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Review Article

Comparative Study of Valacyclovir and Acyclovir for the Improves Therapy of Herpes Zoster in an Immunocompetent Adult

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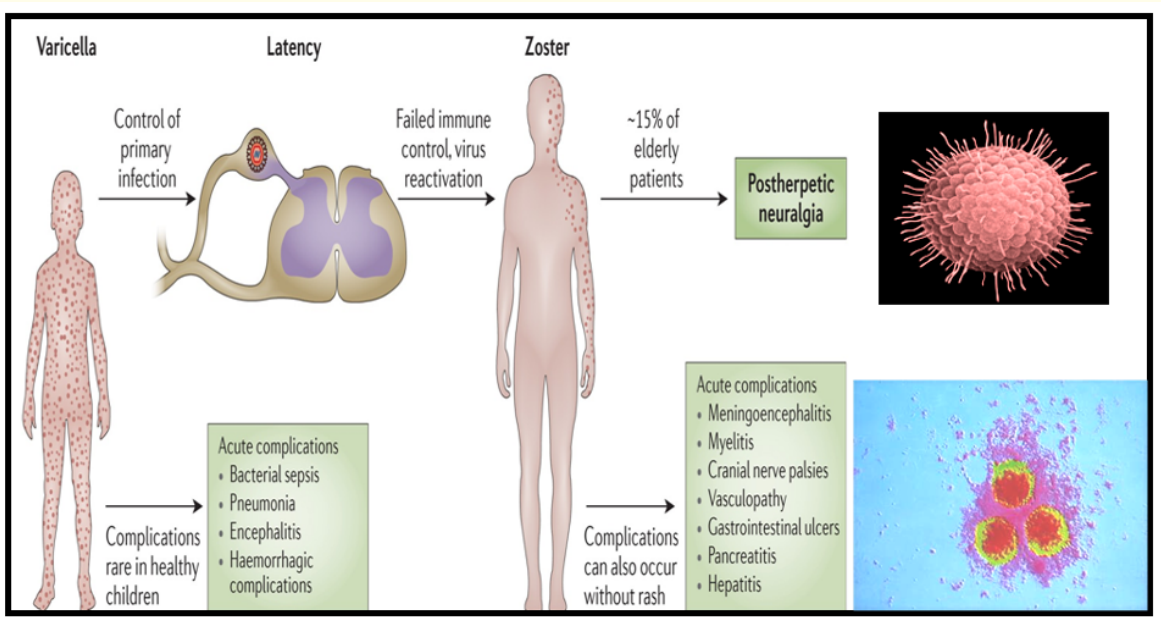
Abstract

Herpes zoster is a kind of viral infection which is known to occur due to the reactivation of virus named varicella zoster virus. This is normally very painful self-limited dermatomal rash. Usually the rashes occur on the body and face, they appear to be in the form of single, wide stripe. Patients who have some other underlying conditions which decrease the cell mediated immunity have 20 to 100 times more chances of getting herpes zoster. Herpes zoster can be treated by acyclovir and its speed of recovery increases when it is taken in early stages of infection and speeds up healing up of rash and decreases pain. As acyclovir has reduced oral bioavailability because of this it requires frequent dosing. Valaciclovir is the form which has more bioavailability almost three to five folds. Valaciclovir is a modified product of acyclovir and after oral administration is rapidly converted to acyclovir in the gastrointestinal tract. Thus, the bioavailability of acyclovir is three to five times greater after the oral intake of valaciclovir compared to taking acyclovir alone. Acyclovir (standard dose for herpes zoster ophthalmicus: 800 mg five times daily for seven to 10 days) and valaciclovir (standard dose for herpes zoster ophthalmicus: 1000 mg three times daily for seven days) have been approved for the treatment of herpes zoster and are widely used. Valacyclovir exhibits the same favorable toxicity profile as acyclovir.

Following absorption, valaciclovir is completely converted to acyclovir and the essential amino acid, L-valine. Other than acyclovir there are other drugs like valacyclovir treats within 72 hours of the development of rash. Thus, in the management of immunocompetent patients > or = 50 years of age with localized herpes zoster, while valaciclovir given in 1,000 mg thrice a day for 7 days increases the reduction of pain and also has simple dosing and also provide favorable safety conditions.

