

Heroin Addiction and Related Clinical Problems



Periodico trimestrale - Sped. in Abb. Post. - D.L. 353/2003 conv. in L. 27/02/2004 n° 46 art. 1, comma 1, DCB PISA - Aut. tirb. di Pisa n.5 del 9-3-2000

the official journal of



Europad

EUROPEAN OPIATE ADDICTION TREATMENT ASSOCIATION

EUROPAD, formerly EUMA, was founded in Geneva (Switzerland) on September 26, 1994. It shall remain independent of political parties and of any government.

The vision

EUROPAD exists to improve the lives of opiate misusers and their families and to reduce the impact of illicit drug use on society as a whole. The Association works to develop opiate addiction treatment in Europe but also aims to make a major contribution to the knowledge of, and attitudes to, addiction treatment worldwide.

BOARD OF DIRECTORS

Icro Maremmani	President	Pisa, Italy
Marc Reisinger	Vice-President	Brussels, Belgium
Andrej Kastelic	General Secretary	Ljubljana, Slovenia

Oleg Aizberg, Minsk, Belarus
Michael Arieli, Jerusalem, Israel
Marc Auriacombe, Bordeaux, France
Safet Blakaj, Pristina, Kosovo
Olof Blix, Jönköping, Sweden
Pascal Courty, Clermont Ferrand, France
Jean Jacques Deglon, Geneva, Switzerland
Sergey Dvoriak, Kiev, Ukraine
Michael Farrell, London, UK
Gabriele Fischer, Vienna, Austria
Milazim Gjocaj, Pristina, Kosovo
Martin Haraldsen, Sandefjord, Norway
Liljana Ignjatova, Skopje, Macedonia
Ante Ivancic, Porec, Croatia
Nikola Jelovac, Split, Croatia
Minja Jovanovic, Kragujevac, Serbia
Euangelos Kafetzopoulos, Athens, Greece
Alexander Kantchelov, Sofia, Bulgaria
Sergey Koren, Moscow, Russia
Alexander Kozlov, Moscow, Russia
Gunnar Kristiansen, Oslo, Norway
Mercedes Lovrecic, Ljubljana, Slovenia
Nermana Mehic-Basara, Sarajevo, Bosnia and Herzegovina

Haim Mell, Jerusalem, Israel
Vladimir Mendeleovich, Kazan, Russia
Genci Mucullari, Tirana, Albania
Lubomir Okruhlica, Bratislava, Slovak Republic
Matteo Pacini, Pisa, Italy
Pier Paolo Pani, Cagliari, Italy
Luis Patricio, Lisbon, Portugal
Tijana Pavicevic, Podgorica, Montenegro
Paul Quigley, Dublin, Ireland
Marina Roganovic, Kotor, Montenegro
Rainer Schmid, Vienna, Austria
Aneta Spasovska Trajanovska, Skopje, Macedonia
Karina Stainbarth-Chmielewska, Warsaw, Poland
Marlene Stenbacka, Stockholm, Sweden
Emilis Subata, Vilnius, Lithuania
Marta Torrens, Barcelona, Spain
Didier Touzeau, Paris, France
Albrecht Ulmer, Stuttgart, Germany
Peter Vossenbergh, Deventer, The Netherlands
Nikola Vuckovic, Novi Sad, Serbia
Helge Waal, Oslo, Norway
Stephan Walcher, Munich, Germany
Wojciech Rudalski, Warsaw, Poland

Editorial Board

Editor

Icro Maremmani "Santa Chiara" University Hospital, Department of Psychiatry, University of Pisa, Italy, EU

Associate Editor

Pier Paolo Pani Social Health Division, Health District 8 (ASL 8), Cagliari, Italy, EU

International Advisory Board

Hannu Alho National Public Health Institute (KTL), University of Helsinki, Finland, EU
Marc Auriacombe Université Victor Segalen, Bordeaux 2, France, EU
James Bell Langton Centre, Sydney, Australia
Olof Blix County Hospital Ryhov, Jönköping, Sweden, EU
Barbara Broers University Hospital of Geneva, Switzerland
Miguel Casas University Hospital of "Vall d'Hebron" - University of Barcelona, Spain, EU
Michael Farrell King's College, University of London, UK, EU
Loretta Finnegan National Institutes of Health, Bethesda, ML, USA, [Retired]
Gabriele Fischer University of Vienna, Vienna, Austria, EU
Gilberto Gerra United Nations Office on Drugs and Crime, Vienna
Gian Luigi Gessa University of Cagliari, Italy, EU, [Emeritus]
Michael Gossop King's College, University of London, UK, EU
Leift Grönbladh University Hospital of Uppsala, Sweden, EU
Lars Gunne University of Uppsala, Sweden, EU, [Emeritus]
Andrej Kastelic Center for Treatment of Drug Addiction, University Hospital, Ljubljana, Slovenia, EU
Michael Krausz St.Paul's Hospital, University of British Columbia, Canada
Mary Jane Kreek The Rockefeller University, New York, USA
Mercedes Lovrecic Institute of Public Health of the Republic of Slovenia, Ljubljana, Slovenia, EU
Joyce Lowinson Albert Einstein College of Medicine, The Rockefeller University, New York, USA, [Emeritus]
Robert Newman Baron de Rothschild Chemical Dependency Institute, Beth Israel Medical Center, New York, NY, USA
Charles P. O'Brien University of Pennsylvania, Philadelphia, USA
Lubomir Okruhlica Centre for Treatment of Drug Dependencies, Bratislava, Slovak Republic, EU
Mark Parrino American Association for the Treatment of Opioid Dependence, New York, USA
Giulio Perugi Department of Psychiatry, University of Pisa, Italy, EU
Marc Reisinger European Opiate Addiction Treatment Association, Brussels, Belgium, EU
Marlene Stenbacka Karolinska Institute, Stockholm, Sweden, EU
Alessandro Tagliamonte University of Siena, Italy, EU
Marta Torrens University of Barcelona, Spain, EU
Ambros Uchtenhagen Research Foundation on Public Health and Addiction, Zurich University, Switzerland
Helge Waal Center for Addiction Research (SERAF), University of Oslo, Norway, [Emeritus]
George Woody University of Pennsylvania, Philadelphia, USA

Editorial Coordinators

Marilena Guareschi

Association for the Application of Neuroscientific Knowledge to Social Aims, AU-CNS, Pietrasanta, Lucca, Italy, EU

Matteo Pacini

"G. De Lisio" Institute of Behavioural Sciences, Pisa, Italy, EU

Publishers

Association for the Application of Neuroscientific Knowledge to Social Aims, AU-CNS
Not for profit Agency

"From science to public policy"

Via XX Settembre, 83 - 55045 Pietrasanta, Lucca, Italy, EU

Phone +39 0584 790073 - Fax +39 0584 72081 - E-mail: info@aucns.org

Internet: <http://www.aucns.org>

Pacini Editore

Via A. Gherardesca - 56121 Ospedaletto, Pisa, Italy, EU

Phone +39 050 313011 - Fax +39 050 3130300 - E-mail: Pacini.Editore@pacinieditore.it

Internet: <http://www.pacinieditore.it>

Cited in:

EMBASE Excerpta Medica Database

SCOPUS

EMCave

Social Sciences Citation Index (SSCI) - Thomson Reuters

Free download at:

<http://www.atforum.com/europad.html>

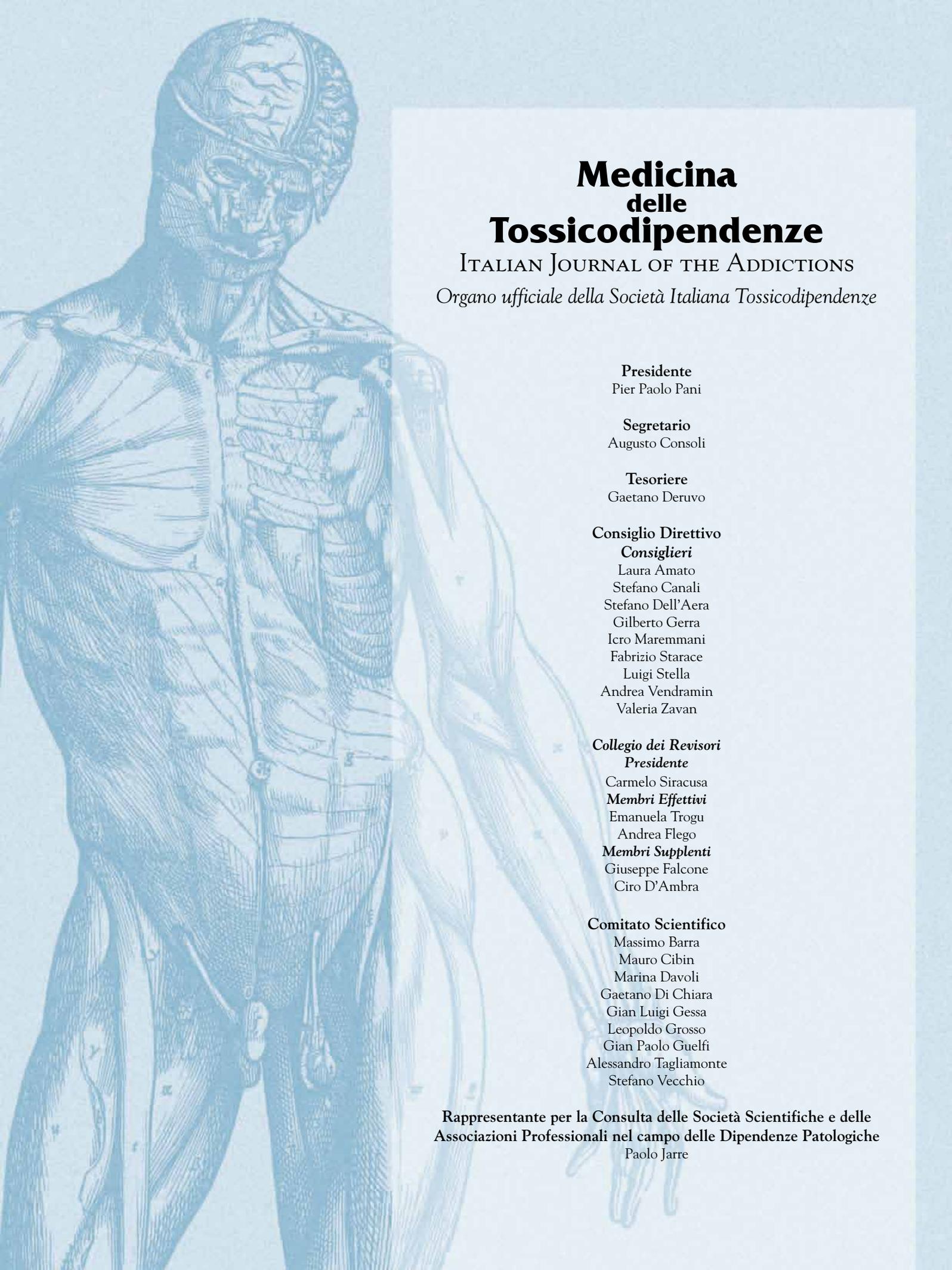
http://pain-topics.org/opioid_rx/europad.php

Open Access at:

<http://www.europad.org>

CONTENTS

Tobacco smoking prevalence in a large sample of heroin users accessing rehabilitation <i>Benedetta Pajusco, Antonio Boschini, Cristiano Chiamulera, Marco Begnini, Camillo Smacchia and Fabio Lugoboni.</i>	5
Housing and employment situation, body mass index and dietary habits of heroin addicts in methadone maintenance treatment <i>Daniela Alves, Ana Filipa Costa, Daniela Custódio, Liliana Natário, Vera Ferro-Lebres and Fernando Andrade</i>	11
Effect of valproate on benzodiazepine withdrawal severity in opioid-dependent subjects: a pilot study <i>Helena Vormaa and Heikki Katila</i>	15
Opioid addiction complicated by alcoholism (in young men) <i>Lev N. Blagov and Dmitry I. Kurgak</i>	21
Dual Diagnosis (Comorbidity): A growing diagnostic and treatment issue in the psychiatric and substance use programmes in the Republic of Macedonia <i>Ivan G. Tulevski</i>	29
Does cannabis have therapeutic benefits for withdrawing opioid addicts? <i>Marcel Peloquin, Lacey R. Peters, Megan E. McLarnon and Sean P. Barrett</i>	35
Is it time for new studies on the level of insight in heroin addicts to promote compliance with methadone treatment? <i>Luca Rovai and Angelo Giovanni Icro Maremmani</i>	37



Medicina delle Tossicodipendenze

ITALIAN JOURNAL OF THE ADDICTIONS

Organo ufficiale della Società Italiana Tossicodipendenze

Presidente

Pier Paolo Pani

Segretario

Augusto Consoli

Tesoriere

Gaetano Deruvo

Consiglio Direttivo

Consiglieri

Laura Amato

Stefano Canali

Stefano Dell'Aera

Gilberto Gerra

Icro Maremmani

Fabrizio Starace

Luigi Stella

Andrea Vendramin

Valeria Zavan

Collegio dei Revisori

Presidente

Carmelo Siracusa

Membri Effettivi

Emanuela Trogu

Andrea Flego

Membri Supplenti

Giuseppe Falcone

Ciro D'Ambrà

Comitato Scientifico

Massimo Barra

Mauro Cibir

Marina Davoli

Gaetano Di Chiara

Gian Luigi Gessa

Leopoldo Grosso

Gian Paolo Guelfi

Alessandro Tagliamonte

Stefano Vecchio

**Rappresentante per la Consulta delle Società Scientifiche e delle
Associazioni Professionali nel campo delle Dipendenze Patologiche**

Paolo Jarre



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2011; 13(1): 5-10

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Tobacco smoking prevalence in a large sample of heroin users accessing rehabilitation

Benedetta Pajusco¹, Antonio Boschini², Cristiano Chiamulera³, Marco Begnini², Camillo Smacchia² and Fabio Lugoboni¹.

1 Department of Internal Medicine, Medical Unit for Addictive Disorders, University of Verona, Policlinico GB Rossi, Verona, Italy, EU

2 San Patrignano Medical Centre, Coriano, Rimini, Italy, EU

3 Neuropsychopharmacology Laboratory, Section of Pharmacology, Department of Medicine and Public Health, University of Verona, Italy, EU

Summary

Although there is a large amount of anecdotal evidence about the association between heroin abuse and tobacco smoking, there have been only a few epidemiological studies. The present report is a cross-sectional survey on tobacco smoking in heroin users. The sample included 10,530 drug users accessing the *Comunità di San Patrignano* during the time period 1st January 1980 to 1st May 2007. Heroin-addicted subjects ($n = 10,181$) were not receiving any type of substitution or detoxification therapy. Tobacco smoking prevalence in the heroin-addicted group was 99.2% (10,095 out of 10,181 subjects). In the large sample of heroin users observed in the present study, this confirms the anecdotal report that most heroin users are smokers.

Key Words: Tobacco addiction; Heroin addiction; Smoking

1. Introduction

Although there is a large amount of anecdotal evidence about the association between drug abuse and tobacco smoking, only a few data have been made available so far on the prevalence of tobacco addiction among current heroin users, probably due to a low degree of compliance with structured interviews or to the presence of other factors, such as concomitant drug therapy, in data pooled in the setting of large epidemiological studies. To date, most of the available data on the association between tobacco and opiate addiction have been obtained from heroin addicts in methadone maintenance, who showed a high prevalence (80-95%) of smoking (1-3,7). To our knowledge, no data have been reported so far on smoking prevalence in heroin addicts who are not in

treatment for opiate dependence.

The present report is a cross-sectional survey on tobacco smoking; it was carried out in a large sample of heroin addicts not under treatment for opiate dependence. The aim of the study is to describe the prevalence of smoking in untreated heroin users who accessed the largest European residential drug-rehabilitation community, the *Comunità di San Patrignano*, Italy, during the period 1980-2007.

2. Methods

2.1 Design of the study

The present report is a cross-sectional survey on tobacco smoking.

Correspondence: Benedetta Pajusco, MD; Department of Internal Medicine, Addiction Unit, University of Verona, Policlinico GB Rossi, 37134 Verona, Italy.

