

Emerging Issues in the Relationship Between Adolescent Substance Use and Suicidal Behavior

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ABSTRACT

Adolescent suicidal behavior poses a major global public health concern as it is highly prevalent and associated with mortality and morbidity worldwide. Substance-use disorders are also an issue of increasing concern among adolescents and have been shown to increase the risk for suicidal behaviors. In this review we address emerging issues in the relationship between adolescent substance use disorders and suicidal behaviors. We focus on common hazardous patterns of substance abuse such as binge drinking and poly-substance abuse and point out developing patterns of substance preferences as evidenced by the contemporary widespread use of synthetic cannabinoids. We address these issues in the context of vulnerable populations such as sexual-minority adolescents and youth with co-occurring mental-disorder diagnoses. Finally, we relate to the present and future challenges presented by these issues to implement effective anti-suicidal treatment and prevention strategies in adolescents with substance use disorders.

METHODS

Papers relating to substance abuse and suicidal behavior in adolescents from the past 10 years were searched in Pubmed by using the terms “adolescent,” “youth,” “teenage,” matched with “substance use/ abuse/ dependence,” “suicide ideation /plan /attempt /completion. . From the resultant papers, those relating to the relationship between substance use disorders and suicidal behavior in adolescents were read and searched for further relevant references. After reviewing the chosen material,

we highlighted several issues which are the focus of this review and chose papers relating to these subjects in order to compile them into a “non-systematic” review. Internet web sites were either individually picked and accessed or referred to from paper references; internet pages relevant to the subject of this review are cited.

INTRODUCTION

Suicidal behavior (SB) is a broad term encompassing a wide scope of self-injurious behaviors with at least a partial intent to die, ranging from ideation to active self-inflicted death. Adolescent SB poses a major global public-health concern since it is highly prevalent and associated with mortality and morbidity. Suicide is currently the third leading cause of death among adolescents in the United States and second in Europe (1, 2). Recent data indicate an alarming rise in adolescent suicide attempts during the past two years (3) although there are conflicting reports regarding adolescent completed suicide attempts mainly due to high cultural and inter-country variability (4). Regardless of the obvious consequences of completed and non-completed suicide attempts, adolescent suicidal ideation by itself has been shown to increase the risk for compromised adult functioning and future psychiatric morbidity (5).

Many risk factors associated with adolescent SB have been described (6-8), and the interplay between them as well as other moderators has been thoroughly studied. In the last two decades many studies have shown substance-use disorders (SUD) to be one of the most prominent risk factors associated with adolescent SB and increased mortality (9-12). On an average day in the U.S. alone about half a million adolescents aged 12 to 17 drink alcohol and an equal number use cannabis (13), and these drug-using teenagers report increased rates of sadness or hopelessness and SB (14).

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Adolescent SUD as well as SB are both central issues in child and adolescent psychiatry and the relationship between them has been thoroughly and systematically described elsewhere (15-17). Nevertheless, several emerging issues regarding this relationship have most recently generated high interest among care-givers from educational, social and health related services in the community as well as the clinical setting, yielding a substantial amount of data which may be used to formulate targeted intervention plans. In this review we will address these emerging issues and offer future perspectives.

PATTERNS OF ADOLESCENT SUBSTANCE USE AND ABUSE

Apart from tobacco, alcohol and cannabinoid-based substances are by far the most widely used (13) and studied abused substances worldwide. Both have been shown in many studies to be associated with elevated rates and increased risk for adolescent SB (16,18,19) and may be associated with increased suicide attempt lethality (20). In this context it is worth mentioning that a wide variability in the temporal patterns of abuse exist prior to the emergence of SB, ranging from acute intoxication (21) adjacent to a suicidal act (i.e., facilitating factor) to chronic abuse that can predate SB by several years (22).

It is evident today that the impact of alcohol and other substance abuse on SB is more complex than was previously thought and is related not only to the amount of substance consumed (light vs. heavy use) but also, and maybe even more so, to the different patterns of substance abuse as detailed below for both alcohol and other substances abused.

