Seroprevalence of hepatitis B and hepatitis C markers in adolescents in Southern Brazil

Soroprevalência de marcadores de hepatite B e hepatite C em adolescentes no Sul do Brasil

> Natália Gazzoni Scaraveli 1 Ana Maria Passos 1 Andréia Royer Voigt 1 Andréa do Livramento 1 Gabriela Tonial 1 Aricio Treitinger 1 Celso Spada 1

Abstract

¹ Universidade Federal de Santa Catarina. Florianópolis, Brasil.

Correspondence

A. M. Passos Universidade Federal de Santa Catarina. Campus Universitário Trindade, Florianópolis, SC 88040-900, Brasil. anampassos@gmail.com

This study was carried out to determine the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) markers among adolescents aged between 10 and 16 years old, who are elementary school students in the city of Chapecó, Santa Catarina State, Brazil. The study involved a crosssectional survey that included 418 volunteers, from March to July, 2008. Serology comprised HBsAg, anti-HBc, anti-HBs and anti-HCV. Tests were performed using automated Microparticle Enzyme Immunosorbant Assay (Abbott, AxSYM System, Wiesbaden, Germany). The prevalence of HBsAg was found to be 0.2% (95%CI: 0.0-1.3), and the prevalence of anti-HBc was found to be 1.4% (95%CI: 0.5-3.1). Regarding anti-HBs, 48.6% had titers greater than 10UI/L. None of the volunteers presented reactive results for anti-HCV. This study showed a low prevalence of HBV and HCV markers of infection and a great number of volunteers immunized against HBV. Finally this study shows the importance of proper health campaigns and policies in reducing those prevalences.

Hepatitis B; Hepatitis C; Vaccination; Seroepidemiologic Studies

Introduction

Infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) are problems that are important to global public health and represent significant causes of morbidity and mortality world-

According to the World Health Organization (WHO) ^{2,3}, approximately 360 million people are chronically infected with HBV around the world, and 170 million with HCV, and are at risk of developing cirrhosis and/or hepatocellular carci-

In Brazil, it is estimated that 15% of the population have been in contact with HBV and 6 million people are HBV or HCV chronic carriers 5. Although several studies have been conducted on hepatitis B and C, especially on blood banks 6,7,8,9,10,11,12, there are few studies carried out among the general population 13,14,15, and due to territorial extension, and cultural and economic differences, the distribution of these diseases in the country differs among regions 16.

Additionally, prevalence studies of HBV and HCV markers in southern Brazil, more specifically in the state of Santa Catarina, are scarce as

Chapecó is located in the western of the state of Santa Catarina, Southern Brazil. In previous studies it has been considered a region of high endemicity of hepatitis B, where vertical transmission played an important role in maintaining

the epidemic. Horizontal transmission also occurs, especially among individuals aged below five years old, through mechanisms that are not yet totally clear 17.

The hepatitis B vaccination began in 1989 in some regions of Brazil, directed primarily to specific groups. Some years later (1998), it became available in more regions and to children aged below one year old, as well as to high risk populations. Afterwards, the coverage of the vaccine was extended to health students, military personnel and adolescents up to 15 years old. Specifically in Santa Catarina, in 1993 the vaccination was recommended to children aged below four years old, and, in 1996, to children up to 15 years old. It was only in 2001 that the National Immunization Program was extended to the population up to 19 years old 18.

The establishment of political health programs requires an awareness of the epidemiological profile of the population in question. In this way, the determination of the prevalence of HBV and HCV infection markers, as well as HBV immunization markers represent fundamental tools. Thus, there is an urgent need to determine the real profile of these infections, so as to, in case of need, establish more effective measures of prevention and awareness.

Hepatitis B and C share common transmission pathways, making it possible to investigate them simultaneously 19. Is it well known that during the ages of between 10 and 16, there is an increase of risk practices which can lead to HBV and HCV infection, such as unprotected sexual relations, tattooing and body piercing 20.

Therefore, this study had a main objective of establishing the prevalence of HBV infection and immunization markers and HCV infection markers in adolescents and elementary school students in the city of Chapecó.

Material and methods

This cross-sectional study included elementary school student volunteers, adolescents aged between 10 and 16, in Chapecó between March and July, 2008.

