Premature Mortality among Males with Substance Use Disorders

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Abstract

Objective—Previous studies have demonstrated that substance use disorders (SUD) are associated with premature mortality in clinical populations, though findings regarding the effect of antisocial personality disorder (ASP) on mortality among persons with SUD are less clear. However, it is unclear to what extent that finding generalizes to persons with SUD in the community, because very little work has been done involving mortality in longitudinal studies of mortality associated with SUD. The objective of this study was to assess whether the presence of SUD or ASP are associated with early mortality among males (fathers) in a predominantly community sample, using a 15-year prospective longitudinal study design.

Method—We conducted a prospective longitudinal study of adolescents and their fathers. The adolescent subjects were recruited at age 10–12 years, with follow-up evaluations at ages 14, 16, 19, 22, and 25. Questions were asked about paternal mortality during each of those visits. The study sample for this study was the 769 fathers of the adolescent subjects, who included N=341 fathers with a DSM-III-R diagnosis of SUD and N=428 control fathers without a SUD. 89% of these fathers were recruited from the community, and 11% were recruited from clinical sources. Comorbidity patterns were described. A multivariate Cox regression analysis was performed with the father's age at death or last assessment as the dependent variable, and education, SUD, and ASP as the independent variables.

Results—Lower education level, the presence of a substance use disorder, and the presence of antisocial personality disorder were significantly associated with earlier mortality (Wald=5.1, df=1, p=0.024; Wald=5.1, df=1, p=0.024, and Wald=5.5, df=1, p=0.019, respectively). Most subjects died from medical illnesses, as opposed to drug overdoses or accidents, which is different from the pattern often noted in clinical samples.

Conclusions—The results of this study demonstrate that the presence of SUD, the presence of ASP, and a lower education level were associated with early mortality in our primarily community-based sample, which extends previous reports of similar findings in clinical samples. The magnitude of the prematurity of the deaths was less that that generally noted in previous studies involving clinical samples, and the causes of death were also somewhat different from those noted in clinical samples. The majority of cases of mortality in our SUD sample resulted from medical illnesses rather than from accidents or overdoses.

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Introduction

According to a meta-analysis of 152 studies from 1966 to 1995, the two disorders with the highest relative risk for premature death from both natural and unnatural causes are substance use disorders (SUD) and eating disorders (Harris & Barraclough, 1998). It is well documented that the course of alcohol use disorders (AUDs) and substance use disorders (SUDs) may end in premature death (Timko et al, 2006; Price et al, 2001). However, data on mortality are much more extensive for clinical populations than for persons in the community, so it is unclear to what extent SUD are associated with premature mortality among community populations (Timko et al., 2006). The objective of this study was to determine whether the presence of SUD is associated with premature mortality in our study sample, which is primarily (89%) a community sample. We hypothesized that the presence of SUD would be associated with premature mortality in our sample.

Method

The study design has been extensively described in multiple recent papers (Cornelius et al, 2001; Tarter et al., 2003; Clark et al., 2001; Clark et al., 2005), including comprehensive descriptions of the participants, recruitment procedures, research procedures, research instruments, rater training, inter-rater reliabilities, and data analyses. Consequently, only the major methodological points will be mentioned in this section.

Prior to participation in the study, written informed consent was obtained from fathers and mothers, and assent was obtained from minor children. The study was approved by the University of Pittsburgh Institutional Review Board. Approximately 89% of the families were recruited from the community through public service announcements and advertisements a well as by direct telephone contact conducted by a market research firm, and 11% were recruited from clinical sources (Tarter et al., 2002). The fathers and their sons (and other family members) were recruited when the sons were 10–12 years of age. Comprehensive evaluations of fathers and sons were made at the baseline assessment. Comprehensive follow-up evaluations of the sons were conducted when the sons were ages 14, 16, 19, 22, and 25. Follow-up evaluations were not conducted involving the fathers. Deaths of fathers and the cause of death were determined by asking family members during each of the various follow-up interviews. Cause of death was confirmed by checking newspaper obituary records, by asking additional family members the cause of death, or by checking government death reports.

Diagnostic evaluation of the subjects was conducted with an expanded version of the Structured Clinical Interview for DSM-III-R (SCID)(Spitzer et al., 1987), which was the most recent DSM edition when the study was initiated. Diagnoses were determined in a consensus conference using the best estimate diagnostic procedure (Kosten & Rounsaville, 1992).

Cox proportional hazards models were utilized to assess the predictors of substance use disorders in our population (Clark et al., 2005). This particular statistical technique was used because the outcome data were "right-censored," since onsets may have occurred in some subjects after the final assessment was conducted for this study. Therefore, survival analysis was the appropriate statistical methodology (Klein & Moeschberger, 1997). The proportional hazards or Cox model performs regression analysis was utilized for conducting these survival analyses (Cox, 1972). Education level was the only demographic variable which showed a significant difference between the SUD+ and non-SUD group in preliminary analyses, so that was the only demographic variable that was entered into the subsequent multivariate analyses. A multivariate Cox regression analysis was performed with the father's age at death or last assessment as the dependent variable, and education, SUD, and ASP as the independent variables, based on our preliminary analyses and our previous work in this area (Tarter et al.,

2003; Clark et al., 2005). As secondary analyses, other diagnoses were also assessed as possible predictors of death, including oppositional defiant disorder, attention deficit disorder, and depressive disorders.

Results

The sample included 769 fathers, 28 of whom died during the course of the study. The entire sample included 581 Caucasians (75.5%), and 185 African Americans (24.1%), and 3 of other ethnicity (0.4%). Of the 28 who died, 20 were Caucasians (71.4%) and 8 were African Americans (28.6%). All subjects were male. The deceased fathers did not differ from the living fathers in race, religion, occupation, household socio-economic states, or age at onset of their substance use disorder. The mean age at the time of death was 50.7 years (+/− 7.8 years).

