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Prevention of herpes zoster: A review

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Abstract
Herpes zoster (HZ) or "shingles" is one of the most common neurological conditions worldwide. It occurs as a result of a reactivated varicella zoster virus (VZV) infection. Anaesthetists and pain specialists may find themselves consulted to manage the often severe and disabling pain of an acute episode. To prevent progression to post herpetic neuralgia (PHN), a potentially crippling persistent disorder, early intervention is imperative. The purpose of this paper is to review current guidelines for the prevention of HZ.

Keywords: RTE Act, Challenges, Remedies and Recommendations

Introduction

Prevention

➢ Infection Control

Since VZV is a highly contagious virus, it can cause potentially life-threatening disease in high-risk patients. Henceforth, appropriate measures for infection control should be taken immediately when a VZV infected patient is hospitalized. Prevention of VZV transmission to susceptible persons is complicated by the fact that patients with varicella are contagious for 24-48 hours before the onset of clinically evident disease. Infection control measures include strict isolation of patients with varicella or disseminated herpes zoster. Precautions regarding the drainage and secretion are sufficient for patients with dermatomal herpes zoster while proper precautions regarding isolation should be followed in cases of herpes zoster with skin lesion until the last skin lesion is completely crusted [1].

Susceptibility of exposed patients and health personnel for varicella zoster virus is assessed by serology in case there is a negative or unknown history of chickenpox. Susceptible patients who got exposed to a VZV-infected patient and are at risk for complications of varicella should receive hyperimmunoglobulin as soon as possible so as to prevent transmission of infection.[161] Since the usual incubation time of varicella is 9-21 days, all susceptible exposed patients should be placed in strict isolation from 9 days after the first to 21 days after the last possible exposure. Some experts recommend that susceptible immunocompromized patients should be placed in strict isolation immediately, because the incubation period in these patients may be even shorter. Exposed VZV seronegative health personnel should be reassigned to a low-risk department or placed on administrative leave from 9 days after the first to 21 days after the last exposure [2].

➢ Zoster Vaccine

The zoster vaccine (ZOSTAVAX) is a lyophilized preparation of the Oka/Merck strain of live attenuated VZV, the same strain which is used in the varicella vaccines (VARIVAX, PROQUAD). The Oka strain was isolated in Japan in the early 1970s from vesicular fluid from a healthy child who had varicella (figure 6.1). The strain was attenuated through sequential propagation in cultures of human embryonic lung cells, embryonic guinea-pig cells and human diploid cells.

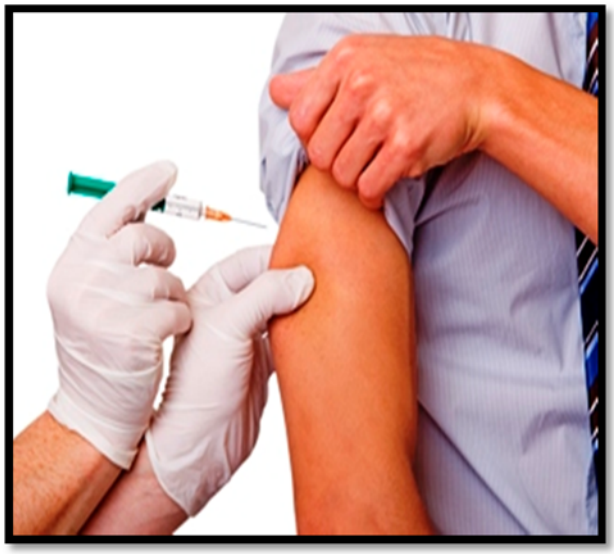
Each 0.65-mL dose contains a minimum of 19,400 PFU of Oka/ Merck strain of VZV when reconstituted and stored at room temperature for up to 30 minutes. Zoster vaccine is similar to VARIVAX. However, its potency is 14-times the potency of VARIVAX, which contains a minimum of 1,350 PFU. Each dose of zoster vaccine also contains additional VZV antigenic component from nonviable Oka/Merck VZV which includes:-

- 31.16 mg of sucrose
- 15.58 mg of hydrolyzed porcine gelatine
- 3.99 mg of sodium chloride
- 0.62 mg of monosodium L-glutamate

- 0.57 mg of sodium phosphate dibasic
- 0.10 mg of potassium phosphate monobasic
- trace quantities of neomycin and bovine calf serum [4, 5, 6].

