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Gender differences in the treatment of the opiate dependence with naltrexone

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Introduction. We want to know the influence of gender factor in the consumption characteristics, social support and evolution in treatment with naltrexone in an opiate addict group.

Material and methods. 1.432 patients (83.1% males and 16.9% females) recruited over a 12 year period who successively initiated treatment period years with naltrexone. Retrospective observance study, with design of treatment group without control group. We evaluated the role of gender in retention with the Mantel-Cox test. The differences were analyzed according to the gender with contingency tables.

Results. One year retention for all of them was 29.75%, this being 30.92% for men and 23.97% for women. This difference is significant at one year according to the Mantel-Cox test (statistics: 8.38%; gl: 1; signification: 0.0038). Women show less frequency of cocaine use (p=0.011) and less use of intravenous cocaine (p=0.048), lower frequency of consumption of alcohol (p=0.000) and cannabis (p=0.002), a shorter period of heroine abuse (p=0.016) and a higher proportion of them only use heroine (p=0.015). They have less economic independence (p=0.001), their partner is more frequently an addict (p=0.000), they have less help for the treatment from a non-consuming partner (p=0.000).

Conclusions. There are outstanding differences with regard to consume characteristics, social support and evolution of the treatment according to the gender (either male or female). Men have better prognosis than women in the population studied. These differences seem to be due to the sociocultural contents of the gender concept.

Key words:
Gender differences. Woman. Heroine. Treatment.

Actas Esp Psiquiatr 2008;36(4):197-204

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Diferencias de género en el tratamiento de la dependencia de opiáceos con naltrexona

Introducción. Se quiere conocer la influencia del factor género en las características de consumo, apoyo social y evolución en el tratamiento con naltrexona de un grupo de dependientes de opiáceos.

Material y métodos. Mil cuatrocientos treinta y dos pacientes (83,1% hombres y 16,9% mujeres) que sucesivamente y durante 12 años inician tratamiento con naltrexona en la unidad de toxicomanías. Estudio observacional retrospectivo con diseño de grupo de tratamiento sin grupo control. Evaluamos el papel del género en la retención con la prueba de Mantel-Cox. Con tablas de contingencia se analizan las diferencias en función del género.

Resultados. La retención al año de iniciarse el tratamiento para el total es de 29,75%, siendo de 30,92% para hombres y de 23,97% para mujeres. Esta diferencia al año es significativa según la prueba de Mantel-Cox (estadístico: 8,38; gl: 1; significación: 0,0038). Las mujeres presentan menor frecuencia de consumo (p=0,011) y uso de la vía intravenosa para cocaína (p=0,048), menor frecuencia de consumo de alcohol (p=0,000) y de cannabis (p=0,002), menor tiempo de consumo de heroína (p=0,016) y mayor proporción consumen sólo heroína (p=0,015). Tienen menor independencia económica (p=0,001), cuentan con mayor frecuencia con pareja consumidora (p=0,000), contando con menor apoyo para el tratamiento de una pareja no consumidora (p=0,000).

Conclusiones. Existen diferencias relevantes respecto a las características del consumo, apoyo social y evolución del tratamiento según el género (sea hombre o mujer). Los hombres tienen mejor pronóstico que las mujeres en la población estudiada. Dichas diferencias parecen deberse al contenido sociocultural del concepto género.

Palabras clave:
Diferencias de género. Mujer. Heroína. Tratamiento.

INTRODUCTION

The study of the analysis of gender in the field of opiate dependency is relatively recent although being a man or woman conditions and shapes the expression of the consumption and problems accompanying them. Although the differences between men and women are well documented, research on the addictions rarely considers gender. In general it contemplates them from a masculine point of view. Up to a few years ago, opiate consumption was predominately masculine and given the predominance of dependent males that requested help, women were seen as atypical cases and no consideration of gender was applied in their evaluation and treatment[1,2].

The differences in addiction according to gender are related with socio-political phenomena and with the specific structure of the subject, family and social networks in which they are immersed. Our society has been experiencing important changes over the last 100 years regarding the female role, and the woman has been acquiring more educational and professional opportunities than previously. Their incorporation into society also supposes their incorporation into its more negative aspects such as addictions. However, social evaluation of consumption in the woman continues to be different from that of the male. When a woman breaks the law such as with the consumption of drugs in general, and opiates specifically, she performs a dual infringement, that of the fact in itself and that assigned to the violation of the role and its expectations. Although there has been greater social acceptance towards alcohol consumption (but not about its dependency), tobacco and tranquilizers by woman in the last two decades, there is still a very negative evaluation towards consumption of heroin and cocaine[1-5].

