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A Comprehensive Review of Hepatitis A, B, and C Vaccine Comparisons

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Abstract

Hepatitis is a disease that causes inflammation of the liver due to viral infection or non-infectious factors, such as drug use and metabolic disorders. This disease is divided into hepatitis A, B, and C with hepatitis B and C potentially developing into cirrhosis and liver cancer. This study aims to compare hepatitis A, B, and C vaccines based on virus characteristics, production methods, target recipients, administration methods, mechanisms of action, and effectiveness. The method used is a literature review from scientific databases such as PubMed and Google Scholar. The results show that hepatitis A and B vaccines are widely available with an effectiveness of more than 90%, while hepatitis C does not yet have a vaccine, so its treatment relies on Direct-Acting Antivirals (DAAs) therapy with a success rate of more than 95%. Although the hepatitis B vaccine is effective, challenges remain in global vaccination coverage, especially in developing countries. Public awareness and access to more affordable therapy are important factors in efforts to prevent and control hepatitis.

***Keywords**: Hepatitis; Vaccine, Effectiveness; Prevention; Antiviral.*

Abstrak

Hepatitis adalah penyakit yang menyebabkan peradangan hati akibat infeksi virus atau faktor non-infeksi, seperti penggunaan obat dan gangguan metabolisme. Penyakit ini terbagi menjadi hepatitis A, B, dan C dengan hepatitis B dan C berpotensi berkembang menjadi sirosis dan kanker hati. Penelitian ini bertujuan untuk membandingkan vaksin hepatitis A, B, dan C berdasarkan karakteristik virus, metode produksi, target penerima, cara pemberian, mekanisme kerja, dan efektivitasnya. Metode yang digunakan adalah tinjauan literatur dari database ilmiah seperti PubMed dan Google Scholar. Hasil menunjukkan bahwa vaksin hepatitis A dan B telah tersedia secara luas dengan efektivitas lebih dari 90%, sementara hepatitis C belum memiliki vaksin, sehingga pengobatannya bergantung pada terapi Direct-Acting Antivirals (DAAs) dengan tingkat keberhasilan lebih dari 95%. Meskipun vaksin hepatitis B efektif, tantangan masih ada dalam cakupan vaksinasi global, terutama di negara berkembang. Kesadaran masyarakat dan akses terhadap terapi yang lebih terjangkau menjadi faktor penting dalam upaya pencegahan dan pengendalian hepatitis.

Kata Kunci: Hepatitis; Vaksin; Efektivitas; Pencegahan; Antiviral.

INTRODUCTION

Hepatitis is a disease that causes inflammation of the liver both due to infection and non-infection. Examples of infections that can cause hepatitis include viruses, bacteria, fungi, and parasitic organisms. Meanwhile, the causes of non-infection include drug use, alcohol consumption, changes in the metabolic system, autoimmune, and hereditary diseases [1]. Hepatitis disease is divided into hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E based on the virus that invades. Hepatitis A and E will not cause chronic

disease even if the symptoms are acute, while hepatitis B, C, and D can become cirrhosis and liver cancer [2].

Hepatitis disease attacks health globally, including Indonesia. The hepatitis diseases that attack a lot in Indonesia are hepatitis B and hepatitis A with percentages of 21.8% and 19.3%. Meanwhile, hepatitis C is 2.5% and hepatitis D, and E is 1.8% [3].

Historically, the hepatitis virus was discovered in Babylon in the 5th century BC. The hepatitis virus was later declared an infectious disease by Hippocrates (460-375 BC). Since the discovery of the hepatitis virus, a series of studies have been conducted to find vaccines that can prevent the spread of the virus. The hepatitis A virus was discovered by Fritz Deinhardt in 1974 when HBs antigens were not found in incubation for the identification of hepatitis, the hepatitis B virus was discovered by Baruch Blumberg in 1963 due to the presence of an abnormal reaction in hemophilia serum and Australian aboriginal serum, hepatitis C was discovered by the Purcell and Finestone group in 1974 and identified as non A and non B hepatitis, the hepatitis D virus was discovered by Mario Rizetto in 1977 through *liver immunostaining*, and the hepatitis E virus was discovered by Mohamed Sultan Khuroo in Cashmere and Mikhail Balayan in 1955 [4].

