

LETTER TO EDITOR/CARTA AO EDITOR

The Hero's Substitution: Cross Sectional Study about Substitution Therapy for Heroin

A Substituição do Herói: Estudo Transversal sobre Terapêutica de Substituição de Heroína

✉ CATARINA CORDEIRO^{*1,2}, ✉ RODRIGO SARAIVA^{1,2}, ✉ INÊS SIMÕES¹, ✉ FÁTIMA ISMAIL^{1,2}, ✉ FILIPA NOVAIS^{1,2}

¹ Department of Neurosciences and Mental Health, Psychiatry Department, Hospital de Santa Maria (CHULN), Lisbon, Portugal

² Clínica Universitária de Psiquiatria e Psicologia Médica, Faculdade de Medicina, Universidade de Lisboa, Portugal

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Dear Editor,

Substance use is an important public health concern, representing an important cause of avoidable mortality.¹ Opioid users show the greatest mortality, being at the highest risk of overdose.¹ Treatment is mostly conducted in specialized outpatient settings, with opioid users being the largest group undergoing such treatment. Heroin remains the most common opioid, currently accounting for around 80% of all new opioid-related treatment demands in Europe.² Substitution treatment remains the preferred method, as it keeps showing a positive outcome in treatment retention, illicit opioid use, risk behavior, and drug-related mortality.³ Methadone is the most prescribed treatment of this kind, followed by buprenorphine.² In this study, we aimed to establish if there were demographical or clinical predictors of the referral to different opioid substitution programs.

We performed a cross-sectional study, where we analyzed data from consecutively recruited patients from the addictive disorders outpatient clinic at the Centro Hospitalar Universitário Lisboa Norte. The recruitment was made from 1st January of 2020 to 31st December of 2020.

Inclusion criteria were: patients with at least one consultation with the addictive disorders center team during the referred period. Exclusion criteria was not consuming opioid substances.

Stata software was used to perform the statistical analysis (version 14.2; StataCorp, Texas, USA). Descriptive statistics were presented as mean \pm standard deviation. For the analysis of our hypothesis, we used a logistic regression model. The outcome was the type of program: methadone versus buprenorphine substitution. Potential predictors, such as age, sex, age at the beginning of drug use, age at the beginning of drug-related problems, consumption of alcohol, cocaine, heroin, and cannabis were studied, first, in univariate models. Then, those that were found to be significant were included in a multivariate model.

Our sample included 154 people, 126 males (82%) and 28 females (18%). Their mean age was 45 ± 11 years old, ranging from 18 to 64 years old. Thirty patients (20%) were included in the buprenorphine program and 117 (80%) were in the methadone substitution program.

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* Autor Correspondente/Corresponding Author: Catarina Cordeiro | catarinarodriguescordeiro@gmail.com | Av. Prof. Egas Moniz MB, 1649-028 Lisboa

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Table 1. Demographical and clinical characteristics of the sample

Age, years	44.9 ± 11.1
Males, n (%)	126 (81.8)
Education, years	9.4 ± 3.9
Employment status	
• Unemployed, n (%)	30 (29.1)
• Retired, N (%)	18 (17.5)
• Active workers, n (%)	55 (53.4)
Marital status	
• Married, n (%)	29 (29.9)
• Single, n (%)	52 (53.6)
• Divorced, N (%)	13 (13.4)
Age at the beginning of drug abuse	19.9 ± 7.9
Age at the beginning of drug related problems	27.9 ± 9.8
Type of drug	
• Alcohol	62 (44.0)
• Cocaine	67 (47.2)
• Heroin	111 (77.6)
• Cannabis	60 (42.3)
• Other drugs	15 (9.7)
Type of program	
• Methadone substitution	117 (79.6)
• Buprenorphine substitution	30 (20.4)

From our logistic regression model, being older and not consuming cocaine were found to be significant predictors of being referred to a buprenorphine program (crude OR 1.07; $p=0.006$; CI 1.02-1.12 – adjusted OR 1.06; $p=0.018$; CI 1.01-1.11) and (crude OR 0.29; $p=0.009$; CI 0.11-0.74 – adjusted OR 0.35; $p=0.034$; CI 0.14-0.92), respectively.

For centuries, heroin was a drug of young, poor, inner-city male minorities. Nowadays we see a change in epidemiology since it has become a popular drug of choice for older, wealthier white men and women in smaller cities and suburban areas.⁵ Although it is still more likely to find a heroin addict among men keep in mind that demographic is changing, to include more women.⁵ Despite this, our population is still constituted mostly by men, which can be explained by more limited access to drugs among females, resulting in a later and less frequent use.⁶ Most of the patients gathered in this study were in the methadone program (80%), like what is found in several other countries⁷. This could be explained by the fact that methadone has been available for much longer than buprenorphine. However, we cannot ignore that patient inclusion in this study took place during the COVID-19 pandemic period, and that only patients attending presential appointments were

included, with a lot of ambulatory service being provided through telemedicine. This might result in a bias, favoring the inclusion of patients in the methadone program, who always maintained presential appointments and had to go to the hospital to take the drug, contrary to patients under buprenorphine treatment.

Our results suggest that being older is a significant predictor of taking buprenorphine. This finding differs from other articles reporting higher rates of methadone use in older patients comparing to buprenorphine.⁷ Perchance, younger patients might have reached our ambulatory service more recently, and as so, most of the time the choice of methadone over buprenorphine might be explained by better rates of treatment retention.⁷ That is particularly urgent in younger patients and those who just began seeking treatment. Furthermore, buprenorphine may precipitate opioid withdraw if patients are not already in withdrawal,⁸ making the induction phase of early treatment more challenging with this drug. On the other hand, it is frequently advantageous to transfer patients from methadone treatment to buprenorphine. Some of the advantages of buprenorphine are the lower risk of overdose, sedation, QT prolongation, and ventricular arrhythmias and the less severe withdrawal if a dose is missed.⁹

Finally, not consuming cocaine was also found to be a significant predictor of taking buprenorphine. Both buprenorphine and methadone have shown efficacy in polydrug use with cocaine and opioids,⁸ but methadone seems to come over the top, showing more efficacy than buprenorphine.¹⁰ This might justify our findings, which suggest that methadone is preferred over buprenorphine in patients with polysubstance use with opioids and cocaine. This study has several limitations. This is a cross-sectional analysis of data that does not consider individual clinical

factors, such as the severity of opioid use disorder. Therefore, our findings indicate associations rather than cause and effect relationships. The covid pandemic period logistic impositions might also have biased our results. Nevertheless, this is an important study that shows that both demographical data and the type of substance may lead to different treatment choices. More studies should be made comparing these types of programs to gather more evidence that should support clinical decisions.

Declaração de Contribuição

CC, RS, IS e FN: Escrita e revisão do manuscrito

FI: Revisão do manuscrito

Contributorship Statement

CC, RS, IS and FN: Writing and review of the manuscript

FI: Review of the manuscript

Responsabilidades Éticas

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Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

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