Attributing of expected behaviors to a group is determined by the socialization form. Woman has different demands, with the assuming of greater responsibility and control of the setting[2,5]. This implies that the consequences of the consumption may be different since social tolerance of the dependency in the woman is lower and the dependent woman may suffer greater social rejection and more discrimination.

The epidemiological studies show greater prevalence of the use of heroin in men. Opiate consumption data in the woman indicates that 0.3% of women over 14 years have consumed heroin at some time, while their regular consumption is less than 0.1%. Heroin dependence is estimated to be 1 to 3 per 1,000 in all. It is calculated that there is one female opiate addict per 4 or 5 males, although the proportion asking for treatment is 1 to 76-13. Women also are overrepresented among opiate dependents who demand treatment in our setting, of which only 15%-20% are women[6,14,15].

Factors associated to treatment evolution

Many variables from different settings have been associated to the evolution in dishabituation therapies in general and in opiate dependency specifically. Individual and socio-environmental factors have been studied as predictors of response and treatment retention.

Severity data of the addiction indicate poor prognosis[16,17], as well as that of alcohol consumption[18,19] and other substances[20,21]. The study of the usual amount of opiates consumed mark treatment prognosis. Consumptions of low amounts in the months prior to the onset of the therapy are considered to be a favorable factor of good outcome[22-26], while prolonged addictions and high heroin doses are a predictive factor of relapse[27]. Worse evolution is found among parenteral drug users versus those who consume by inhaled/smoked pathway[28,29]. The majority of the opinions[30,31] considers that backgrounds of relatively short consumption, normally associated to lower repercussion in other areas of functioning of the individual, determine worse treatment prognosis due to lower motivation and limited seeking of help. Paradoxically, the same occurs with already deeply rooted consumptions, usually associated to numerous attempts of failed dishabituation in which the addiction has become a part of the «life style»[32,33]. Thus, a middle-long period of addictive background, that is still not chronic, is a factor of good prognosis in naltrexone programs, with the same importance as the previous existence of extensive periods of abstinence[34-36]. The number and duration of abstinence periods also play a role, indicating better evolution in the patients who have had prolonged abstinence periods or who come to the program against after a previous relapse[36-40].

Alcohol consumption predicts worse evolution in the treatment[41-43]. Severe alcohol consumption increases mortality[44] and worsens retention[45]. Consumption of other substances, such as cocaine, among addicts to opiates is elevated[46-50]. This consumption of cocaine is negatively related with such diverse areas as exposure to violence, increase of criminal activity[51,52], early drop out[53], relapse in opiate consumption[54,55], greater proportion of psychopathology and HIV markers[56]. In our setting, cocaine addiction establishes worse prognosis regarding the dishabituation program with naltrexone[57].

Having work stability at the onset of the treatment[57,58], greater family stability and involvement[59-62] and higher professional level[63,64] are predictors of good response[65].

Whether the gender factor can establish different evolution in opiate dependency therapy is discussed. Some studies indicate that women are underrepresented among the patients who demand treatment, take longer to initiate treatment and when they do so, their results are worse[4,66,67].

The purpose of this study is to evaluate the predictive importance of the gender factor in the evolution of treatment in a large sample of heron addict patients under treatment with naltrexone. Equally, and assuming the extensive involvement of sociocultural variables in the gender var-

iable, the second objective established is to differentiate, in case of being able to assume the gender as prognostic predictor, that specific characteristics are differentiating both genders. To do so, the influence of said factor in the characteristics of substance consumption and in the support and social setting presented by the dependent subject is studied.

MATERIAL AND METHODS

A sample of 1,432 patients diagnosed of opiate dependency disorder (F11.2, ICD-10)[68], (1,190 men and 242 women) and recruited over a 12 year period who successively initiated treatment with naltrexone, that was prescribed in and monitored by the Drug Addiction Unit of the University Hospital Ramón y Cajal (Madrid), was studied.

