Recent advances in Hepatitis B skin vaccination and immunization

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Introduction

Every year on July 28th, World Hepatitis Day is commemorated to raise awareness on viral hepatitis, a worldwide public health concern affecting millions of people [1]. Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are considered the most concerning ones among the different types of viral hepatitis.

Hepatitis B is a worldwide health concern because of its prevalence, the potential for devastating consequences, and the need for effective preventative interventions. [2]. HBV can spread by unprotected sexual contact, sharing needles, mother-to-child transmission during childbirth, or other situations during which there is exposure to contaminated blood or other body fluids. Hepatitis B is causing both acute and chronic infections, with the latter having the potential to cause liver cirrhosis, liver cancer, and other potentially fatal side effects [2]. An estimated 820,000 people died from hepatitis B in 2019, primarily from cirrhosis and hepatocellular carcinoma (primary liver cancer) [2]. Safe, accessible, and efficient vaccinations help prevent the spread of Hepatitis B.

Hepatitis B contributes to **820,000 deaths** every year

25% of chronic infections progress to **liver cancer**

Adapted from [5]

The role of vaccines in managing Hepatitis B

Vaccination can prevent Hepatitis B and its related conditions. Hepatitis B vaccines are already available since the early 1980s and are considered safe and effective. The vaccine is estimated to prevent 38 million deaths over the lifetime of persons born between 2000 and 2030 in 98 low- and middle-income countries [3]. Currently, over 15 Hepatitis B vaccines are commercially available. They elicit antibodies from the immune system that guard against HBV infection. Three doses of the main immunisation series are most commonly given at 0, 1, and 6 months [4]. Vaccination within 24 hours of birth followed by 2 to 3 additional doses provides life-long protection against Hepatitis B infection [5].

Hepatitis B vaccine offers a variety of advantages. First off, it offers long-lasting defence; research indicates that vaccine-induced immunity can endure for at least 20 years. Secondly, it helps reduce the chance of infants developing chronic infection by preventing the spread of HBV from infected women to their newborn children. Lastly, in many nations, mass immunisation campaigns have been successful in lowering the general prevalence of Hepatitis B and its consequences [4].

Challenges with Hepatitis B vaccines

Although Hepatitis B vaccinations have been quite effective, providing widespread access to vaccinations, especially in environments with low resources, remains a substantial problem. The vaccine coverage required to accomplish disease control is furthermore hampered by barriers including cost, a lack of healthcare infrastructure, and a lack of knowledge [4]. Indeed, incorrect information, false beliefs about the effectiveness and safety of vaccines, particularly for at-risk population, causes immunisation delays or even vaccine rejection [4,6].

Other hurdles encountered with Hepatitis B vaccination include
(1) dose compliancy as some people might not finish the entire vaccine series. The risk of infection from incomplete immunisation highlights the necessity for ongoing efforts to guarantee high rates of vaccination schedule completion [4,7];
(2) immunocompromised people such as HIV patients, elderly , smokers, patients with renal failure, and obese people may not develop protective antibodies [8];
(3) delivering Hepatitis B vaccines outside the cold chain, vaccinating all infants within 24 hours of birth, and fully immunising infants through routine vaccination programmes pose important challenges as well [9]. On top of that, 5% to 10% of people who get the most commonly used second-generation vaccines fail to acquire antibodies that protect them [10].

Skin vaccination: A promising alternative

Skin vaccination requires a vaccine to be injected into the dermis, the skin layer underneath the epidermis. Hepatitis B vaccines are often given intramuscularly, meaning a full dose is needed due to decreased antigen uptake at the muscle location, while the intradermal approach achieves equivalent immunogenicity using a fractional dose, thus a smaller volume and lower antigen concentration. This strategy offers the possibility for broader immunisation coverage while simultaneously conserving vaccine supplies [11,12].

