

Department of Clinical Laboratory Sciences

Graduate Masters Theses

Association Between Positive Cotinine Levels And Increased Factor VIII And Von Willebrand Factor Concentrations. Marium K. Paulsen, MS. May 2009.

ABSTRACT:

Cardiovascular disease (CVD) is the leading cause of death in the United States. Smoking, as well as a sedentary lifestyle, diabetes, hypertension, family history, age, gender, race, and metabolic syndrome and other risk factors, contribute to CVD. It is believed that smoking contributes to CVD through reactive oxygen species, which cause an inflammatory response, may damage cells, and contribute to oxidation of cellular elements such as lipids. Smoking also is a risk factor for thrombosis, a CVD disorder. It seems likely that the inflammatory response associated with smoking could increase the levels of coagulation factor VIII (FVIII), an acute phase reactant, and von Willebrand factor (vWF), which forms a complex with FVIII and is released from Weibel-Palade bodies in endothelial cells. Increased levels of these procoagulants have been shown to be linked to increased risk of thrombosis. In this study, the levels of factor VIII antigen (FVIII:Ag) and von Willebrand factor antigen (vWF:Ag) were measured in 875 subjects of the San Antonio Family Heart Study (SAFHS) (2002-2006) who also completed a questionnaire about their smoking behaviors. Based on their responses, subjects were categorized as: (a) current smokers, (b) former smokers, (c) those that had never smoked, and, a fourth category for those without a smoking behavior recorded (d) unknown smoking behaviors. Plasma cotinine was also measured as an unbiased indicator of nicotine exposure. Other covariates were available such as age, gender, body mass index (BMI), plasma triglycerides (TG), plasma high sensitivity C-reactive protein (hs-CRP), diabetes status, and drinking behavior. Commercially available enzyme-linked immunosorbent assay (ELISA) methods were used to measure the levels of cotinine and coagulation factors in EDTA plasma samples collected. A raw data analysis was performed on the 875 subjects for whom complete data were available including age (46 ± 15 years for males; 48 ± 14 years for females), BMI (30 ± 6 kg/m² males; 32 ± 8 kg/m² females), TG (141 ± 114 mg/dL males; 121 ± 65 mg/dL females). Across the four groups of smoking behaviors (current smokers, former smokers, those who had never smoked, and those with unknown smoking behavior) the females had a higher mean hs-CRP (4636 ± 3986 ng/mL) than males (3074 ± 3413 ng/mL). There was no difference in means for FVIII and vWF according to smoking behavior. The means for cotinine levels correlated with reported smoking behavior, with current smokers having the highest cotinine levels. Furthermore, the former smokers had a higher percentage of participants with diabetes than current smokers or those who had never smoked. It is possible that smoking may put one at a higher risk for developing diabetes, but it is also possible that the smokers gave up the habit after they developed diabetes and implemented a lifestyle change. A Sequential Oligogenic Linkage Analysis Routines (SOLAR) analysis was performed on the 867 subjects for whom complete data were available for the assays and covariates with the outliers removed. A p-value < 0.05 was considered significant. A relationship was found between vWF, hs-CRP, and diabetes and FVIII

(the outcome variable). A relationship was also found between age, and FVIII and vWF (the outcome variable). In conclusion, while this study's aim was to show a relationship between smoking behavior (with cotinine as a marker) and those of FVIII and vWF, no significant relationship was found. However, the observation that females, regardless of their smoking behavior had consistently higher levels of hs-CRP than males, warrants further research because hs-CRP assays are now considered a reliable measure to assess risk for CVD.