This is an observational, retrospective study with design of a treatment group without control group (type-case series, anterograde directionality and mixed temporality. Data collection was performed using a structured protocol of clinical data collection[69,70]. As parameter for evaluation of therapeutic success, retention at one year in the program was chosen. Retention was defined as correct monitoring of the patient according to the appointment established and in abstinence state. Initiation of the retention period is marked by taking the first complete dose of naltrexone after any type of previous detoxification. The end of it is indicated by the discharge date, with the possibility of several causes for this discharge (medical discharge, death, dropout, etc.). Difficulty for data collection (due to the characteristics of the population) the constant process of adaptation of the protocol to the new investigations conditioned the data collection. These circumstances have been taken into account for the statistical analysis. The data were stored in an Access database and developed with the SPSS_8 statistical program. Parameters that were adequate for the descriptive analysis (arithmetic mean and standard deviation in quantitative variables and frequencies in qualitative variables) were used. In the inferential study, survival techniques were adopted that made it possible to establish the likelihood that a subject would survive or remain in therapy for at least the t time[71-74]. To evaluate the role of gender in retention, the Mantel-Cox test was used. This made it possible to indicate the significant presence of different behaviors based on their categories in the variable regarding the likelihood of survival in therapy. Using contingency tables, the differences found based on gender in other variables of the protocol as defined in the structured protocol of clinical data collection that we used were analyzed[69,70].

RESULTS

Out of the total of 1,432 patients, 83.1% were men and 16.9% women. The user profile as a whole had a mean age of 27.3 years (SD: 5.1), were mostly Caucasian (99%), single (71%), and lived with their family of origin (74.1%). Half of the population stated they were inactive and had no right to unemployment benefits or pension (49.3%); 24% having basic school level.

The subjects consumed heroin 0.66 g/d (SD: 0.6), either inhaled or smoked (55.8%), from the age of 19.87 years (SD: 4.2). About 63% of the subjects admitted consuming concomitant cocaine during the last 6 months, most of them (53.3%) intravenously accompanied by heroin. Among those who consumed it, the mean daily cocaine administered was 0.63 (SD: 0.57), and they initiated this consumption at 19.83 years as a mean (SD: 4.1). In relationship with other substances, 44.2% consumed cannabis regularly, 59.2% benzodiazepines and 50.6% alcohol.

Retention for all the patients at one year of initiating therapy was 29.75%. Likelihood of survival in treatment with naltrexone for men was 30.92%, the value for the same parameter for women being 23.97% (table 1 and fig. 1). This difference in the likelihood of survival (retention) at one year is significant according to the Mantel-Cox test (statistics: 8.38; gl: 1; sign: 0.0038).

As seen in table 2 there are relevant differences regarding the characteristics of consumption according to the consumer's gender (whether man or woman). Thus, regarding the toxicological variables, women have less frequency of cocaine consumption (55.1% vs 64.5%; p = 0.011), less use of the intravenous route for cocaine consumption (50.9% smoked vs 38.9% inhaled; p = 0.048), lower frequency of alcohol consumption (49.4% vs 66.5%; p = 0.000), lower frequency of cannabis consumption (34% vs 46%; p = 0.002), less time of heroin consumption (58% less than 7 years 49% of men less than 7 years; p = 0.016), greater proportion of women who only consumed heroin (10.5% vs 5.6%; p = 0.015), with tendency to less use of intravenous route of heroin during the addictive period (20% vs 54%; p = 0.065) and to present a younger age of onset of treatment (26.9% vs 28.4%; p = 0.049). Regarding the relevant differences for the setting and social support according to gender of the addict, we found that women were less frequently single (59.4% vs 72.8%; p = 0.000), had lower proportion of non-qualified work (19.4% vs 46.8%; p = 0.000), and, to a greater degree, we unemployed without unemployment benefits (60.3% vs 47.2%; p = 0.001), had a

Table 1 Survival at one years based on gender factor

	Survival at one year	Median	95% CI
Male	30.92%	164	146.98-181.02
Female	23.97%	119	87.38-150.62

