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Cocaine relapse and health-related quality of life: a 23 weeks study

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Introduction. Cocaine dependence is a disorder where relapses are frequently presented and many factors are involved. Furthermore, cocaine dependence is associated with poor health-related quality of life (HRQoL) outcomes. This study aims to explore perceived HRQoL as an indicator of drug relapse in cocaine-dependent patients (CDP).

Subjects and Methods. A longitudinal study was carried out in CDP during 23 weeks. A consecutive sampling method was applied, 39 participants composed the initial sample (mean age 35.6 years), only 15 participants completed outpatient follow-up period. CDP were assessed with psychiatric and HRQoL instruments (SCID-I, SCID-II, BDI, STAI scale and SF-36) in different points of the study. The patients were followed up, and cocaine relapses were assessed. The sample was divided according with the relapse (early vs. late relapse). Data were compared and analyzed in order to evaluate whether HRQoL measure could be related to cocaine relapse.

Results. There are differences in perceived HRQoL measures between CDP with/without early relapse, especially in Mental health and Social functioning dimensions ($p < 0.05$). Furthermore, Late/relapse-patients have higher improvement of HRQoL than patients with early relapse.

Conclusions. Perceived HRQoL might predict early relapse and could be a possible predictor tool of potential future relapses. More research in this field is needed.

Keywords: Substance-use Disorder, Cocaine, Health-related Quality of Life, Relapse, HRQoL

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Recaída en el uso de cocaína y calidad de vida relacionada con la salud: un estudio de 23 semanas de seguimiento

Introducción. Las recaídas son frecuentes en la dependencia a cocaína, múltiples factores están involucrados en ellas. Además, la dependencia a cocaína se relaciona con un peor pronóstico en relación a la calidad de vida relacionada con la salud (CVRS). Este estudio explora la CVRS percibida como un indicador de recaída en pacientes con dependencia a cocaína.

Metodología. Se llevó a cabo un estudio longitudinal en pacientes con dependencia a cocaína durante 23 semanas. En total 39 pacientes participaron (edad media 35,6 años), aunque solamente 15 completaron el periodo de seguimiento. Se utilizaron varias escalas e instrumentos psicométricos (SCID-I, SCID-II, BDI, STAI y la SF-36) en diferentes puntos del estudio. Los pacientes fueron seguidos y se evaluaron las recaídas. La muestra fue dividida de acuerdo con el momento de recaída (temprano vs. tardía). La información fue comparada y analizada para poder evaluar si la CVRS se podía relacionar con la recaída de cocaína.

Resultados. Hubo diferencias en la CVRS percibida entre los pacientes con y sin recaída temprana, especialmente en las dimensiones de Salud Mental y Funcionamiento Social ($p < 0.05$). Además, los pacientes con recaídas tardías presentaban una mejoría de la CVRS percibida si se comparaba con los que recaían de forma temprana.

Conclusiones. La CVRS percibida podría predecir parcialmente las recaídas tempranas y su medición podría ser una herramienta para evaluar posibles recaídas en el futuro. Sin embargo, es necesaria más investigación en esta área.

Palabras clave: Trastorno por Uso de Sustancias, Cocaína, Calidad de Vida Relacionada con la Salud, Recaídas, CVRS

INTRODUCTION

Cocaine use disorder is considered as a worldwide health problem due to the multiple associated comorbidities and outcomes^{1,2}. Relapses are a frequent issue in substance use disorders (SUD)³⁻⁵, and specifically, high rates of relapse are reported in cocaine use disorder^{3,4}. Thus, some researches described that up to 57.2% of cocaine-dependent patients (CDP) relapse within three months after a detoxification admission³. Consequently, relapses are a major problem in treatment settings and several factors could be related in, such as craving, comorbidities and psychosocial factors, among others⁶. All these factors interrelate and probably none is enough to be a direct cause, although it is important to mention that there are some factors that could have more weight. Hence, some authors describe that psychiatric comorbidity (dual) could be a remarkable factor in SUD, being a risk factor both for substance onset but also for relapse^{6,7}. Besides, CDP could have difficulties in analyzing complex emotions and regulating their emotional response, thus risky situations for relapse may be unrecognized or mishandled^{6,8}. Not for nothing, one of the most studied psychotherapy for cocaine consumption (Cognitive-behavioral therapy) emphasizes on *relapse risk factors* and not other factors of cocaine use disorder⁹.

