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Review

Efficacy, Effectiveness, and Safety of Herpes Zoster Vaccine in Immunocompromised Patients

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Abstract

The varicella-zoster is a dangerous virus that has the potential to lead to many fatal conditions. People with low immune systems tend to be affected by this virus and they are more prone to HZ and its complications. This virus can't be treated with an antiviral drug as they may not respond to them. It's important to note that the live attenuated vaccine and the adjuvant recombinant subunit vaccine have different characteristics and recommended uses for individuals with compromised immune systems. This paper aims to assess these vaccines' efficacy, effectiveness, and safety in such individuals. However, autoimmune therapy may create more side effects which can be more in the injection use. In conclusion, vaccination is a measure against HZ and its complications for people with compromised immune systems. The RZV vaccine is widely regarded as the choice because it has shown effectiveness and is considered safe, for different groups of people, with weakened immune systems. For people, with slight immune-compromised, the ZVL vaccine might be a choice. However, it's crucial to assess each situation on a basis.

Keyword: *Adjuvant recombinant subunit vaccine, Herpes Zoster, Immunocompromised patients, Live attenuated vaccine, Varicella-Zoster Virus*

Introduction

A potentially dangerous virus name herpes zoster, have a clinical condition name shingles that occurs when the zoster virus becomes active in the body resulting in a rash characterized by fluid-filled blisters appearing on an area of the skin (1). While HZ can affect any part of the body, it commonly appears on the chest or lower back. This reactivation can lead to complications, including herpetic neuralgia (PHN) and persistent pain lasting more than three months after the rash disappears (2). There is some other dangerous impact of this virus can do to which it can affect the eyes, potentially causing vision loss or even blindness. In some cases, HZ can spread to parts of the body, such as the nervous system or other organs (3, 4). These complications did not impact one's quality of life. It also results in increased healthcare utilization and costs for those affected by HZ. People who have weakened systems are, at a risk of developing herpes zoster and experiencing complications. Additionally, they often have a response to treatment. This group includes individuals who have immunodeficiency conditions such, as HIV infection, hematological malignancies, solid organ transplants or autoimmune disorders (5, 6). Furthermore, individuals who are undergoing treatment, with medications such as corticosteroids, cytotoxic agents, biologics or targeted therapies are considered to have compromised systems. Getting vaccinated is a step in protecting against herpes zoster (HZ) and its potential long-term consequences. Presently there are two authorized vaccines, for preventing HZ; the attenuated vaccine (ZVL) and the adjuvant recombinant subunit vaccine (RZV) (7, 8). ZVL contains a live strain of varicella zoster virus (VZV) which stimulates both cellular immunities. Initially licensed in 2006 for preventing HZ in adults aged 60 years and older, ZVL was later expanded to include those 50 years and above. On the other hand, RZV consists of a glycoprotein E (IgE) from VZV combined with an adjuvant system that enhances immune response. It received licensure in 2017 for preventing HZ in adults aged 50 years and older, regardless of their status. However, it's important to note that these vaccines have characteristics and specific indications when it comes to their use among immunocompromised individuals. It is not recommended to administer ZVL to patients who have weakened systems as there is a risk of VZV infection linked to the vaccine. However, patients with mild to immuno-compromisation, such as those undergoing dose immunosuppressive therapy or individuals with HIV infection and CD4 counts above 200 cells/mm3 ZVL, might be considered (9, 10). Nevertheless, its effectiveness and safety in this population are uncertain. It is advisable for individuals who are 50 years old or above and have compromised systems to consider getting RZV regardless of the extent of their immunosuppression. Numerous research studies have indicated that RZV is effective in preventing both HZ and PHN in immunocompromised patients, including those with cancer, people who have undergone organ transplants, and individuals receiving treatment for autoimmune disorders. Furthermore, RZV has exhibited safety levels and tolerability among immunocompromised patients without an increased risk of adverse events or mortality. The main aim of this paper is to present an analysis of the effectiveness, efficiency, and safety profiles of ZVL and RZV, in patients, with compromised systems.