A random sampling plan was conducted for the selection of volunteers, so that it would reproduce the distribution of the adolescent population in elementary school (5th-8th grade), according to the administrative category of school of attendance, as well as their dimension and geographic location. Thus, 418 students from 21 schools were enrolled to participate in this study. This sample was considered sufficient to be representative of the student population in question and to determine a prevalence of HBV and HCV markers of 50% (unknown prevalence) with a 95% confidence interval (95%CI), and 0.05 alpha error 21.

A 10mL blood sample was collected from each volunteer by venous puncture. Serology comprised HBsAg, anti-HBc, anti-HBs and anti-HCV. Every test was performed in the Municipal Clinical Analysis Laboratory of Chapecó, using automated Microparticle Enzyme Immunosorbant Assay (Abbott, AxSYM System, Wiesbaden, Germany).

HBsAg, anti-HBc and anti-HCV results were categorized as "reactive" or "nonreactive", strictly according to the manufacturer's instructions.

Protection with hepatitis B vaccination is considered to be achieved when the concentration of anti-HBs antibody titers is greater than or equal to 10IU/L 22,23,24, thus, volunteers with anti-HBs titers greater than or equal to 10IU/L were considered immunized.

Statistical analysis consisted of inferential analysis of data for different proportions.

The study was approved by the Municipal Education Secretary of Chapecó, State Education Secretary of Santa Catarina, Municipal Health Secretary of Chapecó and by the Ethical Committee of the Federal University of Santa Catarina (project 260/07). Informed consent was obtained from each volunteer's parent or guardian.

Results

Among the 418 volunteers, 67.5% studied in public schools run by the state, 28.5% in public schools run by the city hall, and 4.1% in private schools. Regarding gender, 39% were male and 61% female.

The age of the participants varied from 10 to 16 years, with a mean age of 13.7 ± 1.3 years and median of 14 years. According to quartiles, age was distributed as follows: 10-12 years old (21.3%), 13 years old (19.9%), 14 years old (24.4%) and 15-16 years old (34.5%).

The prevalence of HBsAg was found to be 0.2% (95%CI: 0.0-1.3), and the prevalence of anti-HBc was found to be 1.4% (95%CI: 0.5-3.1).

Regarding anti-HBs, 48.6% presented reactive titers, 39% presented detectable titers and 12.4% presented undetectable titers.

Table 1 shows the profile of hepatitis B markers of infection and immunization according to gender.

None of the volunteers presented reactive results for anti-HCV (0%).

Table 1

Profile of hepatitis B serologic markers of hepatitis B and C in volunteer adolescents, according to gender. Chapecó, Santa Catarina State. Brazil. 2008.

Gender	HBsAg (-)				HBsAg (+)
	Anti-HBc (-)		Anti-HBc (+)		Anti-HBc (+)
	Anti-HBs (+)	Anti-HBs (-)	Anti-HBs (-)	Anti-HBs (+)	Anti-HBs (-)
Male	78 (18.66)	84 (20.09)	0 (0.00)	1 (0.24)	0 (0.00)
Female	122 (29.19)	128 (30.62)	2 (0.48)	2 (0.48)	1 (0.24)
Total	200 (47.85)	212 (50.71)	2 (0.48)	3 (0.72)	1 (0.24)

Discussion

A low prevalence of HBsAg and anti-HBc was found in the elementary school volunteers of Chapecó. This HBsAg prevalence is similar to that of 0.7% found in blood donors from Florianópolis ^{7,17} and of 0.6% and 0.7%, respectively, in pregnant women from Londrina and Curitiba, Paraná State ²⁵. However, it was lower than that of 8.5%, reported in Northern Brazil in children aged below 19 years old ¹⁴ and of 3.2% in Southern Brazil among blood donors from Chapecó ⁷. It is also lower than that of 1% found in Pakistan ²⁶ and of 4.3% in individuals from Thailand of a similar age range born before the implementation of the HBV vaccination, but similar to that of 0.7%, in those born afterwards ²⁷.

Our anti-HBc prevalence is lower than that reported in Northern Brazil, 6% in children aged below 19 years old ¹⁴ and in Southern Brazil among blood donors: 5.3% ⁷ and 9.2% ¹⁷ in Florianópolis and 29% in Chapecó ⁷. It is also lower than that found in Thailand, in individuals of a similar age range born before the implementation of the HBV vaccination, 15.8%, and in individuals born afterwards, 2.9% ²⁷.

