

Review Article

Vaccination against Hepatitis B Virus through Various Strategies

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Abstract: Hepatitis is the inflammation of liver which cause liver cirrhosis. It is the health problem. This may be acute or chronic. The chronic stage of hepatitis leads to liver cancer which is the last stage and ultimately causes death. It is the main cause of liver disease. It is much problematic and about 2 billion people infected from this deadly disease. There are three modes of hepatitis B transmission. One from the mother to infant, another one is the sexual transmission, and the last one is through blood transfusion and most in those people who are drug abusers. In 1995, the vaccination system was introduced to cure this disease. To eradicate HBV virus WHO introduced the vaccination system. Then the vaccination dose was given to infants at their birth to eliminate their HBV. This is a three-dose vaccination system and much other vaccination for adults and to eliminate this problem during pregnancy. For combat with this disease, many therapeutically vaccines have been introduced. WHO (World Health Organization) play a major role to eliminate this problem from the society.

Keywords: Cirrhosis, Boost immunization, Alanine aminotransferase, Thimerosal vaccine, Seroprotection, Anaphylaxis.

INTRODUCTION

Hepatitis is the main cause of liver disease. Hepatitis B is a health problem today faced by the public. This extremely problematic disease cause about 686,000 deaths in 2013 & 300,000 deaths through liver cancer & 317,400 deaths through cirrhosis this is actually secondary to Hepatitis B. Hepatitis has actually three models of transmission. In 1991 EPI recommend hepatitis B vaccination which was introduced in different countries with its prevalence in 1995. But in other countries this vaccination was introduced with lower prevalence. In 2014 hepatitis B vaccination was introduced in almost 184 countries. To eliminate hepatitis B virus WHO form strategies which cause 90% decrease in chronic hepatitis B & 65% decrease in mortality rate caused by these infections [1]. World Health Organization (WHO) helping many countries to control their problem & by November 2017, 84 countries have developed many helpful strategies to get rid of this problem and the World Health Organization has developed many strategies and therapeutic vaccination way to eradicate this problem by 2030 [2]. Chronic hepatitis B virus is the main reason to produce liver cirrhosis and hepatocellular carcinoma disease. HBV is transferred from parents via an apparent percutaneous or per-mucous display to blood and other body fluid [3]. Since, the 1980s, primary HBV immunization has been executed to overcome HBV transmission and shown high potency for safest immunity [4]. Immunological analysis of well built, weak or lacking safest antibiotic responses to the HB vaccine must give insights into the small process of fundamental non-responsive to HB [5]. This hepatitis B is actually a virus infection and is a global health problem with 780,000 death rate yearly [6]. Severe hepatitis B become chronic and at least 240 million people in the world suffer from chronic hepatitis B virus [7]. It is estimate that 257 million people in

the world suffer from chronic hepatitis B and cause liver cancer [8]. Childhood vaccination for hepatitis B is suggested in different countries. Mostly European countries and the USA suggested primary vaccination system for grown people and booster vaccination for individuals in which risk of infection is high [9]. The HB genome is one of the most changeable in DNA viruses. Particularly, changes take place in the hydrophobic region of HBsAg which is related to reduce vaccine response [10]. The study of vaccine from the immunological system, a suitable mouse model is required to give the process of HBV elimination and antibody production [11]. The most effective three-dose vaccine for hepatitis B is used [12]. Vaccination coverage is 25% among grown people greater than 19 years. Traditionally, vaccines contain live attenuated or inactivated pathogens which are highly immunogenic, but due to these safety issues new developed vaccines are produced on the use of recombinant subunit antigens [13]. The liver is the immune organ which favored the induction of immune susceptibility rather than immune activation [14]. The main cause of this disease prevalence is that it does not have any early signs and is easily transferred to other people [15]. The B-cell ELIS pot assay is also a good strategy for increasing the amount of HBs-specific B cells [16]. Vaccines of hepatitis B are also being prepared worldwide by using HBc VLP [17]. Vaccines are being used to restore B cell and another CD4 T cell which in return induces an immunological response [18]. The most effective technique by WHO is infants vaccination system in order to eradicate this deadly virus [19]. Infant vaccination is an extremely good strategy but it should be checked that all these infants should undergo serological testing [20]. Now a day prophylactic vaccines are present but a most effective strategy for HBV vaccine is needed [21]. The IFN-3 concentrated is linked with the Hepatitis B vaccination system as it regulates anti-HBs [22]. CD8+ and CD4+ cells play a great role in producing immunological responses and protecting the body against HBV [23]. It is also