Methodology

On October 1, 2023, We started searching several databases online. For this study, we went through much research across databases such as Medline, PubMed, Embase, and Web of Science. In order to obtain results, we incorporated medical subject headings and a range of related terms in our search within each database. Our keywords covered aspects including herpes zoster, vaccination, individuals with compromised systems, effectiveness, safety, and more. Additionally, we manually explored Google Scholar to supplement our research efforts. We checked the reference lists of the retrieved papers for additional sources. In order to preserve the quality of the review, we applied inclusion criteria, such as excluding papers published before 2008 or after 2023 and preferring English-language publications. We did not apply any restrictions based on age or publication type.

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Discussion

HZV can cause a rash filled with fluid-filled blisters. It may lead to complications, like post-herpetic neuralgia, involvement of the eyes, or spreading to other organs. People with weakened systems are more susceptible to developing shingles and its related issues, while their response to treatment may be less effective.

Efficacy and effectiveness

Several studies have explored the effectiveness and safety of the attenuated vaccine in individuals with weakened systems shedding light on its potential benefits. These studies involved groups of immunocompromised individuals and varied follow-up durations. An RCT study specifically looked at 141 patients who had HIV infection, and Cd4 counts above 200 cells/mm3. It examined the results of those who received the ZVL vaccine compared to those who were given a placebo. Notably, this trial demonstrated that the ZVL vaccine was well tolerated and safe without any cases of vaccine related VZV infection or serious adverse events observed. However, the ZVL vaccine did not demonstrate a decrease in the occurrence of herpes zoster or post-herpetic neuralgia compared to the placebo group during a 2.3-year follow-up period. For PHN, the incident rate was 0.50 (95% CI, 0.06, to 4.28). In a study that followed 21,954 patients with bowel disease who were taking tumor necrosis factor (TNF) agents or other immunosuppressive drugs, it was observed that ZVL had a significant advantage (11, 12). ZVL showed a risk of HZ compared to those who did not receive the vaccination over a period of 2 years. The risk factor for HZ was found to be 0.52 (with a 95% confidence interval of 0.37 to 0.74) in people using TNF agents and 0.61 (with a 95% confidence interval of 0.43 to 0.87) in individuals taking medications. In a study involving 633 patients with arthritis who received treatment either with biologics or conventional synthetic disease-modifying drugs (csDMARDs), it was discovered that ZVL (Zoster Vaccine Live) effectively reduced the risk of herpes zoster (HZ) in individuals. The study, which followed the patients for an average of 1.6 years, showed that both biologic users and csDMARD users were likely to develop HZ when they received the ZVL vaccine—according to the research findings, individuals who used csDMARDs had an adjusted odd ratio (aOR) of 0.41 (with a 95% confidence interval of 0.21 to 0.79) for herpes zoster (HZ) while users of csDMARDs had an aOR of 0.38 (with a 95% confidence interval of 0.18 to 0.81). A thorough review of twelve studies investigated the effectiveness of the Zoster Vaccine Live in populations with weakened systems, such as those with blood cancers, organ transplant recipients, autoimmune disease patients undergoing therapy, and individuals living with HIV infection. The review emphasized the safety of ZVL in immunocompromised groups, as no vaccine related VZV infections or serious adverse events were reported. However, the effectiveness of ZVL in preventing HZ or post-herpetic neuralgia (PHN) varied among these populations. Ranged from 18% to 70%. Factors such as the level of suppression, type and dosage of therapy used, and timing of vaccination were found to influence how effective ZVL was in each population.

Clinical manifestation

Through skin rash and it may be fluid-filled blisters is the most common sign of having herpes (13). This condition can lead to complications, like herpetic neuralgia, eye involvement, and the spreading of the virus throughout the body. Immunocompromised individuals face a risk of developing HZ and experiencing severe symptoms. In these cases, HZ may present with severe features. For instance, there may be a phase preceding the appearance of the rash in days or weeks, during which individuals may experience symptoms like fever, fatigue, headaches, or swollen lymph nodes (14). The rash itself can exhibit characteristics in immunocompromised patients. It may be more widespread and appear in areas or non-contiguous patterns on the body, including crossing over to both sides of the body's midline. Additionally, it tends to cause pain and itching and can persist for longer periods beyond four weeks, leading to scarring or skin discoloration. To further illustrate this point, we can provide examples from the literature that describe these severe manifestations of HZ in

