ORIGINAL ARTICLE

Personality disorder and substance related disorders: a six-month follow-up study with a Brazilian sample

Transtorno de personalidade e transtorno por uso de substâncias: experiência brasileira com seis meses de seguimento

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ABSTRACT

Objectives: A few Brazilian researches correlate personality disorders (PD) and substance related disorders (SRD). The aim of the present study is to investigate the association between them, to evaluate the PD frequency among chemical dependents inpatients, this comorbidity association with social and demographic characteristics, used drug of choice, its impact on clinical evolution until the moment of their committal, the frequency of relapse, self-help group – and psychotherapic adherence among SRD patients six months following committal. **Methods:** A 101 inpatients sample of chemical dependents was enrolled in 2 hospitals. The following instruments were applied: a questionnaire for social and demographic characteristics identification and drug use pattern, some questions from the sixth version of the Addiction Severity Index (ASI-6), the SCID-II questionnaire and specific questions concerning psychotherapic and self-help groups participation, and medication use. **Results:** From these 101 patients, 55.4% were diagnosed with PD, being avoidant (14.9%), borderline (11.9%) and antisocial (8.9%) the more frequent ones found. PD patients had an earlier crack use in life ($p = 0.038$) and had also more previous treatments than the ones without PD ($p = 0.005$). Borderline PD patients were less worried to substance use problem ($p = 0.003$). After 6-months follow-up, no statistical significance was found between patients with and without PD regarding drug use or treatment adherence. **Conclusion:** A high PD diagnosis was found in drug use inpatients. Patients diagnosed with SRD and PD need the identification of this comorbidity and of their personality characteristics in order to plan a more comprehensive and effective treatment.

Keywords
Substance related disorders, personality disorder, comorbidity, dual diagnosis.

RESUMO

Objetivos: Poucos estudos brasileiros correlacionam transtornos de personalidade (TP) com transtorno por uso de substâncias (TUS). O objetivo deste estudo é verificar a associação entre eles, avaliar a frequência dos TP na população de dependentes químicos internados, correlacionar com características sociodemográficas, drogas de escolha, frequência de recaída, aderência a grupos de autoajuda e psicoterapia em até seis meses após a alta hospitalar. **Métodos:** Uma amostra de 101 pacientes internados em dois hospitais foi selecionada. Os seguintes instrumentos foram aplicados: um questionário para identificação de características sociodemográficas e padrão de uso de drogas, algumas questões da sexta versão do

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ASI-6 (Addiction Severity Index), o SCID-II e algumas questões específicas sobre participação em grupos de autoajuda e em psicoterapia, bem como o uso de medicações. **Resultados:** Destes 101 pacientes, 55,4% foram diagnosticados com TP, sendo evitativa (14,9%), limítrofe (11,9%) e antissocial (8,9%) as mais frequentemente encontradas. Pacientes com TP demonstraram ter feito uso mais precoce de *crack* na vida (p = 0,038) e também tinham mais tratamentos anteriores do que aqueles sem TP (p = 0,005). Pacientes com TP limítrofe estavam menos preocupados com o problema de abuso de substâncias (p = 0,003). Após seis meses de seguimento, nenhuma diferença estatística significativa foi encontrada entre pacientes com e sem TP acerca do uso de drogas ou aderência ao tratamento. **Conclusão:** Uma alta prevalência de TP foi encontrada em pacientes internados por TUS. Pacientes diagnosticados com TP e TUS necessitam a identificação da comorbidade e das características de sua personalidade, a fim de planejar um tratamento mais abrangente e eficaz.

Palavras-chave
Transtorno por uso de drogas, transtorno de personalidade, comodidade, patologia dual.

INTRODUCTION

Several international studies have correlated substance related disorders (SRD) and personality disorders (PD)[1-6]. In Brazil, however, we have few studies on this association. Besides that, major part of these studies focuses on a specific PD and its prevalence among substance abusers[4,7-9]. Then, little is known concerning the several Axis II diagnosis and its interference on SRD.