The 769 fathers involved in this study included two groups: a SUD+ group consisting of 341 individuals, and a non-SUD comparison group consisting of 428 fathers without SUD. The non-SUD comparison group consisted of two subgroups, including a subgroup with a psychiatric disorder (n=81, 10.5%) and a subgroup with no psychiatric disorder (n=347, 45.1%). The two subgroups were combined in all analytic comparisons with the SUD+ group because of the limited size of these two non-SUD subgroups.

The most common substance use disorders in the sample were alcohol use disorder (alcohol dependence or alcohol abuse)(77.9%), cannabis use disorder (65.7%), cocaine use disorder (49.7%), opiate use disorder (23.2%), amphetamine use disorder (14.2%), sedative use disorder (9.0%), hallucinogen use disorder (4.3%), phencyclidine use disorder (2.8%), and inhalant use disorder (1.5%). Only 12.3% of the fathers involved in this study met DSM diagnostic criteria for only a single substance use disorder, while the strong majority (87.7%) of the fathers met DSM diagnostic criteria for multiple substance use disorders. Specifically, 36.0% met criteria for two DSM substance use disorders, 32.2% met criteria for three SUD disorders, 14.9% met criteria for four SUD disorders, and 4.1% met criteria for five or more SUD disorders. The most common non-SUD psychiatric diagnoses were major depressive disorder (32.5%), anxiety disorder (24.3%), and bipolar disorder (2.4%), while only 43.9% of all fathers had no non-SUD psychiatric diagnosis.

The 28 fathers who died during the course of the study included 18 subjects (5.3%) from the SUD+ group, and 10 subjects (2.3%) from the non-SUD group, which was a significant difference between groups (Pearson Chi-Square=4.68, df=1, p=0.030). In the 769 subject sample, 85 fathers met diagnostic criteria for antisocial personality disorder. The 28 fathers who died included 21 (3.1%) who did not exhibit ASP, and 7 (8.2%) who did exhibit ASP, which was a significant difference between groups (Pearson Chi-Square=5.749, df=1, p=0.016). The Cox regressions demonstrated that three variables were associated with earlier death, including SUD+ vs. non-SUD status (Wald=5.1, df=1, p=0.024), ASP+ vs. non-ASP status (Wald=5.5, df=1, p=0.019), and low education level (Wald=5.1, df=1, p=0.024). Further analyses revealed that the other diagnoses which had been assessed, such as depressive disorders, attention deficit disorder, and oppositional defiant disorder, were not associated with early mortality.

The majority of deaths in both the SUD+ group and the non-SUD group were the result of medical problems rather than resulting from factors such as drug overdoses or accidents. The excess mortality in the SUD+ group compared to the non-SUD group was entirely the result of two diagnoses: liver disease (N=6 in the SUD+ group vs. N=0 in the non-SUD group) and cancer (N=3 in the SUD+ group vs. N=1 in the non-SUD group). Three persons died from myocardial infarctions and one person died from a stroke in both the SUD+ group and in the non-SUD group. Other diagnoses in the SUD+ group included hit and run motor vehicle

accident, suicide, and amyotropic lateral sclerosis in one case each, and two cases in which the cause of death was unknown. Other diagnoses in the non-SUD group included kidney disease, murder, and pulmonary embolism in one case, and two cases in which the cause of death was unknown.

Discussion

The results of this study demonstrate that the presence of a substance use disorder, the presence of antisocial personality disorder, and a lower education level predict premature mortality among males in the community. The mortality rate among the SUD+ fathers (5.3%), which was about two-and-one-half times higher than the mortality rate among the non-SUD fathers (2.0%), which is consistent with findings from most (Harris & Barraclough, 1998; Price et al., 2001) but not all (Fridell & Hesse, 2006) previous researchers. However, the overall mortality rate of our primarily community-based SUD+ group was somewhat lower that has been previous reported for SUD subjects in clinical samples, which may reflect a selection effect associated with the lower level of acuity of persons in the community as compared to clinical samples (Berkson, 946; Timko et al, 2006), or may reflect a decline in mortality rates associated with an improvement in treatment services (Ghodse, et al, 1998).

The majority of cases of mortality in our SUD sample were the result of medical illnesses rather than from accidents or overdoses, which is consistent with the pattern generally shown by non-opiate using SUD subjects (Chen et al., 2001; Meloni et al., 2006). The causes of death were for liver disease and for cancer were higher in the SUD+ fathers than in the non-SUD fathers, but otherwise the causes of death were similar in the two groups. The high mortality rate associated with liver diseases among SUD patients has been noted by other researchers (Chen et al, 2001). The causes of mortality are of interest because they point to the specific interventions that may be lifesaving (Fridell & Hesse, 2006). These findings regarding cause of death in our sample suggest that mortality prevention efforts should focus more on medical disorders associated with substance use disorders, such as prevention and early treatment of liver disease and cancer in persons with SUD.

There are several limitations to our research design that should be noted when interpreting our findings. First, the sample was not a random sample from across the United States, and did not contain women, so the results may not generalize to the United States as a whole. Although the sampling strategy was not random because of the specific recruitment criteria that needed to be satisfied by the family, comparison of the fathers in this study with subjects in epidemiological studies indicated similarity (Tarter et al., 2003). The moderate size of the study sample also limited our ability to assess subgroups or to assess the wide variety of other factors that might contribute to premature mortality among person with SUD. Further large-scale studies are warranted to further clarify the disorders contributing to premature mortality among those with SUD, and to develop effective strategies for prevention and early treatment of those disorders.

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