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noted that a double dose of three dose vaccination system in infants are most effective [24]. Hepatitis B exhibits those routes which are interlinked for other diseases such as HIV so the HIV patients also have HBV [25]. The WHO (World Health Organization) recommends the three-dose vaccination system in infants in order to eradicate this disease [26]. The World Health Organization (WHO) suggested screening all high alerted group of HBV in order to avoid infection [27]. People who are obese, diabetic, older (greater than 50 years) have less effective immunological responses for vaccines [28]. HBV is such a deadliest virus that it can easily lead to liver cancer. So the vaccination system is the key to eradicate hepatitis B virus [29].

VACCINATION TO CONTROL HEPATITIS B

World Health Organization (WHO) introduced the vaccination system to control and prevent Hepatitis B [2].

VACCINATION FOR NEWBORN

Within the 24 hours of the birth of the newborn the vaccination dose must be given in order to prevent Hepatitis B. If the vaccination dose is given within 6-12 month after birth then this dose will be most effective against Hepatitis B. For reduction and prevention from chronic hepatitis B virus this strategy should be follow. The vaccination dose should be given in three intervals. This should be given at 6, 10 & 14 weeks of life to prevent HBV. Those East African countries who worked and applied practically this strategy have found great results and they introduced this vaccination in their daily national infant's immunization program. So the vaccination program at the birth will be the most effective to prevent HB [30].

IMPACT OF VACCINATION IN NEWBORN

The survey was programmed within 1990-2008. The program in the Gambia within 1986-1990. They deliver vaccine at birth and the result was that HBV prevalence reduced from 8% to 14.6% within 6 months to 9-year-old children and there is less than 2% prevalence among 1-5-year-old children. Nigeria also has reduced prevalence because they have given vaccination doses to newborns [30].

IMPACT OF HBV IN COUNTRIES WHICH DOES NOT INTRODUCE A BIRTH DOSE

Countries such as Senegal, Ghana, Cameroon & Tanzania do not introduce the birth dose; have a much higher prevalence [30].

CATCH UP VACCINATION

Those people who do not receive vaccination dose at their birth to prevent from HBV then they should be vaccinated through different years with their age [1].

VACCINATION FOR ADULTS

The risk of HBV increase by using infected tools, by cut & injury of skin, drug injection or dealing with blood or blood products and reuse of HBV infected syringes. The rate of getting HBV in adults is relatively less than the newborns. The vaccination program has been more difficult to be applied to adults which are at risk, they should vaccinate before they get infected [1].

PROGRESS IN THE VACCINE

Prevention from HBV 3 dose vaccination system in newborn is most effective which cover 82% prevention & is near to 90% from HBV and we will control this HBV by 2030 [2].

PERCENTAGE OF HBV PREVALENCE

The World Health Organization (WHO) has divided countries into three classes which depend on the prevalence of seven HBV. First one is lower class which is less than 2%, the intermediate is between 2-8% and the higher one is above 8%. Here the life is at risk and there is more than 60% of HBV prevalence in these countries. All needed is the vaccine for HBV [31].

HBV VACCINES

Firstly plasma-derived vaccines are used which are composed of pure 22nm HBs Ag inactivated through urea, pepsin, formaldehyde, and heat were given in 1982. Then yeast derived HB recombinant vaccines were used in the mid-1980s. They are actually developed by cloning. Also, yeast-derived but free from them serosal vaccines are entirely available. Then the third generation HB vaccine composed of the pre-S region is more immunogenic but these are today not entirely available. The combination of vaccines was also used and available. The HepB3 vaccines which have actually 3 doses are more effective [31].

IMPROVEMENT IN THE EFFICACY OF THE HB VACCINE

Multiple attempts have been done for the betterment of HB vaccine because of the presence of non-responders this is an obstacle. People who do not respond to three injections in the first series are actually being prescribed to do a second 3-dose series and as a result, approximately 50% of individuals are anti-HBs responders. Hemodialysis is a procedure by which patient condition can be improved with double dose vaccination [31].

PROBLEMS IN HB VACCINES

It decrease slowly after 40 years and also reduce antibody response within body. By this 10% of people show poor results [31].