González and García[1] found a 56.4% prevalence of SRD and PD comorbidity. An American observational study showed that, among alcohol-abusers, 28.6% had at least one associated PD and that 47.7% of drug users (but alcohol) have one PD diagnosis either[5]. The prevalence of PD varies according the drug being studied[2,3]. The ones more frequently associated with PD are antisocial, hysterical and dependent[2,5], also paranoid, avoidant and obsessive-compulsive[10]. The borderline PD was evaluated in several studies[2,11], leading to its association with treatment drop-out[8] and with a worse long-term prognosis, as also antisocial and schizotype PD[11]. Concerning specific drug types, a Brazilian study showed that crack users presented a higher rate of antisocial personality disorder (25%) than powder cocaine (9%) and non-cocaine psychoactive substances users (9%)[12].

In Brazil, in a study that evaluated how personality traits are associated with occasional use, abuse, and dependence of psychoactive drugs in a large sample of adults via online questionnaires, it was found that novelty seeking was the trait most associated with increased involvement with alcohol, cannabis, and cocaine. Persistence was lower in cannabis-, benzodiazepine-, and cocaine-dependent subjects, as well as in hallucinogen abusers and self-directedness was reduced in dependents of all drug classes[13]. Another study evaluated the presence of mental disorders among prisoners in the Salvador City pointed to high rates for borderline personality disorder 19.7% and 34.8%; antisocial personality disorder 26.9% and 24.2%; alcohol addiction 26.6% and 35.3%; drug addiction 27.9% and 32.4% among those who were, respectively, in semi-opened or closed regime, reinforcing that disorders comorbid idea is related to psychoactive substances and personality disorders are quite frequent[14].

This frequent association can increase drug prevalence consumption as well as jeopardize these patients to enroll treatment in order to avoid relapse[1,2]. It is known that patients with this association have dysfunctional beliefs related to addiction and are, therefore, more treatment resistant by cognitive therapy for example[15]. A Brazilian trial emphasized the need for strengthening even more the therapeutic alliance in these two diseases diagnosed patients because they are more resistant for changing treatment stages, less adherent to treatment, have earlier and higher relapse rates[16].

Therefore, the identification of this comorbidity is fundamental as it greatly impacts on SRD patients. The aim of this trial is to investigate the association of psychoactive drug dependency and personality disorders, verifying PDs frequency among SRD patients in the studied hospitals, this comorbidity association with social and demographic variables, with identification of drug use pattern and type, the past impact of the SRD/PD comorbidity in patients clinical evolution until the moment of their hospitalization and, at last, to verify relapse rates and adherence adhesion to self-help groups (alcoholic/narcotics) and psychotherapic treatment in this population, with and without PDs associated six months following committal.

METHODS

The sample was composed by inpatients with substance related disorder in a unit for this at São José Clinic, with 90 beds for chemical dependency of the total 200 beds (private and health plans users), and in a psychiatric unit at Parque Belém Hospital, with 120 beds for chemical dependency from 242 beds in total (private and social health plan users). Both hospitals are located at Porto Alegre city, in Brazil. Data collection period was from march/2013 to december/2014. This was a 101 patients convenience sample with a 6-months follow-up period (cohort design).

Patients should be aged 18 years or older and fulfill DSM-IV-TR psychoactive dependency criteria. They should live in Porto Alegre and have a contact phone number for follow-up. Were included patients already interned for at least two weeks so their responses to questionnaires would suffer less interference of psychoactive substances use. Exclusion criteria were: age lower than 18, mental handicap, confusional and/or psychotic states or imbalanced clinical comorbidity. Initially 14 patients were excluded and 3 refused to participate in the study. Patients were excluded by psychiatric evaluation or medical records data. In the analysis of results, was also excluded one patient that did not want to answer SCID-II questions.

