Journal of Infection and Public Health (2017) 10, 76—83

http://www.elsevier.com/locate/jiph

Low prevalence, low immunization and low adherence to full hepatitis B vaccine scheme and high-risk behaviors among crack cocaine users in central Brazil

Leandro N. da Silva[a], Divânia D. da Silva França[a], Nativa H.A. Del-Rio[b], Megmar A. dos Santos Carneiro[b], Regina M.B. Martins[b], Rafael A. Guimarães[c], Raquel S. Pinheiro[c], Ana L.N. Junqueira[c], Karlla A.A. Caetano[c], Sheila A. Teles[c,*]

[a] *Municipal Health Secretary, Goiania, GO, Brazil*
[b] *Postgraduate Program in Tropical Medicine and Public Health, Institute of Tropical Diseases and Public Health, Universidade Federal de Goiás, Brazil*
[c] *Postgraduate Program in Nursing, Faculty of Nursing, Universidade Federal de Goiás, Brazil*

Received 23 November 2015; received in revised form 18 February 2016; accepted 20 February 2016

KEYWORDS
Hepatitis B;
Crack cocaine;
Epidemiology;
Hepatitis B vaccine

Summary Crack cocaine users represent a target group for hepatitis B vaccination. We evaluate the HBV epidemiology, immunization status and compliance with a super-accelerated vaccination schedule among in-treatment crack cocaine users in central Brazil. Six hundred in-treatment crack cocaine users were interviewed, and serum samples were tested for HBV markers. A super-accelerated vaccination schedule of HBV vaccine was offered to all susceptible crack cocaine users. In total, 7.0% of those tested had at least one positive marker of HBV exposure. Age, use of crack cocaine through improvised pipe, exchange of sex for money/drugs and previous sexually transmitted infections (STIs) were predictors of HBV exposure. One hundred six (17.7%) individuals showed a serological profile of hepatitis B vaccination. Of these, 54.7% were less than 25 years old, and only 13% of individuals were more than 35 years old. Although 91.8% of crack users accepted the first vaccine dose, only 21.7% received all three doses. Of the 23 crack cocaine users who

* Corresponding author at: Universidade Federal de Goiás, Prédio da Reitoria — Campus Samambaia, CEP 74 001-970 Caixa Postal 131, Goiânia, Goiás, Brazil. Tel.: +55 6232558483.
E-mail address: sateles@ufg.br (S.A. Teles).

http://dx.doi.org/10.1016/j.jiph.2016.02.010

agreed to have their vaccine response evaluated, 78.3% developed protective anti-HBs titers. Premature termination of treatment was the most common reason for not receiving the full vaccine series. Despite the low prevalence of HBV exposure among in-treatment crack cocaine users in central Brazil, the low rate of immunization and the high frequency of high-risk behaviors highlight the potential for crack users to acquire and disseminate this infection and therefore maintain the viral reservoir. Health practitioners need to keep this in mind, taking advantage of all opportunities to access this population and vaccinate against HBV.

Introduction

HBV infection is a cause of acute and chronic hepatitis, cirrhosis and liver cancer. There are currently approximately 240 million hepatitis B carriers worldwide, distributed predominantly in African and Eastern countries where HBV dissemination occurs mainly by horizontal and vertical routes, respectively. In Western countries, HBV infection is acquired, in general, as a result of high-risk behaviors, such as unsafe sex practices and illicit drug use [1].

Globally, it is estimated that 0.4% of adults aged 15—64 consume cocaine. The major markets of cocaine are American and European countries, and Brazil is the largest cocaine market in South America [2]. Crack cocaine is the base form of cocaine. It is cheaper than cocaine salt and has more intense effects. It is estimated that there are 370,000 crack cocaine users in this country [3], and crack addiction is one of the most common causes of cocaine-related hospitalization [4]. Crack users generally exhibit multiple risk behaviors that expose them to diseases with sexual and parenteral transmission, such as hepatitis B virus (HBV) infection [5—7].

