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RESEARCH ARTICLE

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

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Abstract

TheUsersofopioidsubstances,especiallyinjectingdrugs,areathighriskofinfection 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 approven device in the risk reduction strategy of hepatitis B,C and HIV infection.The aim of this studyis 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.

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,andHIV,which varies geographically from one country to another and even within the same country [2].

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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-demographiccharacteristicsofpatientsintegratedintotheMetahdoneprogram(June2010-September2019).

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

Table 2:- MedicalandpsychiatriccharacteristicsofpatientsintheMethadoneProgram(June2010September2019).

age of patients		32.6
Age of onset consumption		19.2
Comorbidities: - Psychiatric - Somatic - VHB - HCV	 169 (83) 33 (16) 1 (0,48) 20 (11,1)	

- HIV Serological status not known	4 (1,94) 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 - female	 23(92) 2(8)	
How to use - Injected - Smoked - Snorted - Injected+smoked	 11(44) 1040) 1(4) 1(4)	
Average initial dose		26.2mg/d
Average maintenance dose		75.2mg/d
SPA: - Cannabis - Alcohol - Cocaine - Benzodiazepines - Polydruguse(cannabis-alcohol-cocaine- Benzodiazepines)	 15 (60) 6(24) 6(24) 10 (40) 20 (80%)	
Patients on treatment: HBV,HCV: HIV	 18(72) 16 (100)	

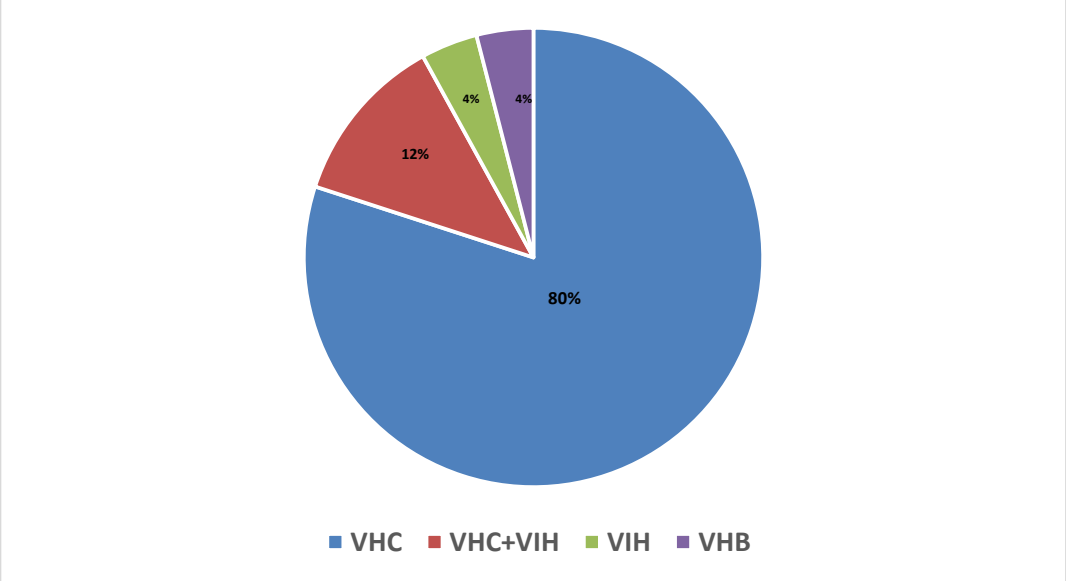

Figure 1:- Prevalence of hepatitis B, C and HIV in patients with positive serology.

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].Inour study theprevalences of hepatitis C, B and HIV were 80%, 13% and4%respectivelyinpatientswithpositiveserology.Theseresultsarecomparabletothose ofastudydoneinMyanmarwhichfoundthatHCVwasbyfarthepredominantinfectionamong 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 systemicreview[2]foundthatHCVprevalenceratesamongIDUvarywithinthecountryand arealwayshigherthanHIVandHBVrates,aglobalHCVprevalencewasestimatedat52.3% (95%IU42.4-62.1)amongIDU.ThissaysthathalfoftheIDUwereinfectedwithHCV.HIV prevalenceamongIDUvariedconsiderablybygeographicregion,rangingfrom1.1%(0.8-1.4) to35.7%(15-56.6),withthehighestraterecordedinEasternEuropeandLatinAmerica, whicharehometothelargestnumberofIDUwithHIV.WhileHBVinfectionamongIDUwas estimatedat9.1%(95%IU5.1-13.2)withapredominanceinEastandSoutheastAsiawhich account for more than half of all HBsAg positive IDU worldwide.

In our study, the doseof 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 holy opioidproductswithmethadonedosesabove80mg[13],this is partlyexplainedbythe 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 withincreasing 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 significantlylowerinHCV-positive(0.31-0.35)thaninHCV-negativepatients(0.72-1.66), they also found significantly elevated levels of CYP2B6 gene expression in HCV-positive patientscomparedtoHCV-negativepatients(P=0,031),thecatalyticactivityofCYP2B6for methadonemetabolitesandessentiallyS-methadoneexplains,amongotherthings,thelow 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 polyconsumptionofpsychoactivesubstances (PAS)(cannabis,cocaine,alcohol,benzodiazepine); it is established in theliterature that polyconsumptionof psychoactive substances constitutes ariskofHCVtransmissionamongIDU[19-20].Onestudyshowedthatpeoplewhoinjected cocaineinadditiontoopioidsweretentimesmorelikelytobeinfectedwithHCV(RER1HR= 3.44), while people who combined opioids with crack cocaine or benzodiazepines (BDZ)had relativerisksof(RR1HR=1.27),(RER1HR=0.8)respectively.Theriskisevenhigherwhen combiningthesethreepsychoactivesubstanceswithinjectedOP($p<0.001$)[21].Thiscan beexplainedbysynergisticinteractionscausedbythecumulativeharmfuleffectsofcocaine and co-injection of OP[22- 23] . Another plausible explanation is that the psychoactive stimulanteffectofcocaine(injectedorsmoked)mayaffectthedecision-makingprocess[24]. FindingssuggestthatopioidsandBDZexertmutualμ-modulatoryeffects[25-26],andthat people who combine the two substances inject more frequently and share injection equipment.ThecumulativeeffectofseveralPASontheriskoftransmissionofblood-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. WhileallHIVpatientswereputonantiretroviralswithgoodadherence,thiscanbeexplained in our case by the free availability of antiretrovirals in our health system.The

resultsdemonstratethatopioidagonisttreatmentcanbeusefulinlinking injectingdrugusers to HCV care, and highlight the need to better engage people who use PAS for care [27]. Studieshavefoundincreaseduseofantiretroviraltherapy(ART)amonginjectiondrugusers 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 significantlyfasterentryintoHIVcarecomparedwiththosewithoutahistoryof MST(relative risk = 2.97; 95% CI: 1.20-6.21) [31].

OnestudylookedatHIVandHCVcontrolstrategiesinmethadonemaintenancetreatment in Guangdong Province, China [32] which found that condom promotion was the most effectivemeansofreducingHIVinfectioninMST,incontrast,psychologicalcounselingand 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 andthe biologicalcharacteristics ofthis population. Moreover,the early diagnosisofHCV,HBVandHIVinfectioninopioidusersoutsidethemethadoneprogramwillbe judicious in order to ensure early management.

Limitationsofthisstudy

Socio-demographiccharacteristicswerenotdiscussedduetotheabundanceofvariables explored.Weonlytargetedopioidusersinourstudy,whileothersubgroupsofdrugusers may also be at risk for infectious diseases.

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