

Substance abuse and suicide risk among adolescents

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Abstract The aim of this paper was to review the literature concerning the relationship between suicide and substance abuse behaviours among adolescents, focusing on epidemiology, comorbidity and preventive programmes. We performed a Pubmed/Medline, Scopus, PsycLit and PsycInfo search to identify all papers and book chapters during the period between 1980 and 2011. Adolescents with substance abuse disorder who attempt or complete suicide can be characterized as having mood disorders, stressful life events, interpersonal problems, poor social support, lonely lives and feelings of hopelessness. The research supports the existence of a strong relationship between suicide and substance abuse. Preventive programmes should be based on the detection of risk factors associated with both suicide and substance abuse disorder. Management programmes should combine different

therapeutic strategies such as peer-to-peer education, school-based programmes, psychotherapy and pharmacological treatment. Evidence suggests that targeted suicide prevention programmes can be delivered which reduce the burden associated with substance abuse and suicide in youths.

Keywords Drug abuse · Alcohol abuse · Suicide · Youths · Prevention

Introduction

Adolescence is a challenging period of cognitive, biological, physiological and psychological transition, occurring between 10 and 19 years of age [22]. The transition to

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adolescence leads to needs for independence, identity formation and acceptance by peers. All of these contribute to risk-taking behaviours, suicidal ideation and suicidal behaviour.

According to the World Health Organization [115], suicide is the third leading cause of death among those aged 15–24, after car accidents and cancer. Additionally, suicide attempts represent the main reason for referral to child and adolescent psychiatric emergency services [77].

Despite the fact that suicide mortality in middle-aged and older persons has recently decreased in several European and North American countries, suicides among youths have risen dramatically in recent decades [76], and researchers have associated this increase in youth suicide with the widespread use of alcohol and other drugs among adolescents [7, 47, 112].

Both cross-sectional and retrospective evidence in adolescent and adult populations have reported an association between suicidal behaviours and substance use. Goldsmith et al. [35] reported a rapid increase in drug abuse in the USA in the years after 1960 especially in adolescents. Adolescent suicidal behaviour also increased by about 300%. Substance using in adolescence has been proposed as a relevant risk factor for suicidal behaviours [97]. Wines et al. [114] found that 28% of inpatients in drug abuse treatment centres had histories of suicidal ideation and 21% had attempted suicide. Additionally, after 2 years of substance abuse treatment, 19% continued to have suicidal ideation and 7% had made suicide attempts. It was also suggested that the estimated risk for suicide in the presence of alcohol-related disorders was about four times greater in men and five times greater in women than in its absence [100]. Shneider et al. [101] reported that alcohol-related disorders (DSM-IV alcohol dependence) were more often diagnosed in suicide victims than in controls (OR = 8.8, 95% CI 4.4–17.7).

Based on the existing literature, this systematic review first aimed to investigate whether there is an association between the substance use/abuse/dependence and suicidal behaviour in clinical and non-clinical samples. Our second aim was to ascertain whether substance use/abuse/dependence may be considered as a specific risk factor for suicide after controlling for a number of potentially confounding factors.

Materials and methods

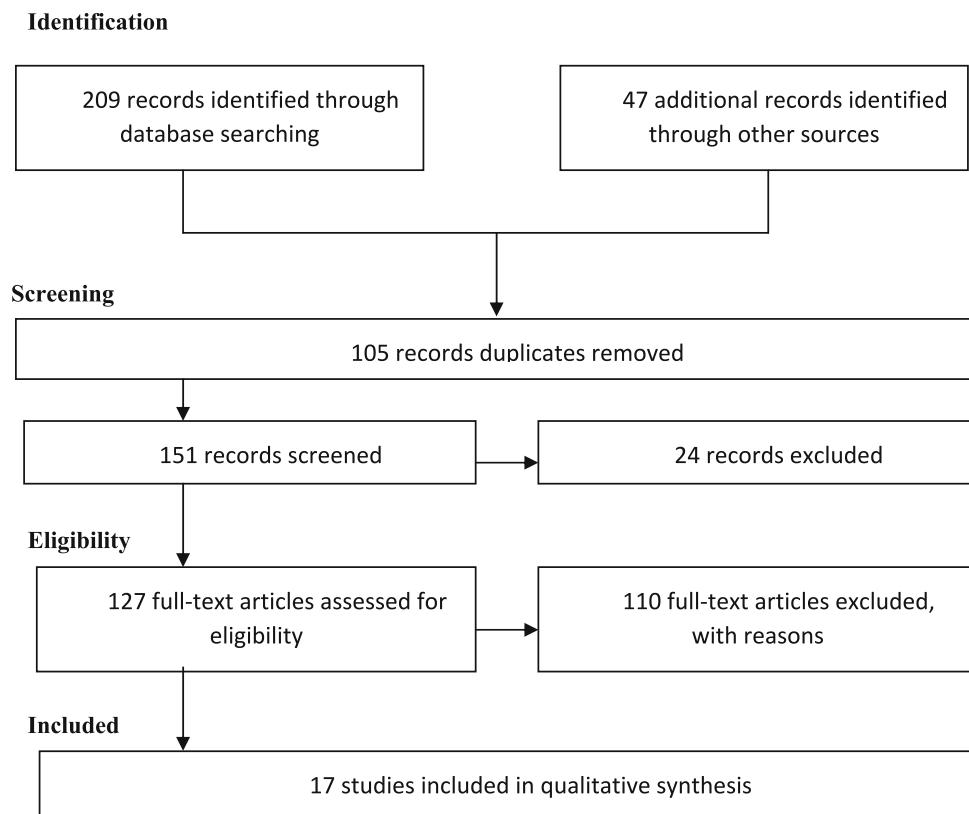
To achieve a high standard of reporting, we have adopted ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ (PRISMA) guidelines [69]. In order to provide a new and timely systematic review of substance abuse and suicidal behaviour, we performed a Pubmed/