The hepatitis B vaccine, which is considered the most effective means of preventing HBV infection, has been recommended for drug users since its creation. It has been available, free of cost, for this population in our country since the 1990s [8]. Despite this availability, the frequency of vaccinated illicit drug users remains low [9]. The difficulty of accessing health services for these individuals coupled with the long interval between the second and third dose of the vaccine appear to contribute to this situation [10]. In this context, accelerated vaccination schemes against hepatitis B [11,12] and vaccinations in areas frequented by drug users could be strategies to help overcome these issues.

The purpose of this study was to investigate HBV epidemiology and HBV vaccination and to evaluate compliance and vaccine response among in-treatment crack users in central Brazil.

Materials and methods

From August 2012 to April 2013, crack cocaine users were recruited in the Chemical Dependency Unit (CDU) of a reference hospital in Goiania (1,256,514 inhabitants), central Brazil. The inclusion criteria for the study were aged 18 years and over, in treatment for drug abuse and used *crack* in the last 6 months. The exclusion criteria were as follows: under the influence of medication at the time of the interview, making it impossible to answer questions, and exhibition of behaviors that would render them unable to participate in the interview process and/or collection of blood sample at the time of blood collection.

Data collection was performed twice a week for a period of 8 months from August 2012 to April 2013. All eligible individuals who were admitted during the study period were invited to participate. The interviews were conducted in a private location on the premises of the CDU. Blood samples were collected in order to detect HBV serological markers, and then the first dose of hepatitis B vaccine was offered. Subsequent doses were offered to individuals identified as susceptible to HBV by serological screening.

In the hospital where the study was conducted, the time of hospitalization for drug detoxification is 28 days. The hepatitis B vaccine was administered according to a super-accelerated regimen: 0, 7 and 21 days [12]. The vaccine administered was the same as that used by the National Immunization Program (NIP), the Brazilian recombinant hepatitis B vaccine (VrHBV) from the Butantan Institute (SP). The vaccine was administered intramuscularly (deltoid muscle). After the third dose, a second blood sample was collected to evaluate the vaccine response.

All samples were tested by ELISA for the detection of HBsAg (Hepanostika HBsAg Ultra, bioMérieux, Boxtel, the Netherlands), total anti-HBc (Eti-Ab-CorekPlus, DiaSorin, Italy) and anti-HBs (Eti-Ab-Auk, DiaSorin, Italy) by immunoassay using commercial kits. Quantitative detection of anti-HBs was performed using the Elecsys anti-HBs assay (Roche, Rotkreuz, Switzerland).

Individuals whose blood samples were negative for all HBV markers were considered susceptible to HBV infection. Subjects whose blood samples were positive for only anti-HBs antibodies were considered vaccinated against hepatitis B. Individuals whose blood samples had titers $\geq$10 mIU/mL were considered vaccine responders.

Interview data and the results of serological tests were entered into a computer and analyzed in SPSS (Statistical Package for Social Sciences) version 17.0 for Windows. Prevalence was calculated with a 95% confidence interval. The χ^2 test (chi-square) and Fisher's exact test (categorical variables) were used to compare variables and to evaluate the association between HBV positivity and risk factors. These results, which were estimated by odds ratio in univariate analysis, were further analyzed using a stepwise logistic regression model. Patients who were only anti-HBs positive were excluded from the association analyses. Pearson correlation was used to assess the relationship between the level of anti-HBs titers and the time of blood collection.

This study was analyzed and approved by the Committee on Ethics in Human Research of Hospital das Clínicas/UFG, case CEP/HC/UFG n° 117/201.

Results

During the study period, 1305 patients were admitted to the Chemical Dependency Unit. Of these, 959 had a history of crack cocaine use. Of them, 266 were excluded due to age (n = 74) or agitation and aggression (n = 192), and 93 refused to participate (Fig. 1). Of the investigated crack users (n = 600), the majority were male (84.5%). More than half self-reported as mixed race (61.5%) and single (66.5%). Only 26% reported formal employment, and 20% reported previously living on the streets. The median age, education and household income of participants was 30 years (IQR: 09), 9 years (IQR: 05), and $445 (IQR: 477), respectively. The median time of hospitalization was 15 days (minimum: 1; maximum: 98).