Quality of life (QoL) has recently been considered in SUD¹⁰. QoL is conceptualized as a multidimensional construct, and in most studies, it has been associated with personal characteristics, social roles, objective circumstances and the subjective perception of life in diverse areas^{11,12}. Some authors define two types of QoL concepts: overall QoL encompasses the patient's satisfaction with life in general and is related to wellness and not limited to diseases limitations¹¹, while health related quality of life (HRQoL) is related to the patient's perception about how health status could affect physical, psychological, and social functioning and well-being^{11,12}. In the field of SUD, there is no working definition of QoL^{10,11,13}. For the patients, some aspects of QoL are more important than the habitual goals of drug treatment (e.g. abstinence)^{10,11}, thus, drug use often does not motivate seeking treatment, but the outcomes and the impairment of some aspects in the patient's life¹¹. In addition, some researches indicate that the greater level of cocaine use, the poorer QoL/HRQoL^{13,14}, and improvements in QoL/HRQoL could be a measure of therapeutic outcome in SUD^{11,13}.

The Short Form 36 (SF-36) is a self-reported HRQoL questionnaire which measures current perceived health status, and therefore, limitations in functioning due to disease^{11,15}. SF-36 consists of 11 items which measure eight health dimensions: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores are calculated for each individual dimension, ranging from 0 (worst) to 100 (best)¹⁵.

Previous researches have used SF-36, and those investigations have suggested helpful applications in SUD¹⁶⁻¹⁹. As far as we know, no studies have been published about correlation between HRQoL (using SF-36) and cocaine relapse.

This research aimed to study HRQoL as an indicator of cocaine relapse in CDP, the hypothesis was: Patients with early relapse would have worse perceived HRQoL than patients with later relapse.

MATERIALS AND METHODS

A longitudinal pilot study was carried out (between January/2005-April/2010) and belongs to a larger clinical trial (FIS EC07/90713, for further information, contact the authors). The study was approved by the Clinical Research Ethics Committee of Vall d'Hebron University Hospital (according to the Declaration of Helsinki). Written informed consent was obtained in all participants.

Preliminar definitions:

- *Cocaine-dependent patient (CPD)*: Patients who met criteria for cocaine dependence, according to DSM-IV-TR.
- *Relapse*: return to substance use. It was defined as three consecutive positive urinalyses or five positive ones in four weeks, this criteria has been used in previous studies³.
- *Early relapse*: defined as the relapse in the first four weeks after detoxification admission. This period (one month) is habitually used in research because some neurobiological modifications have been reported in the first month after cocaine withdrawal in humans and animal models^{20,21}.
- *Late relapse*: the relapse that began after the first month after detoxification admission (see explanation of *early relapse*).

Subjects

A consecutive sampling method was applied. Accordingly, all patients in ambulatory care or admitted to the hospital detoxification Unit (who met the inclusion criteria) received a complete discussion of the study, patients who accepted were recruited. Inclusion criteria were: age 18 years or older, cocaine dependence according to DSM-IV-TR criteria, sufficient cognitive abilities and a good understanding of the information concerning the research (it was assessed by a clinical interview). Participants had to test positive for cocaine by urinalysis at the screening visit. Exclusion criteria were: presence of another drug dependence

(besides cocaine/nicotine-dependence) and/or the concomitance with other major psychiatric or severe medical disorder. Females could not be pregnant or during breastfeeding. Patients did not receive financial compensation for their participation in the study.