Pictorial Abstract



Keywords: *Herpes Zoster; Dermatomal Rash; Bioavailability; Acyclovir; Valacyclovir; Immunocompetent; L Valine*

Introduction

Herpes zoster is a kind of viral infection which is known to occur due to the reactivation of virus named varicella zoster virus. Usually this virus affects people of every age but, the adults above 50 years have increased risk of developing this infection this is caused due to immunosenescence due to increase in age. Irrespective of any age the people who have suppressed cell mediated immunity due to any other underlying disease. This is a very important condition throughout the world.

The rash and pain occurs when varicella zoster virus, it becomes dormant in sensory ganglia following primary virus infection, is re-activated this is related with declining cellular immunity associated with the increase in age.

There are various complications that may include:

- **Dermatological:** Example include secondary bacterial infection,
- **Neurological:** Include long term pain, stroke and segmental paresis,
- **Ophthalmological:** Include keratitis, secondary glaucoma and irridocyclitis,
- **Visceral:** Hepatitis and pneumonia.

Out of all postherpetic neuralgia is the most common condition this occurs in 1 patient among 5 patients. This condition mainly affects the skin and also nerve fibers causing burning pain that last longer even after the rashes has been disappeared. In its treatment topical lidocaine or capsaicin and oral pregabalin, gabapentin and other tricyclic antidepressants are used. In most of the patients i.e. 50% of the

untreated patients the rashes disappeared and this is majorly seen in older people. Some of the abnormal sensations also contain pain. Some of the sensations are tingling, allodynia, numbness and decreases over months in most of the patients. The pain may last upto six months. The safety and efficacy of oral valaciclovir contains high dosage of 1,000 mg three times a day for 7 days or 14 days while the dose of acyclovir is 800mg five times a day for 7 days. When these were compared in immunocompetent adults aged more than or equal to 50 years with herpes zoster. Approximately 22% of patients with herpes zoster still suffer from post-herpetic neuralgia.

The major diagnosis can be done based on signs and symptoms of the patients. Herpes zoster can be completely. It has been proven that oral acyclovir reduces the prevalence and severity of intraocular conditions associated with herpes zoster ophthalmicus [1-9].

Etiopathogenesis

Varicella zoster virus is among the eight herpes viruses that cause disease only in humans. There are 2 types of infections firstly it causes primary infection which is common in children's during this it leads to chicken pox. It is commonly transmitted through air from one person to another by coming in direct contact with the lesions of the infected person. During this phase the virus gets disseminated from the blood stream and reaches to the skin, oral mucosa and also lymph nodes. This leads to the appearance of rashes. The reactivation of endogenous VZV causes herpes zoster. This persists in the latent form within the sensory ganglia. This leads to an early episode of chickenpox. In association with the herpes simplex, herpes zoster is commonly associated with the prodromal severe pain which precedes the rash after many days which den leads to dermatomal rash of herpes zoster this leads to allodynia which may persist for weeks. Months or even a year even after the rash is healed complications like postherpetic neuralgia occurs.

When the primary infection gets treated this virus does not gets removed from the body it stays in the sensory dorsal root ganglion cells. This happens the same even after taking the vaccination. However, after the treatment of primary infection the body retains immunity for such virus and causes induction of varicella zoster virus-specific memory T cells. This memory T cells immunity does not retain forever it gets reduces and then declined by time. The decline below a theoretical "zoster threshold" correlates with an increased risk of herpes zoster infection [10-13]. The exogenous boosting may play an important role in the increase in the memory immunity against the virus. Along with this endogenous boosting also plays an important role.

Even after this the average period of immunity against the virus is around 20 years. There are various factors that play an important role in the virus reactivation. They are: stress, immunocompromised status, immunosuppressive drugs and also plays an important role. According to studies this virus is as common as almost 95% of the adult individuals suffer from this infection and also are at a higher risk of developing the infection. Once the person is infected with this infection it lead to an increase in post herpetic neuralgia which is caused due to the injuries to the peripheral and central nervous system. The patients who have deficiency in T lymphocytes and macrophages mediated immune defense are seen to be more affected by this virus.

