Seasonal Variation in Cholesterol- Basic results

Introduction

During the past half-century several small longitudinal and larger cross sectional studies have been published suggesting that cholesterol levels are higher in the fall and winter than in the spring and summer. [Thomas, 1961 #1; Fyfe, 1968 #2; Thelle, 1976 #3; Buxtorf, 1988 #5; Cucu, 1991 #6; Gordon, 1988 #4] The most striking of these studies suggested that in areas of extreme seasonal climatic variation, such as Finland, there may be as much as a 100mg/dl seasonal variation in serum cholesterol levels. [Keys, 1958 #7] Recently Råstam and colleagues reported a cross-sectional study of seasonal variation in plasma cholesterol levels drawn as part of the screening process for the Minnesota Heart Health Program. [Råstam, 1992 #8] Cholesterol levels were found to peak in January, with a statistically significant seasonal variation evident in men. In women there was a non-significant trend towards higher winter levels. Using the NCEP guideline for hyperlipidemia of >240 mg/dl, 25.4% of men were at or above this level in winter, whereas only 13.5% met this cutpoint in summer. Gordon and colleagues also have pointed out that seasonal variation in cholesterol levels could be responsible for as much as a 30% difference in the number of patients labeled as hypercholesterolemic during the winter season versus the summer. [Gordon, 1987 #9] However, seasonal variation in blood cholesterol level is not considered in the U.S. National Cholesterol Education Program guidelines, including the recent update to those guidelines. [National Cholesterol Education Program, 1988 #10; Expert Panel on detection, 1993 #11] It is also rarely taken into account in the normal clinical management of hyperlipidemia, although the seasonal differences described above would result in large differentials in the frequency of patients being labeled as having “high” cholesterol. The described seasonal variation would also lead to a much lower percentage of patients reaching goal cholesterol levels if treatment were initiated in the summer and remeasurement carried ut in the winter, than if the converse were true.

With these considerations in mind, we carried out a study of seasonal variation of lipids on healthy volunteer patients. We also measured all of those factors that were thought likely to be related to such variation. Our goal was to characterize seasonal changes in lipid values in a healthy adult population, and to determine the extent to which changes in mediating variables (such as physical activity, dietary intake, and light exposure) can account for such seasonal lipid changes. A secondary objective was to identify sub-groups of subjects where seasonal changes in cholesterol were particularly large (or small).

Materials and Methods

Subject selection

Participants in the SEASONS study were recruited from the Fallon Healthcare System, a Health Maintenance Organization serving Worcester, Massachusetts and surrounding communities. Fallon Healthcare System members who were residents of Worcester County, aged 20 to 70 years, and who had telephone service were eligible to participate if they were not taking cholesterol-lowering medications and were not actively on lipid-lowering or weight-control diets, were free from possible causes of secondary hypercholesterolemia (e.g. hypothyroidism, pregnancy), and were free of chronic life-threatening illness (cancer, or renal or heart failure). Subjects were recruited between December 1994 and February 1997 at a rate of approximately 25 subjects per month. Each subject was compensated for their participation in the study with a portable blood pressure monitor, blood lipid and dietary assessment results, and a monetary sum of $70.

Blood Lipid Assessment

Blood lipid values were assessed at baseline and then every three months for one full year (total of five assessments). Potential predictors of seasonal lipid variation to measured within a 6-week window surrounding each clinic visit for blood draws (~ 4 to 2 week post-clinic visit). The Institutional Review Boards of the Fallon Healthcare System and the University of Massachusetts Medical Center approved all subject recruitment and data collection procedures. Each subject signed an approved informed consent form prior to entering the study.

Baseline data collection.

Demographic data (e.g. age, gender, marital status, education, employment) and health habits (e.g. smoking) information were collected by self-administered questionnaire. Anthropometric data, including body mass (kg), height (m), and waist and hip circumferences (cm) were measured at the baseline and each follow-up clinic visit by the SEASONS staff.
Nutritional data collection

Nutritional data were collected by trained dietitians via a set of 3 unannounced 24-hour recall dietary telephone interviews during the protocol period surrounding the clinic visits. Two interviews were conducted on weekdays, with the remaining interview conducted on the weekend. A broad range of summary dietary measures were recorded along with nutrients after processing through the nutrient data bank. Measures of dietary intake were averaged over the interview period corresponding to each lipid measure, with values of total energy (Kcal/d), percent Kcal from saturated fat, and grams of saturated fat used in these analyses.

Physical Activity data collection

Physical activity data were collected at the same time as the nutritional data on a set of 3 unannounced 24-hour recall telephone interviews during the protocol period surrounding the clinic visits. In the interview, participants recalled the number of hours they spent in four intensities of activity in the previous day in three domains (household, occupational, and leisure time). Methods described by Ainsworth and colleagues (Ainsworth, 1993, #64) were employed to calculate estimates of physical activity energy expenditure using standard metabolic equivalent (MET) values. A weighted sum of daily physical activity energy expenditure 9MET-hrs/d was calculated using the time reported (hrs/d) in each intensity of activity and the following MET weights; light (1.5 METS), moderate (4.0 METS), vigorous (6 METS) and very vigorous (8.0 METS). One MET-hr/d is roughly equivalent to 1 kcal/kg body mass/hr, or the resting metabolic rate for a 60-70 kg person.

Statistical Methods

We fit mixed regression models that include sine curves to estimate seasonal effects in lipids. Statistical significance was assessed at the $\forall \leq 0.05$ level. Fixed effects in the models correspond to the crosssectional covariables (age, gender, …) and the time dependent covariates (energy intake, activity, weight, BMI, …), where we include an estimate of the mean value of the time dependent covariate in addition to the deviation from that mean for each subject. The models treat subjects and quarters within a subject as random effects.

Based on the 24-hour data, we first predict average nutrition and activity values for subjects in each quarter accounting for possible day of the week effects and interviewer effects via gender specific mixed models. We considered interviewer and day of the week as fixed effects, and subjects and quarters nested in subjects as random effects. In nearly all models, effects of day of the week and interviewer were statistically significant. We estimated quarterly values for subjects with best linear unbiased predictors from the mixed models (SAS, 1996).