Relationship between alcohol consumption, whether linked to other substance use or not, and antiretroviral treatment adherence in HIV+ patients

Relación entre la adherencia al tratamiento antirretroviral en pacientes VIH+ y el consumo de alcohol, asociado o no al uso de otras sustancias

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Abstract

Hazardous alcohol consumption is a common diagnosis among people living with HIV infection. The relationship between alcohol consumption and poor adherence to antiretroviral therapy has been highlighted in different studies, yet few of them performed a parallel analysis of other substance use. In Spain, alcohol consumption is frequently associated with other substance use, mainly cannabis and cocaine. The aim of this study is to assess the influence of hazardous alcohol consumption both combined with other substances (cocaine, heroin, methadone and/or cannabis) or alone on antiretroviral therapy adherence in our social environment. We performed an observational case-control study including 119 HIV+ individuals. We recruited 40 non-adherent patients, defined by less than 90% compliance according to hospital pharmacy refill data, and corroborated by the *Simplified Medication Adherence Questionnaire* (SMAQ) and referring professional's opinion. Control cases (n=79) were defined as those patients with similar characteristics but considered adherent according to the same parameters. Data collection took place between May 2013 and September 2015. Statistical analysis was performed using a binary logistic regression model. Our results indicate that alcohol consumption decreases adherence to antiretroviral therapy. The use of methadone represents a statistically significant increased risk of poor adherence. No significant differences were found between adherent and non-adherent groups regarding cocaine, heroin or cannabis use in this study. In summary, the detection of substance use and especially alcohol consumption in HIV+ patients can improve the effectiveness of antiretroviral therapy by identifying and treating at-risk individuals for a poor therapeutic adherence.
Keywords: HIV; Highly Active Antiretroviral Therapy (HAART); Medication adherence; Alcohol use; Substance use.

Resumen

El consumo perjudicial de alcohol es un diagnóstico de elevada prevalencia en pacientes VIH+. Distintos estudios han destacado la influencia negativa del mismo sobre la adherencia al tratamiento antirretroviral, aunque pocos de ellos valoran además el consumo de otras sustancias. En España, el consumo de alcohol se presenta frecuentemente en situación de policonsumo, fundamentalmente de cannabis y cocaína. El objetivo es comprobar cómo influye el consumo de alcohol, asociado o no al uso de otras sustancias (cocaína, heroína, metadona y/o cannabis), en la adherencia al tratamiento antirretroviral en nuestro entorno. Se ha realizado un estudio observacional tipo casos y controles sobre una muestra de 119 individuos VIH+. Conforman los casos (n=40) sujetos no adherentes al tratamiento farmacológico según reporte de Farmacia Hospitalaria, corroborado por el *Simplified Medication Adherence Questionnaire* (SMAQ) y la opinión del profesional de referencia. Se consideran controles (n=79) una muestra de pacientes de características similares con buena adherencia terapéutica según los mismos métodos de valoración. La recogida de datos se hizo entre mayo 2013 y septiembre 2015. El análisis estadístico se realizó mediante regresión logística binaria. Los resultados muestran que el consumo de alcohol empeora la adherencia al tratamiento antirretroviral. El uso de metadona supone un incremento estadísticamente significativo del riesgo de no adherencia. No se han encontrado diferencias significativas entre los grupos del estudio respecto a los consumos de cocaína, heroína o cannabis. Por tanto, la detección del consumo de sustancias, especialmente de alcohol, y su abordaje en pacientes VIH+ puede repercutir positivamente en el cumplimiento terapéutico, en beneficio de una mayor efectividad de la terapia antirretroviral.
Palabras clave: VIH; Terapia antirretroviral (TARGA); Adherencia terapéutica; Trastorno por uso de alcohol; Policonsumo.

The hazardous use of alcohol and other substances is a frequent diagnosis in patients with HIV infection. Several authors have pointed out their high prevalence (Parsons, Starks, Millar, Boonrai & Marcotte, 2014; Skalski, Sikkema, Heckman & Meade, 2013). Although estimates vary between 8% and 42% (Williams et al., 2016), it has been pointed out that the prevalence of heavy drinking (Cortés Tomás & Motos Sellés, 2016) in these patients almost doubles the prevalence in the general population (Galvan et al., 2002).