Patients were chosen by lot to avoid a possible selection bias in patients' choice and rather than they were invited to participate on study and to them was explained the interview goals and procedures. In case of agreement, they signed the informed consent form. The Project was submitted to the Porto Alegre Health Science Federal University Institutional Review Board (IRB), opinion approval: 257.251 – and the two mentioned hospitals IRBs, having received approval.

On the first stage, inpatients were inquired by two medical doctors, specializing in psychiatry, with an interview with approximately 50 minutes of duration. On a second stage, six months following discharge, the patients were submitted to a new interview, phone collected, performed by psychology students. Interviewers were trained for the instruments application and periodic interviews evaluations were performed. There were no previous defined criteria for choosing an interviewer to each patient. On the second stage, interviewers were blinded to the presence or not of PDs. A kappa test was performed for instruments application agreement at the first stage with a 0.9 score[17].

On the first stage, the following instruments were applied:

- A social and demographic features questionnaire;
- A Drug Use Pattern questionnaire to characterize quantity, frequency and consumption pattern;
- SCID-I (Semi-structured Clinical Interview based on APA-1994 DSM-IV)[18] to evaluate psychoactive substance dependency presence. The SCID-I, in its clinical version, was translated and adapted to Portuguese, and, in general, it presents good reliability. For treating the disorders related to substance use, the reliability, as the weighted kappa, was K = 0.76[19].
- A questionnaire with some questions from ASI-6 – the Sixth Version of Addiction Severity Index. This is a semi-structured interview used to verify the seriousness of problems in many life aspects related to psychoactive substance consumption like physical and psychological health, job and finances, family and legal problems[20,21]. The psychometric properties' analysis of the ASI-6 indicates good reliability and validity of this instrument for Brazilian culture, both in hospitalized patients as in outpatients treatment. The Cronbach's alpha for subscales of the ASI-6 ranged from 0.64 to 0.95. Correlations between scores of Alcohol and Drugs ASI-6 area and concurrent instrument (ASSIST) were high (0.72 and 0.89, respectively)[22].
- SCID-II (Semi-structured Clinical Interview based on APA-1994 DSM-IV)[23] to verify the PD presence. There are literature's evidences about the consistency between the SCID-II and clinical observation, denoting good reliability and internal consistency of the instrument[24].

On the second step, a questionnaire for Drug Abuse Consumption (adapted for 30-days and the last 3 months evaluations) was applied plus specific questions concerning psychotherapic and self-help groups participation and medication use.

Data were stored in Excel program and then exported to SPSS v. 18.0 for statistical analysis. Categorical values were described by absolute frequency and percentual relative frequency, and then compared between groups by Chi-Square or Fisher Exact test. Quantitative measures were described when they had symmetrical distribution, by mean and standard deviation and t Student test for independent random samples compared. In case of asymmetrical distribution, they were described by median and interquartile interval and were compared by Mann-Whitney test use. Prevalences were described with their own 95% confidence interval. A 5% significance level was considered. It was performed a logistic regression with the variables that had $p < 0.20$ when comparing patients with and without personality disorders.

RESULTS

A 101 patients sample was collected, 70 being male. In sample, 56 patients had PD (55.4%) (IC95%: 45.6-65.3). Following on table 1, frequencies of patients PDs are described.

Table 1. Personality disorders frequency in sample

Personality disorder	n	%
Avoidant	15	14.9
Borderline	12	11.9
Antisocial	9	8.9
Dependent	7	6.9
Paranoid	6	5.9
Obsessive-compulsive	5	5.0
Schizotype	2	2.0
Narcissistic	2	2.0
Hysterical	-	-
Schizoid	-	-
Not elsewhere specified PD	3	3.0

Category variables descried by n (%).

There was no statistical difference for social and demographic patients characteristics with and without personality disorder (Table 2).

In sample, alcohol was consumed during life for 89.1% patients, tobacco 73.3%, cocaine 62.4%, cannabis 55.4%, crack 33.7%, stimulants 21.8%, solvents 18.8%, hallucinatory 15.8%, tranquilizers 6.9%, amphetamines 5.9%, feeding supplements 4.0% and opioids 2%. It was not found a significant statistical difference between groups with and without PD regarding psychoactive substance use.