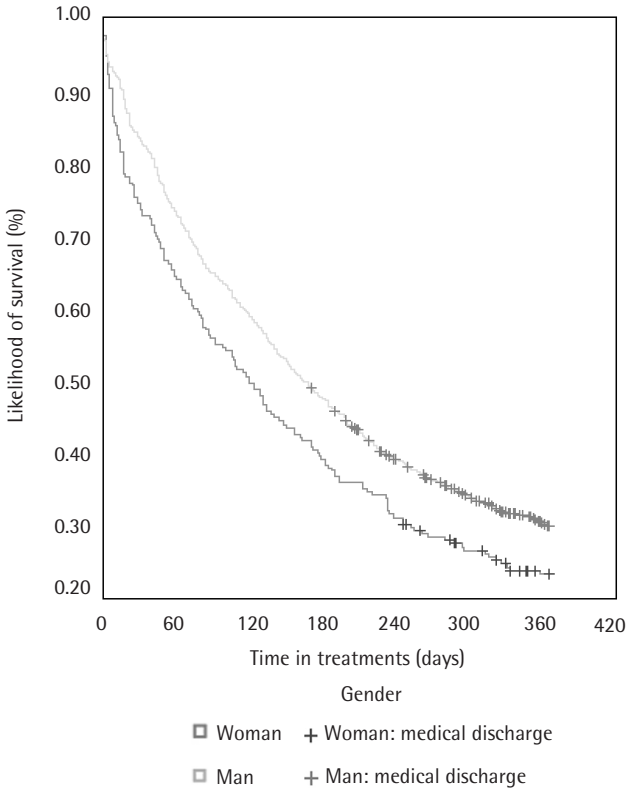

Figure 1 *Survival curves based on gender.*

greater percentage of studies than the male (80% vs 73.3% has completed or passed obligatory basic studies; p=0.044), more frequently had an addict partner (43% vs 10%; p=0.000), and had less support of non-consuming partner (22% vs 35.5%; p=0.000).

DISCUSSION

In spite of the considerable size of the sample and the prolonged duration of the follow-up, the absence of a control group can be criticized methodologically. However, the review of similar studies show that this defect is almost inevitable in this type of study because of methodological, ethical and political-health care reasons. It also must be remembered that the results come from a sample of patients who were exclusively treated with naltrexone. The patients in this study come from several areas of Madrid, but are grouped into a drug addict clinic of a single hospital. The prolongation of the study in time supposes including profile and patterns of difference consumptions, marked partly by successive health care policies, sometime different. This offers heterogeneity to the sample.

The possibility of generalizing the results requires the user profile to be representatives of the most extensive population of heroin addicts possible. The profile of the subjects presented herein regarding gender, age, consumption variables and those related with their social situations coincide in the most important with the data reported by other publications of the setting[6,9,14,15,36,40,75,76], so that the conclusions may be valid for at least the national setting.

In our study, it is confirmed that women have less likelihood of survival at one year in treatment than the men (24% vs 31%). The gender factor, therefore, establishes different evolution in the therapy of opiate dependency. Thus, men have better prognosis than women in the population studied.

When the differences are evaluated compared with the men, we found that women have differences in two fields: in the consumption characteristics and in the support and social situation.

Regarding the characteristics of the consumption, women from our sample have less consumption of cocaine with less use of the intravenous route, less consumption of alcohol and less multiple drug addictions together with less time of heroin consumption when initiating treatment for their addiction. All these characteristics are as indicated in the literature markers of good prognosis, given that prolonged addictions and high doses of heroin[27], alcohol consumption[41-44], and mainly cocaine consumption[53-55,57] are related with worse therapeutic outcome.

From all the differences found between both genders, those regarding setting and social support are relevant. The literature indicates that work stability[27,58], professional level[63,64] and family stability and involvement[59-62] are predictors of good outcome.

On the other hand, presence of a drug dependent mate is fundamental in the identify of gender and an essential component to explain the first contact with the substance. After, the addict woman is more frequently linked to a drug addict partner. The first consumptions of heroin occur together with the partner in most of the women, these being the inductors or modifying the perception towards consumption. The influence of the drug dependent partner on relapses in consumption in the woman is very important[66,77,78].

Female heroin addicts are characterized by greater marginality than men. They frequently have an association with a man who helps them acquire the drug or they may end up dedicating themselves to marginal activities such as prostitution. These women have greater access to drugs and more problems linked to the addiction in general with great precariousness and degradation in their life. Furthermore, they delay initiation of treatment and when they do begin, it is more difficult to do it because they must first get rid of the negative attitude baggage they are carrying[4,78].

The women in our sample have greater work instability and low personal qualification, together with important economical dependence on others as that described by

Table 2 Differences in gender in the significant variables with chi squared and significance