Medline, Scopus, PsycLit and PsycInfo search to identify all papers and book chapters during the period between 1980 and 2010. The search used the following terms: (suicide OR suicide attempt OR ideation OR suicidal behaviour) AND (epidemiology OR rates OR trends OR incidence) AND (drug OR substance abuse OR drug abuse OR substance disease OR comorbidity) AND ('prevention' OR 'intervention' OR 'future implications'). Specifically, in order to adequately focus on the specific field of interest, the following search query was used in Pubmed: (suicid* [TI] AND substanc* [TI]). This search in Medline generated 182 articles. The same search strategy was used in Scopus rendering 4 additional articles and in PsycLit/PsycInfo (specifying 'suicide AND substance abuse' and deleting '[TI]') providing 43 further articles. The reference lists of the articles included in the review were manually checked yielding 27 additional articles that might be potentially considered for screening. The Pubmed, Scopus and PsycLit/PsycInfo databases revealed a total of 151 potentially relevant articles after the removal of duplicates. Figure 1 summarizes the search strategy used for selecting studies (identification, screening, eligibility, inclusion process).

Data collection

Only those articles published in peer-reviewed journals were included. Where a title or abstract seemed to describe a study eligible for inclusion, the full article was obtained and examined to assess its relevance based on the inclusion criteria. Two independent researchers conducted a two-step literature search. Any discrepancies between the two reviewers who, blind to each other, examined the studies for the possible inclusion were resolved by consultations with a senior author. Included were all contributions that explicitly mention the association between substance use and suicidal behaviour in clinical and non-clinical (healthy) samples. Exclusion criteria are the following: (1) studies including samples with mean age >18 were excluded years; (2) studies published before 1980; (3) articles without abstracts or abstracts that did not explicitly mention suicidal behaviour, substance use, abuse and dependence; (4) articles not published in English language; and (5) articles having low relevance to the main theme. Included papers were restricted to those in English with the exception of one Norwegian study [75] included in Table 1 because it was considered to be of particular interest. All 151 articles were critically evaluated: 24 of these were excluded because they were not published in peer-reviewed journals, were without abstracts, had abstracts that did not explicitly mention suicidal behaviour (suicidal attempts and ideation) and substance abuse, and are articles with a

Fig. 1 Search strategy used for selecting studies (identification, screening, eligibility, inclusion in the systematic review)



publication date before 1980. This left 127 full-text articles of which 110 articles were excluded because they were not published in English language, had low relevance to the main theme, included unclear data regarding materials and method and number of patients analyzed. Thus, 17 articles meeting our inclusion criteria were included in the present review.

Data extraction

Data were independently collected by the two reviewers. The following characteristics were extracted from the 17 included articles in Table 1: author/s and publication year, study design, sample size, eventual follow-up, conclusions and main risk factors.

The principal reviewer (MP) inspected all reports. Then, three reviewers (MP, PG and GS) independently inspected all citations of studies identified by the search and grouped them according to the topic of the papers. Reviewers acquired the full article for all papers located. Where disagreement occurred, this was resolved by discussion with MA who also with double-blind features inspected all articles located and grouped them following the major areas of interest identified by all authors. If doubt remained, the study was put on the list of those awaiting assessment, pending acquisition of more information. We excluded from our analysis any studies vaguely reporting

on substance abuse in adolescence or using inadequate or unclear diagnostic criteria for such disorders or those inappropriately assessing the impact of substance abuse on suicide risk. Results of this search are presented in the paragraphs regarding the role of substance abuse in the precipitation of suicide risk.

Summary measures

Studies were rated for quality using the following eligibility criteria: (i) the representativeness of the sample from the general population (0–2 points), (ii) the presence of a control group (1 or 2 points), (iii) presence of follow-up >1 year (1 or 2 points), (iv) evidence-based measures of assessment (e.g. the use of the SCID-I for the diagnosis of the substance abuse/dependence or other psychometric evaluation) (1 or 2 points), (v) the presence of two independent raters who blindly diagnosed the substance abuse/dependence (1 or 2 points), (vi) a statistical evaluation of the interrater reliability (1 or 2 points) and (vii) evidence-based measures for assessing suicide or suicide attempts (1 or 2 points). Quality ratings had 14 as the maximum score.

Studies were differentiated in the following way: good quality (>11 points)—most or all criteria being fulfilled, and where they were not met, the study conclusions were thought very unlikely to alter; moderate quality (6–11

Table 1 Relevant studies about substance abuse and suicide risk in adolescents and young adults

