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Effectiveness of Shingrix versus Zostavax in immunocompromised adults aged 50 years and older.

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EFFECTIVENESS OF THE SHINGRIX VACCINE VERSUS ZOSTAVAX IN IMMUNOCOMPROMISED ADULTS AGE 50 YEARS AND OLDER.

by

An Independent study submitted to the faculty of the College of Nursing and the University of North Dakota in partial fulfilment of the requirements for the degree of

MASTER OF SCIENCE IN NURSING: Family Nurse Practitioner

Sandrine Ndetah, BSN, RN

PERMISSION

Title: Effectiveness of Shingrix versus Zostavax in immunocompromised adults aged 50 years and older.

Department Nursing

Degree Master of Science

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ABSTRACT

This literature review was carried out based on a case report from a successful Simulation Objective Structure Clinical Examination (OSCE). During the OSCE, case report involving an immunocompromised adult with Herpes Zoster (HZ) was analyzed and the effective shingles vaccine was determined. Databases used to search for research articles included UpToDate, and the Cumulative Index to Nursing an Allied Health Literature (CINAHL) through the EBSCOhost search engine. Key words used were "herpes zoster vaccine." The search was limited full text English articles that fell within the years 2015 to 2020 and articles outside the given time period were excluded. A total of 226 articles were located. Recommendations from the Advisory Committee on Immunization practices (AICP) were also reviewed.

According to the research articles, and guidelines in this literature paper addressed, Shingrix is the vaccine of choice for use in the prevention of HZ in immunocompromised adults aged 50 years and older when both doses are taken as prescribed. Immunocompromised refers to having an impaired immune system.

PICO Question

In immunocompromised adults aged 50 years and older, is the use of Shingrix vaccination versus Zostavax more effective in reducing the risk for Herpes Zoster?

Population: Immunocompromised adults 50 years and older

Intervention: Shingrix

Comparison: Zostavax

Outcome: Shingrix will be safer, cost effective and produce longer coverage.

BACKGROUND

Herpes Zoster (HZ), commonly referred to as shingles is a viral infection that occurs with reactivation of the varicella-zoster virus (Janniger, 2020). Initially it presents as pain along the affected dermatome, followed by a vesicular eruption within two to three days. The self-limited rash appears as a unilateral grouped herpetiform vesicles on an erythematous base. Risk factors include age 50 years and older, and prior exposure to the varicella virus also known as chickenpox. This rash can be treated with antivirals if diagnosed within 72 hours of onset, but severe cases of shingles can lead to postherpetic neuralgia (PHN). Postherpetic neuralgia is a persistent pain lasting thirty or more days which can be incapacitating and is very common in older adults. Vaccines are used to prevent the risk of developing herpes zoster and PHN.

There are currently two vaccines approved by the United States Food and Drug Administration (FDA) for use in the prevention of herpes zoster among older adults including Zoster Vaccine Live (ZVL) commonly known as Zostavax, and recombinant zoster vaccine (RZV) commonly called Shingrix (Albrecht & Levin, 2019). Zostavax, a live attenuated vaccine for the prevention for HZ in adults fifty years and older. It was the first vaccine approved to prevent HZ and it did record a decrease in shingles within that age group. Unfortunately, Zostavax being a live attenuated vaccine limits its ability to protect immunocompromised individuals against shingles. This is where the new shingles recombinant vaccine called Shingrix is superior to Zostavax, as it can be administered to everyone including immunocompromised individuals. Shingrix is administered in two doses and the second dose is six months apart. The case report below will demonstrate an example of where shingrix is recommended over the Zostavax.

CASE STUDY

SUBJECTIVE

- **Chief Complaint:** Right sided lower back pain at T12
- **History of present illness:** This is a 60-year-old Caucasian female who presents to the clinic with complains of a right lower back pain at her T12 that started about 2 days ago. Patient describes the pain as a sharp, 6/0 pain that does not radiates, is not affected by time, is alleviated by ice, and aggravated by movement and cloths rubbing on it. Patient has tried prn Tylenol OTC with no relieve. Patient states that she has never had varicella or herpes zoster and neither has anyone in her household.
- **Past Medical History/Current medication**
    - Rheumatoid arthritis: 20mg Prednisone oral as needed
    - Hypertension**:** Lisinopril 20mg oral once daily
- **Allergies:** No food, drug, or seasonal allergies
- **Surgical history:** Hysterectomy at 40 years old
- **Social hx:** Retired secretary, lives with spouse, does not consume alcohol or tobacco
- **Family history:** No pertinent family history
- **Immunization:** Up to date per patient

