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ARTICLE RESEARCH

HEPATITIS B, HEPATITIS C AND HIV AMONG DRUG USERS IN METHADONE MAINTENANCE TREATMENT: PREVALENCE, DOSES, TREATMENT COMPLIANCE

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Abstract

The Users of opioid substances, especially injecting drugs, are at high risk of infection with blood-borne viruses, such as hepatitis B, C and human immunodeficiency virus, due to the sharing of needles and injection equipment. Methadone substitution treatment is approved device in the risk reduction strategy of hepatitis B, C and HIV infection. The aim of this study is to determine: the socio-demographic and medical psychiatric characteristics of patients with hepatitis B, C and HIV under methadone, the prevalence of hepatitis C, B and HIV, the dose of methadone and compliance with treatment in this population.

Materials and methods: This is a retrospective descriptive study of patients admitted to the center of addictology at the hospital Ar-razi of Sale in Morocco, specifically in methadone unit.

Results: The prevalence of hepatitis C, B and HIV were respectively 80%, 13% and 4% in patients with positive serology, the average dose of methadone was higher than the dose of all patients enrolled in the methadone program. 80% of patients under methadone with positive serology to HCV, HBV and HIV had a polyconsumption of psychoactive substances (cannabis, cocaine, alcohol, benzodiazepine). 72% of our patients with hepatitis C received treatment for their infection while all the patients with HIV were put on antiretroviral drugs with good therapeutic compliance.

Conclusion: Methadone substitution therapy has proven to be a successful strategy to reduce the risk of HIV, HCV and HBV infection in opioid-dependent patients. However, the adjustment of methadone doses and systematic screening for HIV, HCV and HBV is essential in this vulnerable population.

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Introduction:-

The Users of opioid substances, mainly by injection, are at high risk of infection with blood-borne viruses such as hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) [1], due to the sharing of needles and injection equipment. Nearly 15.6 million people aged between 15-64 years inject drugs worldwide, which has an impact on the global prevalence of HCV, HBV, and HIV, which varies geographically from one country to another and even within the same country [2].

Methadone is a synthetic opioid whose primary purpose is to replace opioid products and decrease withdrawal symptoms in dependent patients [3]. Methadone substitution therapy (MST) is a proven risk reduction strategy [4-5]. Studies have shown that MST is associated with a decreased risk of HIV and HCV infection [6-7], as well as with treatment compliance [8-9]. The interaction between methadone metabolites and HCV and HIV is beginning to be elucidated by studies, which among other things influence the effective dose of methadone in this particular population.

Materials and Methods:-

This is a retrospective descriptive study. The data were collected from the records of all patients admitted to the Addiction Center at Ar-razi university Hospital in Sale, specifically in methadone unit since its inauguration in June 2010 until September 2020.

The methodology used is based on a exploitation form, studying (age/sex/marital status/region of origin/comorbidities: psychiatric, HBV, HCV and HIV serology /addictive behaviors/dose of methadone/duration of retention). 206 patients since June 2010 have been included in the study, currently 80 patients inactive file (end of September 2020), and 25 patients have hepatitis B, C and /or HIV.

Results:

Table1:- Socio-demographic characteristics of patients integrated into the Methadone program (June 2010-September 2019).

Variables	N(%)
Gender:	
. male	188(92)
. female	18(8)
Marital Status:	
. Single	92(42)
. Married	97(48)
. Divorced	17(10)
. Widow(er)	0(0)
Profession:	
- Without	121 (67)
. Liberal activities	73(27)
. Student	6(3)
. -Public servant	6(3)
Provenance:	
. Urban	197 (95)
. Rural	9(5)
Region of origin:	
. North of Morocco	113 (59)
. Rabat-Salé	33(17)
. Other cities in Morocco:	46(18)
. Foreign	14(6)

Table 2:- Medical and psychiatric characteristics of patients in the Methadone Program(June2010September2019).