	Man (n = 1,190)	Woman (n = 242)	Chi	Sig		Varón (n = 1.190)	Mujer (n = 242)	Chi	Sig
Current heroin consumption route			6.377	0,015	More than 15 years	78	7		
IV route	524	95			NA/DNK	38	11		
Smoked/inhaled	636	136			Studies			4.066	0,044
NA/DNK	30	11			Primary studies	279	41		
Previous route of heroin consumption			3.484	0,065	Graduate or more	765	164		
IV route	429	65			NA/DNK	146	37		
Smoked/inhaled	499	104			Profession			51.256	0,000
NA/DNK	262	73			Without progression	48	26		
Cocaine consumption			6.823	0,011	Workman	387	28		
No	374	97			Starte worker, liberal	392	90		
Yes	680	119			NA/DNK	363	98		
NA/DNK	136	26			Work situation			16.944	0,001
Cocaine consumption route			6.082	0,048	Yes, stable	221	22		
IV + heroin IV	350	49			Yes, unstable	202	33		
IV + smoked heroin	38	7			Unemployed with benefits	166	32		
Smoked/inhaled	247	58			Unemployed wihtout benefits	526	132		
NA/DNK	45	5			NA/DNK	75	23		
Cannabis consumption			9.213	0,002	Civil status			23.137	0,000
No	510	119			Single	820	139		
Yes	437	61			Married	206	52		
NA/DNK	243	62			Others	90	43		
Alcohol consumption			16.519	0,000	NA/DNK	74	8		
No	252	80			Partner			19.831	0,000
Yes, prior to opiates	98	19			No partner	633	81		
Yes	402	59			Non-consuming partner	350	42		
NA/DNK	438	84			Consuming partner	110	96		
Consumption time			8.000	0,016	NA/DNK	99	22		
Less than 7 years	576	136			Support of non-copnsuming partner			4.046	0,000
From 7 to 15 years	492	88			No apoyo	617	160		
					Apoyo	340	45		
					NA/DNK	233	37		

NA: no answer; DNK: does not know.

others[4,66]. Women have less social independence and greater economic dependence in spite of their better educations level and work qualification and initiate consumption through their partners. With greater frequency, they have abandoned the family home and do not have non-consuming partners. Furthermore, more frequently than in the case of men, the woman's partner is a consumer, so that women count on less support for the treatment. Men have more support in their therapeutic attempts from non-consuming partners. The dependent person has important difficulties to abandon consumption if their partner continues to consume drugs. There are more women who live with or are married to a drug-dependent partner than men.

There are the factors, that of less support and worse social situation, that determine the worse prognosis that the women have in the treatments of the addictions.

CONCLUSIONS

Gender of the heroin dependent subjects significantly conditions the response to treatment of their dependence.

Thus, women have worse prognosis than men in the population studied.

The consumption pattern of women is different from that of the men, with less cocaine consumption and less use of the intravenous route, less alcohol consumption and fewer multiple drug addictions together with less time of heroin consumption on initiating treatment for their addiction. These variables should condition a better prognosis, but they do not do so.

The variables related with social independence (work situation, economic independence, etc.) condition the differences between the genders, making the woman depend economically more than the man on her partner or others. Women more frequently have a consuming partner, which significantly conditions her evolution.

Thus, being a women means less social independence (economic dependence on the social setting), less support from the family of origin and less likelihood of having a non-consuming partner as support in the treatment.

It is these factors that determine the worse prognosis that women have in the treatment of the addiction.

