC and its differentials of individuals who had quitted smoking (ex-smokers) and current smokers were compared with those who had never smoked (never smokers). WBC counts equal to or >9.0 × 10^9/L were defined to be increased. For each differential of WBC, neutrophil counts > 7.5 × 10^9/L, monocyte counts > 1.0 × 10^9/L, eosinophil counts > 0.7 × 10^9/L, and basophil counts > 0.15 × 10^9/L were defined to be increased.

2.2. Longitudinal study

Healthy adult smokers who had more than four consecutive annual health check-ups from April 1, 2007 to March 31, 2012 in the same institution were studied. Among 83,752 individuals who had health check-ups during this period, 25,003 had more than four consecutive annual health check-ups. CRP data on one or more occasions were missing in 2822 individuals and they were excluded. Four thousand five hundred fifty-seven patients with hematological and/or solid tumors, who were taking steroids and/or whose CRP value was equal to or above 0.3 mg/dL as well as two individuals with incomplete date were excluded, thus leaving 17,622 individuals. Fifteen thousand eight hundred ninety-two individuals who had never smoked, who had a smoking history but quitted smoking before the study period, and who quitted smoking after the first visit but resumed afterward before the fourth visit were also excluded. The remaining 1730 individuals were current smokers at their first visit, of whom 1499 continued smoking for longer than three years while 231 quitted smoking within one year after the first visit and remained abstinent from smoking until the fourth visit (Fig. 1B). Longitudinal changes of the WBC and differential counts were evaluated retrospectively.

2.3. Hematological analyses

Fasting venous blood samples were drawn from all subjects into vacuum tube containing EDTA. WBC count and differentials were determined by applying the samples within 15 min to Beckman Coulter

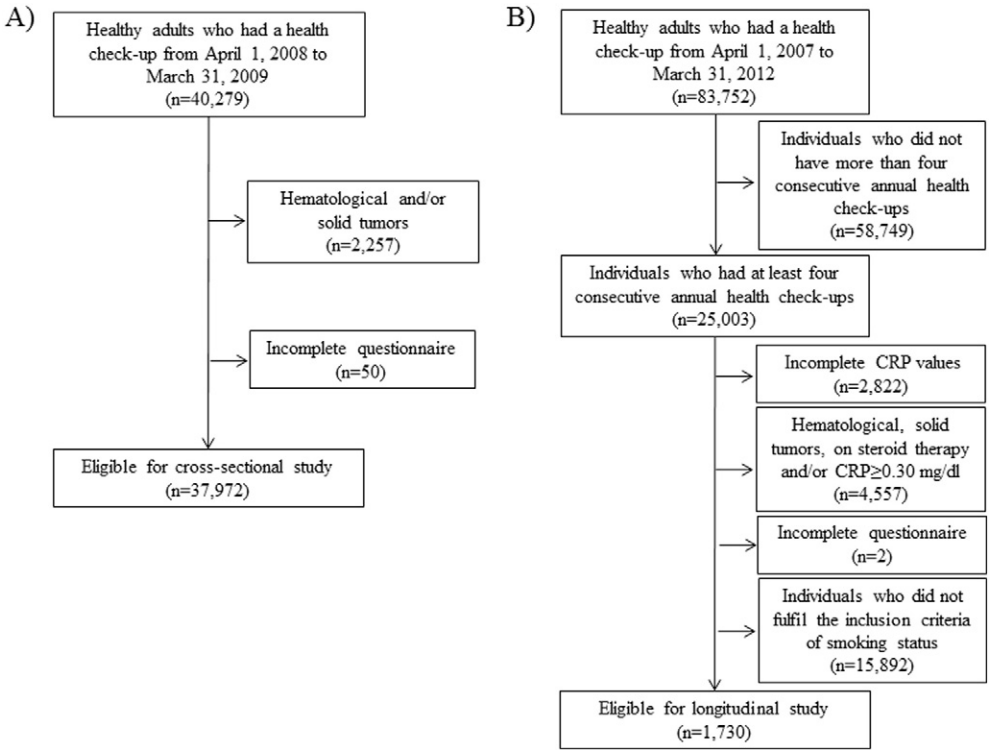

Fig. 1. Study flow diagrams of cross-sectional (A) and longitudinal (B) studies.