Age of patients		32.6
Age of onset consumption		19.2
Comorbidities:		
. Psychiatric	169 (83)	
. Somatic	33 (16)	
. VHB	1 (0,48)	
. HCV	20 (11,1)	
. HIV	4 (1,94)	
Serological status not known	8 (9)	
Judicial history	86 (42)	
Other substance use disorder (non-opioid)	202(99)	
Maintenance Dose (Methadone)		70.7mg
Adverse reactions to methadone	67 (33)	
Retention time in the program		15.2 months

Table 3:- Table 3: Medical and psychiatric characteristics of patients integrated into the Methadone Program with hepatitis C, B and HIV (June 2010- September 2019)

Variables	N(%)	average
age		39.7 years
Gender		
. Male	23(92)	
. female	2(8)	
How to use		
. Injected	11(44)	
. Smoked	10(40)	
. Snorted	1(4)	
. Injected+smoked	1(4)	
Average initial dose		26.2mg/d
Average maintenance dose		75.2mg/d
SPA:		
. Cannabis	15 (60)	
. Alcohol	6(24)	
. Cocaine	6(24)	
. Benzodiazepines	10 (40)	
. Polydruguse(cannabis-alcohol-cocaine- Benzodiazepines)	20 (80%)	
Patients on treatment:		
HBV,HCV:	18(72)	
HIV	16 (100)	

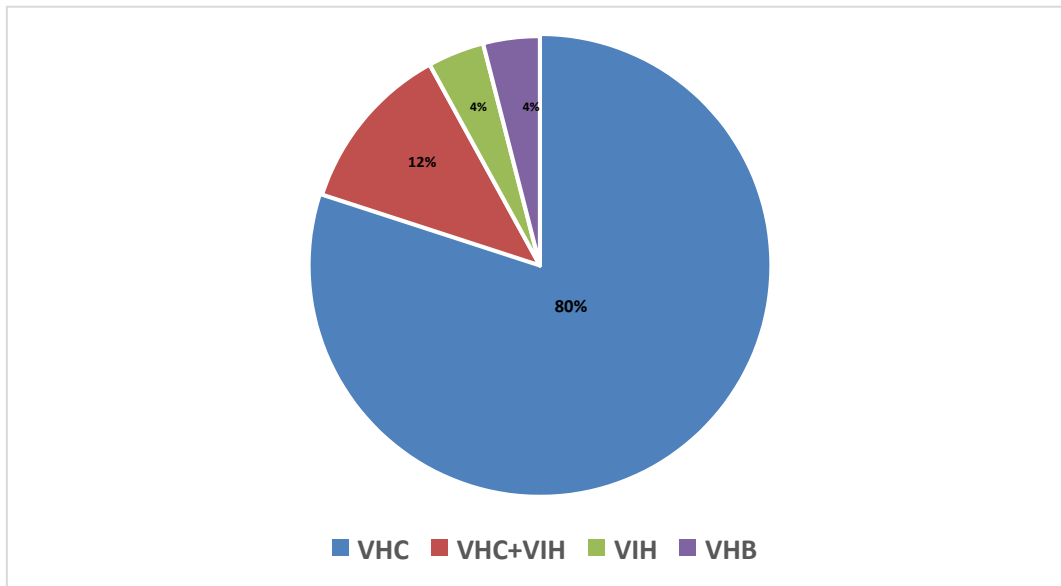


Figure 1:- Prevalence of hepatitis B, C and HIV in patients with positive serology.

Discussion:-

The high risk of infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) [10 - 11] among opioid users and in particular among injecting drug users is established by the literature, given the sharing of syringes and unprotected sexual behavior [10- 11]. In our study the prevalences of hepatitis C, B and HIV were 80%, 13% and 4% respectively in patients with positive serology. These results are comparable to those of a study done in Myanmar which found that HCV was by far the predominant infection among injecting drug users (IDU), with HCV prevalence rates of about 70%, followed by HIV and HBV, with prevalence rates of about 15% and 6%, respectively [12]. In the same vein, a systemic review [2] found that HCV prevalence rates among IDU vary within the country and are always higher than HIV and HBV rates, a global HCV prevalence was estimated at 52.3% (95%IU42.4-62.1) among IDU. This says that half of the IDU were infected with HCV. HIV prevalence among IDU varied considerably by geographic region, ranging from 1.1%(0.8-1.4) to 35.7%(15-56.6), with the highest rate recorded in Eastern Europe and Latin America, which are home to the largest number of IDU with HIV. While HBV infection among IDU was estimated at 9.1%(95%IU5.1-13.2) with a predominance in East and Southeast Asia which account for more than half of all HBsAg positive IDU worldwide.