Apart from the direct harm to the individual's health, other factors have been highlighted among the consequences of alcohol consumption in HIV-positive patients such as the potential increase in the risk of transmission of the virus in situations of alcohol intoxication (Scott-Sheldon et al., 2013), the delay in the diagnosis of the disease (Zarkin, Bray, Babor & Higgins-Biddle, 2004), an increased risk of early cognitive impairment (Anand, Springer, Copenhaver & Altice, 2010) or hepatitis C (Taylor, Denniston, Klevens, McKnight-Eily & Jiles, 2016) and, in general, an increase in morbidity and mortality (Azar, Springer, Meyer & Altice, 2010). In addition, harmful alcohol consumption has been associated with a worsening of immune status independently of treatment (Baum et al., 2010).

In Spain, the rate of new HIV diagnoses continues to be higher than the average for European Union and Western European countries. During 2015, an estimated 9.44 new cases per 100,000 inhabitants (Carlos III Health Institute, 2016) were detected. Since the introduction of highly active antiretroviral therapy (HAART) as the treatment of choice in HIV infection, there has been a significant improvement in the quality and life expectancy of affected individuals (Tancredi & Waldman, 2014; Poorolajal, Hooshmand, Mahjub, Esmailnasab & Jenabi, 2016). The benefits of this regimen, however, are intimately linked to strict treatment compliance, and lack of adherence has been postulated as the first cause of short-term treatment failure (Braithwaite & Bryant, 2010), as well as favouring the development of resistant strains (Cohen, 2006).

There are numerous lines of research regarding factors that may have a negative impact on adherence to antiretroviral therapy, variously highlighting the presence of undesirable side effects of the treatment, emotional stress originating from causes secondary to the core problem treated, lack of social/family support, complexity of the pharmacological regimen, or the lack of efficacy perceived by the patients (Ammassari et al., 2002; Hudelson & Cluver, 2015). Poor treatment adherence has similarly been linked to younger age groups and cognitive impairment (Hinkin et al., 2004), the presence of psychopathology, fundamentally depression (Palepu, Horton, Tibbetts, Meli & Samet, 2004), as well as certain personality traits (Hutton and Treisman, 2008), low socioeconomic status (Bermudez et al., 2016; Peltzer & Pengpid, 2013) and

substance use, particularly alcohol (Azar et al., 2010; Palepu et al., 2004).

It has been posited that adherence to antiretroviral therapy should be understood as a dynamic process in which modifiable risk factors are linked to better or worse compliance (Lazo et al., 2013). In recent years, many authors have focused especially on the impact of alcohol consumption on treatment adherence (Vagenas et al., 2015). Various systematic reviews consistently support the relationship between both factors (Azar et al., 2010, Vagenas et al., 2015; Hendershot, Stoner, Pantalone & Simoni, 2009). Moreover, the consumption of alcohol or other substances may also influence adherence to other medical treatments related to diseases or infections common to HIV-positive patients (Gonzalez, Barinas & O'Cleirigh, 2011). Consequently, treatment intervention programmes have been proposed to decrease alcohol consumption and improve pharmacological compliance, which would translate into an overall improvement in the course of HIV disease (Parry et al., 2014). Thus, it has been pointed out that the transition from active substance use to abstinence would be consistently associated with improved treatment adherence (Lucas, Gebo, Chaisson & Moore, 2002).

In Spain, alcohol consumption is often associated with the use of other substances. According to the household survey on alcohol and drugs (Encuesta Domiciliaria sobre Alcohol y Drogas) carried out by the Spanish Ministry of Health (OEDT, 2015), alcohol is involved in practically all cases of polydrug use: 94.3% of cannabis users and 96.8% of cocaine users also drink alcohol. In addition, among those whose primary substance is alcohol, cannabis is used by 11.1%, and cocaine by 2.7%.