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Darke and Ross [24]	Review article on suicide rates, suicide risk factors and methods employed for suicide among heroin users	Not reported	No	Heroin users are 14 times more likely than peers to die from suicide. They also attempted suicide more frequently than that of community samples. Risk factors for suicide were psychopathology, family dysfunction and social isolation as well as poly-drug use. Drugs but not heroin as a method of suicide appear to play a relevant role in suicide among this group	1. Psychopathology 2. Family dysfunction 3. Social isolation 4. Poly-drug use	I = 2 II = 2 III = 0 IV = 1 V = 2 VI = 2 VII = 2 Total score = 11	Moderate quality
Roy [94]	Case-control study comparing opiate-dependent patients who had and had not attempted suicide	246 opiate-dependent patients	No	One hundred of the 246 opiate-dependent patients had attempted suicide, and significantly more of the opiate-dependent patients who had attempted suicide had a family history of both completed and attempted suicide. Opiate-dependent patients who had attempted suicide reported significantly more childhood emotional abuse, physical abuse, sexual abuse and emotional and physical neglect. Moreover, opiate-dependent patients who had attempted suicide were found to be significantly more introverted, hostile and neurotic. Finally, significantly more of the patients who had attempted suicide were female and unemployed	1. Family history of both completed and attempted suicide 2. Childhood emotional abuse 3. Childhood physical abuse 4. Childhood sexual abuse 5. Emotional and physical neglect 6. Introversion, hostility and neuroticism. 7. Being female and unemployed	I = 2 II = 2 III = 0 IV = 1 V = 2 VI = 2 VII = 2 Total score = 11	Good quality
Havens et al. [42]	Cross-sectional study investigating the relationship between suicidal ideation with injection drug users (IDUs) and non-injection drug users (NIDUs)	244 injection drug users and 73 non-injection drug users	No	Suicidal ideation was present in 27% of the IDU patients vs. 14% among the NIDU patients, $p = 0.003$. After controlling for confounding lifestyle factors, including homelessness, depressive symptoms and gay/lesbian/bisexual identity, the association was no longer significant. The poor sociopsychological background (psychiatric disorders, sexual orientation, isolation), which is frequent among injection drug users may be responsible for the increased suicidal ideation found in IDUs	1. Psychiatric disorders 2. Sexual orientation 3. Isolation	I = 2 II = 2 III = 0 IV = 1 V = 0 VI = 1 VII = 0 Total score = 6	Moderate quality

Table 1 continued

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Kalyoncu et al. [50]	Cross-sectional examination of the socio-demographic and clinical characteristics	108 young adult heroin-dependent inpatients	No	Both the female and male suicide attempters were significantly younger at the onset of heroin use than those who had not attempted suicide. The starting age of heroin use may be a risk factor for suicide attempts. The suicide attempters had experienced greater family psychopathology and dysfunction than the non-attempters and had significantly higher scores on the Childhood Trauma Questionnaire. Previous traumatic experiences are strongly associated with suicide attempts in young adult heroin-dependent patients. In particular, the male suicide attempters more often met the criteria for depressive, anxiety and antisocial personality disorders	1. Younger age 2. The starting age of heroin use 3. Family psychopathology and dysfunction 4. Childhood traumatic experiences 5. Depressive disorder 6. Anxiety disorder 7. Antisocial personality disorder	I = 2 II = 0 III = 0 IV = 2 V = 1 VI = 2 VII = 0	Moderate quality
Marzuk et al. [63]	Individual review of autopsy and toxicological records	Not reported	No	The prevalence of cocaine use among young Hispanic males who committed suicide was 45%. Persons who were young, black or Hispanic and who had used alcohol immediately before the fatal injury were most likely to have been recent cocaine users. After controlling for demographic variables and alcohol use, subjects who committed suicide with firearms were twice as likely to have used cocaine as those who used other methods	1. Cocaine use 2. Younger age 3. Black or Hispanic race 4. Alcohol consumption immediately before the fatal injury	I = 2 II = 0 III = 0 IV = 0 V = 2 VI = 2 VII = 0	Moderate quality
Roy [93]	Case-control study	214 cocaine-dependent patients	No	39% of the cocaine-dependent patients had attempted suicide at some time in their lives, more often had a family history of suicidal behaviour and reported significantly more childhood trauma. They also had higher personality scores for introversion, neuroticism and hostility; they had significantly more comorbidity with the use of other substances, as well as psychiatric and physical disorders	1. Family history of suicidal behaviour 2. Childhood trauma 3. Introversion, neuroticism and hostility 4. Psychiatric disorders 5. Physical disorders	I = 2 II = 2 III = 0 IV = 2 V = 0 VI = 2 VII = 0	Moderate quality

Table 1 continued

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Waldrop et al. [111]	National cross-sectional Survey of Adolescents	2002 adolescents (aged 12–17)	No	Sample prevalences of suicidal ideation and attempts were 24.3 and 3.3%, respectively, yielding weighted population prevalence estimates of 23.3 and 3.1%. Suicidal ideation was positively associated with female gender, age, family, alcohol and drug problems, violence exposure, lifetime depression and PTSD. Suicide attempts were associated with female gender, age, sexual and physical assault, lifetime substance abuse or dependence, PTSD and depression	1. Psychopathology 2. Female gender 3. Age 4. Sexual and physical assaults	I = 2 II = 0 III = 0 IV = 0 V = 1 VI = 2 VII = 1 Total score = 6	Moderate quality
Garlow [33]; Garlow et al. [34]	Retrospective analysis of records of the Office of the Medical Examiner of all completed suicides	416 cocaine users	No	Almost all (94.6%) of the suicides in whom cocaine was detected were male, 51.4% of the cocaine-positive suicides were African American men and 43.2% were white men. Most (86.7%) of African American teenagers did not use substances before committing suicide, whereas 50.0% of the white teenage victims had used one or both substances, with 41.7% of the white teenagers having used ethanol. Ethanol use was much more common among white victims of all age groups	1. Being male 2. Younger age 3. Being white or African American 4. Cocaine or ethanol detected at autopsy	I = 2 II = 0 III = 0 IV = 0 V = 2 VI = 0 VII = 0 Total score = 4	Low quality
Innamorati et al. [48]	Cross-sectional study	340 young adults	No	14.7% were drug users and 24.1% drinkers. Alcohol and drug misuse was significantly associated with reasons for living, hopelessness, suicidal attitudes and depression. After multiple regression analysis, the Drug Abuse Screening Test, the Zung Depression Scale and Loss of Motivation were positive predictors of suicide risk with Survival and Coping Beliefs as negative predictors. Cannabis may be associated with risky health behaviour	1. Alcohol and drug misuse 2. Higher scores on the Zung Depression Scale 3. Loss of motivation	I = 2 II = 0 III = 0 IV = 2 V = 2 VI = 2 VII = 2 Total score = 10	Moderate quality