REFERENCES

1. Stocco P, Llopis JJ, DeFazio L, Calafat A, Mendes F. Women drug abuse in Europe: gender identity. Venice: Irefrea, 2000.
2. Fundación Instituto Spiral. I Symposium Nacional sobre el Tratamiento de la Adicción en la Mujer. Madrid: Debate e Instituto de la Mujer, 2002.
3. Rodríguez E. Perspectiva de género en los problemas de drogas y su impacto. Fundación Instituto Spiral. I Symposium Nacional sobre el Tratamiento de la Adicción en la Mujer. Madrid: Debate e Instituto de la Mujer, 2002; p. 24-7.
4. Llopis JJ, Rebollida M. Clínica de la mujer toxicómana. Un análisis de actitudes. Fundación Instituto Spiral. I Symposium Nacional sobre el Tratamiento de la Adicción en la Mujer. Madrid: Debate e Instituto de la Mujer, 2002; p. 156-72.
5. Morales E, Sánchez Hervás E, Tomás, V. Abuso y dependencia a drogas en la mujer. Conductas Adictivas 2003;3:49-50.
6. Agencia Antidroga. Comunidad de Madrid. Memoria 2005. Madrid, 2006.
7. Plan Nacional sobre Drogas. Encuesta estatal sobre uso de drogas en enseñanzas secundarias 2004. Ministerio de Sanidad y Consumo, 2005.
8. Observatorio Europeo de las Drogas y las Toxicomanías (OEDT). Lisboa, 2006.
9. Observatorio Español sobre Drogas (OED). Plan Nacional sobre Drogas. Informe n.º 6. Madrid, 2003.
10. CND. Situación mundial del tráfico de drogas. Informe de la Secretaría de Comisión de Estupefacientes de Consejo Económico y Social de las Naciones Unidas. Viena, 2007.
11. SAMHSA. Oficina de Estudios Aplicados. National Survey on Drug Use on Health, 2004.
12. National Institute on Drug Abuse. Gender differences in drug abuse risk and treatment. NIDA Notes. National Institute on Drug Abuse. US Department of Health and Human Services, 2000.
13. National Institute on Drug Abuse. Advances in research on women's health and gender differences. National Institute on Drug Abuse. US Department of Health and Human Services, 2002.
14. Carreño JE, Bobes J, Brewer C, Álvarez CE, San Narciso GI, Bascarán MT, et al. 24 hour opiate detoxification an antagonist induction at home- the «Asturian Method»: a report on 1368 procedures. Addict Biol 2002;7:243-50.
15. Madoz-Gúrpide A, Barbudo E, Leira M, Navío M, Villoria L, Ochoa E. Características de la adicción como factor pronóstico en el tratamiento de la dependencia de opiáceos. Actas Esp Psiquiatr 2004;32:199-210.
16. Brewer C, Streel E. Implantes de naltrexona: un avance terapéutico tanto comportamental como farmacológico. Adicciones 2003;15:299-308.
17. Arias F, Ochoa E. Retención en los programas de deshabituación con naltrexona. In: Ochoa Mangado E, editor. Antagonistas opiáceos en las dependencias. Clínica de la naltrexona. Col. Psiquiatría 21. Barcelona: Ars Medica. Psiquiatría Editores, 2001; p. 83-94.
18. Ling W, Wesson DR, Charuvastra C, Klett CJ. A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. Arch Gen Psychiatry 1996;53:401-7.
19. Rounsaville BJ, Weissman MM, Kleber HD. The significance of alcoholism in treated opiate addicts. J Nerv Ment Dis 1982;170: 479-88.
20. Simpson DD, Joe GW, Lehman WE, Sells SB. Addiction careers: etiology, treatment and 12 year follow-up outcomes. J Drug Issues 1986;16:107-21.
21. Ochoa E, Arias F, Somoza JC, López-Ibor JJ. Tratamiento con naltrexona en dependientes de opiáceos: dos años y medio de seguimiento. Arch Neurobiol 1992;55:224-7.
22. Capone T, Brahen L, Condren R, Kordal N, Melchionda R, Peterson M. Retention and outcome in a narcotic antagonist treatment program. J Clin Psychol 1986;42:825-33.
23. Iguchi MY, Stitzer ML. Predictors of opiate drug abuse during a 90 day methadone detoxification. Am J Drug Alcohol Abuse 1991;17:279-94.
24. Simpson DD, Savage LJ, Lloyd MR. Follow-up evaluation of treatment of drug abuse during 1969 to 1972. Arch Gen Psychiatry 1979;36:772-80.
25. Resnick RB, Washton AM, Thomas MA, Kestenbaum RS. Naltrexone in the treatment of opiate dependence. Int Chall Drug Abuse 1978;32:321-32.
26. Babst DV, Chambers CD, Warner A. Patient characteristics associated with retention in a methadone maintenance program. Br J Addict 1971;66:195-204.
27. Bedate J, Bobes J, Ochoa E, Solé J. Evaluación del tratamiento de los heroinómanos con naltrexona. Estudio multicéntrico. Avances en drogodependencias. Barcelona: Ediciones en Neurociencias 1995; p. 129-60.
28. Newman RG. Methadone treatment. Defining and evaluation success. N Eng J Med 1987;317:447-50.
29. Iguchi MY, Stitzer ML. Predictors of opiate drug abuse during a 90 day methadone detoxification. Am J Drug Alcohol Abuse 1991;17:279-94.