There is evidence that the influence on treatment adherence may vary depending on the substance used and the pattern of consumption (Azar et al., 2015; Gonzalez et al., 2011), although the types of substance and the mechanisms that link their use to decreasing adhesion have not been studied in depth (Gonzalez, Mimiaga, Israel, Andres Bedoya & Safren, 2013). In a study carried out by Parsons et al. (2014) on a sample of 557 HIV-positive individuals over 50 years of age, the combined use of alcohol with cannabis or cocaine was associated in a statistically significant way with an increase in forgetting medication when compared to alcohol consumption in isolation.

Treatment adherence requires careful attention to dose times and, in many cases, the coordination of multiple medications, which involves mechanisms related to cognition, planning and decision making. Elements such as lifestyle instability (Tucker et al., 2004), physical and psychic vulnerability, or difficulties in self-control mediated by substance use may interact to weaken adherence. In addition, some patients may discontinue treatment during episodes of consumption if they perceive it to be incompatible with substance use (Kalichman et al., 2015).

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Despite the above, which is based on international data, references in the literature regarding the impact of alcohol consumption on adherence to antiretroviral therapy in HIV-positive patients in Spain are limited (Ortego, Huedo-Medina, Vejo & Llorca, 2011; Pérez-Valero et al., 2016a; Pérez-Valero et al., 2016b). The aim of the present study is to assess whether hazardous alcohol use is linked to poor adherence to antiretroviral therapy in HIV-positive patients once adjusted for use of other substances (cocaine, heroin, methadone and/or cannabis), and to determine the role they play in adherence in a specific care setting and in the cultural context of the Spanish population.

Methodology

Participants

The study population consisted of adult patients undergoing regular outpatient follow-up at the infectious disease centre of a third-level hospital (Ramón y Cajal University Hospital, Madrid), who had been receiving HAART for at least the previous twelve months, dispensed in all cases by the hospital pharmacy. All participants gave informed consent prior to taking part in the study. Regular follow-up was defined as attending at least two scheduled appointments in the previous year (Tripathi, Youmans, Gibson & Duffus, 2011). Exclusion criteria were the presence of acute infectious or active oncological processes, as well as refusal to participate or voluntary withdrawal from the study in compliance with informed consent. In addition, cases with an inconsistency between the SMAQ questionnaire results and/or the opinion of the referring professional regarding adherence according to the hospital pharmacy were excluded from the study. The study was approved by the Clinical Research Ethics Committee of the Hospital before being carried out.

Procedure

This is an observational case-control study. Non-adherent HAART patients make up the cases, and a sample of patients with similar characteristics and good therapeutic adherence are the controls. The selection of cases was carried out by consecutive sampling of a list of non-adherent patients routinely generated on a monthly basis by hospital pharmacy. The controls were selected by consecutive sampling of the patient list for outpatient appointments. Non-adherent patients were considered to be those who, according to the hospital pharmacy refill data, had collected less than 90% of their antiretroviral treatment medication prescribed during the previous year. Adherent patients were those collecting 95% or more of their doses during the last year, according to hospital pharmacy (Paterson et al., 2000). Patients whose adherence was equal to or greater than 90% but less than 95% were excluded from the study on the basis of lack of unanimity in the literature

as to the limits of this differentiation (Viswanathan et al., 2015). All the individuals participating in the study were given a semi-structured clinical assessment interview created ad hoc for the purpose. The SMAQ questionnaire - a brief instrument asking patients six questions about their therapeutic compliance and validated for use in patients with HIV infection (Knobel et al., 2002) - was included in order to corroborate the assessment of treatment adherence according to hospital pharmacy. The assessment process was carried out in its entirety by the researchers. Data collection took place between May 2013 and September 2015.

Variables of the study

Socio-demographic variables such as age, sex, race, marital status, socioeconomic status, educational and work status were included, among others. In addition, a register of variables regarding HIV infection status and treatment was drawn up, which included the progression in time from the beginning of follow-up and treatment, the number of pills and antiretroviral treatment shots per day, as well as whether or not the taking of medication was supervised. Regarding substance use, a history of alcohol, cannabis, cocaine, heroin and methadone (therapeutic use) was recorded covering the 12 months prior to the assessment, with the frequency of their use and the daily amount consumed being taken into account.