Of those tested, three crack users were HBV carriers, and 42 had at least one marker of exposure to

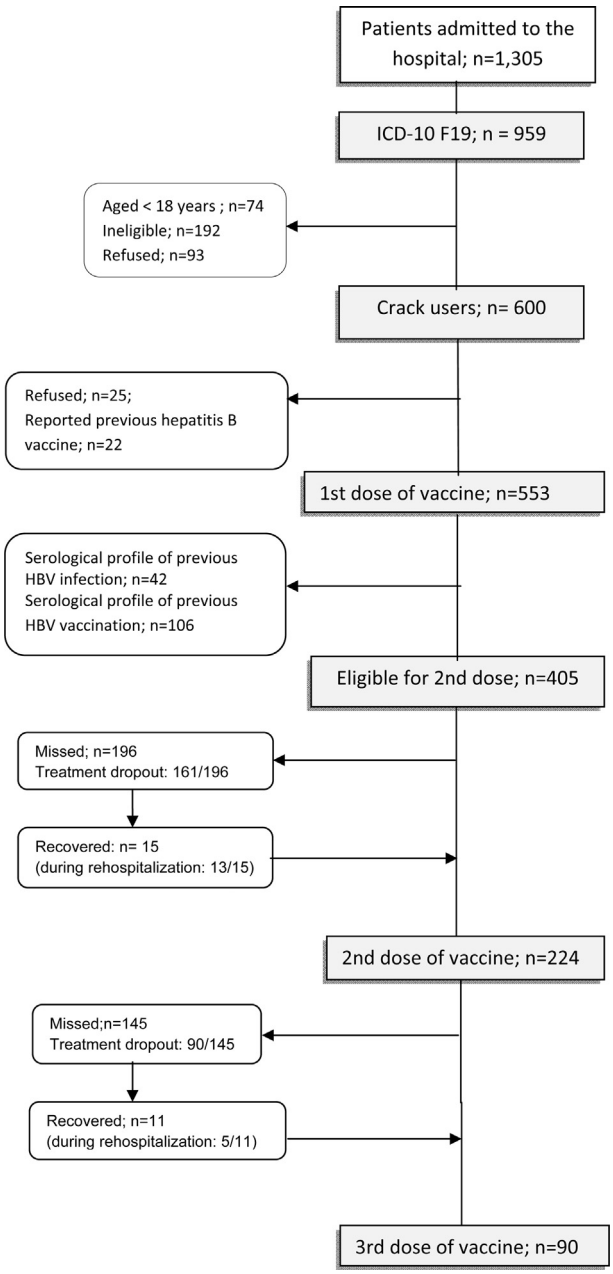

Figure 1 Flow diagram of vaccinations performed on crack users.

HBV, resulting in an overall prevalence of 7.0% (95% CI: 5.22—9.32). In addition, 106 (17.67%; 95% CI: 14.82—20.92) participants were positive for anti-HBs antibodies only, suggesting that they were previously vaccinated against hepatitis B (Table 1). Of crack users under 25 years old, 31.4% had a serologic profile of previous vaccination against hepatitis B, and this percentage declined to 13% in individuals older than 35 years. Conversely, the prevalence of HBV markers was 2.7% among individuals under 25 years old and 11.7% among those aged 35 years old or over (p < 0.001).

Table 1 Prevalence of HBV markers among 600 in-treatment crack cocaine users.

HBV markers	Positive		95% CI[a]
	n	%	
HBsAg	2	0.33	0.09—1.20
HBsAg/anti-HBc	1	0.17	0.02—0.93
Anti-HBc/anti-HBs	29	4.83	3.38—6.85
Anti-HBc	10	1.67	0.90—3.04
Any HBV marker	42	7.00	5.22—9.32
Anti-HBs only	106	17.67	14.82—20.92

[a] 95% CI, 95% of confidence interval.