30. Oppenheimer E, Stimson GV, Thorley A. Seven-year follow-up of heroin addicts: abstinence and continued use compared. Br Med J 1979;2:627-30.
31. Del Río M, Mino A, Perneger TV. Predictors of patient retention in a newly established methadone maintenance treatment programme. Addiction 1997;92:1353-60.
32. Comas Arnau D, García Martín E, Roldán Inchusta G. Políticas sobre drogas a partir de los resultados de un estudio longitudinal retrospectivo de adictos a la heroína (1982-1992). Adicciones 1996;8:75-89.
33. Hser YI, Hoffman V, Grella CE, Anglin MD. A 33-year follow-up of narcotics addicts. Arch Gen Psychiatry 2001;58:503-8.
34. Resnick R, Aronoff M, Lonborg G. Clinical efficacy of naltrexone: a one year follow up. NIDA Res Monogr 1976:114-7.
35. Apodaca I, Montejo E, Lejardi N, Moreno A, Aresti A, Duque J, et al. Características de los toxicómanos que no inician o interrumpen tempranamente el tratamiento. Adicciones 1995;7:159-67.
36. Elizarárate E, Gutiérrez M, Fernández C, Figuerido JL, González-Pinto A, Jiménez JM. Antagonización rápida de opiáceos: eficacia en una muestra de 91 pacientes. Psiquiatría.com (electronic journal) 1998 december (cited 05/05/03);2(4):(27 screens). URL: http://www.psiquiatria.com/psiquiatria/vol2num4/art_4.htm.
37. Resnick RB, Washton AM. Clinical outcome with naltrexone. Ann NY Acad Sci 1978;311:241-46.
38. Shufman EN, Porat S, Witztum E, Gandacu D, Bar Hamburger R, Ginath Y. The efficacy of naltrexone in preventing reabuse of heroin after detoxification. Biol Psychiatry 1994 15;35:935-45.
39. Sansone J. Retention patterns in a therapeutic community for the treatment of drug abuse. Int J Addict 1980;15:711-36.
40. Landabaso MA, Fernández B, Sanz J, Ruíz de Apodanca J, Pérez B, Gutiérrez-Fraile M. Estudio de la evolución (1990-1993) de adictos a opiáceos en programas de antagonistas. Adicciones 1996;8:67-74.
41. Senay EC. Methadone maintenance treatment. Int J Addict 1985;20:803-21.
42. Simpson DD, Joe GW, Lehman WE, Sells SB. Addiction careers: etiology, treatment and 12 year follow-up outcomes. J Drug Issues 1986;16:107-21.
43. Rounsaville BJ, Weissman MM, Kleber HD. The significance of alcoholism in treated opiate addicts. J Nerv Ment Dis 1982;170: 479-88.
44. Joe GW, Lloyd MR, Simpson DD, Singh BK. Recidivism among opioid ad-dicts after drug treatment: an analysis by race and tenure in treatment. Am J Drug Alcohol Abuse 1982;9:371-82.
45. Maddux JF, Desmond DP. Residence relocation inhibits opioid dependence. Arch Gen Psychiatry 1982;39:1313-7.
46. Darke S, Hall W. Levels and correlates of polydrug use among heroin users and regular amphetamine users. Drug Alcohol Depend 1995;39:231-5.
47. Kiddorf M, Brooner RK, King VL, Chutuape MA, Stitzer ML. Concurrent validity of cocaine and sedative dependence diagnoses in opioid-dependent outpatients. Drug Alcohol Depend 1996; 42:117-23.
48. San Narciso GI, Carreño JE, Pérez SF, Alvarez CE, González MP, Bobes J. Evolución de los trastornos de personalidad evaluados mediante el IPDE en una muestra de pacientes heroinómanos en tratamiento con naltrexona. Adicciones 1998;10:7-21.
49. Hobfoll SE, Segal B. A factor analytic study of the relation-ship of experience seeking and trait anxiety to drug use and reasons for drug abuse. Int J Addict 1983;18:448-9.
50. Strug DL, Hunt DE, Goldsmith DS, Lipton DS, Spunt B. Pat-terns of cocaine use among methadone clients. Int J Addict 1985;20:1163-75.
51. Nurco DN. A long term program of research on drug use and crime. Subst Use Misuse 1998;33:1817-37.
52. Greenfield L, Brady JV, Besteman KJ, De Smet A. Patient retention in mobile and fixed-site methadone maintenance treatment. Drug Alcohol Depend 1996;42:125-31.
53. Broers B, Giner F, Dumont P, Mino A. Inpatient opiate detoxification in Geneva: follow-up at 1 and 6 months. Drug Alcohol Depend 2000;58:85-92.
54. Hanbury R, Sturiano V, Cohen M, Stimmel B, Aguillaume C. Cocaine use in persons on methadone maintenance. Adv Alcohol Subst Abuse 1986;6:97-106.
55. Nurco DN, Hanlon TE, Kinlock TW, Duszynski KR. Differential criminal patterns of narcotic addicts over an addiction career. Criminology 1988b;26:407-23.
56. Torrens M, San L, Peri JM, Olle JM. Cocaine abuse among heroin addicts in Spain. Drug Alcohol Depend 1991;27:29-34.
57. Ochoa E, Arias F, Somoza JC, López-Ibor JJ. Tratamiento con naltrexona en dependientes de opiáceos: dos años y medio de seguimiento. Arch Neurobiol 1992;55:224-7.
58. Washton AM, Pottash AC, Gold MS. Naltrexone in addicted business executives y physicians. J Clin Psychiatry 1984;45:4-6.
59. Arias F, López-Ibor JJ, Ochoa E. Predictores evolutivos en un programa de mantenimiento con Naltrexona. Adicciones 1996;8:479-500.
60. Ochoa E, Cebollada A, Ibañez A. Implicación familiar como predictor en un tratamiento de mantenimiento con antagonistas opiáceos. Adicciones 1994;6:51-60.
61. Madanes J, Dukes J, Harbin H. Family ties of heroin addicts. Arch Gen Psychiatry 1980;37:889-94.
62. Kaufman E. Family systems y family therapy of substance abuse: An overview of two decades of research y clinical experience. Int J Addict 1985;20:897-916.
63. Ling W, Wesson DR. Naltrexone treatment for addicted healthcare professionals: a collaborative private practice experience. J Clin Psychiatry 1984;45:46-8.
64. Washton AM, Pottash AC, Gold MS. Naltrexone in addicted business executives y physicians. J Clin Psychiatry 1984;45:4-6.
65. Brewer DD, Catalano RF, Haggerty K, Gainey RR, Fleming CB. A meta-analysis of predictors of continued drug use during y after treatment for opiate addiction. Addiction 1998;93:73-92.
66. Crone B. Gender differences in substance misuse and psychiatric Comorbidity. Current Opinion Psychiatry 1997;10:194-8.
67. Ochoa E, Madoz-Gúrpide A. Situación actual de los programas con naltrexona en la dependencia de opiáceos. Revisión de su efectividad. Adicciones 2005;17(Suppl. 2):223-34.
68. Clasificación Internacional de Enfermedades. Décima revisión. Trastornos mentales y del comportamiento. Descripciones clínicas y pautas para el diagnóstico. Madrid: Meditor, 1993.
69. Baca-García E, García A, Ochoa E. Historia psiquiátrica estructurada en la interconsulta hospitalaria a toxicomanías/sida. Rev Esp Drogodepend 1999;2481:60-70.
70. Baca-García E, Madoz-Gúrpide A. Protocolos de recogida de datos en una unidad de toxicomanías con «clínica de naltrexona». In: Ochoa Mangado E, editor. Antagonistas opiáceos en las de-