Involvement of lungs, central nervous system (CNS), mucous membranes, liver, cardiovascular system (CVS), bladder, skeletal system, blood vessels and gastrointestinal system can be seen among patients with disseminated diseases. Involvement of the lungs, liver and CNS can be fatal.

Clinical features

Herpes zoster virus usually begins with some primary symptoms like fever, pain, itch, malaise, paresthesias and headache which is carried through be rashes on the whole body because of which severe itching gets developed and due to which the diagnosis may be delayed. This is said to be prodromal phase and following this phase comes the active phase. In this phase the patient is observed to be suffering with erythematous papules which then goes into the vessels in 12 to 24 hours and then goes to the pustules in 1 - 7 days and then reaches

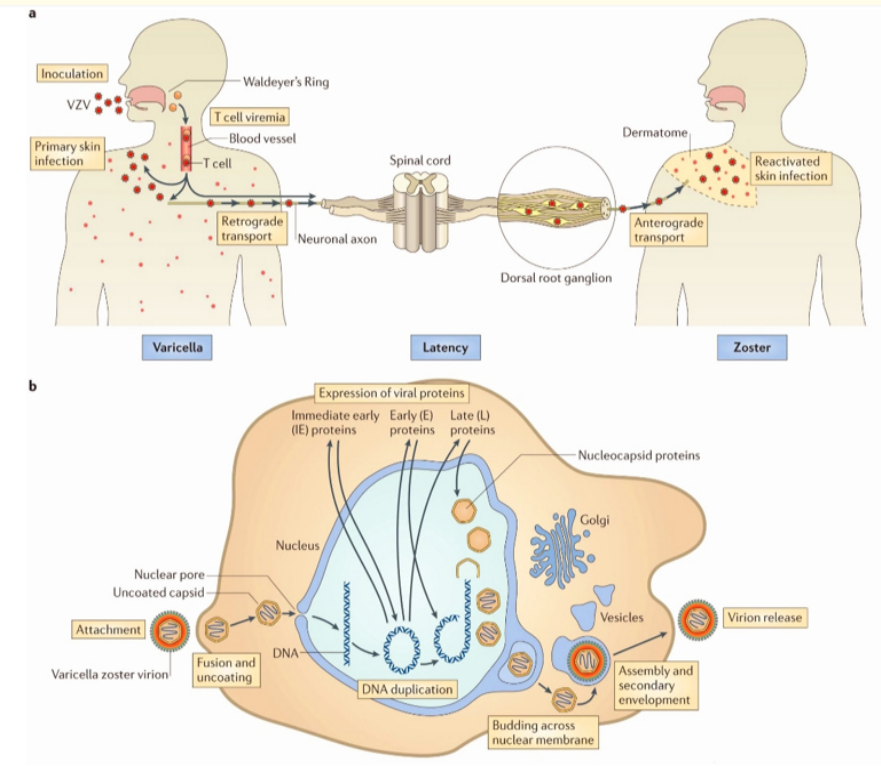


Figure 1: *Etiopathogenesis of VZV.*

to crust in 14 - 21 days. When it reaches to this level it is called as resolution phase. Post herpetic neuralgia is observed in the chronic stage of the disease which involves cranial nerves and other visceral organs.

Due to this many other problems gets arises from simple to severe and may affect the nervous system. A proper care has to be taken for the prevention of the disease. In most of the patients motor weakness occurs and leads to inability in the daily activity. Due to post herpetic neuralgia the patient may experience insomnia, weight loss, depression and chronic fatigue.

The other symptoms that are observed are:

- Abnormal serum iron
- Abnormal liver test
- Lethargy
- Weakness
- Apathy
- Fatigue
- Weight loss.

