Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-8, Issue-6 | November- December 2022
DOI: 10.53339/aimdr.2022.8.6.15
Page no- 113-119 | Section- Research Article (Orthopaedics)

Side Effects of Oral Valacyclovir and Oral Acyclovir in the Treatment of Herpes Zoster

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Received: 10 August 2022
Revised: 19 September 2022
Accepted: 30 September 2022
Published: 22 October 2022

Abstract

Background: Herpes Zoster is a more sporadic disease than a doe's primary VZV infection. Herpes Zoster is typically transmitted person to person by direct contact. The lifetime risk of developing Herpes Zoster is between 25% and 30%, rising to 50% in those aged at least 80 years. The aim is to identify the side effects of oral valacyclovir and oral acyclovir in the treatment of herpes zoster. **Material & Methods:** This randomized clinical trial was conducted in the Department of Dermatology and Venereology, Shaheed Suhrawardy Medical College and Hospital, Dhaka, from April 2016 to September 2016. A total of 60 patients with herpes zoster were enrolled in the study. Group A Valacyclovir was 30 patients, and Group B Acyclovir was 30 patients. **Results:** In Group-A, it was observed that 6(20.00%) patients had nausea found to be the highest, 4(13.33%) patients had Headache, 3(10.00%) patients had vomiting, 2(6.67%) patients had Diarrhea,0(0.00%) patients had anorexia, 3(10.00%) patients had abdominal pain, and 1(3.33%) patients had dyspepsia found to be lowest in Group-A, and 8(26.67%) patients had nausea found to be highest, 5(16.67%) patients had Headache, 4(13.33%) patients had vomiting, 3(10.00%) patients had Diarrhea,1(3.33%) patients had anorexia, 5(16.67%) patients had abdominal pain, and 1(3.33%) patients had dyspepsia found to be lowest in Group-B of study patients as side effects. **Conclusion:** The rate of cessation of abnormal sensations, rash healing, and complications or adverse effects was not similar with both the treatments. There were no clinically significant differences in the nature and frequency but there were clinically significant differences in severity of adverse/side events between the two treatment groups. Thus, we conclude that in the management of herpes zoster, valacyclovir accelerates the resolution of pain and offers simpler dosing, and maintains a favorable safety profile than acyclovir.

Keywords:- Side Effects, Valacyclovir, Acyclovir, Herpes Zoster, Lesions.

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INTRODUCTION

Chickenpox and Herpes Zoster are caused by Varicella Zoster Virus (VZV), human herpes virus type 3 f21'. Herpes Zoster is a more sporadic disease than a doe's primary VZV infection. Primary VZV is transmitted by direct contact, inhalation of aerosols from the vesicular fluid of skin lesions, or aerosolized infected respiratory secretions. Herpes Zoster is typically transmitted person to person by direct contact. Because of its respiratory transmission, VZV can cause an epidemic among susceptible host.[1,2] The lifetime risk of developing Herpes Zoster is between 25% and 30%, rising to 50% in those aged at least 80 years. The estimated average incidence of Herpes Zoster is about 3.4-4.82 per 1000 person-years, which increases to more than 11 per 1000 person-years in those aged at least 80 years.[3] Pain is the most common complaint for patients with herpes zoster seeking medical care.[4,5] Pain persisting after rash healing occurs in more than 50% of untreated patients and is the major complication of older patients.[6,7] The pain is often accompanied by abnormal sensations such as allodynia, tingling, or numbness and decreases gradually over several months in most patients. However, some patients have pain persisting beyond six months.[7,8,9] Postherpetic neuralgia (pain that persists more than 30 days after rash onset or skin healing) is the most feared complication.[10] The duration of postherpetic neuralgia and incidence are directly related to patients aged.[11] The reported incidence of post herpetic neuralgia ranged from 8 to 70% and increased with age. In one study, the overall incidence of postherpetic neuralgia was 8% after 30 days and 4.5% after 60 days. Importantly valacyclovir was more effective than acyclovir in reducing the duration of zoster-associated pain. Thus, valacyclovir ultimately succeeds acyclovir as a first-line treatment for herpes zoster.[12] In Canada, the incidences of medically attended Herpes Zoster and related outpatient visits and hospitalizations were reported to increase with age. Data from a general practitioner network in France showed that 1% of patients with Herpes Zoster were hospitalized, and the death rate was 0.2/100,0003,4. Herpes Zoster associated mortality is rare, with reported incidence ranging from 0 - 0.47 per 100,000-person year, and most deaths occur in those aged at least 60 years. However, many studies use electronic or paper death certificates, leading to underestimating or overestimating the actual mortality rate due to infections other than Herpes Zoster and noninfectious diseases, particularly in older people.[13]

MATERIAL AND METHODS

This randomized clinical trial was conducted in the Department of Dermatology and Venereology, Shaheed Suhrawardy Medical College and Hospital, Dhaka, from April 2016 to September 2016. Sixty patients with herpes zoster were enrolled in the study according to inclusion and exclusion criteria. Group-A Valacyclovir was 30 patients, and Group-B Acyclovir was 30 patients. The purposive sampling method was used. The study aimed to identify the side effects of oral valacyclovir and oral acyclovir in treating herpes zoster. Cutaneous assessments were performed on days 1, 3, 8, 15, 22, and 29. The occurrence of any complications of herpes zoster was also noted. The severity of the rash was graded depending on the number of lesions as mild (<25 lesions), moderate (25-50 lesions), or severe (>50 lesions).