Phone: +39 045 8128291; Fax: +39 045 8128290; E-mail: bene17@live.it

2.2 Subjects

The sample included 10,530 subjects admitted into the Comunità di San Patrignano during the time period 1st January 1980 to 1st May 2007. Heroin-addicted subjects (n = 10,181) were without any type of substitution or detoxification therapies. In fact, the policy of the Comunità di San Patrignano does not require a status of drug abstinence or ongoing detoxification therapy at the time of admission into the community. This policy made it possible to meet the inclusion criteria of 'untreated heroin user' for all the subjects admitted into the Comunità. An on-site hospital was present for the management of acute withdrawal syndrome whenever necessary. The Comunità di San Patrignano does not admit subjects with a diagnosis of neuropsychiatric disorders.

There were more male subjects (n = 8,489; 80.6%) than female ones (n = 2,041; 19.4%). The mean age for all subjects was 28.2 years (SD = 6.2 years). Table 1 shows their characteristics.

2.3 Data collection

Demographics, educational level (8), heroin (daily, non-daily) and other drugs of abuse being used, and tobacco smoking status (smoker, non-smoker) data were collected from an admission log compiled when subjects were admitted into the Comunità during the time period 1st January 1980 to

1st May 2007. For subjects that accessed the Comunità more than once, only data from the first admission were recorded. Non-heroin addicted subjects were mostly cocaine addicts (n = 321/349 subjects; 92%).

2.4 Statistical Analysis

Gender, educational level, heroin use (daily, non-daily), other drug of abuse use, and smoking (smoker, non smoker) status were compared by bivariate statistical analysis with the Chi-square test, or with Fisher's exact test. Comparisons between age or duration of drug use with smoking status (smoker/non smoker) were carried out with Student's t-test. Multivariate analysis was performed by using a logistic regression model with smoking status as dependent variable (non smoker; smokers). Alpha was set at 0.05 (two-tailed) for all statistical analyses, which were conducted using SPSS 11.5 statistical software. (SPSS 11.5, SPSS Inc., Chicago, IL).

3. Results

Of the sample of 10,530 subjects, 10,428 (99.0%) reported current smoking status. No statistically significant differences in current smoking status prevalence were detected between males (8,412 out of 8489; 99.1%) and females (2,016 out of 2,041; 98.8%). Smoking prevalence across years of access to the Comunità di San Patrignano was not statistically significant, with an average of 99.2%

Table 1. Demographics, data for heroin (daily/non-daily) and other drugs of abuse use, history of drug use, route of substance administration and, smoking (smoker; non-smoker) status of study sample.

	Total N (%)
Subjects	10530
Mean Age in years (\pm SD)	28.2 \pm 6.2
Gender	
Males	8489 (80.6)
Females	2041 (19.4)
Education	
Primary education	1042 (9.9)
Lower secondary education	6756 (64.2)
Upper secondary education	1998 (19.0)
First stage of tertiary education	86 (0.8)
Unknown data	648 (6.2)
Primary substance of abuse	
Cocaine	321 (3.0)
Other	28 (0.3)
Heroin	10181 (96.7)
daily use	9290 (87.0)
occasional use	891 (9.3)
Smoking status	
smokers	10428 (99.0)
non-smokers	102 (1.0)
Mean Duration of drug use in years (\pm SD)	10.0 (\pm 5.9)

Table 2. Prevalence data for heroin (daily/non-daily) and other drugs of abuse use, educational level by smoking (smoker; non smoker) status.

	Non smokers		Smokers		Totals	p
	N	(%)*	N	(%)*	N (%)#	
Subjects	102	(1.0)	10428	(99.0)	10530 (100.0)	
Age (M±sd)	29.6±7.2		28.2±6.1		28.2±6.2	0.024
Gender						0.205
Males	77	(0.9)	8412	(99.1)	8489 (80.6)	
Females	25	(1.2)	2016	(98.8)	2041 (19.4)	
Non-heroin (cocaine and other substance)	16	(4.6)	333	(95.4)	349 (3.3)	< 0.001
Heroin	86	(0.8)	10095	(99.2)	10181 (96.7)	
Daily	67	(0.7)	9223	(99.3)	9290 (87.0)	
Non-daily	19	(2.1)	872	(97.9)	891 (9.3)	< 0.001

* percentage of row Totals; # percentage of Subjects Total

(SD = 0.7%) (Table 2).

The average age of smoking initiation (daily use) was 14.1 years (SD = 2.5 years). Average age at the first experience of heroin experience was 18.4 years (SD = 3.8 years). Of those 10,095 subjects addicted to both tobacco and heroin, 8,002 subjects (79.3%) began by smoking first, 1,176 subjects (11.6%) began with both at the same age, and 917 subjects (9.1%) had their first experience of heroin before they started smoking. The non-smoker subjects (n = 102), with a mean age of 29.6 years (SD = 7.2 years), showed a statistically significant greater age than smokers (n = 10,428), who had a mean age of 28.2 years (SD = 6.1 years) (p = 0.024).

A higher prevalence of tobacco smoking was associated with heroin daily use than with: i) the non-daily use of heroin (99.3% vs 97.9%; p < 0.001), and ii) the abuse of other drugs (99.3% vs 95.4%; p < 0.001). A higher prevalence of tobacco smoking was also associated with the non-the daily use of heroin than with abuse of other drugs (97.9% vs 95.4%; p < 0.001) (Fig. 1).

Logistic regression analysis confirmed that smokers were significantly younger than non-smokers (OR 0.97, CI 95%: 0.94-0.99; p = 0.02) and that the prevalence of tobacco smoking was higher in heroin users than in users of other substances (OR 5.66, CI 95%: 3.27-9.81; p < 0.001).

4. Discussion

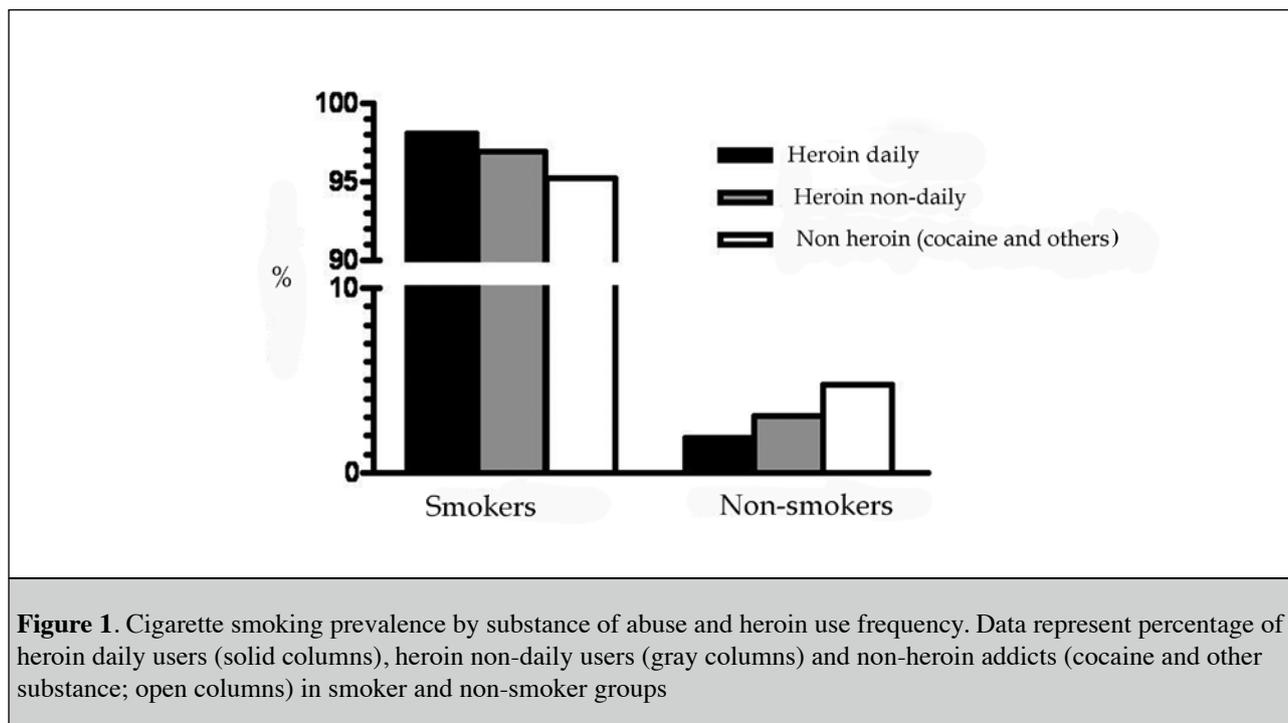
This is the first cross-sectional survey on tobacco smoking to be performed in a large sample of heroin addicts not receiving treatment for opiate dependence. Smoking prevalence in this large sample of heroin users is over 99%, which confirms the anecdotal report that most heroin users are smokers. The prevalence data reported in our survey are greater than those reported (ranging between 80 and 95%) in other studies on heroin addicts receiving methadone maintenance (1-3,7) and over three times the level recorded for

the aged-matched general population in Italy (the smoking prevalence in the Italian population in 2010 was 26%) (5).

Comparisons between different heroin or non-heroin use groups yielded rankings in which smoking prevalence showed its highest values in daily heroin addicts, followed by non-daily heroin addicts and non-heroin addicts. All these prevalence comparisons were statistically significant, but the values recorded were so high (ranging from 99.2 to 95.4%) that it may be concluded that differences in smoking prevalence between these groups are small in size and not relevant in the current sample (most of these subjects were smokers). In fact, smoking prevalence in the non-heroin use group was much greater than that previously reported in the literature (79%) (6).

The present data were collected from an admission log compiled when subjects accessed the community. The smoking data recorded were self-reported current smoking status (yes/no), age at onset of daily smoking (at least 10 cigarettes/day). One major limitation of the present survey is, therefore, that nicotine dependence was not measured (e.g., with the standard Fagerstrom questionnaire) and non-smoking status was not objectively assessed (e.g., by expired carbon monoxide or cotinine assays). An interesting extension of this study would be the collection of more data on smoking history, including, for instance, how many non-smokers were ex-smokers.

Although the data were collected in a specific country (Italy), the present findings demonstrate that smoking shows a strong comorbid association with heroin addiction in a population sample that was not receiving treatment. According to these data, we strongly recommend that the need to halt smoking should be considered for heroin addicts entering a community. Smoking cessation is not currently considered a priority in drug abuse therapy. Even so, being under drug abuse treatment in a residential setting may improve the motivation to stop smoking. There is a limited availability of studies performed in residential therapeutic



communities (4,9) but the data are encouraging. McDonald and coll. (2000) showed that at the time of admission 61% of drug users were responsive to the idea of halting their smoking habit, while implementation of tobacco education and cessation programmes increased this value to 87% at the time of discharge.

A ban on smoking is now in force in most of the therapeutic communities in Italy, including the Comunità di San Patrignano. Admission into a smoke-free environment for drug abuse treatment should therefore be coupled with specific smoking cessation programmes, in order to improve motivation and compliance with therapy.

References

- CLEMMY P., BROONER R., CHUTUAPE A.M., KIDORF M., STITZER M. (1997): Smoking habits and attitudes in a methadone maintenance population. *Drug Alcohol Depend* 44:123-132.
- DU W.J., XIANG Y.T., WANG Z.M., CHY., ZHENG Y., LUO X.N., CAI Z.J., UNGVARI G.S., GEREVICH J. (2008): Socio-demographic and clinical characteristics of 3129 heroin users in the first methadone maintenance treatment clinic in China. *Drug Alcohol Depend* 94(1-3):158-164.
- ELKADER A.K., BRANDS B., SELBY P., SPROULE B.A. (2009): Methadone-nicotine interactions in methadone maintenance treatment patients. *J Clin Psychopharmacol* 29(3):231-238.
- MCDONALD C.A., ROBERTSS., DESCHEEMAER N. (2000): Intention to quit smoking in substance-abusing teens exposed to a tobacco program. *J Subst Abuse Treat* 18:291-308.
- OSSFAD (2010): *DOXA 2010: Il fumo in Italia*. Roma, Italy. 2010.
- PATKARAA., STERLING R.C., LEONE T., LUNDY A., WEINSTEIN S.P. (2002): Relationship between tobacco smoking and medical symptoms among cocaine-, alcohol-, and opiate-dependent patients. *Am J Addict* 11(3):209-218.
- SHADEL W.G., STEIN M.D., ANDERSON B.J., HERMAN D.S., BISHOP S., LASSOR J.A., WEINSTOCK M., ANTHONY J.L., NIAURA R., (2005): Correlates of motivation to quit smoking in methadone-maintained smokers enrolled in a smoking cessation trial. *Addictive Behaviors* 30:295-300.
- UNESCO (1997): *International Standard Classification of Education ISCED 1997*. UNESCO General Conference 29th session, 1997.
- WILLIAMS J.M., FOULDS J., DWYER M., ORDER-CONNORS B., SPRINGER M., GADDE P., et al. (2005): The integration of tobacco dependence treatment and tobacco-free standards into residential addictions treatment in New Jersey. *Journal of Substance Abuse and Treatment* 28(4):331-340.

Role of funding source

This article was supported by internal funds.

Contributors

Benedetta Pajusco, Cristiano Chiamulera, and Fabio Lugoboni conducted literature searches and provided summaries of previous research studies. Antonio Boschini, Marco Beghini, Camillo Smacchia oversaw recruitment

and assessment of subjects and oversaw the development and maintenance of the database. Benedetta Pajusco conducted the statistical analysis. Benedetta Pajusco, Cristiano Chiamulera, and Fabio Lugoboni wrote the first draft of the manuscript and all authors contributed to and have approved the final manuscript.

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present article.

Received October 21, 2010 - Accepted January 30, 2011



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2011; 13(1): 11-14

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Housing and employment situation, body mass index and dietary habits of heroin addicts in methadone maintenance treatment

Daniela Alves¹, Ana Filipa Costa¹, Daniela Custódio¹, Liliana Natário¹, Vera Ferro-Lebres¹ and Fernando Andrade²

¹ School of Health Sciences, Polytechnic Institute of Braganza, Portugal, EU

² Centre for Integrated Responses of Braganza (CRI)

Summary

Forty-nine heroin addicts in methadone maintenance treatment were evaluated with the aim of studying the anthropometric, nutritional and sociodemographic characteristics of these individuals. The BMI of heroin addicts who live with their spouse/partner is significantly higher compared with other housing situations. Most of the heroin addicts evaluated do not consume the minimum servings of fruits, vegetables and grains recommended by the food pyramid, and their consumption of sweets is high. This study reinforced the need for intervention programmes specifically designed to correct the poor nutritional status and diet of drug users, while considering this to be a major public health issue.

Key Words: Heroin addicts; sociodemographic characteristics; nutritional assessment

1. Introduction

Investigations on the interaction between dietary habits and the nutritional status of heroin addicts in methadone maintenance treatment appears to be an important field of research in dietetics, as the drug addicts are a risk group for undernutrition, and little is known about diet and nutrition in this population (1,2).

Previous studies have shown a correlation between drug addiction, education and income levels and body mass index; the lower the educational and income levels, the lower the body mass index (BMI) turned out to be (3,4,9).

Many studies have found that drug abusers have nutritional deficits, including weight loss and changes in dietary patterns. Drug use in itself affects nutritional status for several reasons. A drug may not directly affect energy intake, but it is still likely to affect the frequency and nutritional quality of meals (5,6,10,12).

The aim of this research was to study the anthropometric, nutritional and sociodemographic characteristics of heroin addicts in methadone maintenance treatment.

2. Methods

2.1 Subjects

A cross-sectional study on 49 heroin addicts in methadone maintenance treatment was carried out in the Centre for Integrated Responses (CRI), Braganza, North-East Portugal. Patients who had associated diseases were excluded.

2.2 Data collection

The sample received a previously tested questionnaire consisting of three parts; the first two were answered by the patient, while the third was the documentary result of an interview with him/her. Dietary habits were assessed using a food frequency questionnaire. Anthropometric evaluation was performed by measuring patients' weight and height. Weight was measured with the body analyzer Tanita BC-418 ®. The subjects were weighed without shoes and with light clothes; the figure obtained was accurate to the nearest 0.1 g. Those measured had to keep their feet together, with their heels against the holder of the measuring device, standing upright,

without bending or stretching, and looking straight ahead, without raising or lowering their head. The Frankfurt plane running between the upper end of the ear and the outer corner of the eye had to be kept exactly parallel to the ground. The interviews on dietary habits, designed to facilitate anthropometric evaluations, were conducted by trained dietitians.

2.3 Statistical analysis

All the statistical analysis were carried out using SPSS 17.0 for Windows. The data collected were analyzed using descriptive statistics (means, standard deviations), while the relationships between variables were assessed using non-parametric statistics (the Student t and Mann-Whitney tests). Statistical significance was considered for p values <0.05.