pendencias. Clínica de la Naltrexona. Col. Psiquiatría 21. Barcelona: Ars Medica. Psiquiatría Editores, 2001; p. 135-54.
71. Allgulander C, Fisher LD. Survival analysis (or time to an event analysis), and the Cox regression model-methods for longitudinal psychiatric research. Acta Psychiatr Scand 1986;74:529-35.
72. Juez Martel P, Díez Vegas FJ. Probabilidad y estadística en medicina. Madrid: Díaz de Santos, 1996.
73. Nordstrom P, Samuelsson M, Asberg M. Survival analysis of suicide risk after attempted suicide. Acta Psychiatr Scand 1995; 91: 336-40.
74. Ferrán Aranaz M. SPSS para Windows. Programación y análisis estadístico. Madrid: McGraw-Hill, 1997.
75. Fernández Miranda JJ. Efectividad de los programas de mantenimiento con metadona. Una revisión de los resultados de los estudios de evaluación. Med Clin 2001;116:150-4.
76. Landabaso MA, Fernández B, Sanz J, Ruíz de Apodanca J, Pérez B, Gutiérrez-Fraile M. Estudio de la evolución (1990-1993) de adictos a opiáceos en programas de antagonistas. Adicciones 1996;8:67-74.
77. Torre M, Balboa A, Ayesta F. Situación de la mujer dependiente de la heroína en Cantabria: análisis de los resultados del estado de las pacientes en la última década. Comunicación presentada en el I Symposium sobre Tratamiento de la Adicción en la Mujer. Madrid: Instituto Spiral, 2000.
78. Orte C. Sexualidad en la mujer adulta. Fundación Instituto Spiral. I Symposium Nacional sobre el Tratamiento de la Adicción en la Mujer. Madrid: Debate e Instituto de la Mujer, 2002; p. 30-40.
79. Crone B. Gender differences in substance misuse and psychiatric comorbidity. Curr Opin Psychiatry 1997;10:194-8.