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Long Term Effects of One or Two Doses of Hepatitis B Vaccine in Adults After Five Years

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Abstract: The aim of this study is to evaluate hepatitis B vaccine protection in those adults who have taken one or two does of vaccine before. It was a retrospective cross sectional study was conducted on fifty-six military personnel in Tehran, Iran in the spring 2007. Demographic data such as age, marital status, education level, number of vaccine doses injected and, type of vaccine and date of last vaccination was collected. Their serum was tested for HBs Ab, HBc Ab and HBs Ag and finally the results were analyzed by SPSS software. All individuals were male with the mean age of 33.9±8.9 years. Twelve individuals who had only received one dose of injected vaccine had no antibody against HBsAg and no protection against hepatitis B virus. Of forty-four individuals that had received two doses of injected vaccine, 27 persons (61.4%) were protected and had serum HBsAb more than 10 MIU mL^{-1}. In conclusion one dose of HBV vaccine cannot produce immunity for five years but two doses of HBV vaccine can produce immunity for five years. However, HBsAb should be tested to make sure of immunity.

Key words: Hepatitis B virus, vaccine dose, adult vaccination, prolonged immunity

INTRODUCTION

Viral hepatitis due to hepatitis B virus (HBV) is a major public health concern worldwide which can lead to acute and chronic liver diseases including cirrhosis and hepatocellular carcinoma (Shivananda *et al*., 2006). According to World Health Organization, there were more than 400 million carriers of hepatitis B virus (HBV) in the world by the year 2000 and approximately 5-10% of adult carriers and 80-90% of children carriers became chronic carriers of the virus (Betancourt *et al*., 2007). It is reported that 1.2 million people die from HBV-related diseases every year (Saravananuttu *et al*., 2007).

According to Iranian studies, about 2-3% of Iranian population is HBcAb positive and about 1.3 to 8.69% of the population are chronic HBV carriers (Adibi *et al*., 2004).

Immunization of adolescents against HBV is recommended by international institutions. However, completion of a three-dose vaccination regimen can pose problems in adult population (Wouters *et al*., 2007).

The Geometric Mean Titer (GMT) of anti-HBs is low after the first dose, increases moderately after the second dose, followed by a much higher maximum after a third dose. Two or even one dose of HBV vaccine might be adequate to confer similar protection against HBV similar to the currently recommended three-dose schedule. The increase in GMT may be related to the increased number of doses, but may also be due to a slow accumulation of a memory response. Immune memory can develop indirectly via activation of the effector cells, or directly through clonal expansion. The indirect mechanism would benefit from repeated stimulation by additional doses while the direct mechanism occurs independent of additional dose stimulation. Mathematical modeling suggests that clonal expansion, independent of repeated antigen presentation, is the dominant route by which immune memory following HBV vaccination develops (Sande *et al*., 2007). Three dose vaccination schedule can produce immunity in more than 98% of adults for a minimum of ten years (Yuen *et al*., 2004).

Several studies in adolescents and adults have shown comparable sero-protection (the proportion with peak anti-HBs ≥10 mIU mL^{-1}) and immunogenicity of a two-dose regimen versus a three-dose schedule (Heron *et al*., 2007) and Two-dose regimens of an adult

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formulation of hepatitis B vaccine have been shown to be immunogenic (Cassidy, 2001). In some countries, authorities have also recommended the administration of a two-dose adult formulation hepatitis B vaccine regimen for adolescents and adults (Heron *et al*., 2007).

Other studies have suggested that in children, a sero-protection similar to three-dose schedules could be achieved with two-dose regimens (Akram *et al*., 2005).

The two-dose regimen could improve compliance to vaccination schedule and is expected to be more cost-effective compared to a three-dose schedule. It would also offer fewer health care visits thus could be a helpful immunization program in adults (Wountrs *et al*., 2007) but response to less than three HBV vaccine doses in adults remains largely unknown in our country (Alavian *et al*., 2001).

This study was aimed to evaluate the long term effects of one and two doses of HBV vaccine after five years in military staff in Iran.

MATERIALS AND METHODS

This was a retrospective cross-sectional study that was carried out on fifty-six settled military personnel in the capital city of Tehran, Iran, in the spring 2007. All individuals with their latest HBV vaccine schedule prior to five years ago were recruited to this study. All subjects received adult standard dose of 20 UMg of each type of vaccine. In those who received 2 doses, the second dose was administered one month after the first dose. Persons with history of three doses of HBV vaccine, those without a vaccination card and those with the history of acute or chronic hepatitis were excluded. Demographic data such as age, marital status and education level, type of injected vaccine and date of last vaccination was collected. A blood sample of 5 mL was taken form each subject and then their serum was examined for HBsAb, total HBcAb and HBsAg using ELISA method by Dia-pro kit manufactured in Italy. Anti-HBsAb was measured quantitatively according to the manufacturer's recommendations and was expressed as MIU mL^{-1}.