During last year, alcohol was consumed by 77.2% patients, tobacco 67.3%, cocaine 48.5%, cannabis 35.6%, crack 32.7%, stimulants 16.8%, solvents 5.9%, tranquilizers 5.9%, hallucinatory 5.0%, anabolizer 4.0%, amphetamines 3.0%, feeding supplements 2.0% and opioids 1.0%. During last 30 days, 71.3% patients consumed alcohol, 64.5% tobacco, 40.7% cocaine, 30.7% crack, 28.7% cannabis, 11.9% stimulants, 4.0% tranquilizers, 3.0% hallucinatory and 2.0% solvents.

There were found no differences between groups with or without PD regarding last year/last month on alcohol, tobacco, cannabis, hallucinatory, cocaine, crack, solvents, tranquilizers, stimulants, anabolizer, amphetamines, feeding supplements or opioid use.

For both groups, there were found no differences either concerning age of onset of all drugs use but crack. Patients with PD used crack earlier than the ones without PD with a significant statistical difference ($p = 0.038$).

No significant statistical difference was verified among patients with or without PD that used alcohol only and/or tobacco and the ones that used illicit drugs but did not drank during last 30 days or last year before hospitalization. Also, no significant statistical difference between both groups was found regarding one or multiple drugs use.

When comparing individuals with most frequent PDs in sample (avoidant, borderline, antisocial) among their selves and with those without any PD, there was not found statistical significance neither in 12 months nor in 30 days before hospitalization concerning most used drugs consumption (alcohol, tobacco, cannabis, cocaine, crack).

The ASI scale variables used are described on table 3. Patients with PD had a greater number of previous treatments comparing to those without PD, showing a significant statistical difference ($p = 0.005$) (graphic 1). Patients with PD have presented a higher tendency on longer continuous treatments ($p = 0.085$) and used to consider that cocaine/crack was the most disturbing drug ($p = 0.082$).

Comparing individuals with the most often PDs in sample among them and with those without PD was found that the ones with borderline PD were less worried to substance use problem than all others ($p = 0.033$).

It was performed a logistic regression, including some variables like: education, number of previous treatments, continuous treatment time, degree of treatment importance, the drug considered the leading problem and age of onset crack

Table 2. Social and demographic characteristics of with and without PD patients

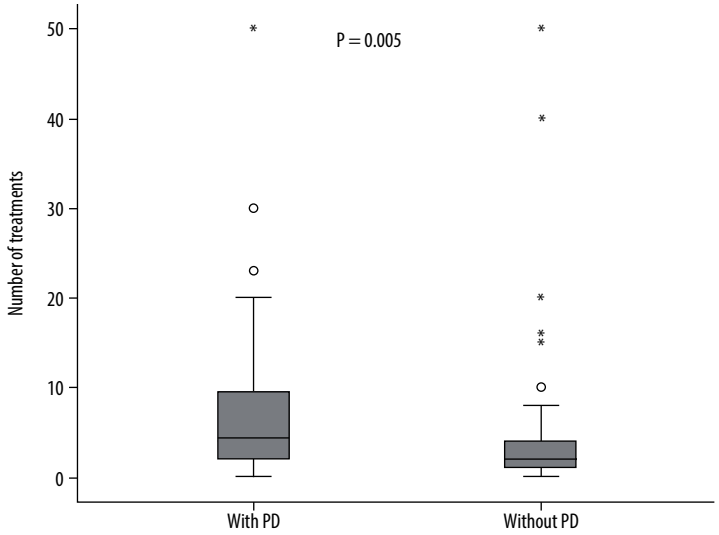
Characteristics	Total	With TP	Without TP	P
Age	40.3 ± 12.6	39.3 ± 1.1	41.5 ± 13.3	0.392
Male	70 (69.3)	36 (64.3)	34 (75.6)	0.316
Civil status				0.651
Single	43 (42.6)	27 (48.2)	16 (35.6)	
Married	30 (29.7)	15 (26.8)	15 (33.3)	
Divorced	24 (23.8)	12 (21.4)	12 (26.7)	
Widow	4 (4.0)	2 (3.6)	2 (4.4)	
Scholarship				0.128
Illiterate	1 (1.0)	1 (1.8)		
Elementary school any level	25 (24.8)	11 (19.6)	14 (31.1)	
High school any level	44 (43.6)	22 (39.3)	22 (48.9)	
University any level	31 (30.7)	22 (39.3)	9 (20.0)	
Family income				0.466
1 to 5 minimum wage	59 (59.0)	30 (54.5)	29 (64.4)	
5 to 10 minimum wage	28 (28.0)	16 (29.1)	12 (26.7)	
> 10 minimum wage	13 (13.0)	9 (16.4)	4 (8.9)	
Actively working until hospitalization				0.533
Yes	56 (55.4)	29 (51.8)	27 (60.0)	
No	45 (44.6)	27 (48.2)	18 (40.0)	