Statistical analysis

The descriptive values and the frequencies of the variables included in the study were obtained in the statistical analysis. Some of the variables were recoded so as not to lose power in the analysis, without this entailing a substantial loss of information and preserving a clinical sense. Cases with financial difficulties with or without external aid, or the impossibility of keeping up payments or debt repayment, or the threat of eviction were classified as having problematic or hazardous socioeconomic status. Alcohol consumption was dichotomously categorized into non-problematic and hazardous consumption, according to the criteria established by the World Health Organization (WHO, 1992). For the remaining substances, their continuous use was considered positive, regardless of the pattern of consumption (all individuals presented at least weekly use). For the description of quantitative variables which did not meet normal distribution criteria, the median and the interquartile range (IQ25-75) were chosen. For the comparative analysis of raw data, the Mann-Whitney U test was used, while the Pearson chi-square statistic was applied to qualitative variables. In both cases, a significance level of $p = 0.05$ was selected.

Finally, we carried out the multivariate analysis using binary logistic regression. The Enter method was used for including the predictor variables in the equation. Variables which in the raw analysis were shown to have a link to treat-

ment adherence were included in the model, and these focus our study in relation to substance use, together with the other variables recommended in the specialised literature. Included in this analysis are: age, gender, socioeconomic level, length of follow-up, number of pills prescribed per day, and use of alcohol, cannabis, cocaine, heroin and methadone.

Results

Descriptive results and raw analysis

Sociodemographic and clinical characteristics of the sample.

A total sample of 119 subjects was analysed, with 40 cases and 79 controls. The median age of the population as a whole was 48.5 years (IQ: 44.3-52.8). The median years of follow-up and treatment time were, respectively, 16.5 (IQ: 9-21) and 15 (IQ: 7-19). The set of subjects took a median of 3 pills per day (IQ: 1-3). Other qualitative data characterising the overall sample are presented in Tables 1 and 2.

The number of males in the control group was 52 (65.8%), with 27 males in the group of cases (67.5%) (Table 3). The median age of the sample was 47.6 (42.5-50.6) in the case group and 49.1 (45.3-53.5) in the control group, with a median follow-up in years in the case group of 17.5 (9.8-22.0) and 15.0 (8.0-21.0) in the controls (Table 4).

The comparative analysis shows that the higher socioeconomic status of the control group is statistically significant. Similarly, among the cases a greater degree of treatment supervision by third parties is evident (Table 3). Regarding the quantitative variables, statistically significant differences between cases and controls were only found in terms of the number of pills per day (Table 4).

Table 1. *Sociodemographic variables of whole sample.*

		n	%
Sex	Male	79	66.4%
	Female	40	33.6%
Race	Caucasian	99	83.2%
	Other	20	16.8%
Marital status	With partner	46	38.7%
	Other	73	61.3%
Employment	In work	53	44.5%
	Unemployed	66	55.5%
Profession	Unqualified	54	46.2%
	Qualified	63	53.8%
Socioeconomic level	Stable	90	75.6%
	At risk	29	24.4%
Supervised treatment	Never	98	82.4%
	Sometimes/always	21	17.6%

Table 2. *Substance use variables of whole sample.*

	Yes	No
	n (%)	n (%)
Alcohol use	27(23.3)	89 (76.7)
Cannabis use	39 (32.8)	80 (67.2)
Cocaine use	29 (24.4)	90 (75.6)
Heroin use	8 (6.7)	111 (93.3)
Methadone use	17 (14.3)	102 (85.7)
Polydrug use	36 (30.3)	83 (69.7)