2.4 Ethical issues

This study has preserved the anonymity of participants and the confidentiality of all the data collected, which are used only for research purposes.

All the participants in this study were adequately informed about its objectives and purposes, and only after due permission had been given by them were they included in the study, in accordance with the Declaration of Helsinki.

3. Results

Table 1 presents the social, anthropometric, nutritional and dietary characteristics of the sample (n = 49). Of the 49 participants, 87.8% were male and 12.2% female, with a mean age of 35.39 ±

8.36 years. The mean body mass index was 22.48 ± 3.47 kg/m².

The index proved to be significantly higher in heroin addicts who live with a spouse (n = 11; 25.03 ± 3.93 kg/m²), compared to other housing situations (n = 38, 21.74 ± 2.99) (p = 0.005), while the energy consumed (kcal) shows no significant differences between the two groups.

All heroin addicts reported having lost weight since the onset of drug use and 71.4% now have a normal weight, with 10.2% underweight.

Total energy consumed averaged 2,324.98 ± 1,021.40 Kcal/day. Those who were unemployed consumed more fat relative to total energy (p = 0.044) and lower amounts of carbohydrates relative to total energy, compared with other work situations.

On eating habits, among all groups, unemployed drug users are those who had the fewest meals per day (2.27 ± 0.94 meals; p = 0.008). All the groups investigated failed to comply with the recommendations on minimum daily consumption of fruit (2 servings), vegetables (3 servings) and grains (6 servings), on the basis of the recommendations of the food pyramid RB. The average daily consumption of sweets was 5.63 ± 2.16 servings per day.

4. Discussion and Conclusion

This study suggests that there is indeed a relationship between the nutritional status and food consumption profile of heroin addicts in methadone maintenance treatment, and sociodemographic factors such as employment and housing situation.

The fact that BMI was significantly higher in heroin addicts living with a spouse may be attributable to the presence of a caretaker figure who instills sensible eating habits and prepares meals. The presence of another person seems to be a factor influencing an

Table 1. Social, anthropometric, nutritional and dietary characteristics of the sample

	Housing Situation			Employment Situation	
	Total N=40	Spouse/Partner N=11	Others N=38	Unemployed N=22	Others N=27
Gender (%)					
Male	87.8	63.6**	94.7**	86.4	88.9
Female	12.2	36.4**	5.3**	13.6	11.1
Age (years)	35.39±8.3	34.18±7.1	35.74±2.9	38.50±7.2*	32.85±8.4*
BMI (Kg/m ²)	22.48±3.4	23.03±3.9*	21.74±2.9*	22.35±2.9	22.59±3.8
Underweight (%)	10.2	9.1	10.5	9.1	11.1
Normal weight (%)	71.4	54.5	76.3	77.3	66.7
Overweight (%)	16.3	27.3	13.2	13.6	18.5
Obesity (%)	2.0	9.1	0.0	0.0	3.7
Qualifications (%)					
1 st cycle	18.4	63.6	5.3	22.7	14.8
2 nd cycle	26.5	18.2	28.9	36.4	18.5
3 rd cycle	30.6	18.2	34.2	22.7	37.0
Secondary education	20.4	0.0	26.3	18.2	22.2
Bachelor	2.0	0.0	2.6	0.0	3.7
Graduation	2.0	0.0	2.6	0.0	3.7

*p<0.05 **p<0.01

Table 1. Social, anthropometric, nutritional and dietary characteristics of the sample

	Housing Situation			Employment Situation	
	Total N=40	Spouse/Partner N=11	Others N=38	Unemployed N=22	Others N=27
Weight loss (%) (yes)	100	100	100	100	100
Weight loss (kg)	8.38±6.6	9.45±7.6	8.04±6.3	7.6±4.7	9.04±7.9
Number of meals daily	2.78±1.1	2.87±1.4	2.76±1.0	2.27±0.9*	3.19±1.1*
Energy (kcal)	2324±98±1021.4	1909.06±582.6	2445.36±1093.3	2301.77±1219.8	2342.84±850.4
Protein (gr)	94.56±32.9	80.98±23.8	98.49±34.4	97.79±38.7*	91.93±27.9*
Protein (%)	16.76±3.1	17.15±2.6	16.64±3.3	17.64±3.3	16.04±2.9
HBP (gr)	69.49±23.8	59.30±18.8	68.58±24.9	69.98±28.1	63.65±19.7
LBP (gr)	25.98±12.6	21.48±5.7	27.29±13.8	24.02±9.2	27.52±14.8
Carbohydrates (gr)	265.25±111.9	229.82±85.1	275.51±117.1	243.76±104.9	282.76±115.6
Carbohydrates (g±sd)	45.73±5.8	47.48±3.6	45.23±6.2	43.27±6.8*	47.73±3.9*
Simple	107.74±52.8	97.37±53.2	110.75±53.0	90.91±46.3*	121.46±54.6*
Complex	142.53±62.1	120.00±33.7	149.06±67.18	134.21±55.4	149.32±67.4
Fat (gr)	77.50±37.4	63.13±21.2	81.95±40.0	82.41±49.0	73.50±24.7
Fat (gr)	30.38±5.89	29.40±4.78	30.54±6.2	32.27±7.29*	23.55±3.8*
Saturated	24.40±8.92	21.28±8.2	25.31±9.0	24.23±9.7	24.54±8.4
Unsaturated	37.87±14.1	31.95±9.3	39.61±14.9	38.88±14.5	37.09±14.0
Fiber (gr)	18.01±8.3	15.87±6.0	18.64±8.8	16.19±6.0	19.50±9.7
Iron (mgr)	13.49±5.2	11.52±3.4	14.04±5.57	12.87±5.33	14.00±5.2
Calcium (mgr)	966.85±485.7	815.43±353.4	1010.39±513.4	926.34±635.28	999.86±327.2
Alcohol (gr)	20.37±25.4	13.78 15.9	22.28±28.6	17.24±20.2	22.93±30.7
Alcohol (% kcal total)	6.07±5.5	5.53±2.2	6.23±6.8	5.54±6.9	6.51±6.5
Energy without alcohol (kcal)	2182.35±959.2	1812.59±507.3	2289.39±1020.6	2181.08±117.2	2183.39±768.5

*p<0.05 **p<0.01

addict's nutritional status, not only because the addict has someone who prepares meals, but the fact of being together itself helps to provide motivation to prepare meals.

The other housing situations (living alone or with parents) show a lower BMI. The average age of respondents is 35.74 years, which suggests that even those who live with their parents have no adult to monitor or take responsibility for meals, since their parents have ages of around 60 years. Usually parents of advanced age experience greater difficulty in performing household chores, including cooking meals; this factor leads to a lower intake by their children.

A normal BMI (71.4%) was recorded for most members of the sample; this result is in agreement with the study by Zador *et al* (12), which gave identical results, and the fact that they are individuals in methadone maintenance treatment leads to an improvement in the general state of health, including nutritional status (8).

Unemployed heroin addicts consume a higher percentage of fat, possibly due to their greater intake of snacks, which have a high concentration of fat and energy, in cafes offering easy access and low prices. Compared with the other groups, participants in this group have fewer meals per day (2.27 ± 0.94/day), which is in agreement with the lower BMI observed in these individuals, which might be accounted for by their limited economic resources.

Failure to comply with the minimum daily intake of servings of fruit, vegetables and grains may be due to the fact that heroin addicts worry mainly about satiety when they have feelings of

scorn about their next meal. These results are supported by a study performed by Smit *et al* (11), which identified low intakes of fruits and vegetables in drug users.

The high consumption of sweets (5.63 ± 2.16 servings/day) may be due to the fact that heroin addicts in methadone maintenance treatment are susceptible to a craving for sweets, as noted in the study performed by Nolan *et al* (7).

These findings agree with the study by Santolaria-Fernández *et al.* (10), which concluded that social and family aspects affect food consumption when they produce an irregular lifestyle and loss of interest in meals.

Sociodemographic conditions must be taken into consideration in the process of intervention with this population. More studies must be performed in order to clarify other nutritional and food behaviour variables in drug user populations.

References

1. Forrester JE, Tucker KL, Gorbach SL. (2004). Dietary intake and body mass index in HIV-positive and HIV-negative drug abusers of Hispanic ethnicity. *Public Health Nutr*, 7(7), 863-870.
2. Forrester JE. (2006). Nutritional Alterations in Drug Abusers With and Without HIV. *Am J of Infect Dis*, 2 (3), 180-183.
3. Himmelgreen DA, Escamilla RP, Milla SS, Daza NR, Tanasescu

Table 1. Social, anthropometric, nutritional and dietary characteristics of the sample

	Housing Situation			Employment Situation	
	Total N=40	Spouse/Partner N=11	Others N=38	Unemployed N=22	Others N=27
Grains (% portion/day)					
<6	93.6	100.0	92.1	95.5	92.6
6-11	6.1	-	7.9	4.5	7.4
Milk (% portion/day)					
<2	34.7	27.3	36.8	54.5**	18.5**
2-3	14.3	18.2	28.9	13.6	14.8
>3	51.0	54.5	2.6	31.8	66.7
Vegetable (% portion/day)					
<3	98	100	97.4	100	96.3
3-5	2	-	2.6	-	3.7
Fruits (% portion/day)					
<2	69.4	72.7	68.4	77.3	53.0
2-4	28.6	27.3	28.9	22.7	33.3
>4	2.0	-	2.6	-	3.7
Meat and Beans (% portion/day)					
<2	38.8	54.5	34.2	36.4	40.7
2-3	32.7	36.4	31.6	27.3	37.2
>3	28.6	9.1	34.2	36.4	22.2
Sweets (% portion/day)	5.63±2.1	5.28±2.1	5.73±2.1	5.53±2.6	5.72±1.7

*p<0.05 **p<0.01

- M, Singer M. (1998). A Comparison of the Nutritional Status and Food Security of Drug Using and Non-Drug-Using Hispanic Women in Hartford, Connecticut. *Am J Phys Anthropol*, 107, 351-361.
- Islam SKN, Hossain KJ, Ahmed A, Ahsan M. (2002). Nutritional status of drug addicts undergoing detoxification: prevalence of malnutrition and influence of illicit drugs and lifestyle. *Br J Nutr*, 88, 507-513.
 - Morabia A, Fabre J, Chee E, Zeger S, Orsat E, Robert A. (1989). Diet and Opiate Addiction: a quantitative assessment of the diet of non-institutionalized opiate addicts. *Br J Addict*, 84 (2), 173-180.
 - National Institute on Drug Abuse. Heroin Abuse and Addiction. 2004. Available at: <http://www.nida.nih.gov/PDF/RRHeroin.Pdf>
 - Nolan LJ, Scagnelli LM. (2007). Preference for sweet foods and higher body mass index in patients being treated in long-term methadone maintenance. *Subst Use Misuse*, 42(10), 1555-66.
 - Observatório Europeu da Droga e Toxicodependência (OEDT). As drogas em destaque – O papel essencial do tratamento de substituição. (2002). Available at: http://www.emcdda.europa.eu/attachements.cfm/att_33470_PT_Dif01pt.pdf
 - Saeland M, Haugen M, Erikson FL, Smehaugen A, Wandel M, Oshaug A. (2008). Living as a drug addict in Oslo, Norway – a study focusing on nutrition and health. *Public Health Nutr*, 12, 630-636.
 - Santolaria-Fernández FJ, Gómez-Sirvent JL, González-Reimers CE, Batista-López JN, Jorge-Hernández JA, Rodríguez-Moreno F, Martínez-Riera A, Hernández-García MT (1995). Nutritional assessment of drug addicts. *Drug Alcohol Depend*, 38 (1), 11-15.
 - Smit E, Graham NM, Tang A, Flynn C, Solomon L, Vlahov D. (1996). Dietary intake of community-based HIV-1 seropositive and seronegative injecting drug users. *Nutrition*, 12(7-8), 496-501.
 - Zador D, Lyons Wall PM (1994). High sugar intake in a group of women on methadone maintenance. *Proc. Nutr. Soc Aust*, 18, 190.

Role of funding source

This study was supported by internal funds.

Contributors

The authors contributed equally to this work.

Conflict of interest

The authors have no relevant conflict of interest to report in relation to the present study.

Received August 9, 2010 - Accepted December 20, 2010



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2011; 13(1): 15-20

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Effect of valproate on benzodiazepine withdrawal severity in opioid-dependent subjects: a pilot study

Helena Vormaa¹ and Heikki Katila²

¹ Helsinki University Central Hospital, Department of Psychiatry

² University of Helsinki, Department of Psychiatry

Summary

This study aimed to determine whether valproate is effective in treating benzodiazepine withdrawal symptoms in subjects receiving opioid maintenance treatment. Thirty patients were randomly selected for benzodiazepine discontinuation with or without valproate. Twenty-eight subjects completed the treatment. No serious adverse events were reported. After randomization, the baseline median diazepam-equivalent doses were 60 mg in the valproate group and 30 mg in the control group. No statistically significant differences were found between the weekly mean withdrawal scores of the two groups; even so, we believe that valproate may be useful in treating benzodiazepine withdrawal in opioid-dependent subjects. More studies are needed to confirm this.

Key Words: Opioid Substitution Treatment; Benzodiazepine; Valproate; Treatment outcome; Random allocation

1. Background

Benzodiazepine use and dependence are widespread among illicit opioid users, with approximately half of opioid maintenance patients reporting recent benzodiazepine use [1, 3, 7, 24, 28]. Benzodiazepine use is associated with more serious drug dependence and psychiatric comorbidity [1, 24]. Interactions between opioids and benzodiazepines may cause sedation, impaired motor and cognitive performance, and respiratory depression. In methadone maintenance treatment, benzodiazepine users may have an eightfold mortality risk compared with other patients [5]. Another medication used in opioid maintenance treatment, buprenorphine, has also been associated with deaths following use in combination with benzodiazepines, but less frequently than methadone [27].

In benzodiazepine-dependent subjects, withdrawal symptoms may occur when use is discontinued. With high

doses, delirium, cerebral seizures, and psychotic reactions are possible. Withdrawal symptoms can be alleviated by gradually tapering doses or by switching to a long half-life benzodiazepine such as diazepam. Slow tapering requires constant management of motivation and may be associated with poor treatment retention as a result. Pharmacological treatments of withdrawal symptoms might allow a more rapid discontinuation of benzodiazepines. However, little information is available on pharmacological strategies. Carbamazepine has demonstrated some efficacy in facilitating gradual benzodiazepine discontinuation [23, 15, 14, 21, 30]. In one randomized, controlled study, carbamazepine improved the outcomes of benzodiazepine tapering more than placebo in subjects receiving benzodiazepine treatment for at least the past year [25]. Due to enzyme induction, there are interactions with other medications, such as methadone, that impair the usability of carbamazepine. In case reports and

small-scale open-label studies, other anticonvulsive drugs, e.g. topiramate (6, 19), gabapentin (13), and pregabalin (20), showed beneficial effects. Some case reports indicate that valproate may improve the results of benzodiazepine withdrawal treatment (21, 30, 11). One randomized, controlled study demonstrated that valproate had no effect on withdrawal severity in a four-week tapering programme, but more valproate patients than placebo patients were able to remain benzodiazepine-free throughout the study (22).

We are aware of only four studies on benzodiazepine discontinuation treatment in opioid or polysubstance users (26, 18, 29, 17). Seifert et al. (26) noted that buprenorphine/carbamazepine was more effective than methadone/carbamazepine for inpatient detoxification in subjects with opioid dependence and additional multiple drug abuse. McGregor et al. (18) compared fixed and symptom-triggered benzodiazepine tapering in a group mainly consisting of polydrug users, concluding that the two methods were equally effective. Weizman et al. (29) compared outpatient clonazepam withdrawal treatment with clonazepam maintenance treatment for benzodiazepine dependence in patients in methadone maintenance treatment in an open-label naturalistic study, and found merits in the maintenance strategy. Kristensen et al. (17) compared buprenorphine/valproate with clonidine/carbamazepine regimen in subjects dependent on at least opioids and benzodiazepines. The buprenorphine/valproate combination seemed to be safe and, over several days, its reduction of withdrawal symptoms proved to be greater than that of the other treatment.

A need exists to identify an effective benzodiazepine withdrawal treatment for subjects with opioid dependence. The aim of this study was to assess whether a rapid benzodiazepine taper combined with valproate medication, carried out in an inpatient setting, is a more effective treatment for withdrawal symptoms than tapering alone in subjects receiving maintenance treatment for opioid dependence.