Showing Zostavax Vaccine

Zoster vaccine should be administered as a single 0.65-mL dose subcutaneously in the deltoid region of the upper arm



Showing Deltoid Region in Upper Arm For Subcutaneous Administration Of The Vaccine

It should only be reconstituted and injected using a sterile syringe free of preservatives, antiseptics, and detergents which can inactivate the vaccine virus.3

➢ Storage and Handling

To maintain the potency, lyophilized zoster vaccine must be stored frozen at an average temperature of ≤5°F until it is reconstituted for injection. Any freezer that has a separate sealed freezer door and reliably maintains an average temperature of ≤5°F is acceptable for storing zoster vaccine [162]. Providers should check the adequacy of their freezer by verifying its temperature before obtaining the vaccine. In general the freezer compartments of dormitory style units are incapable of reliably maintaining temperatures cold enough to store zoster vaccine and are unacceptable for storage.

When a freezer is temporarily unavailable (e.g. during transport or equipment failure) zoster vaccine should be stored in a suitable container (i.e. the original shipping container or a comparable container with a properly fitting lid) with an adequate quantity of dry ice (i.e. a minimum of six pound per box) so that dry ice would persist in the container if not reconstituted vaccine must be transported back to the freezer. Dry ice placed in a suitable container will maintain a temperature of ≤5°F. The diluent which does not contain preservative or other antiviral substances that could inactivate the vaccine virus should be stored separately either at room temperature or in the refrigerator. The vaccine should be reconstituted according to the directions in the package label and only with the diluent supplied. Before reconstitution zoster vaccine should also be protected from light. Withdraw the entire contents of the diluent into a syringe. To avoid excessive foaming, slowly inject all of the diluent in the syringe into the vial of lyophilized vaccine and gently agitate to mix thoroughly. Once reconstituted the vaccine should be used immediately to minimize loss of potency. The vaccine must be discarded if not used within 30 minutes after reconstitution [7, 8].

➢ Efficacy

The efficacy of zoster vaccine was evaluated in a phase 3 vaccine trial termed as the Shingles Prevention Study. It was a double-blind randomized placebo-controlled trial involving 38,546 healthy adults aged ≥60 years who had a history of varicella [162]. Persons were randomized to receive a single subcutaneous dose of zoster vaccine or placebo and were followed for 3.1 years. A total of 957 confirmed cases of zoster occurred among study participants: 315 among vaccine recipients and 642 among placebo recipients.

The vaccine reduced the risk for developing zoster by 51.3%. The vaccine was 66.5% efficacious for preventing PHN. When the definition of PHN was changed from 30 days of pain to 182 days following rash onset, vaccine efficacy increased from 58.9% to 72.9%. Zoster vaccine was shown to have an independent effect of reducing PHN among patients who developed zoster. The mean severity-by-duration of zoster was reduced by 57% in vaccine recipients who developed PHN [9].

In general, with increasing age at vaccination, the vaccine retained efficacy against severity of zoster better than against zoster itself. Thus, efficacy for the prevention of zoster was highest among persons aged 60–69 years and declined with increasing age.

➢ Summary Of Rationale For Zoster Vaccine Recommendations

His availability of a safe and effective vaccine for zoster offers an opportunity to decrease the burden of this disease and its complications among persons with high levels of risk. In the United States, the vaccine is licensed for use among persons aged ≥60 years. Routine vaccination of this population is recommended for following reasons:

1. Zoster causes substantial morbidity in the United States with approximately 1,000,000 new cases occurring annually. Many of these cases cause debilitating pain and when PHN develops the pain can last for months or even years.
2. Although effective antiviral medications for treatment of zoster are available, administration must be initiated within 72 hours of rash onset for maximum benefit. Many patients might not obtain such rapid diagnosis and treatment. Available treatments for PHN often do not completely alleviate the pain and might be poorly tolerated by the older patients.