INTRADERMAL VACCINATION

The intradermal vaccination system is actually more superior to the HB vaccination system. Intradermal vaccines are technically complex. Intradermal vaccination initiates anti-HBs responses in 94% of subjects. Intradermal vaccines show better results than others in health workers, dialysis patients, HIV infected patients & patients with celiac disease [31].

HEPATITIS B IMMUNOGLOBULIN

Hepatitis B immunoglobulin (HBIG) can defend the body until vaccination susceptibility is maintained. It provides defense system and also produces temporary anti-HBs which defend the body for 3-6 months. HBIG products are used that contain no preservatives these are provided only for single use. These products are licensed that is Hepatitis B. These HBIG are formed from the plasma of blood that is rich in anti-HBs and the plasma is taken from the donor.

VACCINE-INDUCED SEROPROTECTION

If the anti-HBs are present in the body then they show immunity against Hepatitis B infection. People who have an anti-HBs level greater than 10IU/mL for 1-2 months and also have complete vaccine series are termed as vaccine-induced or seroprotected respondents. This vaccine induced / seroprotected responders are termed as the surrogate of the clinical defense mechanism.

VACCINE SAFETY

Vaccination for Hepatitis B in adverse event are site injecting reaction, minimal mild systematic reaction and the mild systematic reaction which involves pain (3-29%), erythema (3%), swelling (3%), fever (1-6%) & headache (3%). The anaphylaxis in the HBV vaccine acceptor is 1.1 among per million vaccination dosage and the Institute of medicine (Institute of Medicine is the premier medical institution of Nepal) proposed that there is some relationship between the Hepatitis B vaccine and anaphylaxis in people who were yeast susceptible but the evidence was not enough to check whether there is or not a relationship. The most reported adverse events were nausea (8%) and fever, headache (7%) in the single antigen Hepatitis B vaccination system.

REVACCINATION

In the revaccination system, a dose was given termed as "booster dose" which is given to people to induce a rapid defensive immunity in people suffering from HBV infection and this dose is given after the primary dose of vaccination. People whose vaccinations systems have been completed after one year of birth then they have anti-HBs level less than 10IU/mL. After 18 years, single dose of vaccination system has been given to that people who results in less than 10IU/mL in 60-75% tests.

TARGETS AND FUTURE ASPECTS IN HEPATITIS B VACCINATION

World Health Organization proposed five areas in which by hard work and through strategies, we can eliminate HBV by 2030. These areas are used for treatment of HBV, blood transfusion prevention, transmission of HBV from mother to infant, hepatitis B vaccination, and harm disease. By working on these we can eliminate HBV by 2030. Mother to infant transmission has been avoided and according to the recent update, 4-6% of the newborn with birth vaccine dose has been achieved. In 2015, 3 dose vaccination is used to eliminate HBV at least 82% from the body but according to new updates we achieve 87% which is much near to 90% and by using these 3 dose vaccination system we will eliminate HBV from body in 2030. Blood and syringes safety is much needed and is the main target to resolve the prevalence of HBV is much higher in those people who are drug addicts and inject drugs. The main target is to diagnose 90% of HBV cases which are just diagnosed 11%, GHSS detect HBV cases 90% by 2030. According to a recent report, the HBV treatment system is much lower. According to the Global Hepatitis report 2015, 1.7 million people of HBV undergo treatment. The main achievements are to cure 90% of HBV patients to eliminate Hepatitis by 2030 [2].

CONCLUSION

The major goal is to eliminate this deadly problem by 2030. 3-dose vaccination system must be given to infants in order to control this disease and other therapeutic and novel vaccination system must be applied to eradicate this problem worldwide. Vaccination is the only tool to control and eliminate this problem and it will also then decrease the mortality rate and reduce human distress. The World Health Organization is providing advanced strategies to eliminate this problem by 2030.

CONFLICT OF INTEREST

Declared none.