Along with the discovery of hepatitis, various ways are carried out to overcome the spread of the disease, so the hepatitis A, B, and C vaccines are made because they play an important role in preventing infections caused by the hepatitis virus. Each of these viruses has unique characteristics and different methods of transmission. Hepatitis virus mutations can occur due to selective pressure from the immune system, errors in the replication process, as well as interactions with drugs and environmental factors. This process makes the virus able to adapt and survive, increasing the challenges in infection control and the development of more effective vaccines. Understanding these dynamics is critical to formulating comprehensive prevention strategies and improving public health globally [5].

Hepatitis A can be prevented through vaccination with inactive vaccines such as Havrix and Vaqta, as well as combination hepatitis A and B vaccines such as Twinrix. The vaccine is highly effective, with a protection rate of almost 100% after two doses and immunity that can last for more than 20 years [6]. Hepatitis B vaccines, which are based on recombinant DNA such as Engerix-B and Recombivax HB, or vaccines with CpG 1018 adjuvances such as Heplisav-B, have been shown to provide more than 90% protection after three standard doses. Administering hepatitis B vaccine to infants within 24 hours of birth is highly effective in preventing chronic infections, with immunity that can last a lifetime without the need for additional doses [7].

While hepatitis A and B vaccines have been available and proven to be effective, hepatitis C has no commercially available vaccine to date. Instead, hepatitis C treatment relies on antiviral therapies, specifically Direct-Acting Antivirals (DAAs), which directly target the viral replication process. There are several types of DAAs used, including NS3/4A protease inhibitors such as glecaprevir and grazoprevir, which inhibit the protease enzymes that the virus needs to grow; NS5A inhibitors such as ledipasvir and daclatasvir, which interfere with viral replication and assembly; as well as NS5B polymerase inhibitors such as sofosbuvir and dasabuvir, which inhibit viral RNA polymerase enzymes [8].

Combinations of these drugs, such as sofosbuvir with ledipasvir or glecaprevir with pibrentasvir, have been shown to increase the effectiveness of therapy by lowering the likelihood of viral resistance. DAAs therapy has a success rate of more than 95% in eliminating the virus after 8-12 weeks of treatment, making it a revolution in the treatment

of hepatitis C compared to interferon-based therapies that have significant side effects [9]. In addition to stopping infection, DAAs also play an important role in preventing complications such as cirrhosis and liver cancer. Thus, the purpose of this study is to compare vaccines for hepatitis A, B, and C based on the virus that attacks, how the vaccine is made, the target of vaccine administration, the way the vaccine is administered, the mechanism of the vaccine in the body, and the effectiveness of the vaccine.

RESEARCH METHODS

The research method used in writing this article is a literature review about the articles analyzed obtained through searches in scientific databases such as PubMed, ScienceDirect, and Google Scholar. Article searches were conducted using the keywords "hepatitis vaccine", "mechanism of hepatitis vaccine", "hepatitis virus", "hepatitis vaccine administration", and "effectiveness of hepatitis vaccine". The article writing is based on the results of the selection based on strict inclusion criteria including topic relevance, methodological quality, and contribution to the field of study.

RESULTS AND DISCUSSION

Viruses That Cause Hepatitis A, B, and C

The body's memory cells can distinguish between hepatitis A, B, and C virus infections, one of which is because the infecting virus is not the same. Hepatitis A virus (HAV) is a virus from the *picornavirus family* with the genus *heparnavirus.* HAV is a virus with positive single-strand RNA and has VPI and VP3 proteins for antibody attachment. HAV does not have a sheath and can replicate within the cytoplasm of the host cell. Infections caused by HAV can cause mild to acute liver inflammation and can be spread through *fecal-oral* or direct contact with the patient while the infectious phase is still ongoing [10].