- **Contraindications**

1. Allergy to Vaccine Components

Zoster vaccine is contraindicated for persons who have a history of anaphylactic reaction to any component of the vaccine including gelatin and neomycin. Neomycin allergy is usually manifested as a contact dermatitis which represents a delayed-type immune response [10].

2. Immunocompromised Persons

Zoster vaccine should not be administered to persons with primary or acquired immunodeficiency diseases which include:-

- Persons with leukemia, lymphomas, or other malignant neoplasms affecting the bone marrow or lymphatic system. However, patients whose leukemia is in remission and who have not received chemotherapy (e.g. alkylating drugs or antimetabolites) or radiation for at least 3 months can receive zoster vaccine [163].
- Persons with AIDS or other clinical manifestations of HIV, including persons with CD4+ T-lymphocyte values ≤200 per mm^3 or ≤15% of total lymphocytes.
- Persons on immunosuppressive therapy having high-dose corticosteroids (≥20 mg/day of prednisone or equivalent) lasting two or more weeks. Zoster vaccination should be deferred for at least 1 month after discontinuation of such therapy. Short-term corticosteroid therapy (<14 days) with low-to-moderate dose (<20 mg/day of prednisone or equivalent) are not considered to be sufficiently immunosuppressive to cause concerns for vaccine safety. Persons receiving this dose or schedule can receive zoster vaccine. Therapy with low-doses of methotrexate (≤0.4 mg/Kg/week), azathioprine (≤3.0 mg/Kg/day) or 6mercaptopurine (≤1.5 mg/Kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease and other conditions are also not considered sufficiently immunosuppressive to create vaccine safety concerns and are not contraindications for administration of zoster vaccine.
- Persons with clinical or laboratory evidence of other unspecified cellular immunodeficiency. However, persons with impaired humoral immunity (e.g. hypogammaglobulinemia or dysgammaglobulinemia) can receive zoster vaccine.
- Persons undergoing hematopoietic stem cell transplantation (HSCT) Physicians should assess the immune status of the recipient on a case-by-case basis to determine the relevant risks. If a decision is made to vaccinate with zoster vaccine, the vaccine should be administered at least 24 months after transplantation.
- Persons receiving recombinant human immune mediators and immune modulators especially the antitumor necrosis factor agents like adalimumab, infliximab and etanercept. The safety and efficacy of zoster vaccine administered concurrently with these agents is unknown. If it is not possible to administer zoster vaccine to patients before initiation of therapy the physicians should assess the immune status of the recipient on a case-by-case basis to determine the relevant risks and benefits. Otherwise, vaccination with zoster vaccine should be deferred for at least 1 month after discontinuation of such therapy.

3. Pregnancy

Zoster vaccine is not recommended for use in pregnant women [162]. Moreover, women should avoid pregnancy for 4 weeks following zoster vaccination. Having a pregnant household member is not a contraindication to zoster vaccination. If a pregnant woman is vaccinated or becomes pregnant within 1 month of vaccination, she should be counselled about potential effects on the fetus [2]. Furthermore, virtually all persons receiving the vaccine will have pre-existing VZV immunity which is expected to limit viral replication and presumably further reduce fatal risk. In most circumstances, the decision to terminate a pregnancy should not be based on whether zoster vaccine was administered during pregnancy. Merck & Co. in collaboration with centre for disease control has established a pregnancy registry to monitor the maternal-fetal outcomes of pregnant women who are inadvertently administered live-attenuated VZV-based vaccines within 1 month of pregnancy. Patients and health-care providers are supported to report any exposure to zoster vaccine during pregnancy to this registry.

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