2. Patients and methods

The study was conducted between January 2006 and May 2008 in Helsinki, Finland. Subjects were recruited among patients consecutively admitted to inpatient induction of opioid maintenance treatment ($n = 29$) or to benzodiazepine withdrawal treatment during ongoing opioid maintenance ($n = 1$). Patients had to meet DSM IV-R criteria for opioid dependence and benzodiazepine dependence. Patients were excluded if they were pregnant, had active medical illnesses or severe mental disorders, had a history of convulsions, or were unable to speak Finnish (Figure 1). All participants gave their written informed consent. The Ethics Committee of Helsinki University Central Hospital approved the study protocol. The study was registered at ClinicalTrials.gov registry (Identifier NCT00570219).

Baseline assessments included subjects' medical history

as well as histories of drug and alcohol use investigated by EuropASI (16). Structured diagnostic assessments were performed (SCID I and SCID II) (10, 9). Serum sampling for benzodiazepines and urine sampling for benzodiazepines and illicit drugs were carried out. As a part of the medical examination, routine serum analyses (e.g. C-reactive protein, blood count, aminotransferases) were performed.

To prevent unequal treatment group sizes, we used block randomization in blocks of six subjects. Sealed envelopes were used to keep the randomization sequence unknown. The study was carried out as an open trial, with all outcome ratings assessed blindly to prevent detection bias.

Inpatient treatment lasted 3 weeks. All subjects received gradual benzodiazepine tapering, where the subjects' reported dosage was converted into an equivalent dose of diazepam, with a maximum of 80 mg per day. After the initial dose, dosages were reduced by 10 mg daily until 40 mg per day was reached, after which reductions were only 5 mg daily (18, 12). The experimental treatment consisted of valproate 20 mg/kg per day for 2 weeks, with a reduction during the 3rd week. The patients were maintained during benzodiazepine detoxification on methadone 20-50 mg or buprenorphine 2-16 mg to prevent most opioid withdrawal symptoms. If symptoms occurred, lofexidine was used.

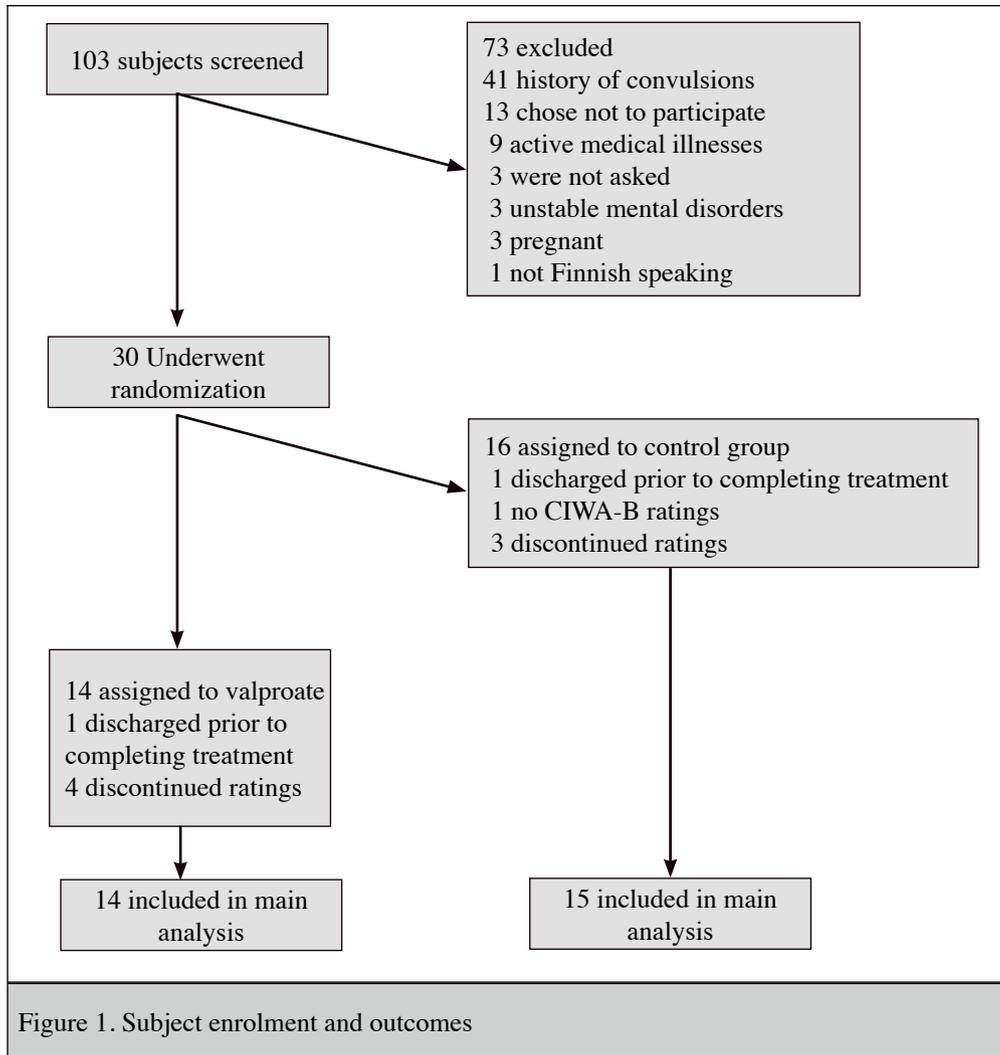
During the inpatient stage, benzodiazepine withdrawal symptoms were measured daily from the day following admission by using a short version of the Clinical Institute Withdrawal Assessment Scale – Benzodiazepines (CIWA-B) (score range 0-18) (18, 4). Serum valproate and aminotransferases were analysed during the treatment for experimental group subjects. Urine screening was repeated at the end of treatment.

The predetermined outcome criterion was withdrawal symptoms as assessed by CIWA-B. Withdrawal symptoms were determined by repeated measures analysis of variance (ANOVA), using the last observation carried forward method (LOCF). The analysis was re-run with adjustment for benzodiazepine dose at baseline. Data were analysed with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

3. Results

One hundred and three patients were screened for the study (Figure 1). Most exclusions resulted from a history of convulsions, patient's choice, or somatic diseases, mainly hepatitis C, presenting as high transaminases. Three patients were pregnant and another 3 were diagnosed as having severe mental disorders. The excluded patients used similar doses of benzodiazepines as participants (median diazepam-equivalent dose 40 mg daily, range 5-712 mg vs. 40 mg, range 8-160 mg, $P = 0.58$, Mann-Whitney U-test).

Table 1 shows the background characteristics of the two groups. At baseline, the median diazepam-equivalent dose was 60 mg daily (range 20-160 mg) in the valproate group



and 30 mg (range 8-75 mg) in the control group. In the valproate group, one subject, according to EuropASI, had used benzodiazepines on 13 days only in the past month, and, in the control group, one subject had used them on 18 days. All the other patients used benzodiazepines daily. In the valproate group, the mean number of compounds used was 2.4 (\pm SD 1.1) and in the control group 2.5 (\pm SD 1.0). No differences emerged between the groups in the compounds used (diazepam, alprazolam, clonazepam, nitrazepam, oxazepam, temazepam, and midazolam). No differences between the groups were recorded either with respect to demographic characteristics, drug history, or diagnoses.

Two subjects were discharged from the benzodiazepine withdrawal treatment for using illicit drugs at the hospital. Another 8 subjects discontinued participation in CIWA-B ratings, but stayed in treatment. No serious adverse effects were reported. For one patient, valproate medication was discontinued on day 9 because of mild liver impairment revealed by liver function tests. Overall, valproate was well tolerated, and no one reported nausea or other side-effects. The mean (\pm SD) serum level of valproate was 564 (156)

μ mol/L. No relationship was found between the serum valproate levels and withdrawal symptoms.

Table 2 shows the weekly mean CIWA-B scores for both groups. The difference between groups was not significant, nor did it become significant after adjusting for baseline benzodiazepine dose. No significant group \times time interaction was found ($F = 0.189$, $df = 1.54$, $P = 0.77$).

4. Discussion

The study subjects were selected from a group of 103 consecutive patients at a dependence clinic that serves the university hospital catchment area. Because the comparison treatment was a rapid benzodiazepine taper without anticonvulsive medication, a history of convulsions was an exclusion criterion. Consequently, 40% of patients were excluded at screening. The benzodiazepine doses of the excluded patients were comparable with those of patients entering the study; thus, it is safe to assume that the study group was representative of opioid users with benzodiazepine dependence of varying severity.

Table 1. Characteristics of study participants

	Valproate group (n = 14)	Control group (n = 16)
Gender: Male (%)	12 (86)	10 (62)
Mean age (\pm SD)	32 (6.7)	32 (5.3)
Living with partner (%)	3 (21)	9 (56)
Employed (%)	0 (0)	3 (19)
Years of opioid use: Mean (\pm SD)	11 (5.5)	10 (4.6)
Years of benzodiazepine use: Mean (\pm SD)	12 (7.1)	9 (5.2)
Benzodiazepine dose (diazepam equivalent): Median (range)	60 (20-160)	30 (8-75)
Alcohol use disorder (%)	2 (14)	2 (12)
Cannabis use disorder (%)	9 (64)	6 (38)
Stimulant use disorder (%)	8 (57)	7 (43)
Mood disorder (%)	1 (7)	5 (31)
Anxiety disorder (%)	3 (21)	2 (12)
Personality disorder (%)	8 (57)	5 (31)

Benzodiazepine use is known to exacerbate opioid withdrawal symptoms (8). In our study, subjects received rapid inpatient benzodiazepine detoxification and were simultaneously stabilized on methadone or buprenorphine. The withdrawal treatment was carried out using a rapid tapering regimen to avoid long hospital stays. Overall, the treatment was well tolerated, as nearly all subjects (n = 28) completed it; two were discharged for using illicit drugs at hospital. No serious adverse effects were reported.

The objective of the study was to determine whether valproate is effective in the treatment of benzodiazepine withdrawal symptoms in opioid-dependent subjects. No significant differences between the groups were found in CIWA-B scores. Several explanations are credible. The difference of 30 mg per day in the baseline benzodiazepine doses between the groups may have lowered the chances of detecting differences in withdrawal scores. A more even distribution might have improved the scope of the results. In addition, if differences did exist between the groups, the sample was apparently too small to allow them to emerge in the wide range of CIWA-B scores. Further, missing CIWA-B ratings might have led to some bias in estimating treatment effects. Eight subjects discontinued participation in CIWA-B ratings, but stayed in treatment. According to hospital notes for them, three subjects in the valproate group reported relief from withdrawal symptoms, while the others experienced no major changes in their clinical condition. In these cases, the patient records supplied information about the missing values of CIWA-B. Willing as we were to err on the conservative side, we decided to adhere, in any case, to the LOCF method.

Only one previous study has examined valproate for withdrawal treatment of polydrug-using opioid-dependent patients (17). In a non-randomized, open-label inpatient detoxification study, the valproate group achieved a reduction in withdrawal symptoms from day one, although no significant differences between the groups overall were found. These results are in line with ours. Two strengths of our study are that we used random allocation and that the ratings were carried out blindly.

The main limitations of our study are that the study participants were not blinded to group assignment and the sample size was small. To minimize the risk for detection bias, blinded evaluation was used. Because open dosing of valproate was applied, there is still the possibility that expectation effects could account for the differences seen between the groups.

No statistical differences can be claimed yet, but we believe that valproate may be useful in treating benzodiazepine withdrawal in opioid-dependent subjects. It was well tolerated, and the weekly CIWA-B scores of the valproate group were similar to those of the control group despite a clinically relevant difference in their baseline benzodiazepine doses. Moreover, valproate may decrease the risk of convulsions, and, as an indirect GABAergic agonist, it may facilitate the transition to abstinence from benzodiazepines (2). In any case, these results are preliminary and require confirmation in more extensive, double-blind, placebo-controlled studies. In particular, more research should be done with subjects using high benzodiazepine dosages or with those who have a history of withdrawal convulsions.

Table 2. Weekly CIWA-B scores (mean \pm SD)

	Valproate group (n = 14)	Control group (n = 15)
Days 1-7	5.1 (2.7)	6.2 (3.5)
Days 8-14	5.8 (3.5)	6.5 (3.6)
Days 15-20	5.2 (3.7)	6.3 (3.9)

References

1. BACKMUND M., MEYER K., HENKEL C., SOYKA M., REIMER J., SCHUTZ C.G. (2005): Co-consumption of benzodiazepines in heroin users, methadone-substituted and codeine-substituted patients. *J Addict Dis* 24: 17-29.
2. BISAGAA. (2008): Benzodiazepines and other sedatives and hypnotics. In: M. Galanter and H.D. Kleber Eds: *The American Psychiatric Publishing Textbook of Substance Abuse Treatment*. American Psychiatric Publishing Washington, DC. pp. 215-235.
3. BLEICHA., GELKOPFM., WEIZMANT., ADELSON M. (2002): Benzodiazepine abuse in a methadone maintenance treatment clinic in Israel: characteristics and a pharmacotherapeutic approach. *Isr J Psychiatry Relat Sci* 39: 104-112.
4. BUSTO U.E., SYKORA K., SELLERS E.M. (1989): A clinical scale to assess benzodiazepine withdrawal. *J Clin Psychopharmacol* 9: 412-416.
5. CAPLEHORN J. (1996): Risk factors for non-HIV related death among methadone maintenance patients. *Eur Addict Res* 2: 49-52.
6. CHESEAUX M., MONNAT M., ZULLINO D.F. (2003): Topiramate in benzodiazepine withdrawal. *Hum Psychopharmacol Clin Exp* 18: 375-377.
7. DARKE S., WILLIAMSON A., ROSS J., TEESSON M. (2006): Reductions in heroin use are not associated with increases in other drug use: 2-year findings from the Australian Treatment Outcome Study. *Drug Alcohol Depend* 84: 201-205.
8. DE WET C., REED L., GLASPER A., MORAN P., BEARN J., GOSSOP M. (2004): Benzodiazepine co-dependence exacerbates the opiate withdrawal syndrome. *Drug Alcohol Depend* 76: 31-35.
9. FIRST M.B., GIBBON M., SPITZER R.L., WILLIAMS J.B., BENJAMIN L. (1997): *Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II): Interview and Questionnaire*. American Psychiatric Press, Washington, DC.
10. FIRST M.B., SPITZER R.L., GIBBON M., WILLIAMS J.B.W. (1997): *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID)*. American Psychiatric Press, Washington, DC.
11. HARRIS J.T., ROACHE J.D., THORNTON J.E. (2000). A role for valproate in the treatment of sedative-hypnotic withdrawal and for relapse prevention. *Alcohol Alcohol* 35: 319-323.
12. HARRISON M., BUSTO U., NARANJO C.A., KAPLAN H.L., SELLERS E.M. (1984): Diazepam tapering in detoxification for high-dose benzodiazepine abuse. *Clin Pharmacol Ther* 36: 527-533.
13. HIMMERICH H., NICKEL T., DALAL M.A., MULLER M.B. (2007): Gabapentin bei einer Patientin mit Panikstörung und Unverträglichkeit von Carbamazepin während des Benzodiazepinentzugs [Gabapentin treatment in a female patient with panic disorder and adverse effects under carbamazepine during benzodiazepine withdrawal]. *Psychiatr Prax* 34: 93-94.
14. KAENDLER S.H., VOLK S., PFLUG B. (1996): Benzodiazepinentzug mit Carbamazepin [Benzodiazepine withdrawal with carbamazepine]. *Nervenarzt* 67: 381-386.
15. KLEINE., COLIN V., STOLK J., LENOX R.H. (1994): Alprazolam withdrawal in patients with panic disorder and generalized anxiety disorder: vulnerability and effect of carbamazepine. *Am J Psychiatry* 151: 1760-1766.
16. KOKKEVI A., HARTGERS C. (1995): EuropASI: European adaptation of a multidimensional assessment instrument for drug and alcohol dependence. *Eur Addict Res* 1: 208-210.
17. KRISTENSEN O., LOLANDSMO T., ISAKSEN A., VEDERHUS J.K., CLAUSEN T. (2006): Treatment of polydrug-using opiate dependents during withdrawal: towards a standardisation of treatment. *BMC Psychiatry* 6: 54.
18. MCGREGOR C., MACHIN A., WHITE J.M. (2003): In-patient benzodiazepine withdrawal: comparison of fixed and symptom-triggered taper methods. *Drug Alcohol Rev* 22: 175-180.
19. MICHPOULOS I., DOUZENIS A., CHRISTODOULOU C., LYKOURAS L. (2006): Topiramate use in alprazolam addiction. *World J Biol Psychiatry* 7: 265-267.
20. OULISP., KONSTANTAKOPOULOS G., KOUZOUPIS A.V., MASDRAKIS V.G., KARAKATSANIS N.A., KARAPOULIOS E., KONTOANGELOS K.A., PAPADIMITRIOU G.N. (2008): Pregabalin in the discontinuation of long-term benzodiazepines' use. *Hum Psychopharmacol* 23: 337-340.
21. PAGES K.P., RIES R.K. (1998): Use of anticonvulsants in benzodiazepine withdrawal. *Am J Addict* 7: 198-204.
22. RICKELS K., SCHWEIZER E., GARCIAESPANA F., CASE G., DEMARTINIS N., GREENBLATT D. (1999): Trazodone and valproate in patients discontinuing long-term benzodiazepine therapy: effects on withdrawal symptoms and taper outcome. *Psychopharmacology* 141: 1-5.
23. RIES R., CULLISON S., HORN R., WARD N. (1991): Benzodiazepine withdrawal: Clinicians' ratings of carbamazepine treatment versus traditional taper methods. *J Psychoactive Drugs* 23: 73-76.
24. ROONEY S., KELLY G., BAMFORD L., SLOAN D., O'CONNOR J.J. (1999): Co-abuse of opiates and benzodiazepines. *Ir J Med Sci* 168: 36-41.
25. SCHWEIZER E., RICKELS K., CASE W.G.,