Category variables descried by n (%) and compared by Chi-square test. Quantitative measures described by mean ± standard deviation and compared by t Student test for independent variables.

Table 3. ASI Scale variables comparison between groups with and without PD

Variables	Total	With PD	Without PD	p
Number of previous treatments	3 (1-8)	4 (2-10)	2 (1-5)	**0.005**
First treatment age	26 (20-38)	25 (20-35)	28 (19-43)	0.406
Treatment days (continuous)	180 (15-730)	360 (38-730)	90 (0-675)	0.085
Continuous treatment days of medications targeting drug use	30 (0-365)	40 (0-365)	0 (0-365)	0.372
Self-help meetings (days)	3(0-180)	5 (0-180)	1 (0-180)	0.745
Self-help meetings twice/week (days)	0 (0-173)	0 (0-150)	0 (0-180)	0.385
Concern regarding substance use				0.258
None	10 (9.9)	8 (14.3)	2 (4.4)	
Slight/Mild/Considerable	17 (16.8)	9 (16.1)	8 (17.8)	
Severe	74 (73.3)	39 (69.6)	35 (77.8)	
Treatment importance				0.174
None	7 (6.9)	6 (10.7)	1 (2.2)	
Slight/Mild/Considerable	14 (13.9)	6 (10.7)	8 (17.8)	
Severe	80 (79.2)	44 (78.6)	36 (80.0)	
Abstinence maintenance importance				0.679
None	4 (4.0)	3 (5.4)	1 (2.2)	
Slight/Mild/Considerable	10 (9.9)	6 (10.7)	4 (8.9)	
Severe	87 (86.1)	47 (83.9)	40 (88.9)	
Most disturbing drug				0.082
Alcohol	41 (40.6)	18 (32.1)	23 (51.1)	
Cannabis	4 (4.0)	4 (7.1)	-	
Sedatives	1 (1.0)	1 (1.8)	-	
Cocaine/crack	55 (54.5)	33 (58.9)	22 (48.9)	
Second most disturbing drug n = 89				0.242
Alcohol	25 (28.1)	14 (28.0)	11 (28.2)	
Cannabis	21 (23.6)	15 (30.0)	6 (15.4)	
Cocaine/crack	17 (19.1)	10 (20.0)	7 (17.9)	
Opioids	1 (1.1)	1 (2.0)	-	
Tobacco	25 (28.1)	10 (20.0)	15 (38.5)	

Quantitative measures with symmetrical distribution described by median (P25-P75) and compared by Mann-Whitney test. Categorical variables described by frequency and percentuals and compared by Chi-Square test.



Graphic 1. Number of treatments comparison between groups with and without PD.