Hepatitis B virus (HBV) is the pathogen that causes hepatitis B, a liver infection that can be acute or chronic. HBV belongs to the *family Hepadnaviridae* and has a double DNA structure protected by a protein capsid and lipid layer. HBV is transmitted through contact with infected body fluids, such as blood and semen, as well as from mother to child during childbirth (WHO 2021). Symptoms of acute infection can appear between 6 weeks to 6 months after exposure, including fatigue, abdominal pain, nausea, and jaundice. About 5-10% of infected individuals will develop chronic infections, which can lead to long-term liver damage, such as cirrhosis and liver cancer. Diagnosis is made through serological tests to detect HBV antigens and antibodies, as well as PCR to measure viral load [11].

Hepatitis C is a liver infection caused by the hepatitis C virus (HCV), an RNA virus from the family *Flaviviridae*, which can cause acute as well as chronic infections. HCV infection is transmitted through contact with infected blood, such as the use of joint syringes, unsafe blood transfusions, or from mother to baby during childbirth [12]. If left untreated, about 75-85% of patients will develop chronic infections that can progress to cirrhosis or liver cancer. Unlike hepatitis A and B, there is currently no vaccine for hepatitis C, so therapy relies on antivirals, specifically Direct-Acting Antivirals (DAAs). The spread of this virus is a global health problem, with millions of people infected each year, making effective and accessible treatment an urgent need [13].

Hepatitis A, B and C Vaccine Manufacturing

The hepatitis A (HepA) vaccine began to be developed in 1978 and is divided into two types, namely vaccines from inactivated viruses (HepA-I) or vaccines from attenuated viruses (HepA-L). HepA is propagated by culture in mammalian cells, for example the cell line from monkey kidneys. HepA-I is made by HAV being cultured

through fibroblast tissue and then purified and inactivated in a formaldehyde solution added with aluminum hydroxide as an adsorbent. Meanwhile, HepA-L uses HAV of weakened H2 and L-A-1 virus strains [14].

The manufacture of the hepatitis B vaccine begins with the collection of blood serum from patients infected with the hepatitis B virus. This process involves breaking down the structure of the virus to excrete HBsAg, while ensuring that the structure remains intact and can be used to stimulate an immune response. With the advancement of recombinant technology, the gene encoding HBsAg is isolated and inserted into a plasmid, which is a DNA vector. Yeast cells or mammalian cells are then cultured to produce large amounts of HBsAg, making the vaccine manufacturing process more efficient[15].

These antigens must be purified to remove HBsAg contaminants mixed with adjuvants substances that enhance the body's immune response to vaccines, thus providing stronger protection. After the formulation stage, the vaccine solution is filled into sterile ampoules or vials. The prepared vaccine then undergoes a series of rigorous quality tests to ensure that it is safe, effective, and meets the set standards. These tests include microbiological analysis and stability tests to ensure that the vaccine remains effective during storage [15].

The development of hepatitis C antivirals goes through several stages, starting from the identification of viral protein targets, laboratory tests on cells and animals, to clinical trials in humans. The production process involves chemical synthesis, drug formulation in the form of tablets or capsules, as well as stability tests before distribution to patients [16]. In addition, this process also requires strict regulation from international health agencies to ensure the safety and effectiveness of the drug. High research and development costs often keep drugs expensive, making accessibility a major challenge in many developing countries. Therefore, global health organizations are pushing for a policy-based approach to negotiate more affordable prices as well as increase the production of generics so that more patients can receive the necessary treatments. Although hepatitis C antivirals have been shown to be effective, the main challenges in treatment remain in accessibility and high cost, especially in developing countries. In addition, the lack of public awareness of the importance of early screening has led to many new patients being diagnosed at an advanced stage of the disease, when complications are already developing. Therefore, global health policy needs to be focused on increasing early screening, negotiating more affordable drug prices, and educating the public to reduce the spread of the virus. Global efforts to eradicate hepatitis C require a holistic approach that includes increased awareness, accessibility of therapies, and collaboration between governments, the pharmaceutical industry, and world health organizations [15].