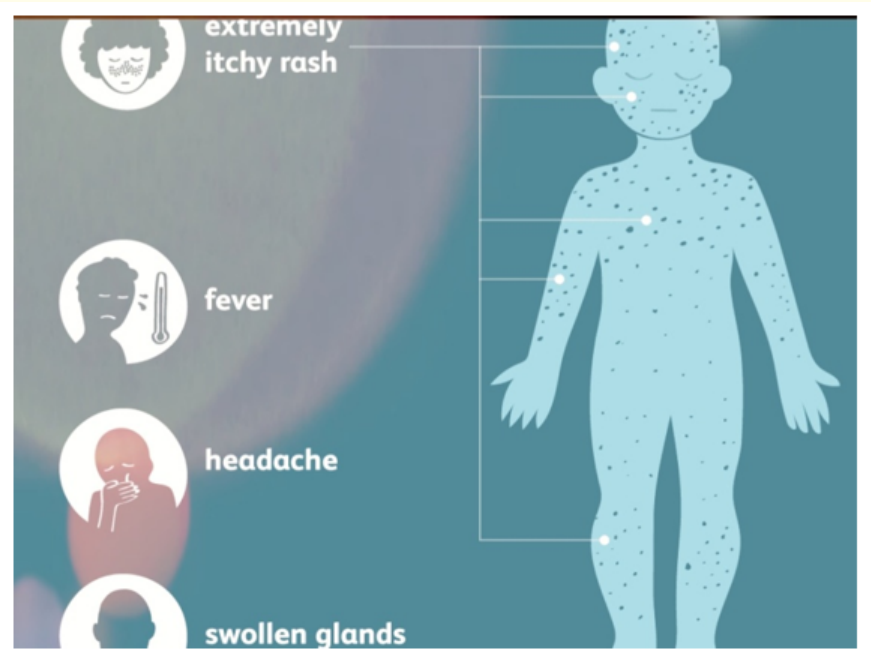


Figure 2: *Primary symptoms of VZV.*

They are many other conditions which also specify this and they affect different organs. They are:

- Heart: Arrhythmias, congestive heart disease
- Pancreas: Diabetes
- Cirrhosis: Impotence
- Hepatomegaly: Abdominal pain
- Arthritis
- Endocrine: Hypothyroidism.

Diagnosis

Its diagnosis can be done my performing various test which are to be done and the major test is the liver test, blood test and MRI.

Particularly this can be detected by the appearance of the rash on the body but the test should also be performed once the rashes appear that should include PCR, VZV DNA, etc.

Management

Paracetamol alone or in combination with a weak opioid (e.g. codeine) is frequently used as analgesia. Addition of drugs active against neuropathic pain (e.g. tricyclic antidepressants such as amitriptyline. Older adults often suffer from adverse effects. PHN treatment needs