Table 4. Patients with and without personality disorders. Logistic regression of variables where p < 0.2

	P	OR	IC95%	
			Lower limit	Upper limit
Schoolarship				
Superior	0.112	17.45	0.51	592.68
High school	0.595	1.84	0.19	17.63
Less than high school	0.282	Ref.		
Number of treatments	0.477	1.03	0.94	1.13
Time duration of treatment	0.736	1.00	1.00	1.00
Self related importance of treatment				
Severe	0.571	2.18	0.15	32.33
None slight mild		Ref.		
Most important drug				
Cocaine/crack	0.222	9.10	0.26	314.38
Alcool cannabis sedatives	.	Ref		
Crack first age of use	0.030	0.90	0.81	0.99

use. After adjusting the factors associated in bivariate analysis with p < 0.20, only the variable age of onset of crack use was significance (p = 0.03), been this use earliest precocious in patients with personality disorder.

During follow-up phase, after 6 months discharge, we could reach only 59.4% of patients, 31.9% were not localized and 8.7% refused to be interviewed. In the PDs group, there was 51.8% losses, while in the group without PDs, there was 26.7% losses, this finding demonstrating to have statistical significance (p = 0.019). Such losses were more frequent among men (p = 0.008), and these patients less frequently found important to reach/keep abstinence (p = 0.04). There were not found any others statistically significant differences regarding other social or demographical variables or to other ASI-6 Scale questions (psychoactive substance disorder, treatment importance and more troubling drug).

After discharge, 66.7% consumed drug (but tobacco), being 18.3% twice to ten times, 10.1% eleven to twenty times and 38.3% more than twenty times. Concerning used drug type, 51.6% had used alcohol, 68.3% tobacco, 18.3% cannabis, 25% cocaine, 25% crack, 10% stimulants (energy drink), 5% tranquilizers, 1.7% solvents during the three months before interview, 43.3% had used alcohol, 66.7% tobacco, 16.6% cannabis, 205 cocaine, 16.7% crack, 5% stimulants (energy drink), 3.3% tranquilizers and 1.7% opioids during the last 30 days before interview.

Only 11.7% patients were participating in self-help groups and 48.3% had psychotherapic treatment, and in this sample, 3.6% had twice a week sessions, 46.6% had a weekly one, 7.1% fortnightly, 39.3% monthly, 3.4% less than once a month ones, and 73.3% were using a psychiatric medication. In 85% of interviews, the interviewers considered to have reliable answers.

There were not found any statistical significant differences between patients with or without PDs regarding every drug use type or treatment adherence rates after 6-months follow-up.

DISCUSSION

A high frequency of PDs was found in patients hospitalized for drug use despite age, civil status, instruction, family earning and work status before admission. More than half patients presented these conditions. This high frequency is according to previous studies like found Langas *et al.*[10] and González and García[1], the former finding almost same results. It is a largely higher PD frequency than in general population that is about 9% to 13% according to Lenzenweger *et al.*[25] and Verheul[6]. A systematic review of personality disorder and addiction show high comorbidity rates too[26]. Regarding social and demographic variables, previous trials show that PD patients are younger, have lower educational level and marry less either[10,27], what is not matching our study findings.

Most frequently found PDs were avoidant, borderline and antisocial, reinforcing literature findings[2,5,10,11,28], although this last one shows a higher prevalence in these studies[6,7]. The presenting authors figure that in Brazil, as in USA, these patients are often in jail or in forensic psychiatric units, which ones were not covered in this study. Regarding borderline PD, a main issue for its high frequency is emotional imbalance and impulsiveness (nuclear aspects), and the last one has been considered the most relevant factor for drug addiction[6,29]. Concerning avoidant PD, a study showed either a high frequency of individuals with phobic symptoms in drug dependents, mainly alcohol users[30].

No significant statistical difference was found related to drugs type, what is not according to a previous study that pointed the fact that alcohol dependents present with less PDs when comparing to other psychoactive drug users[5]. The only significant statistical difference found was that patients with PD aged younger for crack first use that those without PD and had also a tendency to have more troubles with this drug use, maybe because a longer time of consumption. Including, the earliest age for beginning crack use in patients with PD was the only variable that remained with statistically significance, after logistic regression analysis, which presented slightly wider intervals.