In our study, the dose of methadone administered to HIV/HCV patients was as high as 120 mg in some patients. This is consistent with the results of a study that found that HIV/HCV co-infected patients received higher doses of methadone than users of only opioid products with methadone doses above 80mg [13], this is partly explained by the concomitant use of antiretrovirals, efavirenz and nevirapine decrease the blood levels of methadone [14 -15]. The use of higher doses in this context could be explained by the fact that increased adherence to antiretroviral treatment is observed with increasing doses of methadone [16].

In a study [17] that examined the influence of HCV on the plasma levels of methadone metabolites (R-methadone and S-methadone), the results suggest that the mean plasma concentration of methadone and the concentration of R-methadone were higher in HCV positive (340 ± 209 ng/ml and 196 ± 122 ng/ml) than in HCV negative patients (261 ± 204 ng/ml and 142 ± 99 ng/ml) . While the mean ratio of S -EDDP to methadone dose was significantly lower in HCV-positive (0.31-0.35) than in HCV-negative patients (0.72-1.66), they also found significantly elevated levels of CYP2B6 gene expression in HCV-positive patients compared to HCV-negative patients (P=0,031), the catalytic activity of CYP2B6 for methadone metabolites and essentially S-methadone explains, among other things, the low ratio of S-methadone to methadone dose in HIV-positive patients. However, methadone patients with HCV received a 14.13 mg higher methadone dose compared to non-HCV patients. This is consistent with our study in which HCV patients received higher average methadone doses than all patients enrolled in the methadone program. Although HCV infection alters methadone metabolism, HCV-associated liver inflammation has also been associated with reduced methadone doses [18].

In our study, 80% of methadone patients with positive HCV, HIV and HBV serology had a polyconsumption of psychoactive substances (PAS) (cannabis, cocaine, alcohol, benzodiazepine); it is established in the literature that polyconsumption of psychoactive substances constitutes a risk of HCV transmission among IDU [19-20]. One study showed that people who injected cocaine in addition to opioids were ten times more likely to be infected with HCV (RER1HR= 3.44), while people who combined opioids with crack cocaine or benzodiazepines (BDZ) had relative risks of (RR1HR=1.27), (RER1HR=0.8) respectively. The risk is even higher when combining these three psychoactive substances with injected OP ($p < 0.001$) [21]. This can be explained by synergistic interactions caused by the cumulative harmful effects of cocaine and co-injection of OP [22- 23]. Another plausible explanation is that the psychoactive stimulant effect of cocaine (injected or smoked) may affect the decision-making process [24]. Findings suggest that opioids and BDZ exert mutual μ -modulatory effects [25-26], and that people who combine the two substances inject more frequently and share injection equipment. The cumulative effect of several PAS on the risk of transmission of blood-borne viruses (HCV and HIV) has already been demonstrated [19- 20].

In our study, 72% of our patients with hepatitis B or C received treatment for their infection. While all HIV patients were put on antiretrovirals with good adherence, this can be explained in our case by the free availability of antiretrovirals in our health system. The results demonstrate that opioid agonist treatment can be useful in linking injecting drug users to HCV care, and highlight the need to better engage people who use PAS for care [27]. Studies have found increased use of antiretroviral therapy (ART) among injection drug users who are on methadone [16 28]. Findings have sullied the positive role that MST plays in retention, adherence, and viral load suppression among HIV- and HCV-positive IDU [29- 30]. Specifically, a randomized controlled trial found that IDU on methadone reported significantly faster entry into HIV care compared with those without a history of MST (relative risk = 2.97; 95% CI: 1.20-6.21) [31].

One study looked at HIV and HCV control strategies in methadone maintenance treatment in Guangdong Province, China [32] which found that condom promotion was the most effective means of reducing HIV infection in MST, in contrast, psychological counseling and contingency management were found to be the most effective interventions for reducing HCV incidence among MST participants, followed by needle exchange and health education, and finally condom promotion. [33].

Conclusion:-

Systematic screening for HIV, HCV and HBV infection is essential among opioid- dependent people, given the high prevalence of these viruses. However, methadone substitution treatment has proven to be a successful risk reduction strategy, and the adaptation of methadone doses to this population is essential, given the virus/methadone interactions and the biological characteristics of this population. Moreover, the early diagnosis of HCV, HBV and HIV infection in opioid users outside the methadone program will be judicious in order to ensure early management.

Limitations of this study

Socio-demographic characteristics were not discussed due to the abundance of variables explored. We only targeted opioid users in our study, while other sub groups of drug users may also be at risk for infectious diseases.

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