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REFERENCES

- [1] Nelson NP, Easterbrook PJ, McMahon BJ. Epidemiology of hepatitis B virus infection and impact of vaccination on disease. *Clin Liver Dis* 2016; 20(4): 607-28. DOI: 10.1016/j.cld.2016.06.006
- [2] Diarra B, Yonli AT, Ouattara AK, *et al.* World hepatitis day in Burkina Faso, 2017: Seroprevalence and vaccination against hepatitis B virus to achieve the 2030 elimination goal. *Virology* 2018; 15(1): 1-6. DOI: 10.1186/s12985-018-1032-5
- [3] Sintusek P, Posuwan N, Wanawongsawad P, Jitraruch S, Poovorawan Y, Chongsrisawat V. High prevalence of hepatic

- tis B-antibody loss and a case report of *de novo* hepatitis B virus infection in a child after living-donor liver transplantation. *World J Gastroenterol* 2018; 24(6): 752-62. DOI: 10.3748/wjg.v24.i6.752
- [4] Xu X, Li Y, Liang Y, *et al.* MiR-18a and miR-17 are positively correlated with circulating PD-1 + ICOS + follicular helper T cells after hepatitis B vaccination in a Chinese population. *BMC Immunol* 2018; 19: 25. DOI: 10.1186/s12865-018-0263-y
- [5] Cao MZ, Wu YH, Wen SM, *et al.* Mitogen-activated protein kinase eight polymorphisms are associated with immune responsiveness to HBV vaccinations in infants of HBsAg (+)/HBeAg (–) mothers. *BMC Infect Dis* 2018; 18: 274. DOI: 10.1186/s12879-018-3166-x
- [6] Bröker K, Terzenbach R, Bentzien F, Lüth S, Dammermann W. Complement factors C3a and C5a mimic a proinflammatory microenvironment and increase HBV IGRA sensitivity. *J Transl Med* 2019; 17: 6. DOI: 10.1186/s12967-018-1752-8
- [7] Tang AS, Lyu J, Wang S, He Q, Pong P, Harris AM. Disparities in hepatitis b virus infection and immunity among New York city Asian American patients 1997 to 2017. *Am J Public Health* 2018; 108: 327-35. DOI: 10.2105/AJPH.2018.304504
- [8] Weinberger B, Haks MC, Paus RA De, Ottenhoff THM, Weinberger B. Impaired immune response to primary but not to booster vaccination against hepatitis B in older adults. *Front Immunol* 2018; 9: 1035. DOI: 10.3389/fimmu.2018.01035
- [9] Cremer J, Heiningen F Van, Veldhuijzen IK, Benthem BHB Van, Benschop KSM. Genetic variation of hepatitis B surface antigen among acute and chronic hepatitis B virus infections in The Netherlands. *J Med Virol* 2018; 90(10): 1576-85. DOI: 10.1002/jmv.25232
- [10] Journal AI, Dewangan HK, Pandey T, Singh S. Nanovaccine for immunotherapy and reduced hepatitis-B virus in humanized model. *Artif Cells Nanomed Biotechnol* 2018; 46(8): 2033-42.
- [11] Bento D, Jesus S, Lebre F, Gonçalves T, Borges O. Chitosan plus compound 48 / 80: Formulation and preliminary evaluation as a hepatitis b vaccine adjuvant. *Pharmaceutics* 2019; 11(2). pii: E72. doi: 10.3390/pharmaceutics11020072 DOI: 10.3390/pharmaceutics11020072
- [12] Chahal HS, Peters MG, Harris AM, McCabe D, Volberding P, Kahn JG. Cost-effectiveness of Hepatitis B virus infection screening and treatment or vaccination in 6 high-risk populations in the United States. *Open Forum Infect Dis* 2018; 6(1): ofy353. doi: 10.1093/ofid/ofy353. DOI: 10.1093/ofid/ofy353
- [13] Zong L, Peng H, Sun C, *et al.* Breakdown of adaptive immunotolerance induces hepatocellular carcinoma in HBsAg-tg mice. *Nat Commun* 2019; 10(1): 221. DOI: 10.1038/s41467-018-08096-8
- [14] Khan T, Jung IH, Khan A, Zaman G. Classification and sensitivity analysis of the transmission dynamic of hepatitis B. *Theor Biol Med Model* 2017; 14(1): 1-17. DOI: 10.1186/s12976-017-0068-3
- [15] Tian C, Chen Y, Liu Y, *et al.* Use of ELISpot assay to study HBs-specific B cell responses in vaccinated and HBV infected humans. *Emerg Microbes Infect* 2018; 7(1): 1-3. DOI: 10.1038/s41426-018-0197-8
- [16] Ji M, Xie X, Liu D, *et al.* Hepatitis B core VLP-based mis-ordered tau vaccine elicits strong immune response and alleviates cognitive deficits and neuropathology progression in Tau. P301S mouse model of Alzheimer's disease and frontotemporal dementia. *Alzheimers Res Ther* 2018; 10(1): 55. DOI: 10.1186/s13195-018-0378-7
- [17] Zhu D, Liu L, Yang D, *et al.* Clearing persistent extracellular antigen of hepatitis b virus: An immunomodulatory strategy to reverse tolerance for an effective therapeutic vaccination. *J Immunol* 2016; 196(7): 3079-87. DOI: 10.4049/jimmunol.1502061
- [18] Whitford K, Liu B, Micallef J, *et al.* Long-term impact of infant immunization on hepatitis B prevalence: A systematic review and meta-analysis. *Bull World Health Organ* 2018; 96(7): 484-97. DOI: 10.2471/BLT.17.205153
- [19] Markey PG, White HA, Matthews AT, Strebor CR, Krause V. Prevention of perinatal hepatitis B virus transmission: Are we following guidelines? *Commun Dis Intell Q Rep* 2017; 41(3): E195-8.
- [20] Ma S, Chen X, Tan Q, *et al.* An engineered dc-targeting lentivector induces robust T cell responses and inhibits hbv replication in HBV transgenic mice via upregulating T cell autophagy. *Cell Physiol Biochem* 2018; 48(3): 1041-59. DOI: 10.1159/000491972
- [21] Grzegorzewska AE, Świdarska MK, Mostowska A, Jagodziński PP. Circulating interferon- λ 3, responsiveness to HBV vaccination, and HBV/HCV infections in haemodialysis patients. *Biomed Res Int* 2017; 2017: 3713025. DOI: 10.1155/2017/3713025
- [22] Dou Y, Van Montfort N, Van Den Bosch A, *et al.* HBV-derived synthetic long peptide can boost CD4+and CD8+T-cell responses in chronic HBV patients *ex vivo*. *J Infect Dis* 2018; 217(5): 827-39. DOI: 10.1093/infdis/jix614
- [23] De Lima A, Kanis SL, Escher JC, Janneke Van Der Woude C. Hepatitis B vaccination effective in children exposed to anti-Tumour necrosis factor alpha in utero. *J Crohn's Colitis* 2018; 12(8): 948-53. DOI: 10.1093/ecco-jcc/jjy053
- [24] Chawansuntati K, Chaiklang K, Chaiwarith R, Praparattapan J, Supparatpinyo K, Wipasa J. Hepatitis B vaccination induced TNF- α - and IL-2-producing T cell responses in