PDs patients had a higher number of previous treatment episodes. This finding may suggest a more severe disease and less treatment adherence according to literature findings[1,8], although opposing to this, these patients had a tendency to have a higher treatment time for drug related problems. Another study with substance related disorders patients showed that antisocial PD individuals had significantly higher treatment markers like hospitalization days and medical visits[9]. Regarding borderline PD, the patients presenting with this condition had a lower concern level to psychoactive drug related troubles, what can decrease their treatment adherence and worsen evolution, a finding also found in a previous study[8].

Our findings do not allow us to conclude that the comorbidity with PDs leads to worse results on substance related disorders treatment. The absence of difference between groups may be due to the high number of losses, bigger in the group with PDs. It's possible to guess that this comorbidity leads to relapse and can explain such losses. Remarkable findings were the high relapse frequency and low adherence to treatment in both patients groups. A Brazilian study compared alcohol dependents during 6 months, and also found a high relapse frequency and little adherence to psychotherapic treatment or to anonymous alcoholics groups[31].

This study has some limitations like little sample size, what jeopardized comparison among different PDs types, and the fact that was performed in only two hospitals, something that may decrease generalizability. Besides that, the two week drug withdrawal interval can be a bias for proper PD diagnosis. Concerning this issue, PDs prevalence has been shown to be similar in currently drug users and in those with higher abstinence withdrawal. This finding indicates that these diagnosis are not only due to symptoms overlap or diagnostic methodology used[32]. The high number of losses can be a limitation of our study, but can also reflect the challenge of performing follow-up studies in this population, that often change telephones and addresses and have a high relapse rate. Besides that, the data being phone collected could be seen as a potential bias in answers, but 85% of them seemed to be reliable ones to the interviewers. Another aspect that needs to be considered is that a categorical PD diagnosis, based on specific criteria number, has some limitations. The DSM-V personality disorder group has recommended a significant reformulation on psychological personality diagnostic evaluation, proposing a hybrid dimensional and categorical model[33]. However, these recommendations were not available by the moment of our project design and starting data collection.

Patients with PD and psychoactive substance use need the dual diagnosis identification in order to achieve a better therapeutical relationship and treatment conduction, as well as an effective treatment that covers the personality characteristics in a psychoactive substance dependence approach. Integrative treatment represents therapy of choice for patients with this dual diagnoses. Since PD patients tend to start the crack use earlier in their life, it is important to make a prevention regarding the drug's use among these patients. Further studies with a larger sample, using a more rigorous methodology in the attempting of reducing the number of losses in the longitudinal follow-up and focused more in PD more frequently are needed, mainly in Brazilian population to proper map and care this comorbidity as licit and illicit drug consumption is increasing, causing individual, family and social troubles as far as a PD diagnosis in this individuals can lead to a reserved prognosis.

CONCLUSION

A high PD diagnosis was found in drug use inpatients, in our sample, being avoidant, borderline and antisocial the more frequent ones found. PD patients had an earlier crack use in life and had also more previous treatments than the ones without PD. No statistical significance was found between patients with and without PD, after 6-months follow-up, regarding drug use or treatment adherence, however patients diagnosed with SRD and PD need the identification of this comorbidity for to be promoted an integrative treatment for patients with this dual diagnoses.

INDIVIDUAL CONTRIBUTIONS

Débora M. Krieger – Contributed to the collection and analysis of data in the database organization and preparation of the manuscript.

Daniela Benzano – Contributed to the statistical analysis and interpretation of data.

Caroline T. Reppold – Reviewed critically the article and collaborated in the data analysis.

Patrícia O. Fialho – Participated with acquisition of data with patients, interpretation of data and helped do draft the manuscript.

Gabriela B. Pires – Participated with acquisition of data with patients, interpretation of data and helped do draft the manuscript.

Mauro B. Terra – Participated in the conception and design of research, interpretation of data and preparation of the manuscript.

All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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