BINGE DRINKING

Many adolescents display a pattern of excessive alcohol consumption termed “binge drinking,” defined as the consumption of five or more standard alcoholic drinks within less than two hours (23). This pattern is highly prevalent, particularly among youth worldwide (24, 25), and is associated with increased risks for suicidal thoughts and attempts (26). This holds true even when comparing binge drinkers to current alcohol drinkers who do not binge drink (27). Binge drinkers also tend to pursue the concurrent use of other substances of abuse, thus increasing the risk for SB. For instance, a significant correlation with the lifetime use of cannabis has been described for binge drinkers (24), with an elevated risk (OR=5) for concurrent

cannabis use as compared to non-binging alcohol users (27). Binge drinkers who co-abuse cannabis display severe patterns of heavy drinking including increased binge drinking instances as well as elevated alcohol consumption on each drinking occasion (28) both of which are associated with increased risks for suicide attempts (27).

POLY-SUBSTANCE ABUSE

Recent epidemiological studies reveal that adolescent poly-substance consumption is a widespread phenomenon and has become the rule rather than the exception (29). This may hold true even for early adolescent drug abusers as data gathered from youths aged 12-14 admitted to substance-abuse treatment programs in the U.S. reveal that 46% of them were poly-substance abusers (30). Poly-substance use is highly correlated with increased risk for suicide attempts (31) and a strong correlation appears also between the number of substances abused to the probability of a reported suicide attempt (19). In this context, the lifetime number of substances used by itself constitutes an important risk factor for SB (32). Since cannabinoids are perceived as “gateway drugs” to the future use of other illicit substances (33), knowledge of their use by adolescents should warrant questioning regarding the consumption of other substances. Furthermore, regarding adolescents with SUD, some studies even suggest that it may not be cannabis use per se that increases the risk of self-directed injurious behavior, but more so the use of other illicit drugs that may follow the initial use of cannabis (34).

CO-OCCURRING SUBSTANCE ABUSE AND OTHER MENTAL DISORDERS

Psychiatric morbidity and mood disorders in particular are highly associated with increased SB rates among adolescents (35). A recent nationally representative study presenting data on principal diagnoses for hospital stays in the U.S., reported that in 2010 mood disorders were the most common principal diagnosis for all hospital stays among children and adolescents (1-17 years old), and the rate of hospital stays for mood disorders had increased by 80% from 1997 to 2010 (36). Since mood disorders and particularly depression are highly prevalent among adolescents (37) they can be taken as good examples when setting out to describe how mental disorders affect the connection between SUD and SB.

Although depression is the strongest known risk factor for adolescent suicide (11, 38-40), an ongoing debate exists

among clinicians regarding the overall effect that antidepressant drugs have on youth SB (41). This may be in part due to other confounding variables that affect depression, SB or both in an unpredicted manner. One possible explanation for the complex effect of antidepressant medication on adolescent SB is the concurrent use of psychoactive substances which may very well complicate the resolution of a depressive state or the diminution of SB regardless of the therapeutic regimen. Adolescent depression displays high co-morbidity with alcohol and substance abuse (42, 43) and adolescents suffering from major depressive episodes (MDE) are about twice as likely to be using illicit drugs or to be heavy alcohol consumers (37) than non-depressed peers.

Epidemiologic research shows that among adolescents with SUD having a co-occurring diagnosis of other mental disorders, and in particular mood disorders, are the norm rather than the exception. This diagnostic entity is otherwise referred to as “dual diagnosis” or “co-occurring disorders” (COD). Data from 6,886 people presenting to substance abuse treatment in the U.S., of them 4,939 adolescents, revealed that the majority suffered from COD with young adults/late adolescents (aged 18-25) appearing to be the most vulnerable age group (44). In this study, about 90% of early adolescent below 15y of age had suffered at least one mental health problem in the past year and more than half of these reported symptoms of depression (44).

The combination of mood disorders and substance abuse has been shown to elevate the risk for adolescent SB (45, 46) including suicide completion (38). Recent evidence further suggests that increased levels of severity of co-occurring disorders in adolescents lead to a heightened risk for a suicide attempt (47).

Some studies reveal an additive and even a synergistic effect when COD occurs. For instance, the combination of depression and alcohol abuse in adolescents has been shown to be associated with an additive effect on the lifetime probability for suicide attempts in adolescent girls and a synergistic effect for adolescent boys (48). Interestingly, this combined effect may disappear in the transition to adulthood since a recent report suggested that in adults with MDE, alcohol-dependence may not significantly affect the risk for SB (49), although it should be stressed that other reports suggest otherwise (50). In studies of adolescents suffering from bipolar disorder, subjects with SUD demonstrated a significantly greater lifetime prevalence of suicide attempts as compared to those without SUD (51) and those who concomitantly performed a suicidal attempt were more likely to be abusing alcohol or to have SUD as compared to those who did not attempt suicide (52).