Table 3. *Sociodemographic variables compared - cases and controls.*

		Controles	Cases	Pearson test	
		n (%)	n (%)	χ²	Sig.
Sex	Male	52 (65.8)	27 (67.5)	0.033	0.855
	Female	27(34.2)	13(32.5)		
Race	Caucasian	70 (88.6)	29 (72.5)	4.928	0.026
Marital status	With partner	28 (35.4)	18 (45.0)	1.023	0.312
	Other	51 (64.6)	22 (55.0)		
Employment	Unemployed	41 (51.9)	25 (62.5)	1.208	0.272
Profession	Unqualified	31 (40.3)	23 (57.5)	3.148	0.312
	Qualified	46 (59.7)	17 (42.5)		
Socioeconomic level	Stable	69 (87.3)	21 (52.5)	17.490	0.000
	At risk	10 (12.7)	19 (47.5)		
Treatment supervision	Never	71 (89.9)	27 (67.5)	9.146	0.002
	Sometimes/always	8 (10.1)	13 (32.5)		

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Variables related to the use of substances.

Hazardous alcohol use was evident in 15 of the cases (37.5%), compared to 12 subjects (15.8%) in the control group (p = 0.009).

As the analysis of qualitative variables shows, the cases present a profile characterised by higher intakes of each substance assessed except for cannabis, where there are no differences with respect to the controls. Therapeutic use of methadone was observed in 12 of the cases (30.0%), in contrast to 5 subjects in the control group (6.3%) (p = 0.000). The difference in cocaine use was also statistically significant (p = 0.005). In the case of heroin, there were differences between both groups, with p = 0.073 (Table 5).

Logistic regression

Table 6 shows the results of the logistic regression analysis, where the variables that influence treatment adherence in a statistically significant way are highlighted. The applied model correctly classifies about 80% of the subjects, with greater specificity than sensitivity (Hosmer and Lemeshow test: cases = 55.7%, controls = 90.0%, overall = 78.3%) and explains 44.2% of the variability in adherence.

Substance use.

From the above data, it can be deduced that hazardous alcohol consumption represents an average increase of 4.330 (95% CI: 1.157-16.206) in the risk of poor adherence to antiretroviral therapy in a statistically significant way (p = 0.030) as against abstinence or non-detrimental use once adjusted for the variables indicated. The use of methadone increases this risk by 5.074 (95% CI: 1.056-24.379). In contrast, the consumption of cannabis, cocaine or heroin is not significantly associated with decreasing treatment adherence.

Sociodemographic and clinical data.

The results indicate increased risk of non-adherence for males, those in worse socioeconomic situations, and with antiretroviral therapy regimens consisting of a greater number of pills per day.

Discussion

It follows from the above that hazardous alcohol consumption significantly worsens adherence to antiretroviral

Table 4. *Clinical variables and statistical significance of comparisons - cases and controls.*

		n	Median	Interquartile range		Mann-Whitney U
				Q25	Q75	Sig.
Age	Cases	40	47.66	42.50	50.61	0.086
	Controls	79	49.10	45.31	53.47	
Years of follow-up	Cases	40	17.50	9.75	22.00	0.171
	Controls	78	15.00	8.00	21.00	
Years of treatment	Cases	40	17.00	8.25	20.00	0.094
	Controls	78	13.00	5.00	19.00	
Number of pills per day	Cases	40	3.00	3.00	4.00	0.001
	Controls	79	2.00	1.00	3.00	

Table 5. *Substance use and statistical significance of the comparisons - cases and controls.*

	Controls	Cases	Pearson test	
	n (%)	n (%)	χ²	Sig.
Alcohol use	12 (15.8)	15 (37.5)	6.917	0.009
Cannabis use	24 (30.4)	15 (37.5)	0.611	0.434
Cocaine use	13 (16.5)	16 (40.0)	7.987	0.005
Heroin use	3 (3.8)	5 (12.5)	3.207	0.073
Methadone use	5 (6.3)	12 (30.0)	12.151	0.000
Polydrug use	14 (17.7)	22(55.0)	17.489	0.000