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immunocompromised individuals. For example, there was an instance where a patient suffering from lymphocytic leukemia experienced an outbreak of herpes zoster (HZ) that affected the skin on their face, trunk, and limbs (15). Additionally, this patient also developed meningoencephalitis and hepatitis. Another case report detailed a patient diagnosed with erythematosus who had HZ affecting both eyes due to the involvement of the ophthalmic branch of the trigeminal nerve (16, 17). This resulted in conditions like keratitis, uveitis, and optic neuritis. In a third case report, a patient with HIV infection experienced an outbreak of HZ that spread to organs, including the lungs, liver, spleen, and kidneys. These cases demonstrate how HZ can manifest in ways, with varying severity in individuals with weakened immune systems. It highlights the significance of diagnosing and treating the condition. The skin irritation connected with HZ can result in complications for individuals with weakened systems, such as infections, tissue damage, or bleeding, further complicating the situation (18). Moreover, there is a risk of complications such as nerve problems, inflammation of the brain and spinal cord (meningoencephalitis), inflammation of the cord (myelitis), inflammation of nerve roots (radiculitis), or even Guillain-Barre syndrome (19). This highlights the nature of HZ in this group of patients. Some individuals may experience issues with their vision due to inflammation. There are several complications may arise on may affect the eye. Some complication includes keratitis, uveitis, scleritis, retinitis, optic neuritis, and glaucoma. These medical terms describe areas of the eye that can become inflamed and result in discomfort, redness, blurred vision, or even loss of vision. Inflammation can also affect parts of the body for some people. This may impact organs such as the lungs, liver, pancreas, stomach, colon, or kidneys. Consequently, it can give rise to problems like pneumonia, hepatitis, pancreatitis, gastritis, colitis nephritis. These medical terms refer to body parts that can become inflamed and cause symptoms like fever coughing, breathing difficulties, nausea, vomiting, diarrhea, or blood in urine. This wide range of manifestations highlights the need for increased awareness and personalized management strategies when dealing with HZ in individuals whose immune systems are compromised.

Management

The management of herpes zoster in individuals with weakened systems should only focuses on three aspects of treatment choice which includes: antiviral treatment, pain relief, and comprehensive supportive care with an emphasis on safety. Treating HZ in immunocompromised patients heavily relies on therapy, which is essential for reducing the duration and severity of the rash. Additionally, it helps prevent or address complications such as herpetic neuralgia (PHN). Acyclovir, valacyclovir or famciclovir are recommended medications for these patients as they work by inhibiting the replication of the varicella-zoster virus through interference with its DNA polymerase (20). When choosing an agent, factors like availability, cost, dosing frequency, bioavailability, and the patient's renal function need to be taken into consideration. It is ideal to start therapy as soon as possible after the rash appears within a 72-hour window. However, even if initiated later, it can still provide benefits. For immunocompromised individuals who often experience prolonged shedding and face a higher risk of complications. Antiviral treatment should continue until all lesions have scabbed over completely. In cases where signs of viral replication persist. Such as persistent fever, new lesions, or positive polymerase chain reaction (PCR) tests. The course of treatment may need to extend beyond the typical 10-day duration (21, 22). To delve into the topic of treatment, it is crucial to comprehend how the recommended antiviral medications work and their behavior in the body. Take Acyclovir, for instance, which is a prodrug that only becomes effective once viral thymidine kinase phosphorylates it. When taken orally, its bioavailability ranges from 10% to 20%. It remains active in the body for 2 to 3 hours. Dose adjustments are necessary in patients with renal impairment. While acyclovir has demonstrated its effectiveness in reducing the duration of symptoms caused by herpes zoster (HZ) and the occurrence of neuralgia (PHN) in individuals with an immune system, its