Large-scale prospective studies are needed in order to address the causative relationship between substance abuse, depression and SB since current research faces many methodological challenges (17). Pioneering studies such as the Course and Outcome of Bipolar Youth (COBY) (53) may lay the foundations for the clarification of this intricate relationship and lead to the formulation of effective evidence-based treatment plans. An interesting question in this regard is whether early treatment of mood disorders will be efficacious in decreasing future SUD by alleviating the patients' need to “self-medicate” in a similar fashion as was previously demonstrated in ADHD patients (54). Another interesting question is whether early treatment of SUD decreases the occurrence and severity of future affective disorders.

Several barriers exist that hinder the effective treatment of adolescent COD (55). In the latter comprehensive review, the author suggested that the historical separation of the mental health and substance abuse fields should be abolished since both disorders are psychiatric conditions with established neurobiological pathologies that share developmental etiologies and clinical trajectories. The high rates of COD evidenced today and the increased risk for SB that entails this morbidity indeed demands the provision of integrated substance-abuse and mental-health services in the same program.

SUD AND SB IN SEXUAL MINORITIES

Sexual minorities, also referred to as lesbian-gay-bisexual (LGB), suffer from increased rates of social stress and rejection across all age groups (56). However, the assessment of data relating specifically to sexual minorities in the adolescent age group is not a simple task. Most LGBs do not quite openly present themselves as such and a significant portion of them have doubts regarding their sexual preferences. Furthermore, many of them may change their sexual orientation throughout this transitional period (57). Such an assessment is made even harder when trying to retrospectively gauge whether same-gender sexual affiliation was present, requiring the differentiation of self-defined sexual orientation from practiced sexual relationships which may or may not be similar to their sexual affiliation. Nevertheless, it is estimated that LGBs account for at least 5% of adolescents (58, 59), whereas up to an additional 5% present themselves as unsure of their sexual orientation (58) and do not necessarily share similar behavioral patterns as the LGB group.

Several studies report that sexual minority youths are subject to increased rates of social isolation, harassment and

victimization (60, 61). Stressful events such as these may translate into increased rates of mental disorders and most notably depression (62) as well as SB (63, 64). Adolescent sexual minorities compared to their heterosexual peers display increased SB (OR=2.9) and the level of disparity is correlated to the severity of SB observed (OR=1.96, 2.2, 3.18, 4.17 for suicidal ideation, intent, attempt and serious attempt accordingly) (65). Data from the ongoing Youth Risk Behavior Survey (YRBS), a large-scale U.S. national school-based survey, report the prevalence of students having attempted suicide to be 6.4%, 25.8%, and 28% for heterosexual, gay/lesbian or bisexual students respectively (58): these rates are exceedingly high relative to the general population. Adolescent sexual minorities also display an elevated risk for SUD including lifetime use of alcohol (OR=2.23) and cannabis (OR=2.58) (66), earlier initiation of alcohol consumption (67) and a higher prevalence of binge drinking (58, 67).

Since sexual minority adolescents display both increased SB rates and SUD prevalence, one may speculate that the causal relationship between these two behavioral states will be more pronounced in members of this population. Quite contrarily, it has been shown that problem alcohol and drug use was more strongly associated with suicidal ideation and attempts in non-LGB adolescents as compared to LGB adolescents (63). The authors of the former study stressed the importance of elucidating specific suicidal risk-factors relevant to LGB adolescents other than the generally perceived leading risk factors which may be more relevant to non-LGB adolescents. Yet one must interpret these results cautiously given the relatively older age (18-26yrs) of the participants of this study as these results may not be applicable to earlier stages of adolescence (12-19yrs) in which the risk for SB emergence is greatest when compared to non-LGB counterparts (68). Until these results are replicated or refuted it will be safer to assume such a connection exists given the higher prevalence of both phenomena in this population while other specific risk factors for SB are sought for.

A large longitudinal study following a cohort of over 1,000 children from birth to age 21, in which the sexual orientation from age 16 until 21 was retrospectively studied, found a 5-fold increased risk for SB and almost a 2-fold risk for substance dependence among LGBs through the cohort period (69). The prospective nature of the study allowed for the evaluation of social and familial backgrounds of the subjects and indeed some differences were found between LGBs and other cohort members in their familial background, suggesting a more troubled childhood for LGBs.