- GREENBLATT D.J. (1991): Carbamazepine treatment in patients discontinuing long-term benzodiazepine therapy. Effects on withdrawal severity and outcome. *Arch Gen Psychiatry* 48: 448-452.
26. SEIFERT J., METZNER C., PAETZOLD W., BORSUTZKY M., PASSIET., ROLLNIK J., WIESEB., EMRICH H.M., SCHNEIDER U. (2002): Detoxification of opiate addicts with multiple drug abuse: a comparison of buprenorphine vs. methadone. *Pharmacopsychiatry* 35: 159-164.
27. STEENTOFT A., TEIGE B., HOLMGREN P., VUORI E., KRISTINSSON J., HANSEN A.C., CEDER G., WETHE G., ROLLMANN D. (2006): Fatal poisoning in Nordic drug addicts in 2002. *Forensic Sci Int* 160: 148-156.
28. VORMA H., SOKERO P., TURTIAINEN S., KATILA H. (2009): Opioidiriippuvuuden korvaushoito HYKS:n päihdepsykiatrian yksikössä 2003-2005. [Opioid substitution treatment in 2003-2005 at the Psychiatric Unit for Drug Dependence of the Helsinki University Central Hospital (HUCH)]. *Suom Lääkäril* 64: 1853-1857.
29. WEIZMAN T., GELKOPF M., MELAMED Y., ADELSON M., BLEICH A. (2003): Treatment of benzodiazepine dependence in methadone maintenance treatment patients: a comparison of two therapeutic modalities and the role of psychiatric comorbidity. *Aust N Z J Psychiatry* 37: 458-463.
30. ZULLINOD F., KHAZAALY., HÄTTENSCHWILER J., BORGEAT F., BESSON J. (2004): Anticonvulsant

drugs in the treatment of substance withdrawal. *Drugs Today* 40: 603-619.

Role of funding source

The study was supported by Annual EVO Financing (special government subsidies) from the Department of Psychiatry, Helsinki University Central Hospital. No support was provided by any pharmaceutical company.

Contributors

Both authors designed the study. HV was the principal investigator, performed the data analyses, and drafted the manuscript. Both authors contributed to and approved the final manuscript.

Conflict of interest

No conflict of interest.

Acknowledgments

We thank Pia Lahtinen, Jarna Iivari, Tiia Reinholm-Saloma, Petri Tiainen, and the clinical staff of the Unit for Drug Dependence, Department of Psychiatry, Helsinki University Central Hospital, for their collaboration, and Professor Seppo Sarna, Department of Public Health, University of Helsinki, for statistical advice.

Received July 8, 2010 - Accepted November 28, 2010



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2011; 13(1): 21-28

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Opioid addiction complicated by alcoholism (in young men)

Lev N. Blagov¹ and Dmitry I. Kurgak²

¹ Drug Addiction, Russian State Medical University, Moscow, Russia

² Medical Center for Treatment Drug and Alcohol Dependence, Petropavlovsk-Kamchatsky, Russia

Summary

A clinical run of addictive diseases shows a variety of trends. One of these is an amplification of the clinical picture, with the appearance of new structural components whose dynamic psychopathological characteristics tend to increase in severity. It is important here to look at addictive problems not only as constituting a dependence syndrome, but as an ongoing, ever-varying clinical reality, showing the distinctive traits of a specific psychopathological process that comprises post-toxic problems, including combinations of personality disorders and their environmental predisposition. So, opioid addiction complicated by alcoholism can be seen as a prime example of how consistent patterns can be found in the clinically dynamic aspects of addictive diseases. A clinical description of these patterns based on reported cases to be investigated throughout a lifelong period of illness is a step to be taken towards a better understanding of addictive pathology as a severe medical problem.

Key Words: Opioid dependence; Opioid addiction; Alcoholism; Young men; Clinical methodological aspects; Psychopathological diagnostics; Clinical psychopathological Mechanisms; Clinical dynamics

1. Introduction and motivation

Clinical issues in the field of drug addiction problems are highly topical because of the urgent need to encourage better treatment programmes for this difficult clinical group of patients [1, 10, 13]. General methodological evaluations of addictive behaviour problems now include three main approaches. The first is *toxicological*. Here there is a clear possibility of estimating the consequences of chronic intoxication – somatic, neurological and psychopathological [15]. As these consequences are post-toxic, they are retrospective diagnostic elements. A primary consideration here is that the psychopathological consequences demonstrate a psycho-organic syndrome in practically all its possible forms (asthenic, euphoric, explosive, apathetic), as a rule featuring a strongly ‘negative’ psychopathological picture. It includes the well-known, invariably present complex of

asthenia, affective lability and intellectual deficiency (due to the growth of cognitive disturbances). It requires, incidentally, a long time-span and a severe chronic intoxication to become fully implemented. It also changes personality to a ‘simpler’ pattern of reactions whenever environmental factors become critical. This approach, however, cannot account for all the certain, simultaneously specific varieties of addictive behaviour within their relatively individualized, recognizably distinctive model of real clinical appearances. Moreover, any psycho-organic syndrome (here – post-toxic) itself has only ‘negative’ psychopathological potential (with a gradual loss of psychic energy and of the functional capacities of personality, leading to paroxysmal and convulsive disorders in the final stages) and, as presented clinically, there are no ‘productive’ consequences. So, this health deficiency development cannot completely justify or confirm a real pathogenetic model for the formation of pathological addictions in all their variety.

The second approach to the assessment of addictive problems is *psychological* [6, 8, 9, 12, 16]. It aims to complete previous approaches by providing a formal explanation of motivation and of behavioural patterns through their psychological definition. Psychological assessment appeals to strict paradigms of leading, environmentally determined psychological reactions in interpreting most addictive problems as belonging to a typology linked to a 'stress-diathesis' model. Here we discover some elements that are bound to lead to failure, the main one being a *de facto* refusal of strictly academic criteria in identifying addictive problems as a medical priority. This approach claims the right to use medical assessment terminology in order to achieve a literally objective estimation of status, in opposition to any subjective interpretation of personality reactions in all their known variety (considering the usability of mathematics in working with figures in their ordinary variety on the level of symptom assessment). However, this psychological approach to assessment also appeals to a much greater multiplicity of situations, partly determined by personality, than can be identified in a real clinical setting. That means, first of all, known parameters of irritability, hysteroid and asthenic reactions, infantilism and imbalances between forms of behavioural motivation. It also strictly depends on patterns of reaction (which must show differences in each case and depend on concrete situations) and, in every case, personality reactions should be environmentally determined. Nevertheless, any behavioural pattern of pathological addiction is always quite recognizable in its identity and can be represented in general terms, despite recognized personality differences; this applies not only to craving, but to the whole complex of 'addictive situations'. Moreover, these reactions became practically equal in patients with a definite experience of addictive behaviour. Here it is obviously not a matter of 'personality development' (of which type, it must be asked: simple, neurotic or paranoiac?), according to Hans Binder [2]), but of a 'pathological evolution' in the context of pathological processes, as the idea was formulated by Karl Jaspers [11]. And 'processual' characteristics here surely do not just reflect a particular endogenous process, but, because they are included in universal pathological definitions, show a precisely pathogenetic development of addictive illness as part of a continuum within its specific 'endo-form' (endogenous-like) entity.

It is, however, possible to assess an addictive problem complex through psychopathological investigation based on a classical clinical approach that includes psychic status analysis, requiring the collection of completely objective anamnestic data, and clinical supervision over as long a period as possible [4, 5, 7, 10]. This can be considered a very up-to-the-minute *psychopathological* approach allowing a better understanding of addictive behaviour phenomena. This essentially proposes a medical (not only a psychological and social) model for conducting a survey. It calls for

a clinically objective symptomatic and syndromologically accurate description, estimation, definition and classification of this kind of problem as permitting the naming of a disorder and an illness, with each definition specifying their chronic (continual) intrinsic traits.

In developing that thesis, it is possible to enunciate the main goals for long-term psychiatric investigation in the field of addictive behaviour.

It is necessary here to stress and clarify the notion by differentiating between the main definitions. Requiring definition there will always be a *disorder* (an acute disturbance problem with the character of a *reaction*) and an *illness* (a *disease*) viewed as a chronic pathological process that comprises a variety of different disorders (appearing as clinical syndromes). The pathological process in question always has to be characterized by specifying some benchmarks: *debut* (onset), *clinical manifestation* and *outcome*. A chronic process also needs to be defined as a *state* with terms capable of specifying the features of its outcome—*defects* and *regression* as regular personality changes and as the result of psychopathological processes. It is also important for the psychopathologist to supersede the estimation of the level of *symptom* and *symptom complex* (simple syndrome) by clearly formulating the characteristics of that *syndrome* and *syndrome complex* [11]. The clinical dynamism of an illness reveals variants in the clinical dynamics of a disease's trend (transient, remittent, unremitting) and its typology (psychopathology and organic combinations), so revealing the dominant clinical level of damage (neurotic, psychotic, psycho-organic). Only by analysing the psychopathological balance between a 'positive' and/or a 'negative' (defect, regression) clinical evolution in addictive health problems as a specific processual disease does it become possible, objectively and individually, to make a differential diagnosis (with a real comorbidity evaluation) and to speak about remission on the basis of clinically determined psychopathological criteria (but only if validated by a 'sober' formal declaration given by the addict). In this way, the psychopathological addictive complex becomes adequately specified, with the possibility of a fuller description; it does, in fact, need to be described by psychiatrists specialized in clinical addictive behaviour problems. The severity of a addictive disease can be medically assessed only by applying psychopathological criteria, not only toxicological and/or psychological-sociological ones. Lastly, goals for *therapy* and *correction* can, as a consequence, be clearly presented. It is very important here to see the difference between a *symptomatic correction* (of a reversible position) and the *active* (pathogenetically determined) *treatment* of an illness, with its dramatic influence on the dynamic of a pathological process.

No search for stable and prognostic results in this field can be successful without providing marked definitions.

As can be seen at this point, the formulation of a perfect clinical description, with the aim of understanding the clinical

substrate of an addictive disease as completely as possible, is a crucial issue. If this component of clinical estimation can be supplied in a complete form and then be objectively confirmed by independent experts, it is quite probative. So, it is necessary to describe and understand the clinical features of all the main aspects of a ‘natural appearance’, which is what an addictive disease is. Then and only then, after a complete clinical psychopathological (not only a toxic-psychological) description designed to function as the main diagnostic platform, is it possible to elaborate a traditional complex of screening study tests to specify diagnostic goals and successfully implement routine scientific work standards.

Opioid dependence complicated by alcoholism is a good target for clinical psychopathological investigation, because of its frequent occurrence in clinical drug addiction practice. This topic poses a challenge to the feasibility of clinically studying a well-known phenomenology from a dynamic point of view. The goal is that of reliably investigating the clinical structure and dynamics of opioid dependence complicated by alcoholism in young men by means of a complex clinical psychopathological assessment of mental and social status, so as to determine treatment priorities.

2. Materials and method

115 young aged men suffering from opioid dependence, complicated by alcoholism (inpatients and outpatients), were investigated by applying the methods of classical psychopathological analysis and commonly adopted psychological methods, in order to make possible differential diagnosis and a typological description of the clinical subgroups detected. In addition, clinical cases with histories of illness, psychic status, anamnesis and follow-up (catamnesis) were estimated.

- The following clinical and personality (premorbid) pa-

rameters were investigated:

- heredity;
- personality status (normal, accentuation, psychopathy, psychic infantilism);
- pattern of intoxication before addiction has started and during the early stages of its formation;
- the characteristics of craving during the different phases of illness (intoxication, withdrawal syndrome, initial phase of remission).

3. Results

The clinical and social parameters to be investigated were assessed in patients whose age range was 17-27 years, suffering from an addictive illness that lasted from 1 up to 12 years. ‘Opioid onset’ was recorded in 14-25 year-old patients, and ‘alcohol onset’ in 13-23 year-old patients. The other parameters are presented in Table 1.

Heredity status is presented in Table 2.

Two main patterns of diagnostic criteria were used with this group. The first included the traditional criteria for states of abuse, dependence and addiction. The complex involved in these disorders was revealed through the following parameters:

- a) chronic intoxication sessions or a continuum, and their consequences, with complete, objective information about them;
- b) changed biological reactivity to psychoactive substance use;
- c) the presence of a withdrawal syndrome, along with its clinical somatic, neuro-psychological and psychopathological signs;
- d) craving and its equivalents;
- e) behavioural addictive disorders.

Table 1. Demographic characteristics			
	Duration and Specification	Cases	%
Catamnesis	3 years	22	19.1
	2 years	30	26.1
	1 year	27	23.5
Educational level	upper education	5	13.0
	incomplete upper education	24	21.0
	vocational training	38	33.0
	secondary education	19	16.5
	incomplete secondary education	19	16.5
Formal professional status	industrial workers	26	22.6
	students	53	46.1
	commerce	18	15.7
	unemployed and dependants	18	15.7
	de facto involvement in a job, a business or an educational process	24	21.0
	de facto disengagement (idle condition)	91	79.0
Criminal activity	violation of law and police records	34	29.6
	records of conviction	22	19.1
	prison confinement	14	12.2

Table 2. Familiarity

	Patients	%
Alcoholism and Alcohol Addictive Disease in parents	83	72
Personality disorder (psychopathy) in parents	11	9.6
Epilepsy or its equivalents in parents	3	2.6
Drug abuse among helpmates (wife, girlfriends), brothers, sisters (without any events involving parents)	10	8.7

The second diagnostic assessment was based on psychopathological criteria previously described as invariably present syndromes of pathological addiction [3, 5]. This pattern included parameters defining an ‘*addictively predominant psychopathological syndrome complex*, a clinical estimation of ‘*negative*’ psychic status (with a dynamic combination of personality defects and regressive features). Other factors considered were the *structure* and *dynamic diagnosis* of pathological addiction (*kind, form, type, stage, phase* of addictive disease and *main level of psychopathological damage*). The diagnostic criteria of importance were completed by the definition and clinical estimation of the *main psychopathological mechanisms of pathology implementation*, comorbidity status and the final profile of personality changes.

Debut clinical models of opioid dependence complicated by alcoholism showed ‘opioid onset’ in 74 patients (64.4%) and ‘alcohol onset’ in 41 (35.6%). All the clinical material issued was suitably divided into marked cohorts.

3.1. Opioid onset

Premorbid characteristics at ‘opioid onset’ are presented in Table 3. The following premorbid abnormalities were grouped in various combinations in most of these clinical cases, but are shown here as an ‘absolute’ presence.