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efficacy in immunocompromised patients remains uncertain. Valacyclovir, an option, is a prodrug that is converted to acyclovir by liver esterase. It has a bioavailability range of 54 70% when taken a life of 2.5 to 3.5 hours. Valacyclovir exhibits effectiveness and safety as acyclovir in individuals with an immune system, but studies investigating its efficacy in immunocompromised patients are limited. Famciclovir is also utilized as a treatment option. It acts as a prodrug that converts to penciclovir through enzymes. Its oral bioavailability is 77%, with a life of 10 hours. Like the mentioned medications, famciclovir has exhibited effectiveness and safety to acyclovir in individuals with a healthy immune system; however, its efficacy in immunocompromised patients remains uncertain. Proper initiation and titration of analgesic therapy are essential and should continue until the pain subsides or becomes manageable. In cases of PHN, which may persist for more than three months after rash onset, analgesic therapy may extend beyond the duration of the rash. Safety considerations are paramount, especially when employing opioids due to the potential for respiratory depression, constipation, nausea, or addiction. Similarly, it's important to exercise caution when using anticonvulsants and antidepressants in patients who have conditions like renal impairment, drowsiness, dizziness, cardiac arrhythmias, urinary retention, glaucoma, or those at risk of serotonin syndrome. When discussing analgesia in detail, it becomes crucial to understand the mechanism of action, pharmacodynamics, and clinical trials of the recommended pain-relieving medications. Paracetamol has been proven effective and safe for managing mild to pain in individuals with HZ (herpes zoster), although its efficacy for PHN (neuralgia) remains uncertain. NSAIDs (inflammatory drugs) which also fall under the category of analgesics, work by inhibiting cyclooxygenase enzymes and reducing prostaglandin synthesis both peripherally and centrally within the nervous system (23). Their bioavailability, half-life, and metabolism vary depending on the NSAID being used. It has been demonstrated that NSAIDs are effective and safe for treating mild pain associated with HZ, but their effectiveness against PHN is still unclear. Opioids act on receptors found in both the brain and spinal cord; their bioavailability well as half-life, can differ depending on which particular opioid is being used. Opioids have shown efficacy in managing moderate pain experienced by individuals with HZ while also potentially reducing the risk of developing PHN. However, they can cause effects, including breathing problems, digestive issues feeling sick, or dependency. It's important to be cautious when prescribing them to groups of patients. Therefore, caution should be exercised when prescribing them to patients with heart conditions, prostate enlargement issues, elevated pressure concerns, or when used concurrently with serotonergic drugs. In managing herpes zoster infections, among immunocompromised individuals, care plays a role. This comprehensive approach effectively prevents infections while also addressing inflammation management and promoting the healing process. Effective management of this condition involves ensuring care for the skin lesions to keep them clean, maintaining oral hygiene, paying particular attention to eye care when the trigeminal nerve's ophthalmic branch is affected, and effectively managing pain through the use of cold compresses, local anesthetics or capsaicin creams as necessary. Stress management techniques and psychological support can also prove beneficial, as can education and counseling about the natural history, potential complications, and treatment strategies for HZ. Supportive care measures must be tailored to individual patient needs and preferences, coordinated with other healthcare professionals involved in the patient's care, and adapted as necessary to prioritize patient safety and overall well-being throughout the HZ management.

Conclusion

Since herpes can create fatal conditions, it is very important to give protection to immunocompromised patients. It is crucial to take a vaccine for this herpes zoster. Based on research and evidence, RZV is the vaccine that is recommended for this group. It has demonstrated effectiveness and safety among individuals with compromised systems. However, in some situations, ZVL may be

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considered as an alternative for patients with immunocompromisation. The decision to use ZVL should be made after an evaluation of each individual's circumstances. It needs to be noted that while managing herpes zoster in immunocompromised patients, it's nesseccary to consider the patient's condition, preferences, and expectations. Evidence-based guidelines from literature and clinical practice should also inform the treatment approach.

Disclosure

Conflict of interest

There is no conflict of interest

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Ethical consideration

Non applicable

Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

References

1. Gershon AA, Breuer J, Cohen JI, Cohrs RJ, Gershon MD, Gilden D, et al. Varicella zoster virus infection. Nat Rev Dis Primers. 2015;1:15016.

2. Johnson RW, Bouhassira D, Kassianos G, Leplège A, Schmader KE, Weinke T. The impact of herpes zoster and post-herpetic neuralgia on quality-of-life. BMC Med. 2010;8:37.

3. Sabel BA, Wang J, Cárdenas-Morales L, Faiq M, Heim C. Mental stress as consequence and cause of vision loss: the dawn of psychosomatic ophthalmology for preventive and personalized medicine. Epma j. 2018;9(2):133-60.