Table 2 shows the analysis of risk factors for HBV infection among study participants, in which age, use of crack cocaine through an improvised pipe, previous injection drug use, exchange of sex for money/drugs and previous STI were associated with HBV exposure ($p < 0.05$).

These variables were included in a logistic regression model, and the following variables remained independently associated with HBV positivity (Table 3): age [adjusted odds ratio (adjOR): 1.05], use of crack cocaine through an improvised pipe (adjOR: 2.81), exchange of sex for money/drugs (adjOR: 2.52) and previous STI (adjOR: 2.28).

The first hepatitis B vaccine dose was administered in 553 of 600 subjects. After the screening for HBV markers, 405 subjects were eligible for the full vaccine series. Of these, 224 (55.3%) and 90 (22.2%) received the second and third vaccine doses, respectively (Fig. 1). The major reason for withdrawal was treatment dropout. During hospitalization, 68.9% (62/90) of those who eventually dropped out complied with the schedule, and only 25.5% (23/90) were evaluated for vaccine response. Protective titers of anti-HBs were found in 78.3% (95% CI: 58.1—90.3) of these patients: nine between 10 and 100 mIU/mL, five between 101 and 1000 mIU/mL and the remainder with titers greater than 1000 mIU/mL. Among the five individuals who did not respond to the vaccine, three were more than 30 years old, and one was a carrier of HCV. The median time between the third vaccine dose and the sample collection was 77 days (range 49—362 days). There was no association between level of anti-HBs titers and the interval between the third dose and blood draw ($p = 0.579$).

Discussion

In this study, the prevalence of HBV exposure was similar to that found in the general Brazilian population [7% (95% CI: 5.2—9.3) vs. 7.4% (6.8—8.0)]. The participants were mainly young men, and this very likely had an effect on the low HBV prevalence rate found. In Brazil, hepatitis B vaccine has been offered free of charge to infants since 1999, and this program was gradually extended to older ages. This strategy of vaccination virtually eliminates the burden of HBV susceptibility from infancy, promoting barriers against viral dissemination. Currently, this vaccine is offered to all individuals under 50 years old and to those at increased risk, regardless of age [8]. Therefore, in the next decades, a large effort should be made to vaccinate adults and young adults susceptible to HBV, especially those at higher risk for hepatitis B infection, such as illicit drug users. In fact, treatment for chronic hepatitis B is free to those infected through the public health system, and it costs on average US$4526 per year, with the cost doubling if the patient develops decompensated cirrhosis [13]. The cost of each hepatitis B vaccine dose is only US$0.41. Even including expenses involving logistics and health care practitioners, promoting hepatitis B vaccination can cut costs dramatically.

A high frequency of risky behavior was found among the crack users studied, and the following were independently associated with HBV exposure: smoking crack cocaine through improvised pipes, previous STI and exchanging sex for money/drugs.

Here, we found a high frequency of individuals who reported sharing pipes and improvised pipes, with improvised pipes being closely associated with HBV exposure. In our reality, the crack users mainly used empty beverage cans as improvised pipes. This material can cause cuts, sores and burns in and around the users' oral cavities. Once HBV is efficiently transmitted by blood, HBV DNA has been detected in saliva [14]. Therefore, the common behavior of sharing this item used to consume crack can potentially promote viral dissemination.

Table 2 Risk factors for HBV exposure among crack cocaine users not vaccinated against hepatitis B.