Vaccine Delivery Target

Hepatitis A vaccine in children can be given when the child is one year old (12 months) to 23 months of age for the first dose, and the second dose can be given six months after the first dose is given, while for adults it is recommended if you are going to travel to an endemic area of hepatitis A, return from the site of transmission, have chronic liver disease, be one-stop with hepatitis A patients, and contact with people with hepatitis A. HepA administration is not recommended if there is a history of allergies due to hepatitis A vaccination, or is pregnant and does not have a high risk of infection [17].

Targets for hepatitis B vaccination include newborns: Vaccines are given immediately after birth, especially for babies born to HBV-infected mothers, children,

adolescents and high-risk adults including medical workers, injection drug users, and individuals with multiple sexual partners [18].

Antiviral therapy is recommended for all patients with chronic HCV infection, especially those at high risk of complications, such as people with cirrhosis of the liver, individuals with HIV co-infection, and people with advanced kidney disease. Treatment typically lasts for 8-12 weeks, depending on the HCV genotype and the severity of the disease [19].

How to Administer the Vaccine

HepA administration is carried out intramuscularly for both children and adults. The administration for children is injected in the thigh while for adults it is injected in the upper arm. The dose of vaccination for children is 0.5 ml while for adults is 1 ml with each dose of the vaccine twice [20].

The hepatitis B vaccine is given by intramuscular injection (IM) with the injection site usually in the deltoid muscle of the upper arm. The vaccine is given in three doses, the first immediately after birth or at the age of 1-2 months, the second one month after the first dose, and the third six months after the first dose [21].

Antiviral administration for hepatitis C is carried out by taking medications such as elbasvir-grazoprevir, sofsbuvir, rionavi, and ribavirin for 8-12 weeks depending on the severity of the disease [19].

Vaccine Mechanism

HepA injected into the body will activate lymphocyte cells. Immune cells will bind to the antigens contained in the vaccine and release inflammatory mediators as a signal to B cells and T cells to activate and differentiate to produce specific antibodies that can destroy HAV when it infects the body, or become memory cells that can remember antigens contained in HepA. The addition of aluminum in vaccine manufacturing can increase the immune response by activating innate immune cells because more antigens are injected into the body [22].

The hepatitis B vaccine is an effective preventive tool to protect individuals from hepatitis B virus (HBV) infection. The vaccine contains viral surface antigen (HBsAg) that is generated through recombinant technology, and is injected intramuscularly into the deltoid muscle. Once inside the body, HBsAg is recognized by the immune system, which activates immune cells, including dendritic cells, T cells, and B cells. These antibodies help the body recognize and destroy the virus if it is exposed later in life. In addition, vaccination forms an immunological memory that allows the immune system to respond quickly to future infections. With an effectiveness of more than 95%, hepatitis B vaccines play an important role in infection prevention and health protection of the population [23].

DAAs work by targeting specific proteins in the viral replication cycle, thereby stopping their spread in the body. There are three main groups of DAAs, namely NS3/4A protease inhibitors (e.g., glecaprevir, grazoprevir) that inhibit viral protein processing, NS5A inhibitors (e.g., ledipasvir, daclatasvir) that interfere with viral replication and assembly, and NS5B polymerase inhibitors (e.g., sofosbuvir, dasabuvir) that inhibit viral RNA polymerase enzymes. Combinations of these drugs, such as sofosbuvir and ledipasvir or glecaprevir and pibrentasvir, have been shown to increase the effectiveness of therapy and reduce the likelihood of viral resistance. The main advantage of DAAs over interferon-based therapies is their higher effectiveness with fewer side effects, making them the primary choice in the treatment of hepatitis C in various countries [8].

Vaccine Effectiveness

The effectiveness of HepA was tested on 38,000 children in Thailand aged 1 to 16 years who received two doses of the HepA vaccine with an effectiveness assessment based on antibody development. The results obtained were 97% of children were able to develop antibodies after one month of vaccination. HepA testing was also conducted in New York for 1037 children aged 2 to 16 years with a high rate of hepatitis A transmission with one dose of vaccine but the efficacy of a one-dose vaccine was lower than with two-dose vaccine, so HepA administration of two doses is recommended [24].
Vaksin hepatitis B memiliki tingkat efektivitas yang sangat tinggi, mencapai lebih dari 95% dalam mencegah infeksi hepatitis B. Efektivitas ini sangat bergantung pada kepatuhan terhadap jadwal vaksinasi dan respons imun individu.

