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Association between C-reactive protein and suicidal behavior in an adult inpatient population

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ABSTRACT

Objectives: To examine the relationship of inflammation and suicidal behavior in hospitalized adult psychiatric patients.
Method: We retrospectively examined serum high sensitivity C-reactive protein (hsCRP) levels in inpatients at a tertiary-level university hospital (N = 184). The inpatients comprised three cohorts: 1) patients admitted following a suicide attempt, 2) patients with suicidal ideation, and 3) inpatient psychiatric controls. Additionally, we gathered demographic data, clinical data, smoking status, white blood cell count, and fasting lipid panel.
Results: As CRP level increased, the probability of patients belonging to the suicide attempt group increased as compared to both the probabilities of being in inpatient psychiatric control and or suicide ideation groups [OR = 2.09, CI = (1.29, 3.38) and OR = 1.75, CI = (1.15, 2.66) respectively]. We also observed a significant effect of depression in that depressed patients were more likely to have a suicide attempt when compared to patients with no depression or with mania [OR = 10.38, CI = (1.97, 54.70)].
Conclusions: There seems to be an inflammation gradient, measured by CRP levels, from recent suicide attempters, suicidal ideators and psychiatric controls. We replicated the association between a pro-inflammatory state and suicidal behavior in a sample of "real world" severely ill psychiatric inpatients.

1. Introduction

Regarded as the most dreaded of psychiatric disease outcomes, death by suicide was responsible for more than 41,000 deaths and was the 10th leading cause of death in the United States in 2013 (McIntosh, 2014). A variety of risk factors for suicide have been identified (Cáceda, 2014), however a clear understanding of suicide neurobiology is currently lacking. Recent reports link suicide-related events with a pro-inflammatory state, including increased levels of blood tumor necrosis factor-alpha (TNFα), increased levels of interleukin-6 (IL-6), and decreased levels of IL-2 (see Black and Miller for recent meta-analysis (Black and Miller, 2015)). However, most of these studies have examined either suicidal ideation or behavior in relation to healthy controls.

In addition to suicide, inflammation has been linked to depression (Danese et al., 2008; Dowlati et al., 2010), anxiety (Bonaccorso et al., 2001; Maes et al., 1998), bipolar disorder (Dickerson et al., 2007; Maes et al., 1995) and psychotic disorders (Fillman et al., 2013; Miller et al., 2013). Mixed evidence exists for psychosocial stress-derived systemic inflammation (Steptoe et al., 2007). Increased glucocorticoid receptor resistance in patients with long-term life-threatening stress has been suggested as a mechanism for increased systemic inflammation in these individuals, but again, the results are mixed (Cohen et al., 2012; Dunbar, 1939).

C-reactive protein (CRP) is an acute-phase inflammatory protein synthesized by hepatic Kupffer cells signaling other body cells for destruction by the complement system and generated in response to increases in serum IL-6 (Thompson et al., 1999). CRP has also been associated with suicide, although in a more limited fashion (Suchankova et al., 2013; O'Donovan et al., 2013; Courtet et al., 2015). Previous literature has established race (Wee et al., 2008; Khera et al., 2005), body mass index (BMI) (Visser et al., 1999), gender (Khera et al., 2005; Lakoski et al., 2006), and depression

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(Ford and Erlinger, 2004; Howren et al., 2009) as factors influencing serum CRP levels in psychiatric populations, although these factors have not been confirmed in studies with naturalistic designs. A conspicuous gap in the literature is whether the stress of hospitalization may affect the comparison of hospitalized suicidal patients and outpatient psychiatric patients or healthy non-hospitalized individuals.

In the present study, we explore a clinical inflammatory marker (CRP) in psychiatric patients hospitalized in an acute adult inpatient facility following suicidal behavior and ideation with the goal of controlling for the stress of hospitalization itself. We hypothesized that patients hospitalized in a "real world" adult inpatient population following a recent suicidal attempt will display higher CRP values than those with suicidal ideation or psychiatric controls.

2. Methods

2.1. Participants

A retrospective review of the medical records of patients admitted to the two inpatient psychiatric units at the Psychiatric Research Institute (PRI) of the University of Arkansas for Medical Sciences (UAMS) between January 2014 and June 2014 was completed for a total of 577 individual admissions. All procedures were approved by the UAMS Institutional Review Board. The inpatient units make up a 30-bed tertiary care referral center, accepting all patients older than 18 years of age from a geographically diverse range of locations, including the entire state of Arkansas, which is predominantly rural and Caucasian, with 20% of the population living below the poverty line.