Procedure and measures

Patients enrolled were admitted to hospital detoxification, and they were followed up at the outpatient center, the total period of the study was 23 weeks. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)²², Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II)²³, Trait Anxiety Inventory (STAI)²⁴, the Spanish version of Beck Depression Inventory (BDI)²⁵, and the SF-36 Health Survey^{15,26} were administered to all patients during detoxification admission (See figure 1).

During outpatient follow-up period, BDI and STAI were administered once a week, and SF-36 was repeated at the seventh week. Urinalyses were performed three times a week, the first 12 weeks, and two times a week the last 9 weeks. According to relapse, the sample was divided in two groups: the first one was the CDP group with early relapse

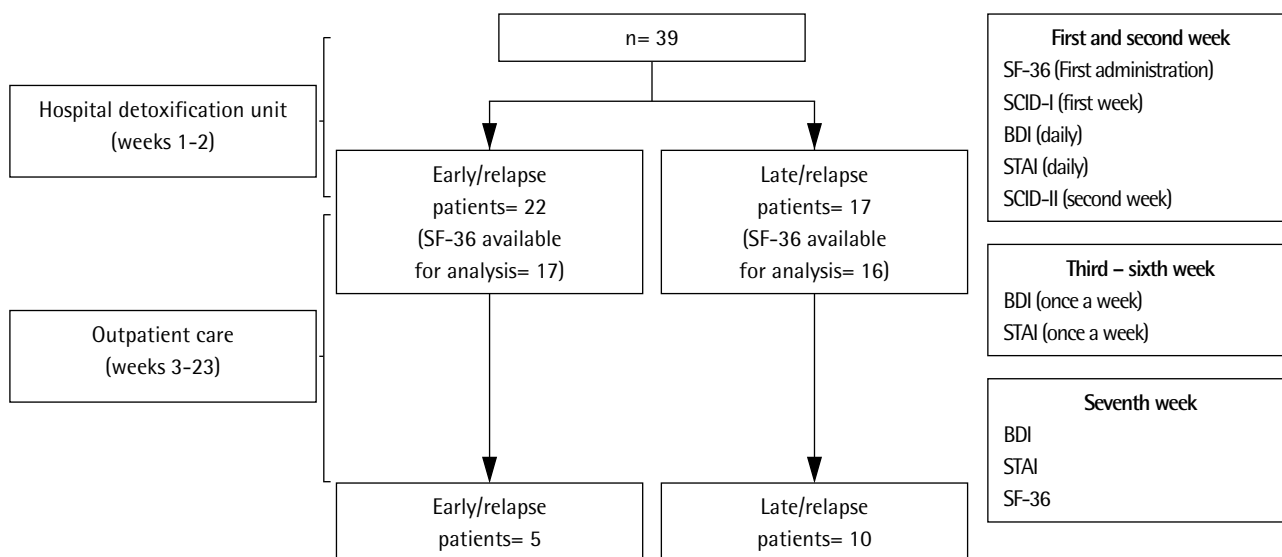
(afterhere, Early/relapse-patients), and the other group was defined as CDP with late relapse (afterhere, Late/relapse-patients).

Statistical analysis

Odds ratio was used for comparisons on socio-demographic and drug abuse use pattern measures between patients with/without early drug relapse. Further, Mann-Whitney test (for independent samples) and Wilcoxon (for repeated measures) were applied for HRQoL dimensions between patients, and additional measures of depressive and anxiety signs/symptoms (SPSS Windows 18.0.0, Inc., USA).