Review of System

- General: Denies any weight changes, fatigue or fever
- HEENT: Denies any burning in the eyes, headache, nasal drainage, sore throat, or dizziness. No visual or hearing changes
- Neuro: Denies any tingling or numbness in extremities
- Cardiac: Denies any chest pain, or palpitations

- Respiratory: Denies any SOB, dyspnea on exertion
- GI: Denies any constipation or diarrhea
- GU: Denies burning sensation or foul odor with void
- MS: Denies any weakness or joint pain
- Integumentary: **+pain and itchiness to lower right back**

OBJECTIVE

Vitals: BP 124/80, HR 78, Temp 99.1, O2Sat 96%, Pain 6/10 (right lower back)

General: Calm and cooperative

CARDIAC: S1S2 with regular rates and rhythm, no extra sounds, clicks, rubs, or murmurs. Cap refill is less than 3 seconds. Pulses are 3+ with no edema.

RESP: Symmetrical chest rise, clear lung sounds, A&P ratio normal, No use of accessory muscles. Tactile fremitus present and equal bilaterally. Diaphragmatic dullness at T10

MS: Symmetrical, full range of motion, and normal muscle tone in all extremities. No crepitus, swelling or deformities noted. Normal range of motion on spine, no scoliosis noted.

Integumentary: *Redness to right lower back with unilateral grouped vesicles and erythematous base at the T12 dermatome*

NEURO: Clear speech, and good muscle tone. Stable balance and normal gait

PSYCH: A&O*3, response appropriately

ASSESSMENT:

- Diagnosis: ICD-10 Codes: B02.9 Zoster without complications.

PLAN

- Valacyclovir 1000mg Orally every 8 hours for 7 days.
- Ibuprofen 400mg Orally every 6 hours as needed.

- Medication education provided to patient.
- Wash hands, cloths, beddings, and avoid scratching or touching affected area
- Patient educated on the possibility of a post neuralgia pain, and to call the clinic for nerve pain medication such as pregabalin.
- Follow up with clinic after 7 days post antiviral medication for first dose of the shingrix vaccine. And then 2 months after for the next dose of vaccine.

LITERATURE REVIEW

Effectiveness

A systematic review by Chiyaka et al (2019), assessed the effectiveness Herpes Zoster Vaccines precisely Zostavax and Shingrix. PubMed and two other databases were searched from inception to March 2018 for original cost-effectiveness, cost- utility, or cost-benefit analyses of the two herpes zoster vaccines. Three investigators reviewed and assessed the articles using the Drummond and Jefferson's checklist, extracted study characteristics, model structure, vaccine characteristics, incidence of HZ and complications, incremental cost-effectiveness ratio, and sensitivity analyses. Inclusive criteria included studies that were original and performed cost effectiveness, cost utility, or cost benefit, of either Zostavax or Shingrix, or both. Studies were excluded if they only assessed the diagnostic test, treatments of herpes zoster and/or PHN, or hypothetical vaccines. A total of 15 studies were reviewed, and results revealed that Shingrix is more effective and less costly than Zostavax and cost effective compared with no vaccine. Limitation included number of studies, and strengths included the level of evidence (I), and the methodology used for the selection and reviewing of the articles.

A systematic review by Symoniak, Farrokh, Gandhi, & Slish (2018), reviewed the effectiveness of Shingrix compared to Zostavax in reducing the risks of herpes zoster and post herpetic neuralgia in adults 50 years and older. A literature review was conducted using PubMed and Google Scholar to report clinical trials and other relevant peer reviewed publications that evaluated Shingrix and or Zostavax. Inclusive criteria included articles that were published through 2017 which evaluated the efficacy and properties of Shingrix and or Zostavax. Exclusive criteria included studies that did not address the efficacy and properties of either vaccines. Results from this systematic revealed that Shingrix had an efficacy of 89.9% to 97.2% in

multiple phase III trials. Based on several Phase III trials, the Advisory Committee on Immunization Practices recommends Shingrix over Zostavax. Limitations in this review included the lack of studies that compared both the Shingrix and Zostavax. Strengths of this study included the level of evidence (I), and number of studies used.

In a randomized, placebo-controlled phase 3 study by Lal et al. (2015), conducted in 18 countries assessed the "Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults," In this study, the inclusive criteria included age of fifty years and above, history of herpes zoster, and previously vaccinated against herpes zoster or varicella. The exclusive criteria included being pregnant or lactating or planning on becoming pregnant. Total participants were 15,411 and 7,698 participants received the vaccine while 7713 participants received the placebo. A follow up at 3.5 years revealed that 6 participants from vaccine group had herpes zoster while 210 participants in the placebo group had herpes zoster. Thereby implying that shingrix effectively reduces the risk of HZ in adults 50 years and older. Limitations included maintaining participant level study blinding. Strengths in this study included the level of evidence (II), sample size, and time period.