4. Atkins EJ, Newman NJ, Biousse V. Post-traumatic visual loss. Rev Neurol Dis. 2008;5(2):73-81.

5. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, Orrico-Sánchez A. Herpes zoster risk and burden of disease in immunocompromised populations: a population-based study using health system integrated databases, 2009-2014. BMC Infect Dis. 2020;20(1):905.

6. Dagnew AF, Vink P, Drame M, Willer DO, Salaun B, Schuind AE. Immune responses to the adjuvanted recombinant zoster vaccine in immunocompromised adults: a comprehensive overview. Hum Vaccin Immunother. 2021;17(11):4132-43.

7. Harbecke R, Cohen JI, Oxman MN. Herpes Zoster Vaccines. J Infect Dis. 2021;224(12 Suppl 2):S429-s42.

8. Levin MJ, Weinberg A. Immune responses to zoster vaccines. Hum Vaccin Immunother. 2019;15(4):772-7.

9. Young J, Psichogiou M, Meyer L, Ayayi S, Grabar S, Raffi F, et al. CD4 cell count and the risk of AIDS or death in HIV-Infected adults on combination antiretroviral therapy with a suppressed viral load: a longitudinal cohort study from COHERE. PLoS Med. 2012;9(3):e1001194.

10. Barnett D, Walker B, Landay A, Denny TN. CD4 immunophenotyping in HIV infection. Nat Rev Microbiol. 2008;6(11 Suppl):S7-15.

11. Willis ED, Woodward M, Brown E, Popmihajlov Z, Saddier P, Annunziato PW, et al. Herpes zoster vaccine live: A 10 year review of post-marketing safety experience. Vaccine. 2017;35(52):7231-9.

12. Xia Y, Zhang X, Zhang L, Fu C. Efficacy, effectiveness, and safety of herpes zoster vaccine in the immunocompetent and immunocompromised subjects: A systematic review and network meta-analysis. Front Immunol. 2022;13:978203.

http://dx.doi.org/10.52533/JOHS.2023.31008

13. Monib S, Pakdemirli E. Shingles (Herpes Zoster) Mimicking Acute Abdomen. Cureus. 2020;12(10):e10762.

14. Kang JH. Febrile Illness with Skin Rashes. Infect Chemother. 2015;47(3):155-66.

15. Tayyar R, Ho D. Herpes Simplex Virus and Varicella Zoster Virus Infections in Cancer Patients. Viruses. 2023;15(2).

16. Naveen KN, Pradeep AV, Kumar JS, Hegde SP, Pai VV, Athanikar SB. Herpes zoster affecting all three divisions of trigeminal nerve in an immunocompetent male: a rare presentation. Indian J Dermatol. 2014;59(4):423.

17. Pelloni LS, Pelloni R, Borradori L. Herpes zoster of the trigeminal nerve with multi-dermatomal involvement: a case report of an unusual presentation. BMC Dermatol. 2020;20(1):12.

18. Nicholson LB. The immune system. Essays Biochem. 2016;60(3):275-301.

19. Brizzi KT, Lyons JL. Peripheral nervous system manifestations of infectious diseases. Neurohospitalist. 2014;4(4):230-40.

20. Kausar S, Said Khan F, Ishaq Mujeeb Ur Rehman M, Akram M, Riaz M, Rasool G, et al. A review: Mechanism of action of antiviral drugs. Int J Immunopathol Pharmacol. 2021;35:20587384211002621.

21. Craviotto V, Furfaro F, Loy L, Zilli A, Peyrin-Biroulet L, Fiorino G, et al. Viral infections in inflammatory bowel disease: Tips and tricks for correct management. World J Gastroenterol. 2021;27(27):4276-97.

22. Ertesvåg NU, Sakkestad ST, Zhou F, Hoff I, Kristiansen T, Jonassen TM, et al. Persistent Fever and Positive PCR 90 Days Post-SARS-CoV-2 Infection in a Rituximab-Treated Patient: A Case of Late Antiviral Treatment. Viruses. 2022;14(8).

23. Jeon YH. Herpes Zoster and Postherpetic Neuralgia: Practical Consideration for Prevention and Treatment. Korean J Pain. 2015;28(3):177-84.

http://dx.doi.org/10.52533/JOHS.2023.31008