Table 6. *Logistic regression, 'Enter' method.*

	B	S.E.	Wald	df	Sig.	Exp(B)	95% CI
Age	-0.092	0.044	4.348	1	0.037	0.912	0.837 − 0.995
Sex	-1.346	0.612	4.834	1	0.028	0.260	0.078 − 0.864
Years of follow-up	0.063	0.041	2.293	1	0.130	1.065	0.982 − 1.154
N° pills per day	0.515	0.203	6.469	1	0.011	1.674	1.126 − 2.491
Socioeconomic level	1.347	0.581	5.374	1	0.020	3.844	1.231 − 12.001
Alcohol use	1.465	0.673	4.735	1	0.030	4.330	1.157 − 16.206
Cannabis use	-0.646	0.588	1.209	1	0.272	0.524	0.165 − 1.659
Cocaine use	0.380	0.715	0.283	1	0.595	1.463	0.360 − 5.943
Methadone use	1.624	0.801	4.112	1	0.043	5.074	1.056 − 24.379
Heroin use	-0.517	1.088	0.226	1	0.635	0.596	0.071 − 5.035
Constant	-2.282	3.062	0.556	1	0.456	0.102	

therapy. This confirms in our own care context and cultural environment what has previously been broadly and consistently described in the literature in other contexts (Azar et al., 2010; Vagenas et al., 2015; Hendershot et al., 2009). Furthermore, the association between alcohol use and lack of adherence is maintained in our research after adjustment for other substance use, so that in the sample studied, alcohol weakens adherence independently of the use of other substances.

A negative influence of the use of methadone on adherence is also evidenced, although doubts as to the meaning of this result exist. The therapeutic use of methadone could, at least in our country, correspond to clinically more deteriorated individuals or to those with a lower socioeconomic profile (Ladero, Orejudo & Carrobles, 2005), which would explain worse adherence and would be congruent with the results obtained. Nevertheless, previous studies have suggested that adherence to a methadone treatment program may lead to an improvement in adherence to antiretroviral therapy in comparison to untreated parenteral drug users (Malta, Strathdee, Magnanini & Bastos, 2008), especially in marginal areas with a high prevalence of this type of consumption (Azar et al., 2015).

Conversely, the present study finds no significant association between the use of cannabis, cocaine or heroin and a decrease of treatment adherence, which differs globally from findings previously reported in the literature in other contexts (Hinkin et al., 2004; Azar et al., 2015). However, the absence of a link between cannabis use and noncompliance has already been pointed out by other authors (Rosen et al., 2013; De Jong, Prentiss, McFarland, Machekano & Israelski, 2005). In this sample, moreover, there are no significant differences in the raw analysis between cases and controls in such consumption. Regarding the use of heroin or cocaine, it is estimated that the absence of a statistically significant relationship could be due to the small

number of individuals that admit to using these drugs, although there is controversy about the capacity of patients to report such consumption (Van Dorn, Desmarais, Swartz, Young & Sellers, 2014).

From the results, it can be concluded that the subjects in worse socioeconomic situations are at greater risk of treatment noncompliance. This would be congruent with other findings described in the literature. It is known that structured social support and a fixed address facilitate adherence (Ruiz-Pérez et al., 2006), thus underlining the importance of psychosocial factors on overall health status and the need to deepen research in this field, which has gained importance in recent years (Ruiz-Pérez et al., 2006; Beer, Mattson, Bradley & Skarbinski, 2016).

In the group of subjects classified as non-adherent, there is a higher percentage of treatment supervision by third parties, which should probably be understood as a consequence of the baseline situation of noncompliance. The superiority - in terms of immunological control of infection and adherence - of supervised medication administration for substance users compared to self-medication has been demonstrated in both randomized studies and systematic reviews (Binford, Kahana & Altice, 2012).

Various authors have previously found that more complicated treatment regimens (greater number of pills per day) worsened treatment adherence (Ammassari et al., 2002; Stone, Jordan, Tolson, Miller & Pilon, 2004; Nachega et al., 2014).

The present study confirms, in our context, most of the findings published in the literature. The reliability of treatment adherence data, in which the objective and quantitative hospital pharmacy reports are consolidated by the SMAQ instrument and the opinion of the referring professional, as well as the inclusion of different consumption and sociodemographic variables can be seen as strengths of the study.

