

Mortality rate in patients on methadone treatment and infected with the human immunodeficiency virus and/or the hepatitis C virus

Mortalidad entre los pacientes en tratamiento con metadona e infectados con el virus de la inmunodeficiencia humana y/o hepatitis C

ROBERTO LOZANO*, NIEVES DOMEQUE**, CONCEPCIÓN PERÁLVAREZ**, MARIA-DOLORES TORRELLAS**, CIELOS GONZALO**.

* Servicio de Farmacia, Hospital Real de Nuestra Señora de Gracia, Zaragoza, SALUD. ** Unidad asistencial especializada en tratamiento ambulatorio de los trastornos adictivos por consumo de sustancias (UASA). Hospital Real de Nuestra Señora de Gracia, Zaragoza, SALUD.

Dear Director,
Heroin addiction is a chronic, relapsing disease with serious consequences, particularly in terms of premature and high mortality (Hser, Hoffman, Grella & Anglin, 2001). Methadone maintenance treatment programs (MMT's) have shown to be effective in reducing illicit opioid use and the risk of infection with human immunodeficiency virus (HIV) and/or Hepatitis C virus (HCV), among other (Kleber, 2008; Pedrero-Pérez & MethaQoL, 2017).

Nevertheless, the approximately 1% annual mortality among MMT patients is more than 10 times that of the general population (Zanis & Woody, 1998); and overdose, HIV infection (VIH), and other viruses transmitted by blood (e.g., HCV infection) constitute the most common causes of death (Roncero, Vega, Martínez-Raga & Torrens, 2017).

In fact, among HIV-infected patients, HIV-HCV co-infection is observed in 50–95% of cases (Muga, Roca, Egea, Tor, Sirera & Rey-Joly, 2000); this simultaneous HIV infection can cause an increased viral load of HCV and a more rapid evolution to liver cirrhosis and its complications (Santos & Sanz, 2004; Elizalde, Iñarraiaegui, Rodríguez & Zozaya, 2004).

Therefore, the objective of this paper was to analyze the influence of HIV and HCV infection on the survival of patients included in MMT's programs.

For this, an observational retrospective study was conducted of mortality over a ten-year period (2005–2014) in a cohort of heroin-dependent patients included in the MMT program of a care unit specializing in the outpatient treat-

ment of addiction and *substance abuse* disorders at the Hospital Real de Nuestra Señora de Gracia in Zaragoza, Spain.

The sample comprised 299 patients at baseline (2004) and 253 patients at the end of the study period (2014). Data concerning gender, age, body mass index, methadone dose, age of inclusion in the MMT, year of diagnosis of HIV and/or HCV infections, and mortality were obtained from electronic and manual clinical records.

The patients were divided into four groups based on the presence or absence of HIV and HCV infections (non-infected, group 1; VIH-infected, group 2; VIH and VHC co-infected, grupo 3; VHC-infected, group 4); then, overall mortality from all causes, as well as the crude mortality rate (CMR) were calculated, the later for each patient group and expressed as the number of deaths per 100 patient-years of follow-up.

Finally, the influence of HIV and/or HCV infections on overall mortality was assessed by comparing the CMR data from groups 2 to 4 (those infected with HIV and/or HCV) versus group 1 (non-infected patients).

By the end of the study period (10 years), there had been 46 deaths (15.4%) and a calculated CMR of 0.9%, 2.2%, 2.6%, and 1.7% corresponding to groups 1 to 4, respectively.

Regarding the influence of HIV or HCV infection, the greatest difference in CMR was between the co-infected group 3 and the control group 1 (0.9% vs .2.6%; $p = .0113^*$). Comparisons among the rest of the groups were smaller and not statistically significant. However, when considering HIV patients in Groups 2 and 3 and HCV pa-

Received: August 2017; Accepted: January 2018

Send correspondence to:

Roberto Lozano. Servicio de Farmacia. Hospital Real de Nuestra Señora de Gracia. Ramón y Cajal 60. 5000 Zaragoza.
E-mail: rlozano@salud.aragon.es

Table 1. Patient characteristics and results.