Variable	Total	HBV positive	ρ
Mean age (years)	31.1 (SD: 8.21)	35.3 (SD: 8.56)	0.001
Length of crack use (months; mean)	54.76 (SD: 45.46)	63.67 (SD: 54.74)	0.185
Number of crack rocks/day (mean)	14.62 (SD: 24.51)	17.16 (SD: 23.29)	0.639
Sex (%)			
Male	423	7.8	
Female	71	12.7	0.173
Use crack through improvised pipes (%)			
No	153	3.3	
Yes	341	10.9	0.005
Sharing of pipes (%)			
No	106	5.7	
Yes	357	10.1	0.164
Refused to answer: $n = 31$			
Use of crack daily (%)			
No	198	6.6	
Yes	291	10.0	0.188
Refused to answer: $n = 05$			
Oral sores (%)			
No	348	9.0	
Yes	146	7.5	0.617
Injection drug use (%)			
No	446	7.6	
Yes	48	16.7	0.033
Previous prison (%)			
No	250	8.4	
Yes	244	8.6	0.934
Exchange sex for money/drugs			
No	351	6.8	
Yes	90	14.4	0.020
Refused to answer: $n = 53$			
Previous sexual coercion (%)			
No	438	8.0	
Yes	56	12.5	0.255
Previous STI[a] (%)			
No	358	5.6	
Yes	127	17.3	<0.0001
Do not remember: 09			
Homosexual (%)			
No	412	9.0	
Yes	31	3.2	0.501
Refused to answer: $n = 51$			
Sex with occasional partner (%)			
No	177	6.8	
Yes	267	9.7	0.275
Refused to answer: $n = 50$			
Condom with occasional[b] partner (%)			
Always	134	9.0	
Sometimes	87	10.3	0.928
Never	46	8.7	

[a] STI, sexually transmitted infection.
[b] Last 6 months.

Table 3 Unadjusted and adjusted odds ratios (OR) for predictors of HBV exposure.

Variable	Unadjusted OR[a] (95% CI)[b]	Adjusted OR (95% CI)[b]	*p*
Age	1.06 (1.02—1.10)	1.05 (1.00—1.10)	0.019
Use of improvised pipe	3.60 (1.39—9.36)	3.49 (1.28—9.47)	0.014
Exchanged sex for drugs/money	2.30 (1.12—4.72)	2.54 (1.17—5.54)	0.019
Previous STI	3.54 (1.86—6.74)	2.36(1.12—4.95)	0.023
Injection drug use	2.42 (1.05—5.58)	2.53 (0.60—3.92)	0.376

[a] OR, odds ratio; adjusted for gender, age, use of improvised pipe, previous injection drug use, exchanged sex for drugs/money, previous STI.
[b] CI, confidence interval.

Interestingly, contrary to other research [15], variables related to unsafe sex remained associated with HBV exposure, even when controlled by injection drug use. The crack users studied who reported previous sexually transmitted infections showed a 2.28-fold greater chance of exposure to HBV. Hepatitis B virus is efficiently transmitted by sexual routes, and analogous to that observed in HIV infection [15,16], curable ulcerative and inflammatory STIs may increase the risk of HBV acquisition.

As shown by others [7,17,18], a high frequency of crack users reported exchanging sex for money or drugs, and those who reported this behavior were 2.5 times more likely to be exposed to HBV. According to an ethnographic investigation carried out by Carlson and Siegal [19], drug users who exchange sex for money/drugs have lost control of their drug use. Further, Vivancos et al. [17] found a close association between severe crack/cocaine dependence and trading sex for money/drugs among crack users in a rural county of England. In this investigation, crack users who reported exchanging sex for money/drugs reported smoking a higher average number of crack rocks/portions than those who denied this behavior (21.5 vs. 12.1; $p = 0.003$) (data not shown). Thus, in these cases, the sex trade funds drug consumption, and as a consequence of this risky sexual behavior, the risk for acquiring sexually transmitted infections, such as HBV, is increased.

The motivation of these patients to start the vaccination schedule was strong — almost all individuals accepted the first dose. However, even with a super-accelerated scheme, the second and third doses were administered in only 55.3% and 22.2%, respectively, of patients eligible for the complete scheme. This rate of completion was lower than those reported by other authors using the same accelerated schemes in vulnerable populations. Rogers and Lubman [12] observed 71% compliance with three vaccine doses among 91 drug users aged 14 and 22 years attended by two outreach services in Australia, and Christensen et al. [20] reported 80.7% among 566 prisoners (most of them were drug users) in Estonia.

