The Effect of Cigarette Smoking on Hemoglobin Levels and Anemia Screening

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The relationships among cigarette smoking, hemoglobin concentration, and carboxyhemoglobin concentration were examined using data from the Second National Health and Nutrition Examination Survey. Among women, smokers had a mean (±SE) hemoglobin level of 137±0.4 g/L, significantly higher than the mean hemoglobin level of 133±0.5 g/L for never-smokers. Among men, the mean hemoglobin levels for smokers and never-smokers were 156±0.4 and 152±0.5 g/L, respectively. No significant difference in mean hemoglobin was noted between ex-smokers and never-smokers. Mean hemoglobin levels and carboxyhemoglobin levels increased progressively with the number of cigarettes consumed per day. Cigarette smoking seems to cause a generalized upward shift of the hemoglobin distribution curve, which reduces the utility of hemoglobin level to detect anemia. Among women of comparable socioeconomic status, the prevalence of anemia was 4.8%±0.6% among smokers, compared with 8.5%±1.2% among never-smokers. This study suggests that minimum hemoglobin cutoff values should be adjusted for smokers to compensate for the masking effect of smoking on the detection of anemia.

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CIGARETTE smoking is known to cause an increase in hemoglobin (Hb) concentration that is believed to be mediated by exposure to carbon monoxide.[1-5] Carbon monoxide bonds to Hb to form carboxyhemoglobin (HbCO), an inactive form of Hb that has no oxygen-carrying capacity.[6,7] Carboxyhemoglobin also causes a shift to the left in the Hb dissociation curve, resulting in a reduction in the ability of Hb to deliver oxygen to the tissues.[6,7] To compensate for the decreased oxygen delivery capacity, smokers maintain a higher Hb level than nonsmokers.[5,8] In addition, a mild decrease in plasma volume may also contribute to the increased Hb levels observed among smokers.[5,9,10]

The increase in Hb levels related to smoking may have important implications for the screening of anemia. Anemia screening based on Hb measurements is routinely performed to identify those at nutritional risk, particularly for iron deficiency, and for early detection of inflammatory processes, chronic disease, or malignant neoplasms.[11] Because anemia is typically defined as an Hb value below a defined cutoff value, the higher Hb values that are a consequence of smoking may decrease their utility as a marker for the presence of nutritional or other health problems. If the elevation of Hb levels is a generalized phenomenon affecting all smokers, Hb cutoffs adjusted for smoking status may be required to identify health and nutrition problems among smokers properly.

This study explores two main questions: (1) What is the magnitude and pattern of elevated Hb values among smokers? (2) What is the effect of cigarette smoking on the screening of anemia?

SUBJECTS AND METHODS

We used data from the Second National Health and Nutrition Examination Survey (NHANES II) 1976-1980, a cross-sectional US probability sample survey with a complex study design.[12] The analysis used data collected from white men (n=2250) and women (n=2454) 18 to 44 years of age for whom smoking status, Hb level, and socioeconomic status were recorded. The study population was restricted to whites 18 to 44 years of age to minimize the influence of chronic disease and hemoglobinopathies that may influence Hb values.

Based on smoking history, the study population was divided into three categories: never-smokers (<100 cigarettes ever smoked), ex-smokers (≥100 cigarettes ever smoked but not smoking when interviewed), and smokers (≥100 cigarettes ever smoked and still smoking when interviewed). Smokers were subdivided into four categories based on the reported number of cigarettes currently smoked per day: 1 to 9, 10 to 19, 20 to 39, and 40 or more.

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Hemoglobin values were measured on an electric cell counter in the mobile NHANES II examination units.[13] The Hbco levels for a random sample of half of the original NHANES II sample were determined with the method described by Small et al[14] and reported as percentage saturation of total Hb. Among women, Hbco measurements were available for 626 (51.9%) of the 1207 never-smokers, 156 (52.3%) of the 298 ex-smokers, and 458 (48.1%) of the 956 smokers. Among men, Hbco measurements were available for 386 (47.0%) of the 822 never-smokers, 222 (51.9%) of the 428 ex-smokers, and 495 (49.1%) of the 1009 smokers. Transferrin saturation was computed by dividing serum iron level by total iron binding capacity and was available for 813 (85.0%) of the 956 female smokers and 1006 (83.3%) of the 1207 female never-smokers. All laboratory methods and quality control procedures for the hematologic and biochemical studies are described elsewhere.[13,15]