The stage of “searching for abuse” within the study cohort revealed a duration ranging between 1 month and 2 years. The clinical phenomenology named as ‘searching for narcotics’ (i.e., initial substance abuse without any signs of dependence, viewed as a pre-nosological stage of addictive illness) was itself specifically focused in Russian investigations 35 years ago by I.N. Pyatnitskaya [14]. In our study the ‘searching for abuse’ of alcohol stage, without signs of dependence and with *initially poor alcohol acceptability* (a very important clinical

notion) was found in 33 cases (44.6%), and cannabis abuse in 31 (41.9%). Based on the clinically assessed data in the opioid debut cohort, two clinical subgroups were found to display a main dynamic pattern of intoxication when opioids was replaced by alcohol. The first demonstrated a substitute (‘vicarious’) form of alcohol abuse, in 51 cases (68.9%). The second showed alcohol abuse taking shape as a change in the pattern of narcotism, with the stability of that changed character in 23 patients (31.1%).

The main clinical features of the *substitution* (“*vicarious*”) alcohol abuse subgroup are listed below:

- A) A substance (alcohol) which is abused during withdrawal, while a patient is in abstinence from the main drug – the drug that had generated dependence (here, opioids), ?bearing in mind that? the reverse occurrence cannot in itself demonstrate dependence.
- B) That abused substance (alcohol) is ‘vicarious’ (i.e., has a substitute function); it also operates at a lower ‘narcogenetic’ level, and does not generally change the main intoxication pattern.
- C) The most important clinical feature of this subgroup was additional systematic intoxication with cannabis, benzodiazepines and/or stimulants completing a specific pattern of intoxication, along with alcohol.
- D) After reversion to the main form of drug-inducing dependence, ‘vicarious’ intoxication fell away and eventually disappeared.
- E) Even when that disappearance was not complete, it did not affect the main intoxication pattern (for example, cannabis smoking along with heroin abuse).

However, the toxicological aspect of substitute drug and alcohol use in opioid addicts can be interpreted through the concept of “cross tolerance”. Also, it is very important to note that, in one chosen subgroup, the opioid onset cohort, the clinical and psychopathological criteria of the withdrawal

Table 3. Premorbid characteristics at ‘opioid onset’

	Cases	% in ‘opioid’ subgroup
Personality accentuation	27	36.5
Psychopathy	7	9.5
Psychic infantilism	48	64.9
Residual psycho-organic signs	9	12.2
Post-traumatic consequences	3	4.1

Table 4. Parameters of premorbid state

	Cases	% in 'alcohol subgroup'
Personality accentuation	19	46.3
Psychopathy	7	17.0
Psychic infantilism	24	58.5
Residual psycho-organic signs	7	17.0
Post-traumatic consequences	3	7.3

syndrome and the characteristics of remission maturation showed that *opioid dependence and addiction continued to be active*.

The main criteria and clinical features in the subgroup where alcohol abuse was revealed as a *change in the pattern of narcotism* can now be presented:

- A) Total refusal of opioid intoxication.
- B) Retention of the episodic use of 'soft' opioids (tramadol and other similar substances), along with continuing alcohol abuse.
- C) The leading form of alcohol abuse was continuous.
- D) A high level of tolerance to alcohol (up to 2 liters or more of strong beverages as daily intake).
- E) A previous invariable stage of opioid dependence with its clinical psychopathological characteristics and withdrawal in anamnesis.
- F) The previous presence of a clinically revealed stage of the abuse of alcohol as a substitute during the main period of opioid intoxication and the continuation of 'vicarious' alcoholism in the subsequent remission maturation phase.

The specific clinical characteristics of the withdrawal syndrome named here as 'complicated' should be described as a distinct clinical composition where the pathological effects of more than one pathogenic substance (here – opioids) change clinical proportions because the specific traits of opioids emerge openly and in most cases come to prevail. As a result, the clinical picture here was characterized by the following positions:

- A) A combination of the traits of 'usual' alcohol withdrawal (involving somatic, neurovegetative and psychopathological components) with significant opioid features (algesic sensitivity, excitement, agitation, aggressiveness, insomnia) in their clinical unity.
- B) A high level of clinical dynamism.
- C) The prevalence of psychopathological components over somatic ones.

D) The protracted character of the *acute period of withdrawal* (we call this the period of 'post-toxic distress'); it lasts as long as 7-10 days, and is followed by the lengthy remission pattern of the *post-withdrawal phase* (we suppose that this phase can be considered the 'real withdrawal', on the basis of psychopathological criteria).

3.2. Alcohol onset

The premorbid characteristics of 'alcohol onset' are presented in Table 4, where the percentages refer to the whole of the 'alcohol debut' cohort.

A comparison between premorbid parameters in the two onset subgroups presented in Table 5 shows some differences, with a prevalence of psychic infantilism in the 'opioid onset' cohort and of personality disorders and psycho-organic components in the 'alcohol onset' cohort.

The premorbid and 'pre-opiate' period, with the intoxication characteristics displayed in the 'alcohol onset' cohort, are presented in Table 6:

Clinical features of opioid addiction with 'alcohol onset' included the following main positions estimated by focusing on psychopathological diagnostic priorities.

- A) A high level of pathological progression of preliminary alcoholism.
- B) Alcohol intoxication with a high degree of irritability, aggressiveness and conflictual behaviour.
- C) Opioid dependence and addiction through preliminary alcoholism lead to a fast clinical dynamic with a short, intensive course tendency.
- D) The psychopathology of the withdrawal syndrome and craving demonstrate their high grades both in the 'alcohol' and in the 'opioid' stage.
- E) As a result of the high degree of progressiveness of addictive illness, there is a rapid transformation to a poly-narco-toxicomaniac pattern, with a return to severe alcohol

Table 5. Parameters of premorbid state

	'opioid onset' (%)	'alcohol onset' (%)
Personality accentuation	36.5	46.3
Psychopathy	9.5	17.0
Psychic infantilism	64.9	58.5
Residual psycho-organic signs	12.2	17.0
Post-traumatic consequences	4.1	7.3

Table 6. Premorbid and 'pre-opiate' period, with the intoxication characteristics displayed in the 'alcohol onset' cohort

	Cases	%
Age at onset of alcohol use:		
10 -13 years old	7	17.0
13 -15 years old	26	63.4
Initially high level of tolerance to alcohol	17	41.5
Quickly emerging alcohol withdrawal (manifested 3-5 years after first experience):	16	39.0
Episodic use of toxic substances:		
Inhalation of organic solvent vapours	8	19.5
Cannabis	4	9.8
Other toxic psychoactive substances	2	5.0

abuse. These are important prognostic characteristics of addictive illness as a pathological process.

- F) In fact, both opioid dependence and alcoholism here show clinical features of 'syndromal comorbidity' because of their relative clinical self-sufficiency.
- G) Poly-toxicomania and definitive alcoholism are clinical characteristics of the final stage of this variant drug dependence (observable in the aged part of the subgroup).

4. Conclusion

The present study shows:

Patterns of clinical dynamics with the clinical and psychopathological structure becoming transformed into opioid addiction complicated by alcoholism.

A clinical movement having the characteristics of a psychopathological process whose onset, manifestation and outcome display quite a 'classic' outcome—the transformation of what was, at the outset, essentially an opioid dependence into poly-toxicomania and alcoholism.

The term 'alcohol onset' used here refers to a prolonged 'search for narcotism' stage located within the main opioid addictive illness. This is one of the debut variants in opioid dependence; it shows a fast dynamic and its advance to an outcome which is poly-toxicomania.

There is an urgent need to extend the scope of the present study, which is based on the priorities set by clinical and psychopathological criteria, by combining it with other methodology complexes so as to gain a fuller understanding of clinical mechanisms and sociopsychological patterns in this population of addicts.

5. Points of special interest

A primary conclusion to be drawn from all the foregoing is the pressing need to investigate the main clinical variants of drug addiction by using a psychopathological phenomenology. The most important question at issue here is the definition of each addictive problem complex as an integral medical substrate showing the prevalence of certain psychopathological markers. Now, clinical descriptions of

the invariably present phenomenological features of addictive diseases prepared in this way on opioid dependence and opioid addiction as a initial sample were completed, some time ago, in Russian studies on psychopathology [3, 5]. These provided clinical descriptions of the 'active' psychopathological syndromes (within the 'addictive predominant' complex) by analysing the psychic status of consciousness, specific thought disorders, affective disorders, bulnesia (disorders of the will), specific intellect and behaviour disorders. This area includes syndromes of 'absolute anosognosia', 'legitimation' of addictive behaviour, and manipulative status of addicts. Descriptions were also given of 'negative' disorders in opioid addiction: psychic defects and psychic regression (as a combination of defects and the psycho-organic consequences of chronic intoxication). The main psychopathological clinical reproduction mechanisms: *obsessive, compulsive, automatism, stereotypical or due to automatisms*, have been reported as the clinical psychopathological content of that dangerous illness, opioid addiction.

Differential diagnosis in clinical investigation and management of the patient are required to reveal some components of the clinical picture. First, there is the identification of leading pathological demonstrations (symptoms and syndromes) viewed as a systemic (rather than an isolated) and recognizable 'addictive syndrome complex' (an 'addictive predominant') which has the characteristics of a *general disease*. Second, there should be the clinical psychopathological assessment of a comorbidity status (dual diagnosis) with the determination of aspects of greater pathological (psychopathological) substance: this should include the whole field of *psychiatric and somatic-neurological* pathology, together with its relative typology (as accepted in Russian psychopathological descriptions [3, 7]). Third, there should be differential diagnosis in the field of personality disorders (psychopathic decompensation), to include critical environmental influences and the inherent properties of essentially addictive psychopathology (whether 'active' or 'negative'). Fourth, there should be a differential diagnosis of the phases of each *addictive disease*. Lastly, (fifth) – there is a need for the differentiation between complex therapy approaches (strategy, tactics) and methods, including psychopharmacology and psychotherapy with their

clear prognostic abilities to achieve positive clinical results. These are needful steps to be taken in acquiring an understanding of such difficult aspects of clinical addictology. We suppose that the formulation of these objectives will favour the opportunity to attain greater precision in developing a diagnostic system.

From this standpoint, therefore, the main goals for treatment can now be presented by listing the following main goals:

- a) the elaboration of tactics and a strategy for therapy;
- b) providing therapy with a level where damage can be determined;
- c) using therapeutic methodology (pharmacotherapy, psychotherapy) to make available aspects of medical technology that offer understandable prognostic criteria;
- d) correction (symptom-oriented therapy) – without intervention in the main pathogenetic mechanisms of illness;
- e) therapy (active treatment) with a capacity to ‘dismantle’ and ‘break down’ the addictive syndrome and the syndrome complex.

References

1. Backmund M., Schutz C.G., Meyer K., Eichenlaub D., Soyka M. (2003): Alcohol consumption in heroin users, methadone-substituted and codeine-substituted patients – frequency and correlates of use. *Eur Addict Res.* 9(1):45-50
2. Binder H. K. (1960): in *Klinische Psychiatrie* (herausgegeben von H.W. Grule, R. Jung, W. Mayer-Gross, M. Muller). Springer-Verlag, Berlin – Gottingen – Heidelberg.
3. Blagov L.N. (2008): *Actual Aspects of Psychopathology in Addictive Disease*. A.N. Bakulev National Cardio-Vascular Surgery Center of Russian Academy of Medicine Sciences Publishers, Moscow.
4. Blagov L. N. (2007): Clinical Features of Heroin Dependence Onset in Young Women. (2007): *Heroin Addict. Relat. Clin. Probl.*; 9 (3): 21-30.
5. Blagov L. N. (2005): *Opioid Dependence: Clinical Psychopathological Aspect*. Genius, Moscow.
6. Brotchie J., Meyer C., Copello A., Kidney R., Waller G. (2004): Cognitive representations in alcohol and opiate abuse: the role of core beliefs. *Br J Clin Psychol.* 43(3):337-42.
7. Chirko V. V. (2002): *Alcohol and Drug Dependence in Patients with Endogenous Psychoses*. Medpractica, Moscow.
8. Flannery W., Keenan E., Fitzgerald M. (2004): Attention deficit hyperactivity disorder (ADHD) and later substance misuse: Annual Symposium of the Society for the Study of Addiction “Advice from on High: Addiction and Government Pronouncements”, Leeds, 6-7 Nov., 2003. *Addict. Biol.*, 9(1) 96.
9. Flynn H.A., Walton M.A., Curran G.M., Blow F.C., Kuntzen S. (2004): Psychological distress and return to substance use two years following treatment. *Substance Use and Misuse.* 39; (6) 885-910.
10. Haastrup S., Jepsen P.W. (1988): Eleven years follow-up of 300 young opioid addicts. *Acta. Psych. Scand.*, 77(1) 22-26.
11. Jaspers K. (1973): *Allgemeine psychopathologie*. Springer-Verlag, Berlin, Heidelberg, New York.
12. Kornreich C., Foisy M.L., Philippot P., Dan B., Tecco J., Noel X., Hess U., Pelc I.,
13. Verbanck P. (2003): Impaired emotional facial expression recognition in alcoholics, opiate dependence subjects, methadone maintained subjects and mixed alcohol-opiate antecedents subjects compared with normal controls. *Psychiatry Res.* 119(3):251-260.
14. Maremmani I. (2009): *The Principles and Practice of Methadone Treatment*. Pacini Editore Medicina, Pisa, Italy; AU-CNS, Lucca, Italy.
15. Pyatnitskaya I.N. (1975): *Clinical Narcology*. Medicina, Moscow.
16. Schuckit M.A. (1989): *Drug and Alcohol Abuse: A Clinical Guide to Diagnosis and Treatment, Third Edition*. New York and London: Plenum Medical Book Company.
17. Teplin D., O’Connell T., Daiter J., Varenbut M. (2004): A psychometric study of the prevalence of DSM-IV personality disorders among office-based methadone maintenance patients. *Amer. J. Drug and Alcohol Abuse.* 30:(3) 515-524.

Role of funding source

This article was supported by internal funds.

Contributors

The authors contributed equally to this article.

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present article.

Received January 18, 2010 - Accepted May 18, 2010



Pacini Editore & AU CNS

Expert Opinion

Heroin Addict Relat Clin Probl 2011; 13(1): 29-34

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Dual Diagnosis (Comorbidity): A growing diagnostic and treatment issue in the psychiatric and substance use programmes in the Republic of Macedonia

Ivan G. Tulevski

Centre for the Prevention and Treatment of Drug Abuse and Abuse of Other Psychoactive Substances, Skopje, The Republic of Macedonia

Summary

The purpose of this paper is to describe several existing problems encountered in the management of dual diagnosis (DD) in the psychiatric and drug treatment institutions in Macedonia. The term DD or comorbidity refers to the co-occurrence of at least one mental and behavioural disorder due to psychoactive substance use with another psychiatric disorder in the same individual. These 'dual' subjects present greater severity from both the clinical and social perspectives than those who have only one type of psychiatric disorder. The cost to the health system for those with DD is significantly higher than it is for someone with a single psychiatric disorder. This presents a significant challenge with respect to the identification, prevention and management of people with DD. According to the 2004 Report by the EMCDDA, the prevalence of DD in treatment settings in various EU countries ranged between 22% and 96%. In the Day Hospital for the Prevention and Treatment of Drug Dependencies in Kisela Voda, Skopje in an 8-year period, 1995-2002, 9.8% – 49 out of a group of 500 heroin users – were diagnosed as 'dual' patients. The unmet need for treatment of people with DD is considerable. People with DD often found themselves in the gap between the relevant services, namely between the Day Hospital in Kisela Voda, and the Psychiatric Hospital in Skopje, or, less frequently, in prison. In Macedonia guidance regarding the best practice for the treatment of individuals with DD is not available. Access to services for people with DD diagnosis is restricted. They are under-diagnosed and receive very little treatment. The present Author has stressed the need for increasing the capacity of the health care system in Macedonia to meet the needs of people with DD. Further research is needed to establish the prevalence of DD, and to improve the diagnosis, treatment and social rehabilitation of people with DD.

Key Words: dual diagnosis; epidemiology; treatment

A Dual Diagnosis of mental disorder, and mental and behavioural disorder due to psychoactive substance use is common. Furthermore, dual diagnosis is often associated with poor treatment outcome, severe illness course, and high service utilization. This presents a significant challenge with respect to the identification, prevention and management of people with dual diagnosis.

The unmet need for treatment within this group is considerable and people with dual diagnosis are often left isolated in the gap left between the relevant services.

Psychopathology coexisting with drug use in adolescents

is often encountered in a variety of clinical settings. Research findings suggest a major role for drug use in the aetiology and prognosis of psychiatric disorders such as affective disorders, conduct disorder and antisocial personality disorder, attention-deficit hyperactivity disorder, and anxiety disorders.