A second randomized, placebo-controlled study by Cunningham et al. (2017), conducted in 18 countries and involving adults seventy years or older, assessed the "Efficacy of the Herpes Zoster Subunit Vaccine (shingrix) in Adults 70 Years of Age or Older." Inclusive criteria included age of 70 and above, and exclusive criteria was age below seventy, being pregnant or lactating. Total participants were 13,900 and half of the participants received the shingrix vaccine while the other half received the placebo (0.9% saline solution). Vaccine or placebo was administered (0.5 ml) into the deltoid muscle at month 0 and month two. Participants were to be followed for at least thirty months post second dose through monthly contacts and annual clinic

visits. Results after 3.7 years revealed that 23 participants in the vaccination group had herpes zoster compared to 223 in the placebo group, and this vaccine also prevented post herpetic neuralgia by 86%. Implying that shingrix is efficient in preventing HZ and HPN in adults 70 years and older. Limitations in this study included maintaining participant level study blinding. Strengths of this study included the level of evidence (II), the sample size, and the time interval of the study.

Co-administration of Shingrix with other vaccines

A phase 3, open-label, randomized, multicenter clinical trial by Schwartz et al (2017), investigated the immunogenicity and safety of Shingrix when co-administered with a quadrivalent seasonal inactivated influenza vaccine (IIV4) in adults 50 years or older. Total participants were 828 and 20 centers were used. Inclusive criteria included individuals 50 years or older. Exclusive criteria included individuals who had taken or planned on taking any investigational drug or vaccine from 30 days prior the study through 30 days after the second dose of the inactivated influenza vaccine, or had received any long term immunosuppressant drugs, had received a previous herpes zoster vaccine, or had a history of herpes zoster. In this study had two groups, including the coadministration group with 413 participants that received both the Shingrix and IIV4 at day 0 followed by a second dose of Shingrix at month 2. And the control group of 415 participants that received the IIV4 at month 0 and the Shingrix at months 2 and 4. The study went through March 3rd, 2013 to March 20th, 2015. Results revealed that the immunogenicity of the two doses of Shingrix was unaffected by coadministration of the first dose with the IIV4. And neither was immunogenicity of the IIV4 affected by coadministration with the Shingrix. The strengths of this study included the participants age group, older adults

who are the population most in need of both the Shingrix and IIV4, the sample size and length of study. Limitations included the fact that the study was open label.

Efficacy of Shingrix in prior Zostavax recipients

Another phase 3 open-label, multi-center study by Grupping et al. (2017), evaluated the immunogenicity and safety of the adjuvanted herpes zoster subunit vaccine (Shingrix) in adults previously vaccinated with the live attenuated herpes zoster vaccine (Zostavax). Inclusive criteria included individuals aged 65 years or older who had received the Zostavax at least 5 years prior to the start of the study. Exclusive criteria included adults who had received or were scheduled to receive a live vaccine within 30 days, had received any investigational vaccine within 30 days, or had received any immunosuppressant within 30 days. A total of 430 participants were included, and grouped into two groups, 215 in the Zostavax pre-vaccinated group and 215 in the Zostavax naïve group. Participants in both groups received both doses of the Shingrix vaccine. The study was done from March 2016 to August 2017. Results from this study revealed that Shingrix induces a strong immune response irrespective of prior vaccination with Zostavax, and no safety concerns were identified from the first vaccination up to one month post the second dose. Strengths in this study included the length of study duration. Limitations included the fact that the study was an open study.

Weinberg et al. (2019), reviewed the persistence of varicella-zoster virus cell-mediated immunity (CMI) after the administration of a second dose of Shingrix. Participants in this study were divided into group 1 which consisted of 201 individuals with a history of HZ and had received Zostavax approximately 10 years prior to enrollment. And group 2 which consisted of 199 individuals who had no history of HZ and had never received Zostavax. All participants

received the Shingrix to the deltoid of their non dominant arm, blood samples were collected immediately before vaccination, and at 1, 6, and 42 weeks, and at 1 and 3 years. Dual-color interferon-gamma (IFN-γ) and interleukin-2 (IL-2) FluoroSpot assays were performed using MabTech Fluorospot kits per the manufacturer's instructions. Results revealed that before and after the first year after vaccination, varicella -CMI was significantly higher in reimmunized compared to the individuals in group 2. And at 3 years, varicella zoster virus CMI differences between groups decreased and only memory responses remained marginally higher in reimmunized participants. In this same study, the authors found Shingrix to confer superior protection against HZ compared with a second dose of Zostavax. Strengths included the length of study, and method used.