Women with Hb levels less than 120 g/L and men with levels less than 135 g/L were defined as having anemia.[16] The analyses that dealt with the effect of smoking on the diagnosis of anemia were restricted to women because the prevalence of anemia among younger white men was very low in NHANES II and because iron deficiency is an important cause of anemia among women of childbearing age.[17] To examine the percentage of female smokers and never-smokers who were iron deficient and who were detected with the established definitions, all women were stratified into three transferrin saturation ranges: low (1% to 11%), moderate (12% to 24%), and high (25% to 95%). Analyses focused on women who were likely to be iron deficient as defined by low transferrin saturation (1% to 11%).[18]

The analyses were statistically weighted to account for probability of selection, nonresponse, and the age-sex-race distributions for the 1978 noninstitutionalized US population.[12] All comparisons were adjusted for socioeconomic status because low socioeconomic status has been associated with a greater prevalence of both anemia and smoking. Adjustment was accomplished through the standardization of comparison groups according to the distribution of the poverty index ratio among all white women or white men 18 to 44 years of age regardless of smoking status for whom a poverty index ratio was available. The poverty index ratio is a measure of household income adjusted for both family size and cost of living for the relevant year.[12] The t test was used as the test of significance for comparing the mean Hb or Hbco values, and Mantel-Haenszel χ^2 tests were used for the comparison of prevalence estimates of anemia. In both cases, never-smokers were the referent group against which the others were compared. Standard errors were calculated for mean Hb and mean Hbco values as well as for the prevalence of anemia. All calculations of SEs took into account the complex survey design.[19]

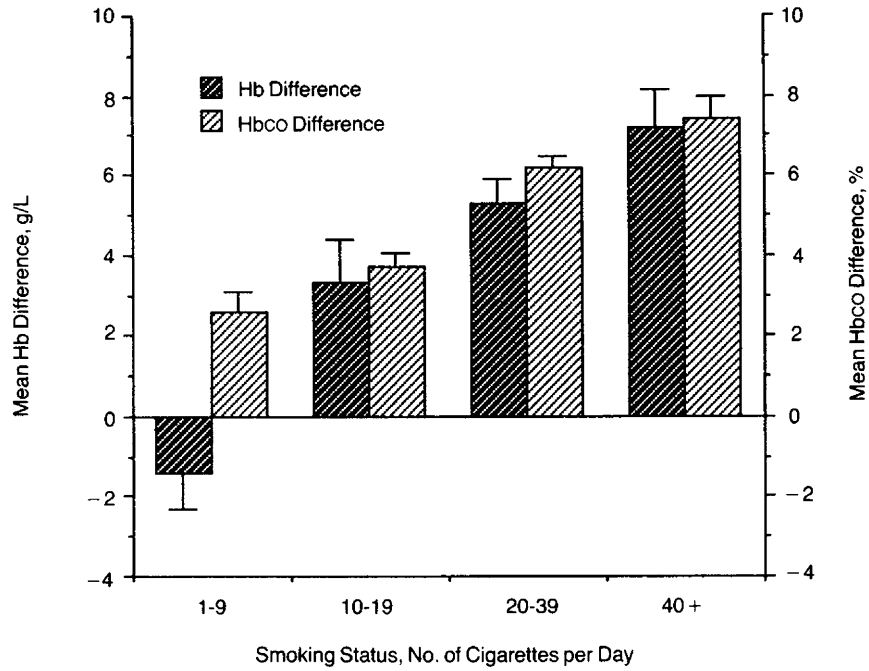

Fig 1.—Increased mean hemoglobin (Hb) difference and mean carboxyhemoglobin (HbCO) difference (±SE) related to increased quantity of cigarettes smoked for female smokers. The mean difference used never-smokers as the baseline comparison group.

RESULTS

Hb Level and Smoking Status

Among women, the mean (±SE) Hb level was 137±0.4 g/L for smokers and 133±0.5 g/L for never-smokers ($P<.001$). Among men, the mean Hb level was 156±0.4 g/L for smokers and 152±0.5 g/L for never-smokers ($P<.001$). For both men and women, a dose-response relationship was observed between mean Hb level and the amount smoked. Figure 1 illustrates the mean Hb level increase for female smokers with increasing quantity of cigarettes smoked after subtracting the mean Hb values of never-smokers. Compared with that in never-smokers, the mean Hb level was significantly higher for those who smoked 10 or more cigarettes per day. The mean Hb value for those who smoked one to nine cigarettes per day and for the ex-smokers was not significantly different from that for the never-smokers.

Hb Distributions of Smokers and Never-Smokers

For both women and men, smokers had a generalized upward shift of the Hb distribution curve when compared with the Hb distribution of never-smokers. Figure 2 illustrates the Hb distribution of female smokers and never-smokers. It is evident that the difference occurs across the entire range of the Hb distribution. Among both women and men, the Hb distribution curve for ex-smokers was very similar to that of never-smokers.