In this investigation, the main reasons for the high number of losses were administrative, as patients prematurely terminated treatment, which seems to be a common problem in our country. According to Duailibi et al. [4], in Brazil, cocaine crack users have the highest treatment dropout rates among all addicts of psychoactive drugs. Out of the hospital, we are unable to contact the majority of them because they did not provide valid addresses and telephone numbers.

The immune system was evaluated in only 23 individuals, and among them, 78% responded with protective titers, with five being strong responders (anti-HBs $\geq$ 100 mIU/mL). This seroprotection rate is within the range previously observed among drug users (54.5—97.1%) [21]. Super-accelerated schemes induce the formation of protective antibodies faster than normal regimens, reducing the period of susceptibility to hepatitis B in high-risk groups. However, the titers of these antibodies may gradually reduce when using accelerated schemes, so a booster dose is recommended at 12 months [22]. Although it is difficult to reach certain populations, such as crack users, for the administration of this additional dose, addiction retreatment, which is common, is an opportunity to provide the booster dose under normal circumstances. Conversely, this population has more opportunities to be exposed to HBV, providing a natural booster and thus ensuring, in theory, the effectiveness of the accelerated schedule.

The convenience sample is one of the limitations of this investigation that prevents further generalization, although the characteristics of the crack users were similar to those found in other Brazilian investigations [3,23,24]. Another limitation of the vaccination is the absence of a control group. Reaching this population is an arduous task, and the number of losses is high even when using a super-accelerated schedule, indicating that a

control group using a standard scheme would be impossible.

Conclusions

Although we found that the prevalence of HBV was low, the low rate of HBV immunization compounded by poor compliance with even the accelerated vaccine schedule and high frequency of risk behaviors among crack users keep this population at high risk for acquiring hepatitis B, highlighting the need for more public investment to reach this target population.

Author contributions

Study concept and design: Da Silva LN, Teles SA.

Acquisition of data: Da Silva LN, Da Silva Franca DD, Del-Rio NHA, Guimarães RA, Pinheiro RS, Junqueira ALN, Caetano KAA.

Analysis and interpretation: Da Silva LN, Da Silva Franca DD, Del-Rio NHA, Teles SA.

Drafting of manuscript: Teles SA, Da Silva LN.

Critical revision: Carneiro MAS, Martins RMB.

All authors approved the final manuscript prior to submission.

Funding

No funding sources.

Competing interests

None declared.

Ethical approval

This study was analyzed and approved by the Committee on Ethics in Human Research of Hospital das Clínicas/UFG, case CEP/HC/UFG No. 117/201.

Acknowledgments

This work was supported by Conselho Nacional de Desenvolvimento Cientifico e Tecnologico — CNPq (Project no. 474713/2012-1). We thank Brian Ream for English language review.

References

[1] Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012;30(March (12)):2212—9.

[2] UNODC. World Drug Report 2015. New York: United Nation Office on Drugs and Crime; 2015. p. 162.

[3] Bastos FI, Bertoni N. Pesquisa Nacional sobre o uso de crack; quem são os usuários de crack e/ou similares do Brasil? Quantos são nas capitais brasileiras? Rio de Janeiro: ICICT, FIOCRUZ; 2014.

[4] Duailibi LB, Ribeiro M, Laranjeira R. Profile of cocaine and crack users in Brazil. Cad Saude Publica 2008;24(Suppl. 4):s545—57.

[5] Comer GM, Mittal MK, Donelson SS, Lee TP. Cluster of fulminant hepatitis B in crack users. Am J Gastroenterol 1991;86(March (3)):331—4.

[6] Brewer TH, Zhao W, Metsch LR, Coltes A, Zenilman J. High-risk behaviors in women who use crack: knowledge of HIV serostatus and risk behavior. Ann Epidemiol 2007;17(July (7)):533—9.

[7] Duff P, Tyndall M, Buxton J, Zhang R, Kerr T, Shannon K. Sex-for-crack exchanges: associations with risky sexual and drug use niches in an urban Canadian city. Harm Reduct J 2013;10:29.