- HIV-Healthy individuals higher than in HIV+ individuals who received the same vaccination regimen. *J Immunol Res* 2018; 2018: 8350862. DOI: 10.1155/2018/8350862
- [25] Bodo B, Malande OO. Delayed introduction of the birth dose of Hepatitis B vaccine in EPI programs in East Africa: A missed opportunity for combating vertical transmission of Hepatitis B. *Pan Afr Med J* 2017; 27(Supp 3): 19. DOI: 10.11604/pamj.supp.2017.27.3.11544
- [26] Ogundele OA. Reducing the risk of nosocomial Hepatitis B virus infections among healthcare workers in Nigeria: A need for policy directive on pre-employment screening and vaccination. *Pan Afr Med J* 2018; 30: 2-4. DOI: 10.11604/pamj.2018.30.133.15954
- [27] Yang A, Guo Z, Ren Q, *et al.* Active immunization in patients transplanted for hepatitis B virus related liver diseases: A prospective study. *PLoS One* 2017; 12(11): e0188190. DOI: 10.1371/journal.pone.0188190
- [28] Shao ER, Mboya IB, Gunda DW, *et al.* Seroprevalence of hepatitis B virus infection and associated factors among healthcare workers in northern Tanzania. *BMC Infect Dis* 2018; 18(1): 1-10. DOI: 10.1186/s12879-018-3376-2
- [29] Breakwell L, Tevi-Benissan C, Childs L, Mihigo R, Tohme R. The status of hepatitis B control in the African region. *Pan Afr Med J* 2017; 27(Supp 3): 17. DOI: 10.11604/pamj.supp.2017.27.3.11981
- [30] Tajiri K, Shimizu Y. Unsolved problems and future perspectives of hepatitis B virus vaccination. *World J Gastroenterol* 2015; 21(23): 7074-83. DOI: 10.3748/wjg.v21.i23.7074
- [31] Komlos J, Landes R. Alice to the red queen: Imperious econometrics. *Econ Hist Rev* 1991; 44(1): 133-6. DOI: 10.2307/2597489

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