Smoking and Elevated Hbco Level

To examine the possible role of Hbco in the smoking-related increase in Hb levels, we examined the relationship between mean Hbco and mean Hb levels according to smoking status. Among women, the mean (±SE) Hbco level was 6.2%±0.2% for smokers and 1.1%±0.1% for never-smokers ($P<.001$). Among men, the mean Hbco level was 7.8%±0.2% for smokers and 1.4%±0.1% for never-smokers ($P<.001$). The mean Hbco level for female ex-smokers was 1.2%±0.3% and that for male ex-smokers was

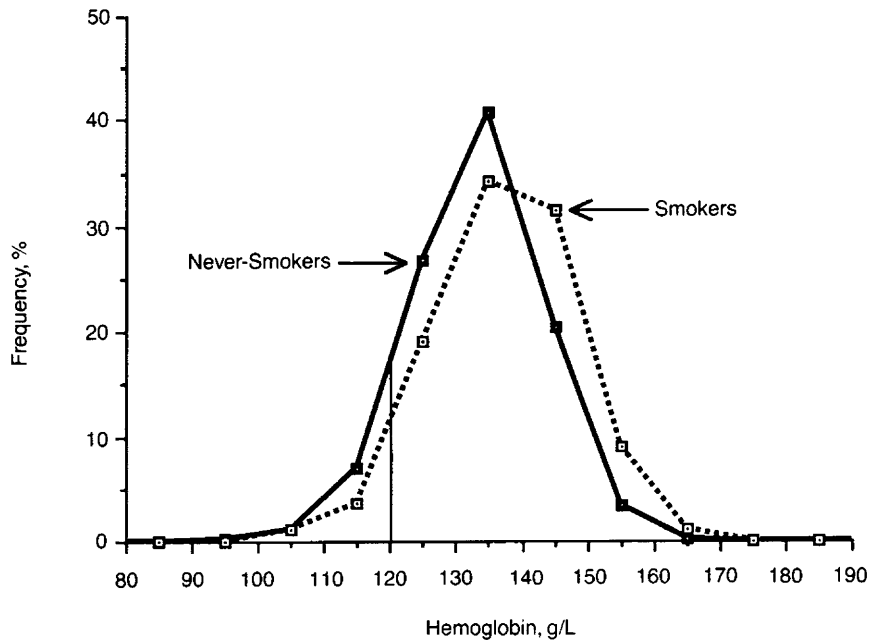

Fig 2.—Hemoglobin frequency distribution curves for female smokers and never-smokers. The hemoglobin distribution curve of smokers showed a pattern of generalized upward shift in contrast to that of never-smokers. The prevalence of anemia was equal to the area under the hemoglobin distribution curve below the cutoff of 120 g/L.

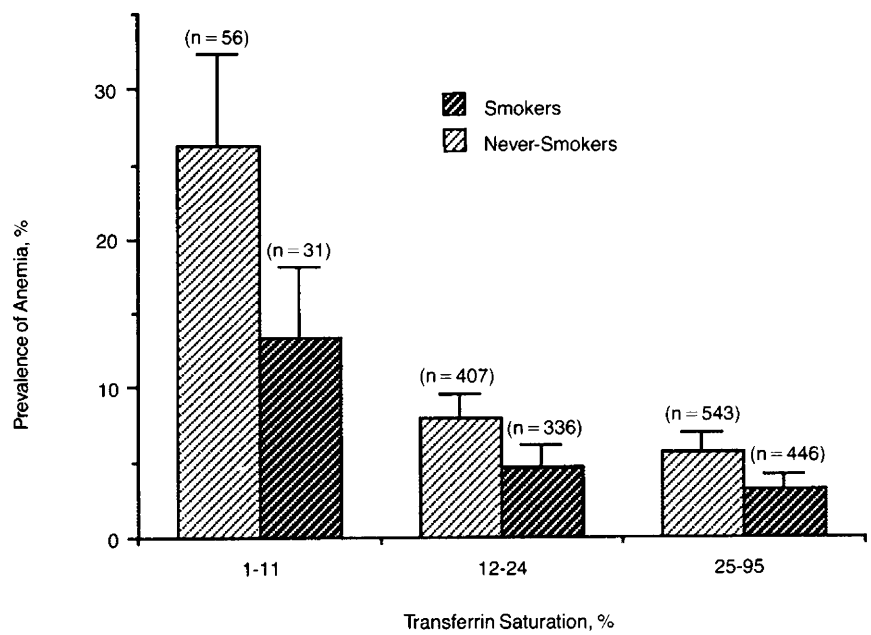

Fig 3.—Prevalence of anemia (±SE) among female smokers vs never-smokers at three different iron nutritional statuses as defined by transferrin saturation.