This lower prevalence for HBsAg and anti-HBc found in our study may be due to the age range of volunteers, who are expected not to have much sexual exposition yet, neither involvement with injected drugs, as well as blood transfusions ²⁸. Additionally, it must be considered that the hepatitis B vaccination may have contributed to this lower prevalence, once mandatory vaccination was introduced in Chapecó in 1994, followed by mass vaccination campaigns which covered all the schools of the city. Therefore, all current city population aged below 25 years old were, theoretically, vaccinated against hepatitis B, including subjects sampled in the present study.

The results found in our study are in part justified by these facts, since a significant proportion (48.6%) of volunteers presented anti-HBs titers greater than or equal to 10IU/L and were, therefore, considered immunized against hepatitis B. Of the excessively, 39% presented detectable titers below 10IU/L and 12.4% presented undetectable titers of anti-HBs.

Several studies argue about the necessity of booster doses of the vaccine for those with anti-HBs detectable titers below 10 UI/L. Also, there are authors who suggest that strong immunologic memory persists for more than 10 years once the complete vaccination scheme has been administered properly and therefore, an anamnestic anti-HBs response is achieved after HBV contact, even if anti-HBs titers are not higher than 10IU/L ^{29,30,31,32,33}. Thus, considering that our volunteers were vaccinated approximately 10 years ago, and that anti-HBs titers wane through the years even though immunologic memory persists, we can consider that the present research found that in Chapecó, there is a vaccine coverage of 87.6% (which corresponds to all subjects with detectable anti-HBs titers).

The coverage rate found in our study is higher than that found in Thailand, where 74.5% of children aged below 18 had received the vaccine, 5.1% had never received the vaccine and 20.4% had unknown vaccination status ²⁷. Although this coverage rate is lower than that expected by the Brazilian Ministry of Health (95%), it must be considered that the expected rates are based on the number of third doses administered, as opposed to the anti-HBs status, and that some percentage of the population may not respond to the hepatitis B vaccine.

Regarding hepatitis C, our study found no cases of reactivity (0%). This prevalence is lower than that of studies with populations of a similar age in Germany (0.7% and 0.8%) 34,35 , and in

the United States (0.3%) 36. It is also lower that that found in Northern Brazil in volunteers aged below 19 years old (2.1%) 14 and in Pakistan in volunteers aged between 6 and 15 (9.6%) 37, and corroborates that found in Spain (0%) in a population aged below 1938.

As foreseeable, due to the young age of participants, our results show a low risk of hepatitis C infection.

It should be noted that all volunteers with reactivity for HBsAg, anti-HBc or undetectable titers of anti-HBs were directed to health units, to receive proper health care and/or immunization.

We acknowledge some limitations to our analysis. It was not possible to perform duplicate analysis or confirmatory tests to evaluate the confiability of our results. Additionally, we did not verify the vaccination cards of the volunteers and therefore, cannot guarantee that all subjects were preciously vaccinated; and possible immigration interferences and forms of exposition to the HBV were not investigated.

Conclusions

This study showed a low prevalence of HBV and HCV markers of infection among adolescent students at elementary schools in Chapecó. Moreover, a great number of volunteers presented anti-HBs titers, which clearly indicates that the National Program of Immunization for hepatitis B is being efficient in the region studied. Finally, our study shows the impact and importance of proper health campaigns and policies in turning a hepatitis B high endemicity area into a low endemicity one for children and adolescents.

Resumo

Este estudo teve como objetivo determinar a prevalência de marcadores do vírus da hepatite B (HBV) e do vírus da hepatite C (HCV) entre adolescentes com idade entre 10 e 16 anos, alunos do Ensino Fundamental da cidade de Chapecó, Santa Catarina, Brasil. Trata-se de um estudo transversal incluindo 418 voluntários, realizado entre março e julho de 2008. As análises sorológicas incluíram: HBsAg, anti-HBc, anti-HBs e anti-HCV. Os testes foram realizados em Ensaio Enzimático de Micropartículas (Abbott, AxSYM System, Wiesbaden, Alemanha). A prevalência de HBsAg foi de 0,2% (IC95%: 0,0-1,3), e a prevalência de anti-HBc foi de 1,4% (IC95%: 0,5-3,1). Quanto ao anti-HBs, 48,6% dos voluntários apresentaram títulos maiores que 10UI/L. Nenhum dos voluntários apresentou resultados reativos para anti-HCV. Este estudo demonstrou uma baixa prevalência de marcadores de infecção HBV e HCV e um grande número de voluntários imunizados contra o HBV. Finalmente, demonstrou-se a importância de campanhas e políticas adequadas de saúde na redução dessas prevalências.