RESULTS

There were 85 potential subjects but only 39 participants satisfied the inclusion criteria and agreed to detoxification admission; only 15 participants completed outpatient follow-up. During detoxification admission, early relapse group was conformed by 22 patients, while 17 patients composed the late relapse group. 89.7% were men, with a mean age of 35.6 years (age range 21-63 years). Most of



SCID-I= Structured Clinical Interview for DSM-IV Axis I Disorders; SCID-II= Structured Clinical Interview for DSM-IV Axis II Disorders; STAI= Trait Anxiety Inventory; BDI= Beck Depression Inventory; SF-36= Short Form 36

Figure 1

Flow chart study, sample size is specified in each step. Urinalyses were performed three times a week, the first 12 weeks, and two times a week the last 9 weeks (see text)

patients had a primary level education (41.0%) and 38.5% were employed. The sample did not differ significantly in marital status, level of education, number of children or employment status (odds ratio, $p>0.05$), as well as, no statistically significant gender-related differences (See table 1). Cocaine was the primary substance of addiction (82.2% patients were also dependent on nicotine), and alcohol, cannabis and sedatives abuse also were reported (71.80%, 35.90% and 23.10%, respectively; see table 1).

No significant differences in depressive symptoms were found in detoxification admission (Mann-Whitney test for two independent samples), although during outpatient follow-up, a significant difference in BDI scores between patients groups (early vs late relapse) were found on the fourth week (11.25 ± 8.96 and 2.00 ± 3.20 , respectively; Mann-Whitney test for two independent groups, $z=-2.123$, $p=0.039$).

Cronbach's coefficient of reliability was 0.90 for SF-36 questionnaire. During detoxification admission, early/relapse-patients showed better HRQoL than late/relapse-patients, in particular, we detected significant differences in Mental health and Social functioning dimensions (all $Zs(31)>-2.17$, $p<0.05$; Table 2). Moreover, patients improved their HRQoL during outpatient follow-up, but only significant differences in late/relapse-patients for General health, Social functioning, Role-emotional and Mental health were detected ($Zs(13)>-2.67$, $p<0.05$; Table 2). This patient's group

also shows significant differences for Mental and Physical Component Summaries (Z with $p<0.05$).

DISCUSSION

The present research explored perceived HRQoL between "Early/Late-relapse" CDP. Such as previous studies have reported, the participants have shown poorer HRQoL than average healthy populations^{27,28}. On the whole, no differences in depressive symptoms and state/trait anxiety symptoms were found at baseline, but some distinctions in HRQoL measures were presented in detoxification admission. Early/relapse-patients presented better HRQoL (*Social functioning* and *Mental health* dimensions, in particular) than Late/relapse-patients during the detoxification period, and this paradoxical finding was opposite during outpatient care. Furthermore, the results overall suggest that, Mental health and Social functioning might predict the presence of early drug relapse.

Regarding differential HRQoL scores between patients during detoxification period, the Early/relapse-patients showed better social functioning and mental health HRQoL compared with their counterparts (see above mentioned), but these differences disappeared during outpatient follow-up. This is an unexpected and paradoxical finding deserving ulterior research. These results could derive from the

Table 1 Comparison between early/relapse-patients vs. Late/relapse-patients according sociodemographic characteristics and abuse consumption of substances

Sociodemographic characteristics				
	Entire Sample (n=39)	Early/relapse-patients (n=22)	Late/relapse-patients (n=17)	Crude OR (95% CI)
Age in years (range)	35.6 (21-63)	32.4 (20-48)	31.5 (22-44)	
Gender (Man %)	35 (89.7%)	20 (90.9%)	15 (88.2%)	1.33 (0.17 - 10.58)
Married/cohabiting	10 (26.2%)	7 (70%)	3 (30%)	2.33 (0.50 - 10.91)
Primary education	16 (41.0%)	12 (63.2%)	10 (62.5%)	1.02 (0.26 - 4.10)
Children	11 (28.2%)	6 (27.2%)	6 (35.3%)	0.90 (0.22 - 3.66)
Employment	15 (38.5%)	7 (31.8%)	6 (35.3%)	1.27 (0.34 - 4.70)
Characteristics of substance abuse consumption: drug use history and current use patterns				
Alcohol	71.80%	68.20%	76.50%	1.51 (0.36 - 6.37)
Cannabis	35.90%	31.80%	41.20%	1.50 (0.40 - 5.61)
Nicotine	87.25	95.50%	76.50%	0.16 (0.20 - 1.54)
Sedatives	23.10%	27.30%	17.60%	0.57 (0.12 - 2.72)