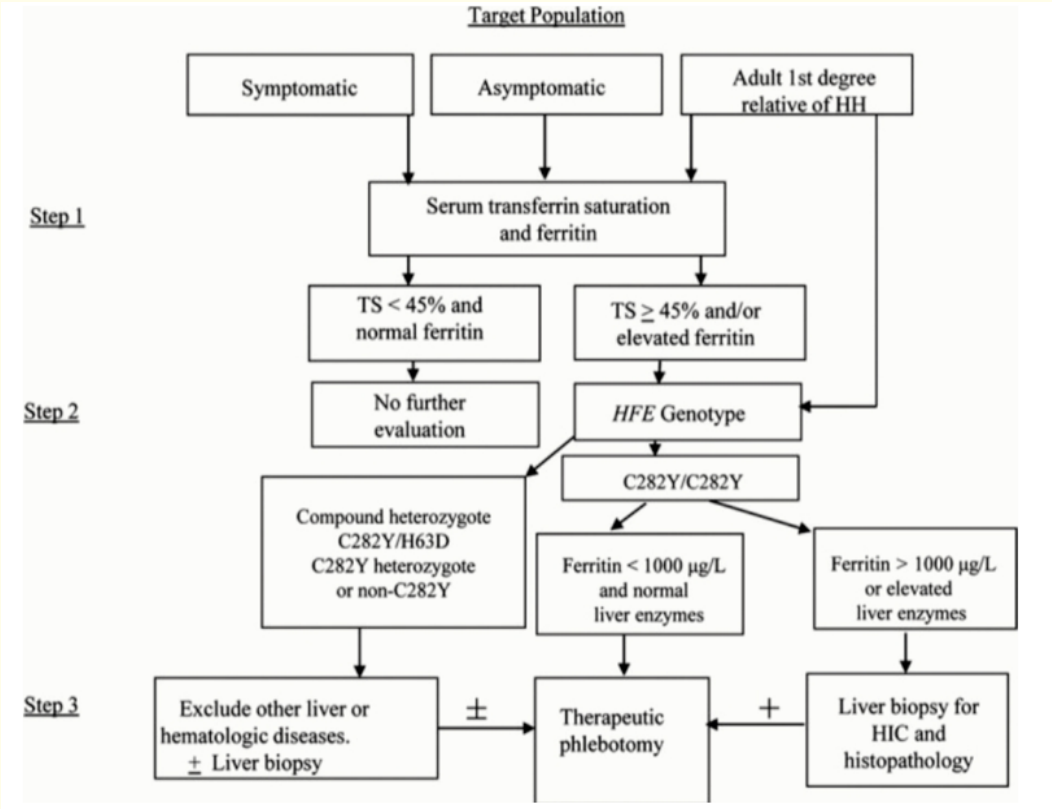


Figure 3: *Target population in which there is higher chances of the spread of the disease and various test that are being performed for its diagnosis.*

to not only be effective but to have an acceptable side-effect profile. Generally, systemic drugs are poorly effective for the treatment of PHN (pain reduced by 50% in 50% of patients at best) and they have significant side effects. Pain can also be reduced by the use of corticosteroids. Topical application of lidocaine patches and treatment with 8% capsaicin patches may provide relief for some patients and avoids systemic side effects. Antiviral drugs have been shown to reduce acute pain and rash severity, accelerate rash resolution and reduce duration of pain. However, many patients suffer from PHN despite antiviral drug use. The prodrugs valacyclovir and famciclovir have a more convenient dosing schedule and more constant blood concentrations than acyclovir. Antiviral therapy is used to reduce the risk of post-herpetic neuralgia.

Antiviral agents

Acyclovir, famciclovir, and valacyclovir are some of the antiviral agents these are used in the treatment acute herpes zoster. These are the agents these helps in reducing pain, prevent post-herpetic neuralgia and promote fast healing. It is more effective when treatment is started within 72 hours. Acyclovir dose is to be 800 mg five times a day and the dose of valacyclovir should be 100 mg 3 times a day.

Corticosteroids

These can be used in gel form and also oral/IV form. They benefit in the reduction of pain. Acyclovir along with steroids has shown very much positive effects. In IV form 250 mg 3 times a day.

Comparative study of acyclovir and valacyclovir

They can be compared by looking at doses in which they are given and the time duration at which it is taken. A complete evaluation need to be done by looking at various parameters at which it is being taken.

	Acyclovir	Valacyclovir
Dose	800 mg	1000 mg
Dosage	5 times a day	3 times a day
Efficacy	Less effective	More effective
Onset of action	1.5 to 2 hrs	Less than 30 minutes
Adverse drug reactions	Muscle/joint ache, confusion	No harmful side effects found

Table 1: *Comparision of acyclovir with valacyclovir.*

By the above table it clearly signifies that valacyclovir in all the aspects is better treatement than that of acyclovir as the dose variation is limited and the dosage time of valacyclovir is lesser than that of acyclovir. Hence, it will be very much easier for the patient to take the drug regularly. The onset of action of valacyclovir when compared to acyclovir is very less. Although there was not much difference in the duration of action of both the drugs.

The other major point is that in an immunocompetent patient acyclovir gets easily resistant and because of that they cause mutation in the viral thymidine kinase which causes the drug to be less effective. The adverse effects that are caused due to acyclovir may lead to many serious mental and physical illness [14,15].

Conclusion

Herpes zoster is a kind of disease which can effect anyone of any age group but immunocomprasant adults are at higher risk of it. Treatment of rash in less than 78 hrs has shown a very positive response and early diagnosis of various other associated conditions can also increase the life expectency of the patient. Use of vitamine C and vitamine B12 is shown to lessen the cause of post herpetiic neuralgia. Hence, by this study we conclude that valacyclovir is better than acyclovir in various aspects and should be prefered over it. This medicine is more effective when taken within 48 hrs to the apperance of the rashes.

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Conflict of Interest

Authors declare that there is no conflict of interest.

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