Psychiatric disorders also appear to have an important role in the aetiology of and vulnerability to drug use problems in adolescents. Dual diagnosis in adolescents is recognized as an important factor in deciding how they should be treated [2].

Dual diagnosis, as it applies to people with mental health and with mental and behavioural disorders due to psycho-

active substance use, has been researched internationally and treatment models have been developed over three decades. There is still, however, no consensus on the precise meaning of the term, the implications of that diagnosis for the health and well-being of an individual, or the most effective treatment models.

People with dual diagnosis are not a homogeneous group. The diagnosis is not clear, whether in comparing classification systems, or going outside them, or else within or between countries. Research methodologies adopt a wide spectrum of definitions, making comparison, replication and the application of findings very difficult in practice.

The term 'dual diagnosis' is perhaps a misnomer, though it has been adopted internationally to represent a range of clinical presentations associated with people who have mental health or mental and behavioural disorders due to psychoactive substance use. Related terms sometimes used interchangeably with dual diagnosis are: 'Dual disorder', 'Mentally Ill Chemical Abusers' (MICA) or 'Chemical Abuse and Mental Illness' (CAMI) in the USA [18] and 'co-occurrence' of psychosis and substance abuse in Australia [7].

Dual Diagnosis was defined by the UN Office for Drug Control and Crime Prevention as "a person diagnosed as having alcohol or drug abuse problem in addition to some other diagnosis, usually psychiatric, e.g. mood disorder or schizophrenia" [17].

Dual diagnosis was defined by the World Health Organization in 1995 as the "co-occurrence in the same individual of a psychoactive substance use disorder and another psychiatric disorder" [19].

According to Maremmani, in the fields of psychiatry and addictive diseases the term "dual diagnosis" has taken on the meaning of "the coexistence of a psychiatric disorder with a substance use disorder" [9].

People with mental disorders are more likely to have mental and behavioural disorders due to psychoactive substance use than people without them. Similarly, people with mental and behavioural disorders due to psychoactive substance use are more likely to have a mental disorder than people without them [2,14]. The association between mental disorders and drug use is a complex one. People with such co-existing disorders are not a homogenous group; they suffer a range of disorders which vary in severity and fluctuate over time.

Determining the aetiology of dual diagnosis results in a chicken and egg discussion: what came first? Existing research about the causal relations between mental disorders and mental and behavioural disorders due to psychoactive substance use is inconclusive [3]. The symptoms of mental disorder and addiction problems interact and mutually influence each other. Kessler [8] and Bakken [1] consider that research evidence shows that mental disorders generally precede mental and behavioural disorders due to psychoactive substance use i.e.

they increase individuals' susceptibility to such problems. However, mental disorders may also be aggravated by drug use (e.g. for depression [10]), or occur in parallel.

Schuckit [15] points out that DSM-IV recognizes at least two types of dual diagnosis. The most common type includes individuals who have a major substance use disorder but who demonstrate symptoms of intoxication or withdrawal that resemble problems observed in other psychiatric diagnoses. The second, less common, type of dual diagnosis involves individuals who, perhaps by chance alone, actually have an independent major psychiatric disorder besides their alcohol or drug dependence.

Despite the difficulty of establishing prevalence, the literature indicates high rates of dual diagnosis that are steadily increasing over time [6]. Two factors may have led to this increase. First, individuals with a mental illness may be increasingly exposed to illicit drugs. Second, there is a general increase in experimentation with illicit drugs in the population as a whole.

According to the EMCDDA publication *Drugs in Focus*, [4] two main groups of comorbid drug users can be recognized, each with a distinct profile. One group is dominated by people with a psychiatric illness and the second is characterized by drug dependency. According to the same publication in 2004 about 30-50% of psychiatric patients in Europe had a mental illness as well as mental and behavioural disorders due to psychoactive substance use, mainly alcohol, sedatives or cannabis. Among patients from drug treatment centres, dual diagnosis mostly implies a different profile, with heroin, amphetamine or cocaine use, together with one or several personality disorders as the dominant diagnostic features, followed by diagnoses of depression and anxiety and, to a lesser degree, psychotic disorders.

The co-occurrence of personality disorders and drug use was only recently described in the general population. The US National Epidemiologic Survey on Alcohol and Related Conditions firmly established a relationship between mental and behavioural disorders due to psychoactive substance use and personality disorder, with about half of all drug users having at least one personality disorder [5]. In terms of clinical prevalence, samples of people with mental and behavioural disorders due to psychoactive substance use, personality disorders (50-90%) prove to be the most frequent form of comorbidity, followed by affective disorders (20-60%) and psychotic disorders (15-20%).

Available European data provide a different picture. In various clinical studies, personality disorders range from 14% to 96% – the dominant types being antisocial and borderline disorders – while depression ranges from 5% to 72%, and anxiety disorders from 4% to 32%. These large variations are probably due to differences in the focus of diagnostic assessment and the types of sample chosen.

In the Republic of Macedonia general population-based studies and clinical studies of dual diagnosis prevalence have not been carried out so far. In the Day Hospital for Prevention and Treatment of Drug Dependencies in Kisela Voda, Skopje in the period of eight years (1995-2002) 9.8% – 49 out of a group of 500 heroin users – were diagnosed as ‘dual’ patients [16]. It is hard to believe that the prevalence of dual diagnosis among a group of 500 heroin-dependent subjects was so low. Despite the high prevalence of heroin users with other mental disorders, in our clinical practice the distinction between drug use symptoms and symptoms of other mental disorders did not receive particular attention, and the specific treatment of comorbid disorders was not provided in accordance with good clinical practice. Routine assessment for mental symptoms and disorders seldom was a part of the standard diagnostic procedures performed during the initial treatment of heroin users in the Day Hospital in Kisela Voda.

The team of psychiatrists, psychologists and social workers in the Day Hospital in Kisela Voda failed to utilize methodological advances which could have improved the diagnosis of both psychiatric and substance use disorders. There was no attempt to use standardized, validated instruments available for the measurement of psychiatric symptoms and personality disorders; the same is true of various instruments that assess levels of drug use and addiction. Even if the Addiction Severity Index (ASI) [11], Brief Psychiatric Rating Scale (BPRS) [13], the Zung Self-rating Depression Scale [20] and the Zung Self-rating Anxiety Scale [21] have been translated into the Macedonian language, they have practically never been used.

Another problem in our practice with regard to the provision of services for people with dual diagnosis is an artificial separation of treatments for mental and behavioural disorders due to psychoactive substance use and those for other mental health disorders. There was pressure to place people with dual diagnosis in one system or the other by determining which disorder was primary for them. This can result in no treatment for the disorders that are not considered primary. In Macedonia there are currently no clear rules for the referral of clients from drug treatment services to mental health services, and there is resistance in mental health services because of a lack of expertise. People with dual diagnosis have tended either to be treated within one service alone, which has meant that some aspects of their cluster of problems have not been dealt with as well as might have been wished, or they have been shuttled between services, with a consequent loss of continuity of care. The provision of integrated care for people with dual diagnosis requires a radical rethinking of the way services are organized – they need to be organized around the user rather than around social, professional or service constructions of ‘abnormal’ behaviour.

The fact that many other mental disorders are associated

with increased rates of mental and behavioural disorders due to psychoactive substance use, including mood disorders (alcohol, stimulants), personality disorders, particularly anti-social and borderline personality disorder (alcohol, polysubstance), anxiety disorders (alcohol, benzodiazepine), PTSD (alcohol, cannabis), eating disorders (alcohol, stimulants), and conduct disorders (alcohol, polysubstance), [15; 13] was not clearly recognized either in drug treatment services or in psychiatric hospitals in Macedonia. As a result, the treatment of people with dual diagnosis has mainly been focused on psychotic disorders such as schizophrenia and depression.

People with dual diagnosis, through their disruptive and aggressive social behaviour and due to a failure to comply with treatment rules and requirements, are very often a cause of frustration to the staff of the Day Hospital in Kisela Voda, who, understandably, often experience impatience, suppressed aggression and symptoms of burn-out. This has substantially diminished their chances that those people will get psychosocial support, adequate pharmacological management and social support. In their case it has been difficult to ensure liaison with relevant agencies (e.g. social services, courts, lawyers and prisons) and other health institutions (primary health care, obstetric services, surgery clinics, clinics for infective diseases, dental clinics and so on).

The restricted use of newer (‘atypical’) antipsychotics and SSRI medicaments in treating people with dual diagnosis in Macedonia could be explained by the lack of dual diagnosis good practice guidelines and the scarcity of financial resources.

Conclusions and recommendations

Estimates of the numbers of people with dual diagnosis in Macedonia are still unavailable because of the lack of formal registration and a total lack of prevalence studies.

Assuming that clinical cohorts of people accessing addiction and mental health services in Macedonia show similarities in the problems they experience, high prevalence rates are likely to emerge in future prevalence studies in Macedonia.

Dual diagnosis needs to be recognized and addressed in the national health policy of the Republic of Macedonia.

Dual diagnosis potentially involves a significant number of people accessing primary care, social services and addiction and mental health services. Provision should be made for the treatment of people with dual diagnosis in all relevant institutions at the regional and local level.

Drug treatment services and psychiatric hospitals in Macedonia do not offer a specific treatment model for dual diagnosis.

Macedonia should introduce specific multidisciplinary educational programmes on dual diagnosis that will enable various disciplines to understand and respect each oth-

ers' roles in providing people who have a dual diagnosis with health care.

The role of primary health care in providing services for dual diagnosis is not yet clear. The role of primary care, in particular that provided by GPs, is integral to the management of dual diagnosis.

New studies are needed to identify the needs of people with dual diagnosis and models of assessment and treatment appropriate to the clinically effective provision of services. Thus, some areas yet to be researched include: prevalence, needs assessment and the role of GPs in providing primary care.

Continuing education programmes for different disciplines working in addiction and mental health services could incorporate dual diagnosis in their syllabi.

Several countries have dealt with the complexities of managing dual diagnosis by developing national guidelines for the services that provide care. It is necessary to develop dual diagnosis good practice guidelines for Macedonian services for people with dual diagnosis.

References

- Bakken K., Landheim A. S., Vaglum P. (2003): Primary and secondary substance misusers: do they differ in substance-induced and substance-independent mental disorders? *Alcohol Alcohol.* 38:(1) 54-59.
- Bukstein O. G., Brent D. A., Kaminer Y. (1989): Comorbidity of substance abuse and other psychiatric disorders in adolescents. *Am J Psychiatry.* 146:(9) 1131-1141.
- Emcdda (2004): Annual Report 2004. The State of the drugs problem in European Union and Norway. Selected Issue 3. Comorbidity Office for Official Publications of European Commission, Luxembourg
- Emcdda (2004): Drugs in Focus. Comorbidity - drug use and mental disorders. 14th issue. EMCDDA, Lisbon.
- Grant B. F., Stinson F. S., Dawson D. A., Chou S. P., Dufour M. C., Compton W., Pickering R. P., Kaplan K. (2004): Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 61:(8) 807-816.
- Jackson-Koku G. (2001): Mental illness and substance misuse: a nursing challenge. *Brit J Nursing.* 10:(242-246).
- Kavanagh D. J., Young R., Boyce L., Clair A., Sitharthan T., Clark D., Thompson K. (1998): Substance Treatment Options in Psychosis (STOP): A new intervention for dual diagnosis. *J Mental Health.* 7:(2) 135-143.
- Kessler R. C., Aguilar-Gaxiola S., Andreade L., Et Al (2001): Mental-substance comorbidities in the ICPE surveys. *Psych Fennica.* 32 62-79.
- Maremmani I., Pacini M., Lubrano S., Lovrecic M., Perugi G. (2003): Dual diagnosis heroin addicts. The clinical and therapeutic aspects. *Heroin Addict Relat Clin Probl.* 5:(2) 7-98.
- Mcintosh C., Ritson B. (2001): Treating depression complicated by substance misuse. *Advances in Psychiatric Treatment.* 7 357-364.
- McLellan A. T., Luborsky L., O'brien C. P., Woody G. E. (1980): An improved diagnostic evaluation instrument for substance abuse patients: The Addiction Severity Index. *J Nerv Ment Dis.* 168:(1) 26-33.
- Ouimette P. C., Wolfe J., Chrestman K. R. (1996): Characteristics of posttraumatic stress disorder-alcohol abuse comorbidity in women. *J Subst Abuse.* 8:(3) 335-346.
- Overall J., Gorham D. (1962): The Brief Psychiatric Rating Scale. *Psychol Rep.* 10 799-812.
- Regier D. A., Farmer M. E., Rae D. S., Locke B. Z., Keith S. J., Judd L. L., Goodwin F. K. (1990): Comorbidity of mental disorders with alcohol and other drug abuse. *JAMA.* 19 (264) 2511-2518.
- Schuckit M. A. (2000): Drug and Alcohol Abuse. A Clinical Guide to Diagnosis and Treatment. Kluwer Academic/Plenum Publishers, New York.
- Tulevski I. G. (2009): Duevni rastrojstva i rastrojstva vo obnoskite predizvikani so upotreba na droga i druga du{evna bolest (dvojna dijagnoza – dual diagnosis, komorbiditet). In: Tulevski I. G. (Ed.) *Zavisnost od droga.* Matica Makedonska, Skopje. pp. 194-242.
- United Nations Office for Drug Control and Crime Prevention (2000): Demand Reduction. A Glossary of Terms. UNODC, New York, NY.
- Us Department of Health and Human Services (2000): Assessment and Treatment of Patients with Coexisting Mental Illness and Alcohol and Other Drug Abuse: Treatment Improvement Protocol TIP. DHHS, Washington, D.C.
- World Health Organization (1995): Lexicon of alcohol and drug terms. WHO, Geneva.
- Zung W. W. (1965): A Self-Rating Depression Scale. *Arch Gen Psychiatry.* 12 63-70.
- Zung W. W. (1971): A rating instrument for anxiety disorders. *Psychosomatics.* 12:(6) 371-379.

Role of funding source

This article was supported by internal funds.

Conflict of Interest

The author has no relevant conflict of interest to report in relation to the present article.

Received October 5, 2010 - Accepted January 28, 2011



Pacini Editore & AU CNS

Letter to the editor

Heroin Addict Relat Clin Probl 2011; 13(1): 35-36

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Does cannabis have therapeutic benefits for withdrawing opioid addicts?

Marcel Peloquin, Lacey R. Peters, Megan E. McLarnon and Sean P. Barrett

Department of Psychology at Dalhousie University, Nova Scotia, Canada

TO THE EDITOR: Evidence suggests there is a high rate of comorbid cannabis use among opioid addicts [1,9] and that cannabis use frequently occurs during the course of opioid substitution treatment [6,8,9]. Although such cannabis use is often regarded as problematic [4], cannabis is known to have analgesic (e.g. [2]), antiemetic (e.g. [5]), and neuronal (e.g. [7]) effects that may have therapeutic benefits for withdrawing opioid users. Despite this, relatively little attention has been paid to cannabis use by opiate users who are trying to manage the gruelling effects of withdrawal [3]. Nobel et al. (2002)[8] reported that cannabis use is a common strategy for self-detoxification from opioids without medical assistance and there have been reports that cannabis use has been associated with improved medical compliance as well as a decrease in the number of opioid- positive urines among individuals receiving naltrexone treatment [1,9]. Despite such findings, the extent to which cannabis has therapeutic benefits for opioid withdrawal symptoms remains unknown.

As part of a larger study, we recently surveyed 72 individuals (age range of 18-64; 20 female) enrolled in a low-threshold methadone maintenance program in Halifax Nova Scotia. During face-to-face interviews participants were asked; "Have you ever used cannabis/marijuana to reduce the symptoms of withdrawal? If yes, from which drug(s)?" 62.5% (45/72; 7 female)

of those surveyed said they have used cannabis in the past to reduce withdrawal symptoms from some type of drug and of these 86.6% (39/45; 6 female) specified that this included opioids. Although participants were not asked for further elaboration, 8 male clients made spontaneous reports about cannabis' effectiveness for assisting with opioid withdrawal. While the majority of such statements (6/8) are consistent with a therapeutic benefit; (e.g. "That's why I use it", "...helped with the come-down," "...used it to sleep," "...to counterbalance effects of methadone and increase my appetite"), one client reported a null effect; ("It doesn't work, but you try,"), and one client reported a negative effect; ("I tried, but it didn't help - it made me more sick"). Individuals that reported having used cannabis to reduce the symptoms of opioid withdrawal reported using cannabis more days during the previous month ($n = 39$, mean = 14.2, SD = 12.5) than those who had never done so ($n = 33$, mean = 5.8, SD = 11.0) ($t(70) = 2.99$; $p < 0.01$), but because we did not collect the data about the frequency of cannabis use for withdrawal relief purposes, it is not clear the extent to which such usage accounts for this difference .