Table 1 continued

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Beautrais et al. [2]	Case–control study	302 cases vs. 1,028 controls	No	Subjects who had made serious suicide attempts had significantly higher rates of cannabis abuse/dependence than comparison subjects presumably related to the socio-demographic disadvantages and disadvantaged childhood family circumstances. After controlling for confounding factors and comorbid psychiatric disorder, the odds ratio between cannabis abuse/dependence and making a serious suicide attempt was 2.0 and only marginally statistically significant	1. Cannabis abuse/dependence 2. Socio-demographic disadvantaged childhood family circumstances 3. Comorbid mood disorder, other substance use disorder and antisocial personality disorder	I = 2 II = 2 III = 0 IV = 2 V = 1 VI = 2 VII = 1 Total score = 10	Moderate quality
Fergusson et al. [32]	21-year longitudinal study	1,265 adolescence/young adults	First evaluation = at birth T_1 = 4 months T_2 = 1 year T_3 = annual intervals up to age 16 years T_4 = at age 18 years T_5 = at 21 years	Regular cannabis use was associated with a dramatic increase in the risk of other illicit drug use, even when confounding variables were taken into account. In addition, regular cannabis abuse was associated with increases in delinquency, depression and suicidal behaviour. The adverse effects of cannabis on adjustment seemed to be most pronounced for younger users and declined with increasing age	1. Cannabis use 2. Younger age 3. Delinquency in cannabis users 4. Depression in cannabis users	I = 2 II = 0 III = 2 IV = 2 V = 2 VI = 2 VII = 2 Total score = 12	Good quality
Rey et al. [89]	Cross-sectional study	1,261 adolescents using cannabis	No	1/4 of the sample reported having used cannabis and males were twice as likely as females to have used cannabis before the age of 13. An association between depression and cannabis use was found. Cannabis use increased the incidence of disruptive behaviours such as conduct problems, tobacco smoking, excessive drinking and the use of illicit drugs	1. Being male 2. Depression 3. Conduct problems, tobacco smoking, excessive drinking and excessive use of illicit drugs in cannabis users	I = 2 II = 0 III = 0 IV = 2 V = 2 VI = 2 VII = 0 Total score = 8	Moderate quality

Table 1 continued

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Chabrol et al. [18]	Cross-sectional study	248 high school students	No	Those who had used cannabis at least once in the last six months had significantly higher rates of suicidal behaviour, depression symptoms and anxiety symptoms compared to non-users. Cannabis use appeared to be an independent predictor of suicidal behaviour after controlling for depression and anxiety symptoms	1. Cannabis use 2. Depression symptoms and anxiety symptoms in cannabis users 3. Injection drug use 4. Being forced to have sex 5. Smoking in girls 6. Fighting for girls and fighting in school for boys	I = 2 II = 0 III = 0 IV = 1 V = 0 VI = 0 VII = 2 Total score = 5	Low quality
Epstein and Spiritio [30]	Cross-sectional study	13,917 high school students	No	Early alcohol onset, having had sex before age 13, injection drug use and being forced to have sex were associated with suicidality across gender. Smoking in girls was associated with making a plan to attempt suicide and actual suicide attempts. Fighting was related to suicidality for girls, while fighting in school was related to suicidality for boys	1. Early alcohol onset 2. Having had sex before age 13 3. Injection drug use 4. Being forced to have sex 5. Smoking in girls 6. Fighting for girls and fighting in school for boys	I = 2 II = 0 III = 0 IV = 1 V = 0 VI = 2 VII = 0 Total score = 5	Low quality
Price et al. [86]	Longitudinal study together with a cross-sectional investigation using the National Cause of Death Register to correctly identify suicides and undetermined deaths	50,087 male military conscripts	33-year follow-up	5,380 (10.7%) of subjects admitted to having used cannabis while 41,394 (82.6%) had not. The association between cannabis use and risk for suicide was present using a crude analysis (crude OR for 'ever use' 1.62, 95% CI 1.28–2.07), but after adjustment for social and personal factors, they failed to confirm the increased risk for suicide in cannabis users adjusted OR = 0.88, 95% CI 0.65–1.20. A significant association was found between the use of other drugs, instead of cannabis, with undetermined deaths (adjusted OR = 2.06, 95% CI 1.11–3.80) but not with definite suicides (adjusted OR = 1.13, 95% CI 0.73–1.75)	1. Use of other drugs than cannabis 2. Depressive symptoms 3. Psychotic symptoms 4. Being forced to have sex 5. Fighting for girls and fighting in school for boys	I = 2 II = 0 III = 2 IV = 2 V = 2 VI = 2 VII = 1 Total score = 11	Good quality

Table 1 continued

Study	Design	Sample size	Eventual follow-up	Conclusions	Main risk factors	Quality score	Quality differentiation
Pedersen [75]	Longitudinal study	2033 young adults	13-year follow-up	No association between early adolescence, suicidality and later depression, while in the group in their twenties, a highly significant association was found between cannabis use, suicide ideation and suicide attempts even after controlling for confounding factors. Subjects who had used cannabis 11 + times during the past 12 months had an OR for later suicide attempts of 2.9 (95% CI 1.3–6.1) and for suicidal ideation an OR of 2.7 (95% CI 2.8–6.4)	1. Cannabis use 2. Younger age	I = 2 II = 0 III = 2 IV = 2 V = 2 VI = 2 VII = 1 Total score = 11	Good quality