[8] Brasil Programa Nacional de Imunizações (PNI): 40 anos. Brasilia: Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica, Coordenação Geral do Programa Nacional de Imunizações; 2013.

[9] Ferreira RC, Rodrigues FP, Teles SA, Lopes CL, Motta-Castro AR, Novais AC, et al. Prevalence of hepatitis B virus and risk factors in Brazilian non-injecting drug users. J Med Virol 2009;81(April (4)):602—9.

[10] Daughtridge GW, Ross TW, Ceballos PA, Stellar CE. Getting the shots: methods to gain adherence to a multi-dose vaccination program for inner city, drug-involved prostitution communities. J Prim Prev 2014;35(April (2)): 93—102.

[11] Hwang LY, Grimes CZ, Tran TQ, Clark A, Xia R, Lai D, et al. Accelerated hepatitis B vaccination schedule among drug users: a randomized controlled trial. J Infect Dis 2010;202(November (10)):1500—9.

[12] Rogers N, Lubman DI. An accelerated hepatitis B vaccination schedule for young drug users. Aust N Z J Public Health 2005;29(August (4)):305—7.

[13] Castelo A, Pessoa MG, Barreto TCBB, alves MRD, Araujo DV. Estimativas de custo da hepatite crônica B no Sistema Único de Saúde Brasileiro em 2005. Ver Assoc Med Bras 2007;53:486—91.

[14] Kidd-Ljunggren K, Holmberg A, Blackberg J, Lindqvist B. High levels of hepatitis B virus DNA in body fluids from chronic carriers. J Hosp Infect 2006;64(December (4)):352—7.

[15] Hwang LY, Ross MW, Zack C, Bull L, Rickman K, Holleman M. Prevalence of sexually transmitted infections and associated risk factors among populations of drug abusers. Clin Infect Dis 2000;31(October (4)):920—6.

[16] Gottlieb SL, Low N, Newman LM, Bolan G, Kamb M, Broutet N. Toward global prevention of sexually transmitted infections (STIs): the need for STI vaccines. Vaccine 2014;32(March (14)):1527—35.

[17] Vivancos R, Maskrey V, Rumball D, Harvey I, Holland R. Crack/cocaine use in a rural county of England. J Public Health (Oxf) 2006;28(June (2)):96—103.

[18] Nunes CL, Andrade T, Galvao-Castro B, Bastos FI, Reingold A. Assessing risk behaviors and prevalence of sexually transmitted and blood-borne infections among female crack cocaine users in Salvador — Bahia, Brazil. Braz J Infect Dis 2007;11(December (6)):561—6.

[19] Carlson RG, Siegal HA. The crack life: an ethnographic overview of crack use and sexual behavior among African-Americans in a midwest metropolitan city. J Psychoact Drugs 1991;23(January—March (1)):11—20.
[20] Christensen PB, Fisker N, Krarup HB, Liebert E, Jaroslavtsev N, Christensen K, et al. Hepatitis B vaccination in prison with a 3-week schedule is more efficient than the standard 6-month schedule. Vaccine 2004;22(September (29—30)):3897—901.
[21] Kamath GR, Shah DP, Hwang LY. Immune response to hepatitis B vaccination in drug using populations: a systematic review and meta-regression analysis. Vaccine 2014;32(April (20)):2265—74.
[22] Tosun S, Yuceturk M, Donmez AB, Gunduz T. Rapid immunization scheme for spouses of individuals established as hepatitis B carriers during premarital tests. Clin Dev Immunol 2012;2012:843134.
[23] Bertoni N, Burnett C, Cruz MS, Andrade T, Bastos FI, Leal E, et al. Exploring sex differences in drug use, health and service use characteristics among young urban crack users in Brazil. Int J Equity Health 2014;13(1):70.
[24] Horta RL, Horta BL, Rosset AP, Horta CL. Crack cocaine users who attend outpatient services. Clinics 2011;69(7):497—9.