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Pain severity and unpleasantness were scored by using gracely scales. Group A was treated with oral valacyclovir l000mg 3 times daily for seven days, and group B was treated with oral acyclovir 800mg daily for seven days. The data were analyzed using the Chi-square test and unpaired t-test. Statistical analysis of the results was obtained using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-17) (SPSS Inc, Chicago, IL, USA). Prior to the commencement of the study, the ethical committee of Shaheed Suhrawardy Medical College, Dhaka, approved the thesis protocol.

Inclusion Criteria

- All patients above 18 years of age with clinical diagnosis of herpes zoster.
- Sex: Both sexes
- New untreated cases of herpes zoster.
- Presentation within 72 hours of onset of zoster rash.
- Participants who gave the written consent and willing to comply with the study procedure.

Exclusion Criteria

- Pregnant and nursing women
- Patients treated with other antiviral medications and immunomodulator agents.
- Known immunocompromised status.
- Patients with pre-existing renal and hepatic impairment.
- Patient unwilling to take part in the study.

RESULTS

In the group, a male was more predominant than the female who was 17(56.7%) cases and 13(43.3%) cases, respectively. In group B, the male was more predominant than the female, with 16(53.3%) cases and 14(46.7%) cases, respectively. The difference between these two groups was not statistically significant (p=O.795) [Table 1]. In-group, a majority of the patients were in the age group of 30-50 years which was 13(43.3%) cases, followed by > 50 years and 18-30 years, which were 11(36.7%) cases and 6(20.0%) cases respectively. In group B majority of the patients were in the age group >50 years which was 15(50.0%) cases, followed by 30-50 years and 18-30 years which were 12(40.0%) cases and 3 (10.0%) cases respectively. The mean age with SD in groups A and B was 38.93 ± 8.29 years and 41.3.6 ± 8.36 years, respectively. The difference between the two groups' ages was insignificant (p=0.263) [Table 2]. There were four types of herpes zoster patients in this study. Among them, the thoracic type was the commonest in both groups which were 17(56.7%) cases, followed by cervical, lumbosacral, and trigeminal dermatomes which were 8(26.7%) cases, 4(13.3%) cases, and 1(3.3%) cases respectively in group A. In-group B cervical, lumbosacral, and trigeminal dermatome which was 9(30%) cases, 2(6.7%) cases, 2(6.7%) cases respectively. The difference between the two groups was insignificant (p=0.616) [Table 3]. In group A, erythema was present in 29(96.7%) cases, maculopapular rash present in 28(93.3%) cases, vesical was present in 22 (73.3%) cases, bullae present in 22(73.3%) cases, crusting was present in 14(46.7%) cases, the pain was present in 5(16.37%) cases. In-group B erythema was present in 30(100.0%) cases, the maculopapular rash was present in 30(100.0%) cases, vesical was present in 29(96.7%) cases, bullae were present in 25(83.3%) cases, crusting was present in 17(56.7%) cases; the pain was present in

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5(16.07%) cases. The only difference between the two groups was found significant in vesical (p=0.011) [Table 4]. It was observed that 6(20.00%) patients had nausea found to be the highest, 4(13.33%) patients had Headache, 3(10.00%) patients had vomiting, 2(6.67%) patients had Diarrhea,0(0.00%) patients had anorexia, 3(10.00%) patients had abdominal pain, and 1(3.33%) patients had dyspepsia found to be lowest in Group-A, and 8(26.67%) patients had nausea found to be highest, 5(16.67%) patients had Headache, 4(13.33%) patients had vomiting, 3(10.00%) patients had Diarrhea,1(3.33%) patients had anorexia, 5(16.67%) patients had abdominal pain, and 1(3.33%) patients had dyspepsia found to be lowest in Group-B of study patients as side effects. [Table 5].

Table 1: Distribution of patients according to sex (n=60).

Group			
Sex	**Group- A**	**Group-B**	**p value**
	Valacyclovir	**Acyclovir**	
Male	17(56.7)	16(53.3)	0.795
Female	13(43.3)	14(46.7)	
Total	30(100.0)	30(100.0)	
Chi-square test was done to measure the level of significance			

Table 2: Distribution of patients according to age group (n=60).

Group			**p value**
Age	**Group- A**	**Group-B**	
	Valacyclovir	Acyclovir	0.263
18-30	06 (20.0)	03(10.0)	
30-50	13(43.3)	12(40.0)	
>50	11 (36.7)	15(50.0)	
Total	30(100.0)	30(100.0)	
Mean = SD	38.93 ±8,29	41. 36 ±8,36	
T test was done to measure the level of significance			

Table 3: Distribution of patients according to involved dermatome (n=60).