Studies were rated for quality using the following eligibility criteria: (i) the representativeness of the sample from the general population (0–1 points); (ii) the presence of a control group (1 or 2 points); (iii) presence of follow-up >1 year (0–2 points); (iv) evidence-based measures of assessment (e.g., the use of the SCID-I for the diagnosis of the substance abuse/dependence or other psychometric evaluation) (0–2 points); (v) the presence of two independent raters who blindly diagnosed the substance abuse/dependence (0–2 points); (vi) a statistical evaluation of the interrater reliability (0–2 points); (vii) evidence-based measures for assessing suicide or suicide attempts (0–2 points). Quality ratings had 14 as the maximum score

Studies were differentiated in the following way: (1) good quality (≤ 11 points)—most or all criteria being fulfilled, and where they were not met, the study conclusions were thought very unlikely to alter; (2) moderate quality (6–11 point)—some criteria being fulfilled, and where they were thought very likely to alter; and (3) low quality (≤ 5 points)—few criteria were fulfilled, and the conclusions of the study were thought very likely to alter. Caution was required in interpreting the results of these trials

points)—some criteria being fulfilled, and where they were not met, the study conclusions were thought unlikely to alter; and low quality (>5 points)—few criteria were fulfilled, and the conclusions of the study were thought very likely to alter. Caution was required in interpreting the results of these trials.

Results

According to our quality score system, the mean quality score of the 17 studies that were included is of 7.7 points. Based on quality differentiation, most of studies (ten) resulted of moderate quality, four contributions were judged of good quality and three of low quality, respectively.

Suicide risk in alcohol users/abusers

Some of the studies included showed an association between alcohol use disorders and suicidal risk (Table 1). Rey et al. [89] in a cross-sectional study on 1,261 adolescents with cannabis use found a close relationship between cannabis use and excessive drinking plus cannabis use increasing the incidence of disruptive behaviours.

Garlow [33] and Garlow et al. [34] in a retrospective analysis found that ethanol use was much more common among white completed suicides of all age groups. The authors reported that 50.0% of the white teenage victims had used ethanol or cocaine alone or both ethanol and cocaine, with most of them (41.7%) having used predominantly ethanol.

In 2008, Innamorati et al. [48] performed a cross-sectional study of 340 young adults and reported that 24.1% were drinkers. Alcohol misuse was significantly associated with reasons for living, hopelessness, suicidal attitudes and depression. After multiple regression analysis, the Drug Abuse Screening Test was a positive predictor of suicide risk.

Epstein and Spirito [30] in a cross-sectional study on 13,917 high school students later reported that early alcohol use onset was significantly associated with suicidality across gender.

Suicide risk in other substance users/abusers

Several other studies showed an association between substance use disorders (SUD) and suicidal risk. Beautrais et al. [2] in a case-control study on 302 cases versus 1,028 controls found that subjects who had made serious suicide attempts had significantly higher rates of cannabis abuse/dependence than comparison subjects presumably due to the socio-demographic disadvantages and to childhood

adverse family circumstances. After controlling for confounding factors, the odds ratio between cannabis abuse/dependence and making a serious suicide attempt was 2.0. Fergusson et al. [32], in a 21-year longitudinal study conducted on a sample of 1,265 adolescence/young adults, reported that regular cannabis use was associated with a increased risk of other illicit drug use, increases in delinquency, depression and suicidal behaviour.

Also, Rey et al. [89], in a cross-sectional study on 1,261 adolescents, have found that 25% reported having used cannabis and males were twice as likely as females to have used cannabis before the age of 13. Additionally, an association between depression and cannabis use was reported.

Pedersen [75], in a 13-year follow-up study conducted in a sample of 2,033 young adults, found a highly significant association between cannabis use, suicide ideation and suicide attempts even after controlling for confounding factors. Subjects who had used cannabis 11 times or more during the past 12 months had an OR of 2.9 for later suicide attempts and an OR of 2.7 for suicidal ideation.

However, not all studies included in the present review reported a positive correlation between cannabis use and suicidal risk. Price et al. [86], in a 33-year follow-up study conducted together with a cross-sectional investigation using the National Cause of Death Register on 50,087 male military conscripts, reported that after adjustment for social and personal confounding factors, the increased risk for suicide was not confirmed in cannabis users (adjusted OR = 0.88). They instead suggested that a significant association exists between the use of other additional drugs, instead of cannabis, and undetermined deaths (adjusted OR = 2.06) but not definite suicides (adjusted OR = 1.13).

Some studies have reported an association between heroin/opiate-dependent patients and suicidal risk. Darke and Ross [24] wrote a review article on this topic finding that heroin users are 14 times more likely than peers to die from suicide. They also attempted suicide more frequently than those in community samples.

Kalyoncu et al. [50], in a cross-sectional study of 108 young adult heroin-dependent inpatients, reported that both the female and male suicide attempters were significantly younger at the onset of heroin use compared to those who had not attempted suicide. They concluded that the starting age of heroin use may be a risk factor for suicide attempts. Also, Roy [94], in a case-control study comparing 246 opiate-dependent patients who had and had not attempted suicide, found that significantly more of the opiate-dependent patients who had attempted suicide had a family history of both completed and attempted suicide. Opiate-dependent patients who had attempted suicide reported significantly more childhood emotional, physical, sexual

abuse and emotional and physical neglect, and they were predominantly female, unemployed, significantly more introverted, hostile and neurotic.

Havens et al. [42] conducted a cross-sectional study investigating the suicidal ideation in injection drug users (IDUs). They investigated a sample of 244 injection drug users and 73 non-injection drug users (NIDUs) finding that suicidal ideation was present in 27% of the IDUs versus 14% of the NIDUs. However, after controlling for confounding factors, the association was no longer significant. The authors suggested that psychiatric disorders, sexual orientation and isolation which are frequent among IDUs may represent risk factors for increased suicidal ideation.