Among its limitations, it should be noted that its statistical power is diminished due to the small sample size, as well as the low incidence of heroin and cocaine use, which appears to limit the role of these variables in our sample. It must be emphasised that data regarding the individual history of substance use were obtained solely via an interview with the patient. In addition, given the requirements of regular outpatient follow-up, it is likely that subjects with more acute consumption patterns and more severe markers of social and clinical deterioration have been excluded from this study. It should be assumed that the results obtained may be applied and extrapolated only to those populations that share a similar profile. It is therefore recommended that the study be extended to populations in environments with greater problems in accessing health care, with more acute consumption patterns or greater psychosocial deterioration in order to study the impact of alcohol and other substances on treatment adherence in subjects with this profile.

Substance use was measured qualitatively, following the WHO criteria for hazardous drinking in the case of alcohol, and quantitatively, without assessing whether patients met criteria for the diagnostic categories of substance abuse or dependence. However, considering the damage linked to the use of substances on a continuum rather than assigning it to static entities increases sensitivity in the detection of the influence of hazardous use in non-adherence, and is the line followed by the current DSM-5.

It should be noted that the adherence estimate according to the hospital pharmacy refill data is based on the withdrawal or otherwise of the medication, and not strictly on its consumption. Other limitations include the inability to determine whether medication was taken at the correct time, whether extra medication was taken in compensation, or whether pills were lost (Berg & Arnsten, 2006). Nevertheless, this method has been shown to be highly specific but not very sensitive, thus the use of complementary methods in the present study decreases the risk of a possible overestimation of adherence (Henegar et al., 2015).

Among the limitations of the study it should finally be stressed that the analysis of the sample presented lacks variables related to the presence or otherwise of psychopathology (Torrens, Mestre-Pintó, Montanari & Vicente, 2017) as well as the cognitive status of the participants. The possibility of selection and survival biases inherent in the study design should also be taken into account. No patients were excluded for non-consent. Data on patients excluded on other grounds were not collected.

It is well known that adherence to antiretroviral therapy plays a vital role in preventable morbidity and mortality in HIV-positive patients (Braithwaite & Bryant, 2010). In light of the results obtained, it is therefore essential to address the possible existence of substance use - especially of alcohol - in the daily clinical setting, questioning the type, frequency and amount of the substance consumed in order to be able to carry out measures that reduce the impact of consumption on treatment compliance (Parsons et al., 2014). In addition to improving the detection of possible risk patterns, it would be important to provide patients with access to specific resources to treat these problems (Gonzalez et al., 2013). Based on the above, new research should focus on the behavioural, structural, social or psychological factors related to adherence in different groups of substance users in order to develop specific interventions (Azar et al., 2015).

Conclusions

The study highlights the importance of alcohol consumption as a factor negatively affecting adherence to antiretroviral therapy. This importance is maintained even when the consumption of other substances is considered, and adjustments are made for other variables that influence adherence, such as being male, having a problematic socioeconomic situation or a regimen with a high number of pills. The assumption that treatment adherence is a dynamic and modifiable process justifies intervention at different levels in order to minimise the factors associated with its decline. Carefully exploring the use of alcohol (and other substances) is essential in the treatment of patients with HIV and highly active antiretroviral therapy (HAART), and could thus facilitate the advancement of better outcomes for the disease, with decreases in morbidity, mortality and the risk of virus transmission, as well as the development of resistant strains. In studies with HIV-positive subjects, the great degree of heterogeneity among patients must be taken into account. Therefore, in clinical practice it will be important to individualise each case and to identify which factors, both risk and protective, can condition adherence to antiretroviral therapy.

Conflict of interests

The authors state that there is no conflict of interest with regard to the present study. Enriqueta Ochoa Mangado states that in recent years she has received funding as a speaker and has collaborated on projects by *Lundbeck, Servier, Reckitt Benckiser / Indivior,* and *Ferrer-Brainfarma.*

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