Hepatite B; Hepatite C; Vacinação; Estudos Soroepidemiológicos

Contributors

N. G. Scaraveli, A. M. Passos, A. R. Voigt, A. Livramento, G. Tonial, A. Treitinger and C. Spada participated in designing the project, the research, and writing up and revising the article.

Acknowledgments

The authors thank the volunteers for their receptivity, the Municipal Health and Education Secretariats of Chapecó and the Chapecó City Hall for logistical sup-

References

- Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J Hepatol 2006; 45:529-38.
- World Health Organization. Hepatitis B. http:// www.who.int/immunization_delivery/new_vac cines/hepb/en/index.html (accessed on Jul/2009).
- World Health Organization. Programmes and projects. Fact sheet no. 164 Hepatitis C. http://www.who.int/mediacentre/factsheets/fs164/en/ (accessed on Jul/2009).
- 4. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics. CA Cancer J Clin 2002; 55:74-108.
- World Health Organization. Global distribution of hepatitis A, B and C, 2001. Wkly Epidemiol Rec 2002; 77:45-7.
- Brandão AB, Fuchs SC. Risk factors for hepatitis C virus infection among blood donors in southern Brazil: a case control study. BMC Gastroenterol 2002; 2:18.
- Rosini N, Mousse D, Spada C, Treitinger A. Seroprevalence of HbsAg, Anti-HBc and Anti-HCV in Southern Brazil, 1999-2001. Braz J Infect Dis 2003; 7:262-7.
- 8. Andrade AFB, Oliveira-Silva M, Silva SGC, Motta IJF, Bonvicino CR. Seroprevalence of hepatitis B and C virus markers among blood donors in Rio de Janeiro, Brazil, 1998-2005. Mem Inst Oswaldo Cruz 2006; 101:673-6.
- Nascimento MC, Mayaud P, Sabino EC, Torres KL, Franceschi S. Prevalence of hepatitis B and C serological markers among first-time blood donors in Brazil: a multi-center serosurvey. J Med Virol 2008; 80:53-7
- Kupski C, Träsel FR, Mazzoleni F, Winckler MA, Bender AL, Machado DC, et al. Serologic and molecular profile of anti-HBc-positive blood bank donors in an area of low endemicity for HBV. Dig Dis Sci 2008; 53:1370-4.
- Torres KL, Malheiro A, Tateno A, Lima TA, Viana-Maia LP, Diniz-Pimentel JP, et al. Hepatitis C virus in blood donors, Brazil. Emerg Infect Dis 2009; 15:676-8.
- Garcia FB, Pereira GA, Martins PRJ, Moraes-Souza H. Epidemiological profile of hepatitis C in blood donors at the Uberaba Regional Blood Center. Rev Soc Bras Med Trop 2009; 42:1-4.
- Miranda AE, Figueiredo NC, Schmidt R, Page-Shafer K. A population-based survey of the prevalence of HIV, syphilis, hepatitis B and hepatitis C infections, and associated risk factors among young women in Vitória, Brazil. AIDS Behav 2008; 12(4 Suppl):S25-31.
- 14. Aquino JA, Pegado KA, Barros LP, Machado LFA. Soroprevalência de infecções por vírus da hepatite B e vírus da hepatite C em indivíduos do Estado do Pará. Rev Soc Bras Med Trop 2008; 41:334-7.
- 15. Ferrão SBRL, Figueiredo JFC, Yoshida CFT, Passos ADC. Prevalência elevada de hepatite C no distrito de Botafogo, cidade de Bebedouro, interior do Estado de São Paulo, Brasil, 2007. Cad Saúde Pública 2009; 25:460-4.