Adverse Effects

A research article by Hesse et al (2019), outlined the post-licensure safety surveillance of the Shingrix vaccine from October 2017 to June 2018 (Hesse et al, 2019). In this article, the centers for disease control and prevention (CDC), and FDA investigators conducted descriptive analysis of reports from the Vaccine Adverse Event Reporting System (VAERS). VAERS is a national surveillance system for adverse events after administration of U.S licensed vaccines. VAERS received 4,381 Shingrix reports, for a rate of 136 reports per 100,000 doses distributed for the first 8 months. Results revealed that with Shingrix, self-limited local and systemic vaccine reactions were common, while serious adverse effects were rare. Unlike Zostavax which has common reports of herpes zoster and rash. Therefore, Shingrix is an effective shingles vaccine that is recommended for adults fifty years and older. Limitations of this study included

the fact that some providers did not administer the complete dose of the Shingrix. And strengths include the study size and the credibility of the methodology used.

Cost Efficiency

A cohort study by Prosser et al (2019), evaluated the cost effectiveness of vaccination with Shingrix compared to the Zostavax and no vaccination, the cost effectiveness of vaccination with Shingrix for persons who have previously received the Zostavax, and the cost effectiveness of preferential vaccination with Shingrix over Zostavax. The authors used a simulation model through the United States (US) epidemiologic, clinical, and cost data. Participants included immunocompetent U.S. adults aged 50 years or older, and the study ran for a lifetime period. Results revealed that vaccination with Shingrix after previous administration of Zostavax yielded an incremental cost effectiveness (ICER) of less than $60,000 per quality-adjusted life-yearly (QALY) for persons 60 years or older. For vaccination with Shingrix versus no vaccination, ICERS ranged from ten thousand dollars to forty-seven thousand dollars per QALY. According to this study, vaccination with Shingrix yields cost-effectiveness ratios lower than those for Zostavax. Limitations included adherence to the recommended two dose regimen, and few data available on risk for serious adverse events. Strengths included the reliability of source and methodology.

Le & Rothberg, (2018), used the Markov model to compare the cost effectiveness and QALYs for the Shingles versus no vaccination with variation of vaccination age from 50 to 59 years, and adults 60-80 who had received the Zostavax within ten years. The process involved a base-case, 1-way, and probabilistic sensitivity analysis from the societal perspective, using TreeAge Pro 2017 software. The study went on for a month and results from this study revealed

that immediate Shingrix booster had an ICER of greater than one hundred QALY at all ages, meanwhile people vaccinated with Zostavax at 60 years of age needed a Shingrix booster after six and four years to meet cost effective thresholds at fifty thousand and one hundred thousand respectively. Strengths in this study included the reliability of data, and limitations included the fact that the study was modeled using data extracted from the literature with no participant data involved.

Recommendation from AICP

Dooling et al., (2018), reviewed the recommendations of the Advisory Committee on Immunization Practices (AICP) for use of herpes zoster vaccines. According to this article, the AICP herpes zoster vaccine work group participated in a monthly/bimonthly teleconference to review herpes zoster epidemiology from March 2015 to October 2017. This work group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to define critical and important outcomes, conduct a systemic review of evidence and review and discuss findings and evidence quality. On October 25, 2017, the AICP recommended Shingrix vaccine for use in immunocompetent adults aged 50 and older.

CONCLUSION/SYNTHESIS

According the results from the literature reviews and research studies, it is evident that compared to Zostavax, Shingrix is a more efficient vaccine for use in the prevention HZ in immunocompromised adults 50 years and older. Shingrix is also known to be safe, cost effective and provides long term protection. The patient from the case report will receive the first does of Shingrix 7 days post her antiviral treatment, and the next dose will be administered within two

months. Education on common side effects and side effects reporting will be discussed with patient. This patient was a great candidate for the vaccine due to her age and being immunocompromised. Research from this literature review reveals that there are limited research studies comparing both Shingrix and Zostavax. Future research should focus on comparing both vaccines.

LEARNING POINTS

- Shingrix is safe for use in immunocompromised patients unlike Zostavax.
- Shingrix induces a strong immune response irrespective of prior vaccination with Zostavax.
- Patients need to receive both doses of Shingrix in order to ensure effectiveness of the vaccine.
- Shingrix can be co-administered with the seasonal influenza vaccine without any effects on the immunogenicity of both vaccines.
- Compared to Zostavax, Shingrix is cost effective with mostly localized side effects such as pain at injection sites.

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