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Introducing the wide range C-reactive protein (wr-CRP) into clinical use for the detection of microinflammation

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Abstract

Background: The determination of low grade inflammation in apparently healthy individuals (microinflammation) has prognostic significance in terms of future vascular events and accelerated atherothrombotic disease.
Methods: We compared the Bayer wide range (wr)-C-reactive protein (CRP) immunoturbidometric assay on the ADVIA 1650 system to the Dade Behring high sensitivity (hs)-CRP on the BNII Nephelometer in 1446 apparently healthy individuals having a relatively low (<10 mg/l) concentration. The correlation between the 2 assays was also analyzed in relation to other commonly used microinflammatory biomarkers.
Results: A significant ($p<0.0005$) correlation was noted between the hs-CRP and the wr-CRP for the entire cohort ($r=0.99$) as well as for both women ($r=0.99$ $n=483$) and men ($r=0.99$ $n=963$). The mean difference between the measures (hs-CRP minus wr-CRP) was -0.039 (SD 0.317). The Deming regression results for the entire cohort showed a slope of 1.112 ± 0.004 and an intercept of -0.263 ± 0.01.
Conclusions: The Bayer wr-CRP assay performed presents a reasonable alternative to the Behring Dade hs-CRP assay. The advantages of the wr-CRP assay are its online and real time availability as well as lower costs.

Keywords: Microinflammation; Wide range C-reactive protein; High sensitivity C-reactive protein

Abbreviations: hs-CRP, high sensitivity C-reactive protein; wr-CRP, wide range C-reactive protein; BMI, body mass index; CVA, cerebrovascular accident; PAOD, peripheral artery obstructive disease; ESR, erythrocyte sedimentation rate; WBCC, white blood cell count; PMN, polymorphonuclears; CAP, College of American Pathologists; FCRS, Framingham Coronary Heart Disease Risk Score.

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1. Introduction

It has been repeatedly shown that atherothrombosis is associated with the presence of low grade, subclinical and smoldering internal inflammation (herewith denoted as microinflammation) [1–3]. High sensitivity C-reactive protein (hs-CRP) assays have emerged as promising laboratory methods for the determination of the presence of this microinflammation and for the assessment of its intensity [4]. In fact, the determination of CRP concentrations might help to single out individuals with an increased atherothrombotic risk [5,6]. In addition, it might have also a direct pathogenetic role as well [7].

2. Participants and methods

2.1. Study population

We prospectively determined the concentrations of CRP in a group of apparently healthy individuals and those with atherothrombotic risk factors who are routinely recruited into the Data Base of the Tel Aviv Medical Center Inflammation Survey (TAMCIS) [8–10]. This is a relatively large cohort to whom we invited apparently healthy employees of the Tel Aviv Medical Center and the Tel Aviv Municipality (Israel) in addition to individuals with atherothrombotic risk factors who are being followed-up in the medical center's outpatient clinics. Members of the medical staff, retired employees of the medical center and the municipality as well as individuals being evaluated in our outpatient health screening program were also recruited. All the individuals included in the present survey gave their written consent according to the instructions of the Institutional Ethics Committee. Appeals to participate were distributed on bulletin boards and in notes that were included with the monthly paycheck of the medical personnel as well as personal invitations to the patients in various outpatient clinics. Excluded were any individuals with an underlying inflammatory disease (arthritis, inflammatory bowel disease, etc.) as well as those with any infections or other inflammatory conditions, including infarction, surgery or angiography during the 6 months preceding study enrollment. We also excluded individuals with anemia (hemoglobin 13.5 g/dl for men and 11.7 g/dl for women) and those treated with steroid or non-steroidal anti-inflammatory medication, except for aspirin (at doses <325 mg/day). They were examined following an overnight fast.

2.2. Definition of risk factors

Diabetes mellitus was defined as fasting blood glucose of >125 mg/dl, the use of insulin or oral hypoglycemic agents, hypertension as blood pressures of $>140/90$ mm Hg, the use of anti-hypertensive medications while hyperlipidemia was defined as cholesterol or triglyceride concentrations of >200 mg/dl, or the use of HMG-CoA reductase inhibitors or fibrates. We included smokers both present (≥ 5 cigarettes/day) and past (none for ≥ 30 days). For the definition of the metabolic syndrome we used The National Cholesterol Education Program (NCEP) Adult Treatment Panel-III guidelines [11] defining the metabolic syndrome as the presence of ≥ 3 of the following risk determinants: (1) increased waist circumference (>102 cm for men, >88 cm for women), (2) increased triglycerides of 1.70 mmol/l (≥ 150 mg/dl), (3) low HDL cholesterol (1.03 mmol/l for men [<40 mg/dl], 1.29 mmol/l for women [<50 mg/dl]), (4) hypertension (systolic blood pressure ≥ 130 mm Hg or diastolic pressure ≥ 85 mm Hg) or antihypertensive medication use, and (5) impaired fasting glucose 6.1 mmol/l (≥ 110 mg/dl). The Framingham Coronary Heart Disease Risk Score (FCRS) was calculated based on the LDL points according to the formula of Wilson et al [12].

2.3. Laboratory methods

2.3.1. Analyses

2.3.1.1. High sensitivity C-reactive protein (hs-CRP). High-sensitivity C-reactive protein (hs-CRP) was analyzed by an immunonephelometric assay on a BN II analyzer (Dade Behring, Marburg, Germany) using Dade Behring kit for hs CRP assay. This assay is based on particle-enhanced immunonephelometry and it enables the measurement of CRP concentrations as low as 0.16 mg/l. The assay is based on the measurement of polystyrene particles coated with monoclonal antibodies specific to human CRP that aggregate when mixed with samples containing human CRP. These