Variable	Group 1 Non-infect.	Group 2 VIH-infect.	Group 3 VIH-VHC co-infect.	Group 4 VHC-infect.
Patient characteristics				
Age, years	47(7.7)	48 (7.5)	47 (8)	46 (6.6)
Female, No. (%)	26 (28)	20 (43)	16 (19)	22 (32)
BMI, kg/m ²	25.6 (3.4)	24 (4)	23 (4)	26 (6)
Years on TMM	15 (7.7)	16 (7.6)	15.3 (8)	13.8 (6.6)
MTD dose, mg	56(32)	61 (41)	65 (35)	55 (31)
Results				
Patients, No. (%)	92 (30.8)	54 (18.1)	85 (28.4)	68 (22.7)
Exitus, No. (%)	9 (9.8)	10 (18.5)	18 (21.2)	9 (13.2)
Patient-years	87	45	69	53
CMR, (%)	0.9	2.2	2.6	1.7
Fisher's test (p)	comparator	.0734	.0113*	.092

Note. All data are expressed as mean (\pm SD), unless otherwise indicated.

* $p \leq .05$; DS = standard deviation; BMI = body mass index; MTD = methadone, No. = number, CMR= crude mortality rate; MMT = methadone maintenance treatment.

tients in Groups 3 and 4, the differences in CMR were also more than double and statistically significant, when compared to the control group: 28 deaths (114 patient-years) vs 9 deaths (87 patient-years, $p=.0104^*$) and 27 deaths (122 patient-years) vs 9 deaths (87 patient-years, $p = .0271^*$) for HIV and HCV, respectively.

The obtained data seem to indicate that HIV and HCV infection, and especially co-infection, along with factors directly related to the treatment of co-morbidities, such as antiretrovirals, tuberculostatic drugs, and psychotropic drugs, which can often be hepatotoxic, play a key role in morbidity and mortality in this cohort of patients.

Therefore, the introduction of new antiretroviral and therapeutic regimens and pharmacotherapeutic follow-up of both adherence to treatment and its side effects for patients with *acquired immune deficiency syndrome*; as well as the adoption of new antivirals for the treatment of hepatitis C, would be key factors to increase survival in this type of patient.

Finally, it should be noted, as the most important limitations of this analysis of mortality, due to sample size and absence of data, that it could not assess the influence of other factors, such as gender, age, or concomitant treatments for infectious and psychiatric co-morbidities.

Conflict of interests

The authors declare no conflict of interest.

References

- Elizalde, I., Iñarrairaegui, M., Rodríguez, C. & Zozaya, J. M. (2004). Treatment of chronic hepatitis C virus infection. *Anales del Sistema Sanitario de Navarra*, 27, 81-90.
- González-Álvarez, S., Madoz-Gúrpide, A., Parro-Torres, C., Hernández-Huerta, D. & Ochoa Mangado, E. (2019). Relationship between alcohol consumption, whether linked to other substance use or not, and antiretroviral treatment adherence in HIV+ patients. *Adicciones*, 31, 8-17. doi:10.20882/adicciones.916.
- Hser, Y. I., Hoffman, V., Grella, C. E. & Anglin, M. D. (2001). A 33-year follow-up of narcotics addicts. *Archives of General Psychiatry*, 58, 503-508. doi:10.1001/archpsyc.58.5.503.
- Kleber, H. D. (2008). Methadone maintenance 4 decades later: Thousands of lives saved but still controversial. *Journal of the American Medical Association*, 300, 2303-2305. doi:10.1001/jama.2008.648.
- Muga, R., Roca, J., Egea, J. M., Tor, J., Sirera, G. & Rey-Joly, C. (2000). Mortality of HIV-positive and HIV-negative heroin abusers as a function of duration of injecting drug use. *The Journal of Acquired Immune Deficiency Syndromes*, 23, 332-338.
- Pedrero-Pérez, E. J. & MethaQoL, G. (2017). Methadone dosage and its relationship to quality of life, satisfaction, psychopathology, cognitive performance and additional consumption of non-prescribed drugs. *Adicciones*, 29, 37-54. doi:10.20882/adicciones.831.
- Roncero, C., Vega, P., Martínez-Raga, J. & Torrens, M. (2017). Chronic Hepatitis C and people with a history of injecting drugs in Spain: population assessment, challenges for effective treatment. *Adicciones*, 29, 71-73. doi:10.20882/adicciones.908.
- Santos, I. & Sanz, J. (2004). Tratamiento con interferón y ribavirina de la hepatitis crónica por virus C en pacientes con infección por VIH. *Anales de Medicina Interna*, 21, 369-372.
- Zanis, D.A. & Woody, G. E. (1998). One year mortality rates following methadone treatment discharge. *Drug and Alcohol Dependence*, 52, 257-260. doi:10.1016/S0376-8716(98)00097-0.