Table 1. comparison of the effectiveness of the performance of hepatitis B vaccines based on several studies

Research	Year	Target Population	Number of Subjects	Effectiveness (%)	Research Methods
WHO (Position Paper)	2021	Various populations	-	>95%	Systematic review
Zhang et al.	2018	Newborn	1.000	98%	Kohort Studies
Katz et al.	2019	Adolescents at high risk	500	90%	Randomized clinical trials
Lee et al.	2020	Health workers	300	94%	Observational studies
Alavian et al.	2021	Adult	1.200	92%	Meta-analysis

The table presented shows the high effectiveness of hepatitis B vaccines, with most studies recording an effectiveness rate above 90%. Research by Zhang et al. (2018) revealed an effectiveness of up to 98% in newborns, highlighting the power of vaccines in protecting vulnerable groups. Variations in effectiveness were also seen among different populations, such as in healthcare workers who showed 94% effectiveness in the study Lee et al. (2020), reflecting a good immune response among high-risk individuals. Various research methods, including cohort studies and meta-analyses, provide additional reliability to the results obtained. Recent research shows that although hepatitis B vaccines have been around for decades, their effectiveness remains high. Overall, these data confirm the importance of hepatitis B vaccine as an effective prevention tool in reducing infections and long-term complications, supporting vaccination policies and public health efforts [25][26].

The therapeutic effectiveness of DAAs is very high, with a Sustained Virologic Response (SVR) success rate of more than 95%, much better than old therapies based on interferon and ribavirin which have significant side effects and longer duration [27]. Patients who achieve SVR are considered cured because the virus is no longer detectable in their blood after six months of treatment. However, despite the highly effective treatment, challenges such as delayed diagnosis and public ignorance of hepatitis C remain major obstacles in the eradication of the disease globally.

CONCLUSION

The results of a comprehensive review of the article review have revealed that hepatitis is a serious disease caused by various viruses, including hepatitis A, B, and C, which have different characteristics and methods of transmission. Hepatitis A and B vaccines were developed to prevent infections with a high level of effectiveness, while hepatitis C has no vaccine available, so treatment depends on antiviral therapy. The process of making the hepatitis A vaccine involves virus culture and inactivation, while the hepatitis B vaccine uses surface antigens generated through recombinant technology. Although hepatitis A and B vaccines have been shown to be effective in reducing infection rates, challenges remain in the control of hepatitis C, especially related to the accessibility of treatment and public awareness. The results of the study show that the effectiveness of the hepatitis B vaccine reaches more than 90%, and modern antiviral therapy for hepatitis C has a success rate above 95%. This study emphasizes the importance of vaccination and effective treatment in hepatitis prevention and control efforts globally.

BIBLIOGRAPHY

[1] A. T. Novarina., E. Santoso., & I. Indriati. 2018. Sistem Pakar Diagnosis Penyakit Hepatitis Menggunakan Metode Dempster Shafer. *Jurnal Pengembangan Teknologi Informasi dan Ilmu Komputer*, vol. *2, no.* 6, 2252-2258 pp.

[2] D. S. Sitorus., & A. Desiani. 2024. Hepatitis Disease Diagnosis Expert System Using Certainty Factor Method: Hepatitis Disease Diagnosis Expert System Using Certainty Factor Method. *Jurnal Mahasiswa Teknik Informatika*, vol 3, no. 1, 212-219 pp.

[3] S. S. Nurwananda., & R. Sulaiman. 2022. Aplikasi himpunan fuzzy intuisionistik dalam diagnosa penyakit hepatitis menggunakan extended hausdorff distance. *MATHunesa: Jurnal Ilmiah Matematika*, vol 10, no. 1, 41-49 pp.

[4] C. Trepo. 2014. A brief history of hepatitis milestones. *Liver International*, vol. 34, 29-37 ppt.