Although these preliminary findings should be interpreted with caution, they suggest that cannabis may be used for therapeutic purposes by at least some opioid addicts. Additional research into the reasons

for and effects of cannabis use among opioid addicted individuals is warranted.

References

1. CHURCH, S.H., ROTHENBERG, J.L., SULLIVAN, M.A., BORNSTEIN, G., NUNES, E.V. (2001): Concurrent substance use and outcome in combined behavioral and naltrexone therapy for opiate dependence. *Am J Drug Alcohol Abuse* 27: 441-452.
2. ELIKOTTIL, J., GUPTA, P., GUPTA, K. (2009): The analgesic potential of cannabinoids. *J Opioid Manag* 6: 341-357
3. GOSSOP, M., BRADLEY, B., PHILLIPS, G.T. (1987): An investigation of withdrawal symptoms shown by opiate addicts during and subsequent to a 21 day in-patient methadone detoxification procedure. *Addict Behav*: 12, 1-6.
4. HALL, W., DEGENHARDT, L. (2009): Adverse health effects of non-medical cannabis use. *Lancet*, 374: 1383-1391.
5. ROCHA, F.C.M., STEFANO, S.C., HAIK, R.D.C., OLIVEIRA, L.M.Q.R., SILVEIRA, D.X.D. (2008): Therapeutic use of cannabis sativa on chemotherapy induced nausea and vomiting among cancer patients: Systematic review and meta-analysis. *Eur J Cancer Care* 17: 431-443.
6. MANNELLI, P., PEINDL, K., PATKAR, A.A., WU, L-T., PAE, C-U., GORELICK, D.A. (2010): Reduced cannabis use after low-dose naltrexone addition to opioid detoxification. *J Clin Psychopharmacol* 30: 476-477.
7. MUNTONI, A.L., PILLOLLA, G., MELIS, M., PERRA, S., GESSA, G. L., PISTIS, M. (2006): Cannabinoids modulate spontaneous neuronal activity and evoked inhibition of locus coeruleus noradrenergic neurons. *Eur J Neurosci* 23: 2385-2394.
8. NOBLE, A., BEST, D., MAN, L-H., GOSSOP, M., STANG, J. (2002): Self-detoxification attempts among methadone maintenance patients: What methods and what success? *Addict Behav* 27: 575-584.
9. RABY, W.N., CARPENTER, K.M., ROTHENBERG, J., BROOKS, A.C., JIANG, H., SULLIVAN, M., BISADA, A., COMER, S., NUNES, E.V. (2009): Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence. *Am J Addict* 18: 301-308.

Role of funding source

This study was supported by a grant to SPB from the Canadian Institutes of Health Research. The funder did not have a role in the study design; the collection, analysis or interpretation of data; in writing the report or in the decision to submit this work for publication.

Contributors

The authors contributed equally to this letter

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present letter.

Received and Accepted December 1, 2010



Pacini Editore & AU CNS

Letter to the editor

Heroin Addict Relat Clin Probl 2011; 13(1): 37-40

HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS

www.europad.org

Is it time for new studies on the level of insight in heroin addicts to promote compliance with methadone treatment?

Luca Rovai and Angelo Giovanni Icro Maremmani

"Vincent P. Dole" Dual Diagnosis Unit, "Santa Chiara" University Hospital, Department of Psychiatry, University of Pisa, Italy, EU

TO THE EDITOR: Patients' lack of insight into their mental illness is a complex and poorly investigated phenomenon which seriously influences psychosocial functioning, shows a clear correlation with the severity of psychiatric symptoms, and has been seen as related to treatment compliance, with important prognostic implications [3, 6, 15].

In the literature the degree of awareness of mental illness has been studied in a wide range of psychiatric conditions, including mood disorders, anxiety disorders, psychotic disorders and obsessive-compulsive disorder. Special attention has been paid to three different elements that are involved: insufficient awareness in patients of specific aspects of each form of the disease, the neuro-cognitive impairment entailed in each case, and consequent failures to comply with treatment.

With reference to mood disorders, patients' level of insight has been shown to be related to the polarity of mood episode; patients with mania have shown significantly poorer insight compared with those with mixed mania, bipolar depression and unipolar depression. The lack of association between level of insight and total number of manic symptoms or with specific manic symptoms could be related to the persistence of subsyndromal symptoms in patients in remission from a manic episode [2]. On the other hand, the awareness of illness has been compared between groups of bipolar I and II patients during a phase of clinical stabilization, the apparent

conclusion being that a severe deficit in self-awareness may constitute a distinguishing psychopathological characteristic of patients with bipolar II disorder [12]. All these observations, even if conflicting data are present, tend to support the hypothesis that impaired insight and other neurocognitive dysfunctions characterize not only symptomatic but also already remitted bipolar patients [14].

With regard to anxiety disorders, a paper assessing the relationship between the impairment of insight and the long-term outcome of illness in several psychiatric disorders has shown a greater relative impairment of insight in mood versus anxiety disorders, prompting the conclusion that awareness of illness is a feature that is relatively stable in this latter group of diseases [4].

Patients' awareness of their own illness has also been studied in psychotic disorders, which classically reveal a poor degree of insight. In schizophrenic patients too, impaired insight is clearly related to a poorer course of the illness and non-compliance with necessary treatment [6]. Deficits in insight have been found to be more common and severe in patients with schizophrenia than in those with schizoaffective and major depression, with or without psychosis, but not more severe than they are in patients with bipolar disorder – a finding that has strong clinical, theoretical, and nosological implications [13].

Given the controversial data on the degree of insight to be found in obsessive-compulsive disorder, one controversial issue has been whether or not OCD patients with poor insight should be considered a distinct sub-group of patients. In a paper exploring insight in that disorder, almost half of the patients showed an excellent level of insight, whereas 15% showed little or none. No correlation between levels of insight and clinical features has been observed, except for a negative trend that emerges when somatic obsessions are present. In addition, a trend towards a lower level of insight has been noted in obsessive-bipolar patients who have a positive history of repeated manic or hypomanic episodes [9].

Neuropsychiatric disorders are often characterized by impaired insight into behaviour. This kind of deficit has been suggested and sometimes explored in drug-dependence disorders, too.

Substance abusers usually deny, or lack awareness of, their problem. Recent neuro-scientific evidence suggests that the denial of problems related to drug use could be associated with alterations in frontostriatal systems, which play a critical role in executive functions and self-awareness [16].

As to alcohol, a close relationship has been observed between the state of patients' insight and their level of motivation to change their own behaviour [7]. Some papers have pointed out the effect of insight on patients' willingness to change their life-style, suggesting the need for brief insight-enhancement interventions addressed to patients with alcohol dependence [8]. When a contemporary mental illness is present (in cases with dual diagnosis), this has been hypothesized to act as a fundamental factor in impairing insight level [17].

A few studies have been dedicated to investigating the role of insight in cocaine dependence. Some authors have examined the potential association between awareness of illness and drug-seeking behaviour, and have gone on to propose, especially with cocaine subjects who are urine-negative, interventions to enhance insight, in order to improve their longer-term clinical outcomes [11]. Active cocaine abusers display a diminished neural response to errors, with particular reference to the anterior cingulate cortex, which is so closely involved in error processing. The inability to detect or adjust performance in response to errors has been linked with clinical symptoms, including the loss of insight and perseverative behavior. On this theory, behavioural deficits that probably contribute to the maintenance of drug dependence could derive directly from a cognitive dysfunction [5].

Switching now to cannabis, there has been a great deal of debate over the role of THC in the pathogenesis of psychotic disorders; to date, cannabis use has been considered to be one of the most important risk factors for schizophrenia. Whatever the cause, for many subjects ending cannabis use during the early phases of recovery is very difficult, not only because of prior habits of use, but also because of the attendant psychotic symptoms, including poor insight and judg-

ment, lack of impulse control, and, most crucially, cognitive impairment. Moreover most of these subjects are unable to understand that cannabis use is connected with the onset of symptoms. Of course, patients' insight is a basic condition for understanding the need for treatment programmes, and it is further damaged by ongoing substance use [10].

Lastly, it is correct to assess dependence on nicotine as a severe form of dependence; it is, consequently, distinguished by impairment of awareness and reward system. The description of smoking as an autonomously chosen lifestyle appears to be cynical and calls for vigorous rejection. Most older smokers would, in fact, like to quit smoking and have repeatedly tried to do so, without ever succeeding. In particular, high-risk patients with comorbidities, who are highly motivated to quit smoking, often fail to achieve this, even if they are fully aware of the major benefits that come from effective smoking cessation [1, 11].

Lack of insight in patients has been explored in several psychiatric conditions, including substance abuse and dependence. In the literature there is a worrying and unjustified shortage of data in the field of heroin addiction, which can be viewed as the prototype of substance dependence disorders. This fact is even more disquieting when it is borne in mind that heroin addicts often fail to comply with methadone treatment when this is prescribed at blocking dosages. Lack of insight is a very difficult state for building the motivation that is indispensable to compliance or abstinence.

On the basis of these observations it would be appropriate to extend the study of insight into the field of heroin dependence, so as to improve the degree of compliance of heroin addicts who are receiving opioid agonist treatment.

References

1. Breitling L. P., Rothenbacher D., Stegmaier C., Raum E., Brenner H. (2009): Older smokers' motivation and attempts to quit smoking: epidemiological insight into the question of lifestyle versus addiction. *Dtsch Arztebl Int.* 106:(27) 451-455.
2. Dell'Osso L., Pini S., Cassano G. B., Mastrocinque C., Seckinger R. A., Saettoni M., Pappasogli A., Yale S. A., Amador X. F. (2002): Insight into illness in patients with mania, mixed mania, bipolar depression and major depression with psychotic features. *Bipolar Disord.* 4 315-322.
3. Francis J. L., Penn D. L. (2001): The relationship between insight and social skill in persons with severe mental illness. *J Nerv Ment Dis.* 189:(12) 822-829.
4. Ghaemi S. N., Boiman E., Goodwin F. K. (2000): Insight and outcome in bipolar, unipolar, and anxiety disorders. *Compr Psychiatry.* 41:(3) 167-171.
5. Hester R., Simoes-Franklin C., Garavan H. (2007): Post-error behavior in active cocaine users: poor awareness of

- errors in the presence of intact performance adjustments. *Neuropsychopharmacology*. 32:(9) 1974-1984.
6. Husted J. R. (1999): Insight in severe mental illness: implications for treatment decisions. *J Am Acad Psychiatry Law*. 27:(1) 33-49.
 7. Jung J. G., Kim J. S., Kim G. J., Oh M. K., Kim S. S. (2011): Brief insight-enhancement intervention among patients with alcohol dependence. *J Korean Med Sci*. 26:(1) 11-16.
 8. Kim K. M., Kim J. S., Kim G. J., Kim S. S., Jung J. G., Kim S. M., Pack H. J., Lee D. H. (2007): The readiness to change and insight in alcohol dependent patients. *J Korean Med Sci*. 22:(3) 453-458.
 9. Marazziti D., Dell'Osso L., Di Nasso E., Pfanner C., Presta S., Mungai F., Cassano G. B. (2002): Insight in obsessive-compulsive disorder: a study of an Italian sample. *Eur Psychiatry*. 17:(7) 407-410.
 10. Miller R., Caponi J. M., Sevy S., Robinson D. (2005): The Insight-Adherence-Abstinence triad: an integrated treatment focus for cannabis-using first-episode schizophrenia patients. *Bull Menninger Clin*. 69:(3) 220-236.
 11. Moeller S. J., Maloney T., Parvaz M. A., Alia-Klein N., Woicik P. A., Telang F., Wang G. J., Volkow N. D., Goldstein R. Z. (2010): Impaired insight in cocaine addiction: laboratory evidence and effects on cocaine-seeking behaviour. *Brain*. 133:(Pt 5) 1484-1493.
 12. Pallanti S., Quercioli L., Pazzagli A., Rossi A., Dell'Osso L., Pini S., Cassano G. B. (1999): Awareness of illness and subjective experience of cognitive complaints in patients with bipolar I and bipolar II disorder. *Am J Psychiatry*. 156:(7) 1094-1096.
 13. Pini S., Cassano G. B., Dell'Osso L., Amador X. F. (2001): Insight into illness in schizophrenia, schizoaffective disorder, and mood disorders with psychotic features. *Am J Psychiatry*. 158:(1) 122-125.
 14. Varga M., Magnusson A., Flekkoy K., Ronneberg U., Opjordsmoen S. (2006): Insight, symptoms and neurocognition in bipolar I patients. *J Affect Disord*. 91:(1) 1-9.
 15. Vender S., Poloni N. (2006): [Is the insight a favourable prognostic factor in the treatment of mental disorders?]. *Recenti Prog Med*. 97:(10) 565-570.
 16. Verdejo-Garcia A., Perez-Garcia M. (2008): Substance abusers' self-awareness of the neurobehavioral consequences of addiction. *Psychiatry Res*. 158:(2) 172-180.
 17. Yen C. F., Hsiao R. C., Chen C. C., Lin H. C., Yen C. N., Ko C. H., Yen J. Y., Chen C. S. (2009): The role of insight to alcohol use disorders in insight to schizophrenia. *Compr Psychiatry*. 50:(1) 58-62.

Role of funding source

No funds for this letter

Contributors

The authors contributed equally to this letter

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present letter.

Received and Accepted February 14, 2011

INFORMATION FOR CONTRIBUTORS

The Editor of *Heroin Addiction & Related Clinical Problems* welcomes contributions of original manuscripts that are not under consideration for publication elsewhere. The *Journal* publishes research reports, proposals, letters to editor.

Peer Review: All manuscripts, including those written at the invitation of the editor, are subject to peer review by at least two experts to determine the originality, validity, and significance of the submitted material. Authors will usually be advised within eight weeks on the decision on their manuscript. All reviewers will remain anonymous.

Manuscript Specifications: Manuscript must be typed double-spaced with one-inch margins on A4 paper (Max 29.952 characters). The cover page must contain the article title, authors' full names and affiliations, and address for correspondence and telephone number of corresponding author. Please, submit your paper only by E-mail in Rich Text Format Saved File. Please provide figures in .pdf or .tiff, .jpeg format or as Microsoft Power Point Presentation. Each article must include an abstract (100-word maximum) and a reference list.

Bibliography must be ordered by authors' names alphabetically. Start each reference with bibliography number; use these numbers, in squared parentheses, for in-text citations. Personal communications, unpublished manuscripts, manuscripts submitted but not yet accepted, and similar unpublished items should not appear in the reference list. Such citations may be noted in the text.

Please use the following guidelines for arranging references:

Journal article:

1. Dole V.P., Nyswander M.E., Warner A. (1968): Successful treatment of 750 criminal addicts. *JAMA* 206: 2708-2711.

Book:

1. Tagliamonte A., Maremmani I. (1995): *Drug Addiction and Related Clinical Problems*. Springer-Verlag, Wien, New York.

Book Chapter:

1. Dole V.P. (1995): Methadone Maintenance. Comes of Age. In A. Tagliamonte and I. Maremmani Eds: *Drug Addiction and Related Clinical Problems*. Springer-Verlag, Wien New York. pp. 45-49.

Journal names should be abbreviated as they appear in *Index Medicus*, journals not currently indexed there should not be abbreviated.

Submission Procedure: Submit the files to Icro Maremmani, MD, Editor, <maremman@med.unipi.it> and a Cc copy to <info@aucns.org>

Submissions should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the journal it is being submitted (Regular Article, Preliminary Communications, Reports, Proposals, Letters to the Editor);

Author Disclosure

Role of Funding Source. Authors are kindly requested to briefly describe the role of the study sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. If the funding source(s) had no such involvement, authors should so state.

Following the Role of the Funding Source text, authors are required to declare their individual contribution to the manuscript under a subheading *Contributors*.

Conflict of Interest. ALL authors are requested to disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations that could inappropriately influence, or be perceived to influence, their work. If there are no conflicts of interest, authors should state that there are none.

Acknowledgements, before the reference list and not as a footnote on the title page.

Ethics of Experimentations: Authors must declare in the cover letter that their studies submitted to *Heroin Addiction & Related Clinical Problems* have been conducted in accordance with Declaration of Helsinki.