Marzuk et al. [63], in an individual review of autopsy and toxicological records, have reported that the prevalence of cocaine use among young Hispanic males who committed suicide was 45%. Young, black or Hispanic males who had used alcohol immediately before the fatal injury were most likely to have been recent cocaine users. After controlling for demographic variables and alcohol use, subjects who committed suicide with firearms were twice as likely to have used cocaine as those who used other methods.

Roy [93], investigating 214 cocaine-dependent patients, found that at least 39% of the cocaine-dependent patients had attempted suicide, more often had a family history of suicidal behaviour and reported significantly more childhood trauma. Cocaine-dependent patients also had higher personality scores for introversion, neuroticism and hostility and had significantly more comorbidity of substance use and psychiatric and physical disorders.

Finally, the National Survey of Adolescents, conducted to assess several suicidal risk factors, recruited 2002 adolescents (aged 12–17) from the general population. Major depressive episodes, post-traumatic stress disorder (PTSD) and SUD were positively associated with an increased risk for suicide attempts (as were female gender, age and experience of sexual and physical assaults) [111].

Prevalence rates of substance use/abuse among adolescent completed suicides

Back in the 1980s, Shafii and colleagues [103] reported a dramatic increase in the referral of children and adolescents with suicidal behaviour to their Child Psychiatric Service in Louisville. They undertook psychological autopsies of all children and adolescents who committed suicide as determined by the Jefferson County coroner between 1980 and 1983. Twenty-four cases satisfied the criteria, but only 83% of the families agreed to participate in the study. Compared to matched controls, suicides were more likely to use non-prescribed drugs or alcohol (70 vs. 24%).

Marttunen et al. [62] investigated the prevalence of mental disorders among 53 adolescent suicides in a nationwide psychological autopsy study in Finland. The authors reported that 26% of the suicides had alcohol abuse or dependence. A more recent study of 106 adolescent suicides aged 13–22 years old [78] indicated that 42% of the victims had an alcohol use disorder or diagnostically subthreshold alcohol misuse (16% alcohol abuse and 11% alcohol dependence).

Brent et al. [11] investigated the psychiatric risk factors for adolescent suicides in 67 suicides from 28 counties of Western Pennsylvania. Suicides had an odds risk of 8.5 of having substance abuse compared to matched controls. The risk was even higher when substance abuse was comorbid with affective disorders (OR = 17.0 vs. 3.3). Brent et al. [10] also investigated the characteristics of 27 adolescent suicides from the Pittsburgh area. The authors found higher incidences of alcohol and drug misuse in the suicides (40.7 vs. 17.9% as best estimate for overall substance abuse, and 37.0 vs. 16.1%, and 29.6 vs. 14.3%, respectively, for alcohol abuse and other drug abuse).

More recently, Renaud et al. [88] compared fifty-five adolescents who committed suicide with a control group of living subjects using psychological autopsies. The prevalence rates for current substance and alcohol abuse were 13% (OR = 5.365) for the suicides compared to 3% for the control group. Furthermore, current mood disorders were more common in suicides than in living subjects, 33 and 2%, respectively.

Prevalence rates of substance use/abuse among adolescent suicide attempters

Several research studies have indicated that suicide attempts are common in adolescents with SUD [5, 17, 26], and that substance use is common in those seeking treatment for suicidal behaviour [29–31, 106, 112]. Vajda and Steinbeck [107], in a retrospective record review of 112 adolescents (13–20 years old) who presented after a suicide attempt at an emergency department, found that 35% met the criteria for an alcohol use disorder and 27% met criteria for an SUD at the time of the attempt. Moreover, the study found that a diagnosis of alcohol abuse increased the risk of a repeat suicide attempt threefold, while a diagnosis of illicit drug abuse increased the risk of a repeat suicide attempt fourfold in the subsequent 12 months. Spirito et al. [106] reported that 12% of adolescent suicide attempters (12–18 years old) who presented at an emergency department met the criteria for an alcohol use disorder (6% alcohol abuse and 6% alcohol dependence) and 18% met the criteria for cannabis use disorder (8.4% cannabis abuse and 9.6% cannabis dependence).

Waldrop et al. [111] found that the weighted population prevalence of suicidal ideation and attempts was 23.3 and 3.1%, respectively. The Mexican Adolescent Mental Health Survey found associations between suicidal attempts and drug use/abuse ($OR = 1.1$ and 3.8 , respectively), and alcohol use and abuse ($OR = 2.4$ and 5.4 , respectively) [67]. Furthermore, in this cohort, the onset of substance exposure and attempting suicide occurred in the same year in 42% for the use of drugs and in 14% for the use of alcohol.

Suicide, substance abuse and other psychiatric disorders: comorbidity matters

Co-occurring substance use and other psychiatric problems are a prominent characteristic of those seeking help at mental health services [13, 15, 44, 80, 91]. In a clinical population of adolescents from substance abuse treatment settings, Diamond and colleagues [27] found that 72% of adolescent marijuana users had two or more psychiatric disorders when entering treatment. In a case-control study of adolescents with alcohol dependence, compared with adolescents residing in the community without alcohol dependence, Clark et al. [20] found that the most common types of psychopathology observed in alcohol-dependent adolescents included conduct disorder, ADHD, major depressive disorder and PTSD.

Comorbidity increases the risk of suicidal behaviour and the severity of the psychiatric illness, especially mood disorders [8, 9, 11, 52, 56] and disruptive behaviour disorders [38, 62].