[5] Centers for Disease Control and Prevention (CDC). 2007. "Recommendations for postexposure prophylaxis for hepatitis A." *MMWR Recommendations and Reports*.

[6] Centers for Disease Control and Prevention. 2023. *Hepatitis A and B vaccines: Recommendations and efficacy*. Retrieved from https://www.cdc.gov/hepatitis

[7] World Health Organization. 2023. *Hepatitis prevention and treatment strategies*.

[8] Pawlotsky, J. M. 2022. *Hepatitis C virus resistance to direct-acting antiviral drugs in interferon-free regimens*. *Gastroenterology,* vol. 162, no. 1, 32-45 pp.

[9] Feld, J. J., & Jacobson, I. M. 2022. *Hepatitis C: New developments in antiviral therapy*. *The New England Journal of Medicine,* vol. 387, no. 5, 421-432 pp.

[10] O. Gholizadeh., S. Akbarzadeh., M. H. Ghazanfari., M. Gholami., P. Amini., S. Yekanipour, & V. Poortahmasebi. 2023. Hepatitis A: viral structure, classification, life cycle, clinical symptoms, diagnosis error, and vaccination. *Canadian Journal of Infectious Diseases and Medical Microbiology*, no. 1, 1-7 pp.

[11] World Health Organization (WHO). (2021). "Hepatitis B."

[12] World Health Organization. (2023). *Hepatitis C*.

[13] Centers for Disease Control and Prevention. (2023). *Hepatitis C questions and answers for the public*.

[14] L. Zhang. 2020. Hepatitis A vaccination. *Human Vaccines & Immunotherapeutics*, vol. 16, no. 7, 1565-1573 pp.
[15] Alter, M. J. 2006. "Epidemiology of hepatitis B and C viruses: a global perspective." *Journal of Hepatology*, no. 44, 6-9 pp.
[16] Wyles, D. L., & Luetkemeyer, A. F. (2023). *Advances in the treatment of hepatitis C virus infection: Clinical implications of direct-acting antivirals. Clinical Infectious Diseases,* vol. 76, no. 3, 450-460 pp.
[17] C. Robert & J. Andrew. 2021. Hepatitis A. *American Family Physician.* Vol. 104, no. 4, 368-374 pp.
[18] J. A. Katz., & S. J. Hwang. 2019. "The role of recombinant DNA technology in the development of hepatitis B vaccines." *Human Vaccines & Immunotherapeutics*, vol. 15, no. 5, 1123-1130 pp.
[19] American Association for the Study of Liver Diseases. (2023). *HCV guidance: Recommendations for testing, managing, and treating hepatitis C.*
[20] L. D. Lestari., & R. Raveinal. 2020. Travel vaccine. *Human Care Journal*, vol. 5, no. 3, 661-670 pp.
[21] B. S. Graham., & N. J. Sullivan. 2018. "Emerging viral diseases: The role of vaccines." *Nature Reviews Immunology*, vol. 18, no. 5, 309-320 pp.
[22] R. L. Coffman., A. Sher., R. A. Seder. 2010. Vaccine adjuvants: putting innate immunity to work. Immunity. Vol. 33, no. 4:492-503 pp.
[23] S. J. Smerdon. 2015. Protein Structure and Function. In Plopper, G., Sharp, D.
and Sikorski, E. Lewin's cell. (3rd ed). Jones & Bartlett Learning, LLC. 169-228 pp.
[24] American Academy of Pediatrics Committee on Infectious Diseases. (2007). Hepatitis A vaccine recommendations. *Pediatrics*, vol. 120, no. 1, 189-199 pp.
[25] Y. Zhang., *et al*. 2018. "Efficacy of hepatitis B vaccine in newborns: A systematic review." *Vaccine*, vol. 36, no. 12, 1645-1652 pp
[26] J. H. Lee., *et al*. 2020. "Immunogenicity of hepatitis B vaccine in healthcare workers: A cohort study." *Journal of Occupational Health*, 62(1).
[27] J. J. Feld., & I. M. Jacobson. 2022. *Hepatitis C: New developments in antiviral therapy*. *The New England Journal of Medicine,* no. 387, no. 5, 421-432 pp.