Inclusion criteria were: age 18–65 years, hospitalization between January 1, 2014 and June 31, 2014, and presence of all laboratory data in question. The only exclusionary criterion was multiple hospitalizations during the study period. Patients were included if they had been admitted prior to the study period, but only data from the first admission during the study period were included. No data from admissions outside the specified interval were obtained or considered in the analysis. In selecting medical records for review, no prejudice was allowed toward current or past medication trials, medication class, method of suicide attempt, or avenue for admission (e.g. transfer from outside hospital, transfer from the medical floor, admission from outpatient clinic, or admission through emergency department). Admission laboratory data, from which the study data were pulled, are routinely used to screen patients for medical instability prior to admission. These labs are drawn routinely within 24 h of admission. Patients are evaluated and admitted continuously, thus labs are drawn as the patient presents, not on a pre-defined schedule.

2.2. Procedures

For those patients meeting inclusion but not exclusion criteria, demographic, laboratory, and clinical data were collected. Demographic data included age, gender, and race. Laboratory data routinely obtained for all patients and included in our analysis were: high-sensitivity CRP (hsCRP) and a fasting lipid panel consisting of triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Given that patients admitted to the inpatient units frequently begin second-generation antipsychotic titrations, a lipid panel is obtained as a standard part of the work-up to expedite appropriate treatment. This data collection was included given recent literature suggesting a correlation between serum lipids and suicide attempt (da Graça Cantarelli et al., 2015). At UAMS hospitals, CRP is measured according to clinical standards using a single UniCel DxC 600 Synchron Clinical Systems (Beckman-Coulter, USA), which is calibrated daily with reference standards between 1.0 and 80.0 mg/L. There were no laboratory personnel changes during the study period.

Six elements of clinical data were included. First, psychiatric diagnostic assessments were performed by or directly under the supervision of a board-certified adult psychiatrist as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition (Association, 2000). Patients were then categorized by authors as having a mood disorder, a psychotic disorder, or both a mood and a psychotic disorder. Mood disorders included diagnoses of major depressive disorder, depression not otherwise specified, bipolar disorder, substance-induced mood disorder, and mood disorder not otherwise specified; psychotic disorders included schizophrenia, schizoaffective disorder, substance-induced psychotic disorder, and psychosis not otherwise specified; a designation of "both" was included when the primary diagnoses included some combination of the above, and the patient exhibited both mood and psychotic symptoms. Second, the affective state of the patient on admission was described as euthymic, depressed, or manic, independent of primary diagnosis. These data were determined by reviewing the mental status exam and reports of the patient included in the history and physical. Third, the presence of an active substance use disorder other than tobacco was assessed. An active use disorder was considered present if either the urine/serum drug screen was positive or the patient endorsed current drug use. Substances of abuse included methamphetamines, cannabinoids, phencyclidine, cocaine, alcohol, and non-prescribed opioids or benzodiazepines. "Fourth, smoking status was included as "current," "past," or "never smoker."" No smoking was allowed while patients are hospitalized. Fifth, medical records were reviewed for a history of suicide attempt not including the episode leading to admission. Patients were assessed first by the admitting physician for a history of suicide attempts, and second by the nursing staff as part of an adult patient profile, a standardized assessment completed on every patient admitted to the inpatient units. Suicidality status, suicide attempt was defined as "self-harm with intent to die," and suicidal ideation was defined as thoughts of self-harm or suicide in the absence of a recent suicide attempt. In order to characterize the suicidality of the suicide attempt group, we used the actual lethality/medical damage subscale from the Columbia Suicide Severity Rating Scale (0: No physical damage or very minor physical damage; 1: Minor physical damage; 2: Moderate physical damage, medical attention needed; 3: Moderately severe physical damage; medical hospitalization and likely intensive care required; 4: Severe physical damage; medical hospitalization with intensive care required; 5: Death) (Posner et al., 2007). Patients meeting criteria for admission (grave disability) without suicidal ideation or recent suicide attempt were considered psychiatric controls. Attempts were made to establish BMI, however the required data were missing for an unacceptably high percentage (33%) of the population, therefore it was excluded from further analysis.

2.3. Data analysis

Descriptive statistics were calculated for the three suicidality groups. Bivariate analysis was performed between suicidality groups and variables involved in the analysis. Chi-square independence test was used for categorical variables, and Kruskal-Wallis test was used for continuous variables due to violation of normality. A generalized logit model was performed to examine the association between serum CRP and the probability of suicidality adjusting for demographic and clinical covariates. The dependent variable was suicidality, which included suicide attempt, suicidal