However, reanalyzing the results after controlling for these differences produced similar results with negligible effects on the unadjusted ones (69). One may speculate that other risk factors such as developmental and behavioral factors should be sought to account for the increased rates of SB in the LGB population. Additional prospective studies are sorely needed to facilitate the identification of distinct attributes and risk factors concerned with SB in the LGB population through their transition into adulthood and maturation of sexual preference.

THE EMERGENCE OF NEW “DESIGNER DRUGS”

From ongoing efforts to monitor adolescent drug-abuse habits, it is evident that temporal preference trends in adolescent substance use exist. For instance, the abuse of non-medical analgesic opioids has become second in prevalence to cannabis usage, surpassing the use of inhalants and hallucinogens (70). Recently, the rise in adolescents' usage of synthetic cannabinoids (SC) and cathinones, also termed “new designer drugs,” “spice products” or “legal highs,” has become a source of major concern due to high rates of reported usage and relative ease of availability. In Israel, for instance, dozens of “spice delivery services” exist, responding to real-time phone calls or online internet orders promising the delivery of a wide variety of “spice” products within an hour, thus offering their clients maximal discretion and surpassing the need to expose oneself in the process of substance acquisition. Off-shore orders and practically all urban corner shops provide other convenient alternatives for fast and easy access to these substances.

The prevalence of adolescent SC use worldwide is not yet clear due to a limited amount of large scale epidemiological studies available, although initial reports from select populations displayed lifetime prevalence rates of 8-9% (71, 72). Since 2011, questions addressing the use of SC have been added to U.S. national drug monitoring questionnaires. The first results obtained from these large scale surveys were dramatic; apart from alcohol and tobacco, SC were the second most widely abused substances among 10th and 12th graders (after cannabis) and third among 8th graders (after inhalants), with a two-year stable result of past-12-months prevalence rates among 12th graders of 11.3% (25). Also, the highest rate of emergency department visits involving SC use was within the 12-17 years age group (73). These high prevalence rates are alarming considering the intensive worldwide legislative efforts administered to prohibit the sale and distribution of SC (74, 75). Apart from a few case-reports (76), no studies have yet reported a direct

association between SB and SC usage in adolescents. Our group is currently designing such a study among adolescent psychiatric inpatients, as the rapid growth of the use and harm of SC is already clinically evident.

The military setting offers another challenging front in the struggle against adolescent SC abuse. Late adolescents joining the armed forces comprise the age group in the military which is most prone to be drug abusers, as most (75%) of military personnel with SUD are under 25 years old (77). In some armies such as the Israeli Defence Force (IDF), most of the soldiers are aged 18-21 years and therefore in that setting the problem of SC is even more relevant. In one case series almost 10% of 155 U.S. army personnel admitted to military hospitals suspected of or admitting to the use of illegal substances were found positive for SC and most of these were under 24 years old (78). Many factors contribute to the increased prevalence of SC among military personnel (e.g., ease of availability, low detectability, vagueness of legality and questionable prosecution liability). Unfortunately, other factors such as increased access to firearms and stressful life events, which are associated with military service, also contribute to increased suicidal attempts, which in the military are more likely than in the general population to result in death (79). The evident increase in SC usage in a setting of chronic stress coupled with a direct access to firearms should warrant an examination of the possible association of SC with the prevalence and outcome of suicide attempts in the military setting, this association has not yet been explored despite a clear association previously found among military personnel between completed suicides and alcohol or other substance use (80). An array of suicide prevention programs, a "mutual responsibility" gatekeeper program, was recently employed in the IDF to encourage soldiers to report alcohol and substance abuse including SC in their units, aiming at decreasing these behaviors and possibly the associated SB.

Legislative initiatives coupled to strict and timely law enforcement activity to reduce SC retailing should be encouraged. Judging by the number of calls made to nationwide U.S. poison centers consequent to SC exposures during the first half of 2013, the number of exposures has more than halved compared to the corresponding period in 2012. This offers circumstantial evidence for the success of such legislative actions (81).

CONCLUSIONS

Although recent data reveal an encouraging decrease in adolescent suicide attempts and death rates during the

past decade (2, 3), suicide in this age group remains by and large a major public-health concern. Adolescent substance abuse has also become a heavy burden on society and the need for its successful management poses many challenges on healthcare, psycho-social, and educational caregivers. The association of adolescent SUD with SB has been substantiated for more than two decades, yet global efforts to reduce substance abuse or SB have displayed a relative lack of success. There are almost no prospective randomized controlled trials from which one can devise and implement evidence based treatment plans specific for adolescents with SUD and SB. Data derived largely from adult studies suggest that interventions schemes that rely on or integrate cognitive behavioral treatment (CBT) techniques may be efficacious in reducing both suicidal behavior as well as substance use among adolescents with co-occurring problems (82). Reductions in suicide attempts, binge drinking and cannabis use were all considered part of the 21 critical national health objectives prioritized by the Healthy People 2010 initiative (HP2010), devised to improve the health and well being of U.S. adolescents and young adults. Although an improvement was reported in all these objectives during the decade in which these were to be achieved, none of the declared target rates were ultimately reached (83). In order for these goals, set by policy makers and guided by expert consultants, to be attained, novel strategies and policies clearly have yet to be formulated.