Harrington et al. [40] found that depression in childhood was a strong predictor of a suicide attempt in early adult life. The risk is increased when depression is associated with drug abuse, cognitive distortions, hopelessness and low self-esteem, a passive coping style, social maladjustment, interpersonal problems and familial and environmental stresses [6].

Goldstein et al. [36] who studied 249 adolescents (aged 12–17 years) with bipolar disorders (BD) in a long-term naturalistic study found that the lifetime prevalence of SUD was 16% in these adolescents and that cannabis use disorder was the most common form of SUD, followed by alcohol use disorder. They also found that conduct disorder was significantly associated with SUD and may be considered a predictor of SUD among adolescents with BD. Moreover, they reported that SUD was associated with an increased risk for suicidal behaviour and troubles with the police (similar to results with adults with BD). In adolescent females with BD, SUD was associated with an increased rate of pregnancy and abortion.

Discussion

The high incidence of completed and attempted suicide in substance abusers, as well as the elevated comorbidity between suicide, substance abuse and psychiatric conditions among adolescents, forces clinicians to deal with a difficult task. Given the association between substance abuse and suicidality, the next question is why are these two behaviours associated.

Substance abuse is a well-known risk factor for attempting suicide, but some authors raise the question of whether it is a proximal or a distal risk factor. Hufford [46] suggested that the acute effects of intoxication may represent a proximal risk factor for suicidal behaviour. There is evidence that excessive alcohol use heightens psychological distress, aggressiveness and suicide-specific alcohol expectancies and inhibits adaptive coping strategies. This additional burden may be sufficient to move suicidal thoughts into action. Support for this theory comes from research suggesting that adolescents who make fatal and non-fatal suicide attempts exhibit elevated rates of alcohol use and intoxication at the time of the attempt [43, 55, 61, 95].

However, substance use may also function as a more distal risk factor for suicidal behaviour [46]. Hufford [46] suggested that SUD may be associated with increased stress and co-occurring psychopathology, which in turn increases the risk of suicidal behaviour [105]. Some studies reported that substance use among adolescents is positively related to heightened levels of stress across many areas of life. For example, it has been associated with poor academic performance, legal and disciplinary problems and interpersonal conflicts among adolescents [56, 71]. Therefore, some adolescents who attempt suicide may be motivated by a desire to escape from unbearable stressors, difficulties or aversive self-awareness such as the realization of inadequacies and unmet expectations [37].

Bukstein et al. [14] investigated the risk factors for suicide in 23 adolescent suicides compared to 12 community controls with a lifetime history of substance abuse. They found that suicides were more likely to be active substance abusers and to have comorbid major depression, suicidal ideation within the past week, a family history of depression and substance abuse, legal problems and the presence of lethal weapons in the home than controls. Following Bukstein et al. [14], three main hypotheses can be postulated to explain the escalation process in substance use and suicide:

1. Substance abuse → breakdown in personal relationships → increased suicide risk;
2. Substance abuse → change in mood → suicidal ideation or depression → suicide attempt;

3. Substance abuse → intoxicating effects → impaired judgement → increased suicide risk.

The presence of a mood disorder (depression or hypomania) may also determine the onset of a secondary substance use. Following the hypothesis of ‘self-medication’, some authors have suggested that suicidal behaviour could also be a reflection of an underlying mood disorder [46]. Some vulnerable individuals with painful affective states due to psychiatric conditions or having some affective temperaments traits [82] seem to be predisposed to addiction. The ‘self-medication’ properties of some substances may reduce stress [57] or increase the drive to use drugs [54, 90, 98]. A mechanism of ‘relief/escape’ may be frequently associated with both the choice of suicidal and substance use behaviours.

Moeller et al. [68] described poor impulse control as a core behavioural feature of SUD and reported impulsivity as a behavioural characteristic of suicidal subjects [28, 45, 60]. In one study, even after controlling for hopelessness, neuroticism, external locus of control and extroversion, poor impulse control remained significantly associated with adolescent suicidal behaviour [3]. Several authors have shown that poor impulse control may predict suicidal behaviour [1, 28, 45, 60, 85].

In adolescents and young adults, traumatic events (a poor family environment and interpersonal and intrapersonal events), which have been shown to contribute to suicide risk [41], are frequent. Stressful life events are risk factors both for suicidal behaviour and for the onset/escalation of substance use [72, 108, 113]. Negative consequences often result from a combination of poor impulse control, stressful life events, suicidal behaviour and substance use [12, 23, 87].

Both acute effects (judgment impairment, reduced inhibitions and worse impulse control) [58] and long-term effects (neurocognitive dysfunctions and reduced behavioural control) may increase the risk for suicidal behaviour [12, 99, 102, 110]. Adolescent substance users often experience behavioural, affective and cognitive changes, resulting in dysregulation of aggression, sensation seeking and impulsivity [19, 64, 65]. Finally, altered serotonergic functioning has also been found in suicides and suicide attempts [59, 60, 105]. Alterations in serotonergic functioning have also been found to be associated with the abuse of some substances [70]. Initial abnormalities in serotonin regulation, together with cell signalling and signal modulation related to the differential expression of the serotonin transporter and low levels of brain serotonin, may increase with an increase of substance use [98]. Volkow [109] has suggested that physiological changes such as serotonergic abnormalities secondary to substance abuse may gradually worsen mood, increasing the

likelihood of suicidal behaviours, particularly in vulnerable populations.