Group			
Dermatome	**Group-A**	**Group-B**	**p value**
	Valacyclovir	**Acyclovir**	
Thoracic	17(56.7%)	17(56.7%)	
Cervical	8 (26.7%)	9 (30%)	
Lumbosacral	4(13.3%)	2 (6.7%)	0.616
Trigeminal	1 (3.3%)	2 (6.7%)	
Total	30 (100.0)	30 (100.0)	
*Chi-square test was done to measure the level of significance			

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Page no- 113-119 | Section- Research Article (Orthopaedics)

Table 4: Distribution of patients according to clinical findings of the integumentary system (n=60).

Group			
Clinical findings of	**Group-A**	**Group-B**	**p-value**
integumentary system	Valacyclovir	Acyclovir	
Erythema	29 (96.7)#	30(100.0)	0.313
Maculopapular rash	28 (93.3)	30(100.0)	0.150
Vesical	22 (73.3)	29 (96.7)	0.011
Bullae	22 (73.3)	25 (83.3)	0.347
Crusting	14(46.7)	17(56.7)	0.438
Pain	05(16.7)	05(16.7)	1.00
*Chi-square test was done to measure the level of significance			

Table 5: Side effects of study patients (N=60)

Event	**No. of occurrences (% patients)**			
	Group-A		**Group-B**	
	Valaciclovir for 7 days (n=30)		**Acyclovir (n=30)**	
	n	**%**	**n**	**%**
Nausea	6	20.00	8	26.67
Headache	4	13.33	5	16.67
Vomiting	3	10.00	4	13.33
Diarrhea	2	6.67	3	10.00
Constipation	1	3.33	2	6.67
Asthenia	1	3.33	2	6.67
Dizziness	1	3.33	2	6.67
Anorexia	0	0.00	1	3.33
Abdominal pain	3	10.00	5	16.67
Dyspepsia	1	3.33	1	3.33

DISCUSSION

In this study, the male was more predominant than the female who was 17 (56.7%) cases, 13 (43.3%) cases in group A and 16 (53.3%) cases, and 14 (46.7%) cases in group B, respectively. Overall, women may have a slightly greater risk of developing zoster when compared to men 14, but in this study, statistically, the difference was not so significant. (P=0.795) in our study. In this study, in-group A majority of the parents were in the age group of 30-50 years which was 13 (43.3%) cases. In group B, most patients were in the age group >50 years, which was 15 (50.0%). The mean age with SD in groups A and B was 38.93 ± 8.36 years and 41.3.6± 8.36 years, respectively. Usually, the chance of developing herpes zoster increases with age, as proved in previous studies.[14,15] Here the differences between the age group were not statistically significant (P=0.263). In our study, the most common dermatome was the thoracic in 17 (56.7%) cases, followed by cervical, lumbosacral and trigeminal dermatome, which were 8(26.7%) cases, 4(13.3%) cases, and 1(3.3%) cases respectively in group A. In-group B cervical,

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lumbosacral, and trigeminal dermatome which was 9 (30%) cases, 2 (6.7%) cases, 2(6.7%) cases, respectively. The difference between the two groups was not significant (p=0.616)[16]. Skin lesions improved faster in patients on Valacyclovir compared to Acyclovir, and in table 4, the difference was statistically significant in the case of vesicle where (p=0.011). An earlier study also noticed the faster resolution of a skin lesion in the Valacyclovir group, but their findings were not statistically significant. Pain is the most common debilitating feature of herpes zoster[16]. Most patients experience pain immediately before and during the acute rash phase. However, a more crucial clinical concern is to prevent or reduce the possibility of persistent pain. However, a sizeable multi-centric study found that treating Valacyclovir for seven days significantly reduced the incidence of post-herpetic neuralgia compared to acyclovir.[15] The safety profile of Acyclovir has been carefully established during >18 years of clinical use. In the present study, there was no clinically significant difference in nature. Frequency of severity, and adverse events between the two treatment groups, as reported in the earliest studies.[15,16]

Limitations of the study

There are some limitations in this study, patients who have Pregnant and nursing women, patients treated with other antiviral medications and immunomodulator agents, known immunocompromised status, and patients with pre-existing renal and hepatic impairment. Also, the sample size was small with probability sampling technique could not be employed to recruit the study unit; they were selected purposively due to time constraints. Therefore, the study population might not represent the whole community.

CONCLUSIONS

This study demonstrates that the administration of valacyclovir three times daily is a safe treatment for acute herpes zoster. Valacyclovir treatment has the benefits of rapid resolution of the signs and symptoms of herpes Zoster and a better safety profile to acyclovir. Furthermore, using valacyclovir has the convenience of three-times daily dosing, thereby ensuring better patient compliance, which makes this regimen an excellent choice for the treatment of herpes zoster having low side effects.

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Page no- 113-119 | Section- Research Article (Orthopaedics)

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Source of Support: Nil, Conflict of Interest: None declared