HBsAb titer higher than 10 MIU mL^{-1} was accounted as protective. This data was analyzed via SPSS 13 and Chi-Square and students t-test was used for statistical association between HBsAb and other variants. p-values less than 0.05 were considered significant.

RESULTS AND DISCUSSION

All individuals in this study were male. Mean age was 33.9±8.9 years old (rang: 19-50 years old). Of all subjects, 39 (69.4%) individuals had college education and 38 (67.8%) persons were married. Forty four individuals (78.5%) received 2 doses of HBV vaccine and 12 (21.5%) took one dose. None of the persons who took one dose of vaccine were protected (Table 1).

Table 1: Demographic data of the subjects

Variants	Number	Percent
Korean vaccine	33	58.90
Cuban vaccine	23	41.10
Married	38	67.86
Unmarried	18	32.14
Age <25	10	17.80
Age 25-35	25	44.60
Age >35	21	37.50
High school diploma and less education	17	30.60
College education	39	69.40
One dose vaccine	12	21.40
Two dose vaccine	44	78.60

Table 2: HBV markers in the military personnel with two doses of HBV vaccine

Virology markers	Positive N (%)	Negative N (%)
HBcAb	3 (6.8)	41(93.2)
HBsAg	0 (0.0)	44 (100.0)
HBsAb	27 (61.4)	17 (38.6)

Korean vaccine was injected in 33 (58.9%) cases and other persons took Cuban vaccine which did not propose a significant association with HBsAb titre. Anti HBcAb was positive in 3 (6.8%) subjects but none of them had positive HBsAg. In those who took 2 doses, 27 (61.4%) were immune and they had HBsAb more than 10 MIU mL^{-1}. The Geometric Mean Titer (GMT) of anti-HBs antibody is 137.16±113.69 MIU mL^{-1} (95% Confidence Interval [CI]; 92.18-182.13). Other results of hepatitis B virus markers are shown in Table 2.

Present study suggested that individuals who had received one dose of hepatitis B vaccine had no detectable anti HBsAb five years after the vaccination; so none of them were immune against Hepatitis B and must restart their HBV vaccination program. But in more than 61% of individuals with two doses HBV vaccine, anti HBsAb was detected (HBsAb titre more than 10 MIU mL^{-1}) and they were immune. In fact, receiving only one dose of HBV vaccine is futile. It may produce anti HBsAb and temporary immunity but it is not permanent (Sande *et al*., 2007).

More than 61% of the individuals who received two doses of HBV vaccine were immune after five years. If this group is at a high risk of hepatitis B infection, their HBsAb should be titrated and if less than 10 MIU mL^{-1}, a booster dose of HBV vaccine has to be injected after five years. In these individuals, mean titer of HbsAb may increase after one booster dose so they become protected against hepatitis B but further study is needed (Sande *et al*., 2007).

Two-dose vaccine regimen offers fewer injections for satisfactory protection against hepatitis B virus infections (Wouters *et al*., 2007) but can not produce a high titer of HBsAb for a long time. So immunity of two-dose vaccine regimens has to be evaluated after five years (Yuen *et al*., 2004) and a booster dose may then be needed (Shivananda *et al*., 2006).

Two-dose HBV vaccine regimen mandates fewer clinic visits, lower administration costs, better compliance and higher coverage rate. Therefore, it can be considered an appropriate regimen for the immunization against hepatitis B infection, but titration is needed to make sure of the results (Kurugöl *et al*., 2005).

HbcAb is an index for previous infection with hepatitis B virus. If an individual is infected by hepatitis B, vaccination does not benefit him. Therefore in regions with a high prevalence of hepatitis B virus (HBcAb positive in more than 30% of individuals), screening is essential. But in this study the prevalence of hepatitis B infection was about 6% and for this reason there was no need for HBcAb screening before vaccination (Tsebe *et al*., 2001).

In this research, the relationship between HBsAb titer and factors such as education, marital status and type of vaccine was not significant but in other studies, a significant relationship was seen between HBsAb titer and factors such as type of vaccine and gender (Zhang *et al*., 2006).

Also in our study, five years after the last dose of HBV vaccine, anti-HBsAb mean titer was 137 MIU mL^{-1} which was lower than other studies. The reason for this difference might be a higher dose of administered vaccine, lower mean age of subjects and examination of anti-HBsAb shortly after the vaccination in their studies (Kurugöl *et al*., 2005).