OR: Odds ratio; 95% CI: confidence interval. No consumption of amphetamine or heroin/morphine/opium drugs

Table 2 Comparison between early/relapse-patients vs. Late/relapse-patients according to SF-36 at beginning and at the seventh week. SF-36 dimensions are specified

SF-36 at first treatment week (Mean±SD)		
	Early/relapse-patients (n=17)	Late/relapse-patients (n=16)
Physical functioning	90.6 ± 16.3	89.7 ± 11.2
Role-Physical	56.41 ± 38.3	47.50 ± 41.2
Bodily Pain	56.41 ± 38.3	47.50 ± 41.2
General Health	56.8 ± 22.9	60.0 ± 22.3
Vitality	45.0 ± 17.8	47.6 ± 22.7
Social Functioning	58.8 ± 23.7*	40.6 ± 28.3
Role-Emotional	51.0 ± 39.3	31.2 ± 39.4
Mental Health	48.2 ± 12.6*	37.5 ± 15.6
Summary		
Mental Component summary	203.0 ± 69.2	157.0 ± 85.1
Physical Component Summary	266.5 ± 73.8	261.6 ± 70.20
SF-36 at seventh treatment week (Mean±SD)		
	Early/relapse-patients (n=5)	Late/relapse-patients (n=10)
Physical functioning	94.0 ± 8.2	90.0 ± 19.3
Role-Physical	55.0 ± 51.2	75.0 ± 35.4
Bodily Pain	85.6 ± 14.0	84.0 ± 17.8
General Health	62.2 ± 20.8	78.3 ± 16.1**
Vitality	61.4 ± 22.5	67.5 ± 15.1
Social Functioning	67.5 ± 37.1	82.3 ± 19.9**
Role-Emotional	66.7 ± 40.8	79.9 ± 32.2**
Mental Health	65.6 ± 28.8	76.1 ± 7.6**
Summary		
Mental Component summary	261.2 ± 124.7	309.8 ± 59.3**
Physical Component Summary	296.8 ± 88.9	327.6 ± 75.1**
*Z with p<0.05 (significant Mann-Whitney test for two-independent samples),		
**Z with p<0.05 (significant Wilcoxon signed-rank test for two-related sample test)		

lack conscience of their addiction or maybe for denying their mental illness¹⁶, and it may be possible that these patients could not perceive the severity of self-impairment²⁹. As similarity, in schizophrenia it has been reported that patients with poor insight could overestimate QoL scores because the consequences of the disease are not perceived³⁰. In any event, these results suggest that the relationship between relapse, addiction severity and subjective HRQoL have not linear interpretation and several factors are involved.

Moreover, a significant improvement in some dimensions of HRQoL was detected in the late/relapse-patients, and in coherence with previous studies, these results suggested that, the higher addiction severity of the early/relapse-patients, the poorer HRQoL and a worse prognosis than late/relapse-patients⁵. Social functioning and Mental Health dimensions were better at the beginning of the study in early/relapse-patients, but they improved more in late/relapse-patients during follow-up (with statistical significance). These dimensions are components of the Mental Component Summary, which reflects psychological distress of patients (along with Role-emotional and Vitality)³¹. In particular, high Mental health scores reflect feelings of happiness, peace and calm^{32,33}, and high Social-functioning scores are related with social performance without interference from some physical/emotional problems. This latter dimension does not reflect the presence/absence of physical/emotional problems, but rather, alerts if these problems could interfere with social common activity^{32,33}. Thus, from our results, future researches in HRQoL and relapse should study further these two dimensions in order to establish the accurate relation with relapses.

Life experience and subjective perception of the level of life satisfaction have been relatively uncommon considered in addiction treatment programs^{10,17,19,34}. One of the reasons why health professionals have begun to consider patient's experiences is that patient's perception is often different to specialist's evaluation^{16,35}. New researches have focused on family and social aspects in substance use¹⁴, some of those investigations have found poor QoL with worse social functioning and different family structures in CDP¹³. Those aspects (social functioning and family environment) are related to greater risk of relapse⁶, and also those factors are associated with QoL measures and should be part of future investigations in cocaine relapse factors and also as part of prevention.