Emerging patterns and norms of substance abuse such as poly-substance abuse and binge drinking emphasize the need to rely on real-time research which may assist in the formulation of time and place-relevant prevention plans and treatment options. Recent studies highlight specified populations with increased risk for both SB and SUD, such as LGB and COD adolescents, the latter displaying a stronger association between the two phenomena. These may suffer from increased vulnerability or decreased resilience to the perilous effects of SUD, social stress or genetic predisposition for mental pathologies. Healthcare personnel should pay heightened attention to observed SB when encountered in LGB youth, even when they are most subtly presented. They should aspire to initiate a suicidality-assessment as soon as possible since the increased risk for LGB SB does not dissipate through sexual identity maturation but rather tends to persist through the transition into adulthood (84).

Many adolescents suffering from psychiatric conditions do not turn to treatment (85). Only a minority of completed adolescent suicides are diagnosed with mental problems and many of these go untreated for such problems prior to the

suicidal act (86). SUD are most common among adolescents with psychiatric morbidity (87, 88) and increasingly often patients are diagnosed as suffering from “dual diagnosis” or COD. Unfortunately, for most of these patients this does not translate into an integrated treatment plan and a duality in treatment focus invariably exists. This is evident in all the treatments’ levels such as its setting, the professional training of the caregivers (i.e., psychiatry vs. drug rehabilitation) and the type and duration of treatment administered. In an editorial published by Bertolote et al. (89) they wrote: “Effective treatment for chronic conditions requires a transformation of health care systems, away from delivery focused on episodic care in response to acute illness, and towards a comprehensive system of care that is designed to meet the long-term needs of patients.” We propose that it is high time to end the artificial dichotomy between psychiatric and substance-abuse directed healthcares and to focus on the adolescent patient as suffering from a chronic illness that has the potential to manifest itself in either direction at a given time and under different circumstances.

The rapid emergence and spread of new “designer drugs,” such as hundreds of SC products, offers new challenges to health systems. Legislative efforts to ban these substances should ideally be easy to implement by law enforcement agencies and have a generalized formulation so as to capture a wide range of substances in their legal definition. Despite the paucity of current data relating to the connection between SC use and SB, it is at least prudent to assume such a connection exists until tested, given the shared neuronal target-receptor profile with cannabis and relying on clinical data from cannabis users which firmly establish this connection.

Other factors may influence the success of suicide prevention plans in adolescents with SUD. For instance, adolescents are highly peer-influenced and follow the norms of their birth cohort and it has been recently shown that members of birth cohorts with more restrictive social norms regarding alcohol use have a lower likelihood to be abusing alcohol (90). This stresses the potential utility of adolescent-targeted as opposed to population-targeted prevention plans and restrictive measures regarding substance use and may also hold true for SB as well, given the “contagious” effect of suicide in youth (91). In this regard, the timing of prevention plan initiation may be critical. It has been shown that about a third of early adolescent admissions to rehabilitation centers report using their primary substance of abuse at age 11 or younger and many of these are CODs (28). Most recently it was reported that at 12 years of age there is a marked increase in the prevalence of SB (92)

and that most of the transitions from suicide ideation to plan or attempt and also from plan to attempt, occur in adolescents within the first year of onset of ideation or of developing the plan (92) as was previously shown for adults (93). Since differences in rates of SB among adolescents with substance use as compared to those without are apparent by age 13 years and become more pronounced thereafter (22), it may therefore be wise to target the implementation of anti-suicidality and SUD prevention and intervention plans to the junior- high school age group. In addition, age-restriction legislative acts, such as increasing the minimum legal alcohol drinking age from 18 to 21, have been shown to reduce completed suicides among 18-23 years old (94), suggesting that postponement of exposure to potentially harmful substances by early educational initiatives coupled to age-limiting legislative acts should be an integral part of adolescent anti-suicidality strategies.

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