- 16. Toledo Júnior AC, Greco DB, Felga M, Barreira D, Gadelha MFS, Speranza FAB. Seroprevalence of hepatitis B and C in Brazilian army conscripts in 2002: a cross-sectional study. Braz J Infect Dis 2005; 9:374-83.
- 17. Treitinger A, Spada C, Ferreira LA, Strazer Neto MS, Reis M, Verdi JC, et al. Hepatitis B and hepatitis C prevalence among blood donors and HIV-1 infected patients in Florianópolis, Brazil. Braz J Infect Dis 2000; 4:192-6.
- 18. Secretaria de Vigilância em Saúde, Ministério da Saúde. Material instrucional para capacitação em vigilância epidemiológica das hepatites virais. Brasília: Ministério da Saúde; 2008. (Série A. Normas e Manuais Técnicos).
- Centers for Disease Control and Prevention. Viral hepatitis. http://www.cdc.gov/hepatitis/index. htm (accessed on Jul/2009).
- 20. Meheus A. Teenager's lifestyle and the risk of exposure to hepatitis B virus. Vaccine 2000; 18:26-9.
- 21. Motta VT, Wagner MB. Bioestatística. Caxias do Sul: Educs/São Paulo: Robe Editorial: 2003.
- Centers for Disease Control. Recommendations for protection against viral hepatitis. MMWR Morb Mortal Wkly Rep 1985; 34:313-24.
- Centers for Disease Control. Update on hepatitis B prevention. MMWR Morb Mortal Wkly Rep 1987; 36:353-60.
- 24. Immunization against hepatitis B. Lancet 1988; 1:875-6.
- Bertolini DA, Pinho JRR, Saraceni CP, Moreira RC, Granato CFH, Carrilho FJ. Prevalence of serological markers of hepatitis B virus in pregnant women from Paraná State, Brazil. Braz J Med Biol Res 2006; 39:1083-90.
- 26. Jafri W, Jafri N, Yakoob J, Islam M, Tirmizi SFA, Jafar T, et al. Hepatitis B and C: prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. BMC Infect Dis 2006; 6:101.
- 27. Chongsrisawat V, Yoocharoen P, Theamboonlers A, Tharmaphornpilas P, Warinsathien P, Sinlaparatsamee S, et al. Hepatitis B seroprevalence in Thailand: 12 years after hepatitis B vaccine integration into the national expanded programme on immunization. Trop Med Int Health 2006; 11:1496-502.
- Souto FJD. Distribuição da hepatite B no Brasil: atualização do mapa epidemiológico e proposições para seu controle. GED Gastroenterol Endosc Dig 1999; 18:143-50.
- 29. Zanetti AR, Mariano A, Romanò L, D'Amelio R, Chironna M, Coppola RC, et al. Long-term immunogenicity of hepatitis B vaccination and policy for booster: an Italian multicentre study. Lancet 2005; 366:1379-84.

- 30. Fitzsimons D, François G, Hall A, McMahon B, Meheus A, Zanetti A, et al. Long-term efficacy of hepatitis B vaccine, booster policy, and impact of hepatitis B virus mutants. Vaccine 2005; 23: 4158-66.
- 31. Hammitt LL, Hennessy TW, Fiore AE, Zanis C, Hummel KB, Dunaway E, et al. Hepatitis B immunity in children vaccinated with recombinant hepatitis B vaccine beginning at birth: a follow-up study at 15 years. Vaccine 2007; 25:6958-64.
- 32. But DY, Lai CL, Lim WL, Fung J, Wong DK, Yuen MF. Twenty-two years follow-up of a prospective randomized trial of hepatitis B vaccines without booster dose in children: final report. Vaccine 2008; 26:6587-91.
- 33. Banatvala JE, Van Damme P. Hepatitis B vaccine do we need boosters? J Viral Hepat 2003; 10:1-6.
- 34. Vogt M, Lang T, Frösner G, Klingler C, Sendl AF, Zeller A, et al. Prevalence and clinical outcome of hepatitis C infection in children who underwent cardiac surgery before the implementation of blood-donor screening. N Engl J Med 1999; 341:866-70.

- 35. Gerner P, Wirth S, Wintermeyer P, Walz A, Jenke A. Prevalence of hepatitis C virus infection in children admitted to an urban hospital. J Infect 2006; 52:305-8.
- 36. Alter MJ, Kruszon-Moran D, Nainan OV, McQuillan GM, Gao F, Moyer LA. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. N Engl J Med 1999; 341:556-62.
- 37. Idrees M, Lal A, Naseem M, Khalid M. High prevalence of hepatitis C virus infection in the largest province of Pakistan. J Dig Dis 2008; 9:95-103.
- 38. Riestra S, Fernández E, Leiva P, García S, Ocio G, Rodrigo L. Prevalence of hepatitis C virus infection in the general population of northern Spain. Eur J Gastroenterol Hepatol 2001; 13:477-81.

Submitted on 23/Nov/2009 Final version resubmitted on 22/Dec/2010 Approved on 24/Jan/2011