Regarding to depressive symptoms and HRQoL, the sample presented differences in these symptoms only at the fourth week (specifically in early/relapse-patients). Depression and depressive symptoms are related to cocaine relapses⁴, and in addition, depression is associated with poor QoL and HRQoL^{12,36,37}, and it is reported as a further decrease factor for HRQoL in patients with alcohol use³⁸. Be that as it

may, early/relapse patients presented a decrement of HRQoL during follow-up period that could be associated to either variable (depressive symptoms and cocaine use)²⁷. No depressive symptoms were found in later/relapse-patients, thus, late relapse probably indicates a better outcome.

According to these results, HRQoL could have some predictive skill about outcomes, and therefore, HRQoL might reflect the major concerns for patients in each concrete phase of the illness. In this regard, the HRQoL assessment may be useful to know how the patients evaluate their current state, and also, how patients feel that they have covered their needs and hopes³⁹.

This is the first study about HRQoL as a predictor of relapse in CDP seeking treatment without other drug dependences and for the most part, the findings are consistent with previous studies. However, due to the characteristics of the study (no control group and a small and convenience sample) and a significant lost in follow-up could limit the generalizability of the present findings. In this regard, it is important to point out that patients who relapse usually drop out continued treatment programs⁵, and this could be one reason why some part of the sample was lost during follow-up period, particularly early/relapse patients. On the other hand, the study did not discriminate or divided the sample between patients with dual diagnosis or not, as dual diagnosis has been related with worse HRQoL³⁷. This issue is relevant regarding personality disorders due to high prevalence of personality disorders with SUD, and also, because some personality disorders and traits could be related to relapse and even prognosis³⁹⁻⁴¹. Furthermore, other factors such as nicotine dependence and somatic comorbidities may affect HRQoL⁴². Also, it is important to establish in future researches whether there are differences in HRQoL between crack cocaine users from crack non-users, because some studies point out worse outcomes in crack users¹⁴.

According to the current results, HRQoL may be useful in orienting choice between different therapeutic options in order to avoid relapses and provide a more accurate treatment. The current research was performed on CDP, hence, the results could be cautiously extrapolated to users of other substances. Overall, SUD is related to worse HRQoL independently of the substance^{11,17-19}, but milestones, outcomes and prognosis of each substance is generally different^{43,44}. Plus, cocaine use is often associated with other substances or even be presented as polysubstance use^{43,45}. However, many of therapeutic interventions and goals are similar independently of the substance⁴⁶, therefore, the current results could be used in those approaches. In any event, it is important to research more in this issue. To conclude, perceived HRQoL could predict early relapse and confirms the following: (i) there are differences in perceived HRQoL measures between CDP with/without early relapse and (ii) Late/

relapse-patients have higher improvement of HRQoL than patients with early relapse.

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CONFLICT OF INTERESTS

Carlos Roncero received compensation to give talks for Janssen-Cilag, Bristol-Myers Squibb, Ferrer-Brainpharma, Pfizer, Reckitt-Benckiser, Lundbeck, Otsuka, Servier, Lilly, Shire, GSK, Rovi, and Adamed. He received financial compensation for his participation as a member of the Janssen-Cilag, Lilly, and Shire boards. He carried out the PROTEUS project, which was funded by a grant from Reckitt-Benckiser and Indivior. The author has no other relevant affiliations or financial involvement with any organization or entity that has a financial interest in or is in financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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Sira Díaz-Morán declares no conflict of interest.

Lara Grau-López received compensation to give talks for Janssen-Cilag, Otsuka, and Pfizer. She has no other relevant affiliations or financial involvement with any organization or entity that has a financial interest in or a financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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Ana I. Álvarez declares no conflict of interest.

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Constanza Daigre declares no conflict of interest.

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