Individuals in this study took less than three doses of HBV vaccine and did not complete the vaccination course mainly due to being reassigned to another city. Two-dose vaccination regimen with a higher dose may resolve this problem and reduce the number of required visits for vaccination and therefore reduce the risk of HBV infection (Francois *et al*., 2002; Levie *et al*., 2002).

Ultimately we conclude that two doses of HBV vaccine can produce immunity for five years, however HBsAb should be tested to make sure of immunity.

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REFERENCES

Adibi, P., M.R. Rezailashkajani, D. Roshandel, N. Behrouz, S. Ansari and M.H. Somi, 2004. An economic analysis of premarrage prevention of hepatitis B transmission in Iran. BMC. Infect. Dis., 4 (4): 31-35.

Akram, S., S. Maqbool, D.S. Khan, R. Jafri, S. Rondhawa and C. Valenzula-Silva, 2005. Immunogenicity of a recombinant, yeast-derived, anti-hepatitis-B vaccine after alternative dosage and schedule vaccination in Pakistani children. Vaccine, 23 (50): 5792-5797.

Alavian, S.M., M. Saadati and A. Mirzadehetal, 2001. Frequency of HBV vaccination and their related variants in health worker of sepah pasdaran in Iran. Military. Med. J., 3 (3): 107-111.

Betancourt, A.A., C.A. Delgado and Z.C. Estévez, 2007. Phase I clinical trial in healthy adults of a nasal vaccine candidate containing recombinant hepatitis B surface and core antigens. Int. J. Infect. Dis., 11 (5): 394-401.

Cassidy, W.M., 2001. Adolescent hepatitis B vaccination. A review. Minerva Pediatr., 53 (6): 559-566.

Francois, G., J. Hallauer and P. Van Damme, 2002. Hepatitis B vaccination: How to reach risk groups. Vaccine, 21 (2): 1-4.

Heron, L., O. Selnikova, A. Moiseieva, P.V. Damme, M. Vander and K. Levie, 2007. Immunogenicity, reactogenicity and safety of two-dose versus three-dose (standard care) hepatitis B immunization of healthy adolescents aged 11-15 years: A randomized controlled trial. Vaccine, 25 (15): 2817-2822.

Kurugöl, Z., F. Mutlubaş and T. Ozacar, 2005. A two-dose schedule for combined hepatitis A and B vaccination in children aged 6-15 years. Vaccine, 23 (22): 2876-2880.

Levie, K., I. Gjorup, P. Skinhoj and M. Stoffel, 2002. A 2-dose regimen of a recombinant hepatitis B vaccine with the immune stimulant AS04 compared with the standard 3-dose regimen of Engerix-B in healthy young adults. Scand. J. Infect. Dis., 34 (8): 610-614.

Sande, M.A., M. Mendy, P. Waight, C. Doherty, S.J.M. Conkey and J. Hall, 2007. Similar long-term vaccine efficacy of two versus three doses of HBV vaccine in early life. Vaccine, 25 (8): 1509-1512.

Saravanamuttu, G., I. Samreen, M. Joanne, M. Ramsay and G. Jonathan, 2007. International public health repository for hepatitis B. Nucleic Acid Res., 35 (2): 367-370.

Shivananda, S., V. Somani, B.S. Srikanth, M. Mohan and P.S. Kulkarni, 2006. Comparison of two hepatitis B vaccines (GeneVac-B and Engerix-B) in healthy infants in India. Clin. Vaccine Immunol., 13 (6): 661-664.

Tsebe, K.V., R.J. Burnett, N.P. Hlungwani, M.M. Sibara, P.A. Venter and M.J. Mphahlele, 2001. The first five years of universal hepatitis B vaccination in South Africa: Evidence for elimination of HBsAg carriage in under 5-year-old. Vaccine, 19 (29): 3919-3926.

Wouters, K., E. Leuridan, K. Herck, N.V. Ardenne, I. Roelofs and R. Mak, 2007. Compliance and immunogenicity of two hepatitis B vaccination schedules in sex workers in Belgium. Vaccine, 25 (10): 1893-1900.

Yuen, M.F., W.L. Lim, A.O. Chan, D.K. Wong, S.S. Sum and C.L. Lai, 2004. 18-year follow-up study of a prospective randomized trial of hepatitis B vaccinations without booster doses in children. Clin. Gastroenterol. Hepatol., 2 (10): 941-945.

Zhang, H., J.X. Ma, X.H. Gong, L.R. Liu, K. Wu and F.J. Luo, 2006. Observation on two kinds of recombinant hepatitis B vaccines used in populations with different immunity. Zhonghua. Liu. Xing. Bing. Xue. Za. Zhi., 27 (8): 690-693.