Dawes et al. [25] proposed a developmental-transnational model integrating a stress-diathesis model [58] including precursors, prominent risk factors and also possible mechanisms involved in suicidal behaviour. They suggested that precursors such as familial factors lead to neuroticism, hopelessness, mood symptoms and then to depression while other precursors produce altered serotonin function and deficits in executive functioning resulting in impulsive-aggressive traits. Three possible causal pathways underlying the vulnerabilities leading to adolescent suicidal behaviours and having bidirectional interactions were reported: (1) stressful life events ↔ genetic markers of serotonin dysregulation ↔ suicide attempts, (2) substance use ↔ impulsivity and (3) substance use ↔ suicide attempts.

Mood disorders interacting with stressful life events may lead in adolescents first to suicidal ideation and then to suicide attempts. Recent findings in adolescents and young adults have demonstrated that functional serotonin transporter polymorphisms interacting with stressful life events may predict depression, suicidality [16] and substance abuse [21, 51, 74]. As Bridge [12] suggested, the presence of other risk factors, such as current drug intoxication, exposure to suicide or availability of a lethal agent, may increase the risk of suicidal behaviour.

Finally, another hypothesis such as a desire to escape problems or the above-mentioned desire for ‘self-medication’ [46, 53] may be proposed to explain the co-occurrence of suicidal and substance use behaviours.

That in young substance users, often aggravated by stigmatizing attitudes [79], contributes to the excess of mortality in adolescence.

In the meantime, a proper assessment based on the evaluation of the most relevant specific risk factors and aimed at identifying those individuals considered to be at risk is crucial. Several risk factors for suicide must be assessed. The frequency of drug use, as well as environmental stressors, should be carefully considered by clinicians when approaching patients with comorbid SUD and suicidal risk because they can significantly impact an adolescent’s emotional well-being. The burden of the comorbid psychopathology should not be ignored. The presence of multiple coexisting disorders can be considered to be a strong predictor of poor outcome in substance users, increasing both the risk of suicidal behaviour and the severity of substance abuse.

An investigation of access to lethal weapons, especially firearms, in the home is necessary. A recent paper [49] reported that four-fifths of adolescent suicides took place in the decedents’ homes, and most of the firearms were owned

by parents, highlighting the importance of limiting youth access to firearms. Overall, the presence of available firearms is a relevant factor in establishing the risk of suicidal behaviour.

Sometimes, in acute cases, hospitalization may be required; in this case, treatment should be individualized to address the myriad of potential diagnoses [92]. There is frequently a need for multi-modal treatment including group, family, individual and milieu therapy, as well as crisis-oriented interventions.

The CDC's National Centre for Injury Prevention and Control has published a programme with guidelines for intervention strategies for communities that are interested in developing prevention programmes for adolescents [73]. The strategies for suicide prevention for adolescents concentrate on two general themes: strategies to identify subjects at risk so as to direct them to healthcare centres and strategies to increase their social support network and their management of stress.

Patients often avoid bringing up their suicidal thoughts and plans, but they are more willing to discuss these if the clinician asks specific questions about any intention to commit suicide [83, 84]. Educating general practitioners [96], nurses [81] and paediatricians [104] about suicide, depression and substance abuse can have a major impact on how patients at risk are evaluated and managed [66]. In a qualitative study, Bergmans et al. [4] interviewed 25 repeated substance-using suicidal patients about suicidality, substance use and service use, and also 27 emergency department staff about their attitudes when providing care to these men. There was frequently a negative interaction between the two groups due to feelings of frustration experienced by the emergency department staff. Moreover, suicidal patients seemed not to be able to express their needs and feelings during crises. This can be ameliorated by the inclusion of social workers as part of the emergency department team when working with suicidal patients.

One of the most effective strategies for suicide prevention is to teach people how to recognize and respond to the signals of suicidal tendencies since this increases the likelihood of at-risk youths seeking help. Everyone can be a source of encouragement, strength and optimism, teaching and practising problem-solving methods with the affected person and inculcating a sense of optimism [115].

Treatment compliance is another critical problem, although only few studies have focused on the long-term consequences of treatment non-adherence. Groholt and Ekberg [39] conducted a 9-year follow-up study in a population of 71 adolescents who had attempted suicide. They found that 44% of the adolescents made another suicide attempt; the majority of them received psychiatric treatment but about half of them attended fewer than three sessions.

This review should be considered in the light of the following limitations. First, meta-analytic techniques were not used to evaluate the results of the research. Second, the authors chose to report those studies that could support a broad analysis of the topic. Despite the careful and systematic search, a number of additional papers may have been missed. The heterogeneity of the studies presented a challenge for quality assessment. However, studies included in this review were assessed for quality allowing us to ascertain the relative contribution of each study to the systematic review.

The majority of the studies raised many questions without giving definitive answers. Bias may be introduced by the inclusion of cross-sectional studies of highly selected clinical samples. Prospective studies of samples from clinical settings would permit the investigation of the timing, duration, and severity of predictors of suicidal behaviour in populations of substance abusers [114].

The relationship between suicide and drug use in adolescents over time is not necessarily linear, and rates of adolescent substance abuse have fluctuated in recent decades [49]. Similarly, the drugs abused vary over time. Finally, research on adolescent suicide and substance abuse has been confounded by changes in diagnostic criteria, lack of age-specific criteria to diagnose adolescent SUD, changes and advances in the treatment of adolescent substance abuse and a failure to investigate the presence of substance use in the earlier studies of adolescent suicidal behaviour [92].

Conclusions

In summary, the present review confirmed the frequent association between substance use/abuse and adolescent suicidal behaviour. Remediating the actual deficits of the research about the association between suicidal behaviour and SUD as well as exploring possibilities for making suicide prevention more effective in clinically at-risk groups are key issues for the future. Future longitudinal studies, including samples from epidemiologically representative populations as well as clinical samples, are required to better understand how targeted resources can be selectively oriented to particular at-risk groups.

Conflict of interest None.

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