Benefits and advantages of intradermal Hepatitis B vaccination

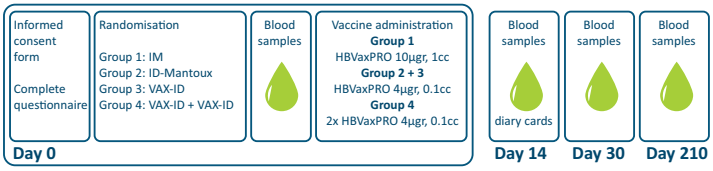
The efficiency of Hepatitis B immunisation following intradermal vaccination has been shown in several studies. Hereby the seroprotection rates of vaccinations given intradermally at fractional doses (dose sparing potential of the intradermal route) are equivalent to those of vaccines given intramuscularly at the recommended dose especially for women and children population [13]. Some other studies however showed that in comparison to intramuscular immunisation, intradermal Hepatitis B vaccination provided less seroprotection [13], which can possibly be explained by the Mantoux technique being error prone. The dose-sparing benefit is especially important in environments with low resources where the availability of vaccines may be limited. By lowering the vaccine volume, more people can be immunised with the same number of doses, increasing vaccination coverage and accessibility.

Additionally, the intradermal approach may augment the immune response because of the extensive network of immune cells in the skin, improving vaccination effectiveness [14], which could be a more effective technique for non-responders [14,15,16]. Studies indeed demonstrated superior seroconversion and response rates compared to the intramuscular route [16].

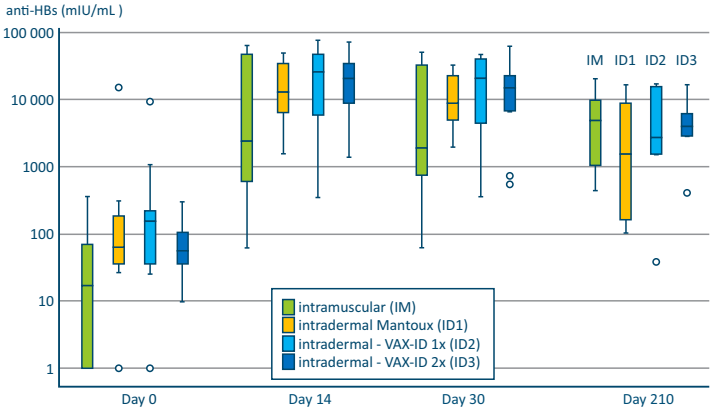
Overcoming the challenges of the intradermal vaccination: Clinical evidence

Although Hepatitis B skin vaccination shows promise, there are challenges to its widespread use. The Mantoux technique is the current standard of care for intradermal injection, but it is notoriously difficult and prone to failure, thus requiring a lot of training for healthcare professionals [17]. Furthermore, the administration is considered painful for the vaccinees.
To overcome the challenges of the Mantoux technique, VAX-ID® has been developed as a novel intradermal drug delivery device with a high ease of use. It is suited for standardized, accurate and reliable intradermal injection to overcome the challenges of the Mantoux technique.

Van Mulder et al. investigated the immunogenicity and safety of intradermal delivery of a hepatitis B booster vaccine using this novel drug delivery device, VAX-ID® [18]. A total of 48 healthy adults were enrolled for the study and divided over 4 groups: (1) standard Intramuscular (IM) injection in the deltoid region (HBVAXPRO® 10 µg, 1 mL), (2) Intradermal (ID) injection in the proximal posterior area of the forearm using the Mantoux technique, (3) ID injection with VAX-ID® in one forearm, or (4) ID injection with VAX-ID® in both forearms. The ID groups received a fractional dose of the HBVAXPRO (1/4th, HBVAXPRO 4µg, 0.1mL) compared to full dose in the intramuscular group.



The results of the study demonstrated promising immunogenicity of the intradermal Hepatitis B booster vaccine using VAX-ID®. The vaccine delivered through the intradermal route produced robust antibody responses, indicating its ability to stimulate the immune system effectively. The immunogenicity of the intradermal vaccine was non-inferior to the standard intramuscular vaccination [18].



Furthermore, the study reported a favourable safety profile for the intradermal delivery method. The incidence of local and systemic adverse reactions was minimal and comparable to those observed with the Mantoux. The findings of this study highlight the potential of the intradermal route using VAX-ID® as a viable option for Hepatitis B vaccination [18].

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