2.2% ± 0.3%; both values were not significantly different from the mean HbCO values of never-smokers. The mean HbCO for both women and men showed a dose-response increase with an increase in daily cigarette consumption. For example, the mean HbCO level for female smokers was 3.7% ± 0.2% for those who smoked one to nine cigarettes per day; 6.9% ± 0.3% for those who smoked 10 to 19 cigarettes; 8.3% ± 0.1% for those who smoked 20 to 39 cigarettes; and 9.7% ± 0.2% for those who smoked 40 cigarettes or more. In comparison with the never-smokers, the mean increase of HbCO level with increasing cigarette consumption correlated well with the increased mean Hb level (Fig 1).

Effect of Smoking on the Use of Hb for Detection of Anemia

Among women, the prevalence of anemia was 8.4% ± 1.2% (SE) for never-smokers and 4.8% ± 0.6% for smokers ($P<.001$) (Fig 2). Lower transferrin saturation was associated with an increased prevalence of anemia for both smokers and never-smokers (Fig 3). Among women with iron deficiency (defined by a transferrin saturation <12%), the prevalence of anemia among never-smokers was 26.6% ± 6.1%, compared with a prevalence of 14.2% ± 4.7% for smokers ($P=.1$).

Hb Correction Factor for Smokers

In an attempt to improve the ability of anemia screening to identify iron deficiency among women smokers, adjusted Hb cutoffs for anemia were developed. Based on the difference in mean Hb level between female smokers and never-smokers, the adjusted cutoffs were 123 g/L for women who smoked 10 to 19 cigarettes per day, 125 g/L for women who smoked 20 to 39 cigarettes per day, and 127 g/L for those who smoked 40 or more cigarettes per day. No adjustment was used for women who smoked less than 10 cigarettes per day (120 g/L).

With the use of the smoking-adjusted cutoffs, anemia among smokers with a transferrin saturation value in the iron-deficient range increased from a pre-adjustment prevalence of 14.2% ± 4.6% to 34.4% ± 6.4%. The effect of the adjusted cutoffs among all female smokers, regardless of iron nutrition status, was an increase in the prevalence of anemia from 4.8% ± 0.7% to 9.6% ± 1.0%, comparable with the prevalence of 8.5% ± 1.2% for never-smokers ($P=.38$).

COMMENT

This study confirmed that Hb levels are significantly higher for smokers than for never-smokers and demonstrated that this increase is directly related to the number of cigarettes smoked daily. The increased mean Hb level among smokers is the result of a generalized upward shift of the Hb distribution curve. This suggests that smoking results in an elevation of Hb level among most, if not all, smokers.

This analysis suggested that the Hb level increase among smokers is largely

related to increased levels of HbCO, an inactive form of Hb resulting from exposure to carbon monoxide. Most smokers in this study had HbCO levels that have been shown to be associated with decreased exercise tolerance and increased myocardial ischemia during exercise among subjects with coronary artery disease.[20] In contrast, most exsmokers had Hb and HbCO levels similar to those of never-smokers. The low level of HbCO observed among never-smokers likely represents a combination of environmental exposure to carbon monoxide and in vivo production of carbon monoxide during Hb catabolism.[16,21]

This study suggests that the Hb values currently used to define anemia lead to an underestimation of the prevalence of anemia among smokers when compared with never-smokers of comparable iron nutrition status. For women who have iron deficiency based on a low transferrin saturation value, the elevated Hb value related to smoking can mask almost half the cases of anemia, hence reducing the usefulness of the Hb test as a clinical screening method. The fact that the observed effect of smoking on Hb distribution is a generalized one provides the justification to adopt higher Hb cutoff values for screening of anemia in smokers. Similar justification has been used for adopting different Hb cutoffs for children and adults, for men and women, and for residents at higher altitudes compared with residents at sea level.[22,23]

Based on our results, we recommend the following stepwise upward adjustment of Hb values to define anemia: 3 g/L for those smoking 10 to 19 cigarettes per day, 5 g/L for those smoking 20 to 39 cigarettes per day, and 7 g/L for those smoking 40 or more cigarettes per day. This adjustment can be applied to improve estimates of anemia prevalence for health surveys or nutrition surveillance. In a clinical setting, a single uniform adjustment of 4 g/L for all smokers may help improve the efficiency of Hb as a screening tool for anemia or iron deficiency. From a health education perspective, the significantly elevated HbCO level related to carbon monoxide exposure can be used to illustrate another toxic consequence of cigarette smoking.

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