



Compare the Efficacy and Safety Profile of Valacyclovir vs. Zinc Sulphate in Verrucae

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Abstract: Warts are very serious skin diseases while the incidence of spontaneous recovery is strong, it typically takes a long time, so, certain patients do not undergo spontaneous treatment. A hospital based comparative study was conducted to compare the efficacy and safety profile of valacyclovir vs. zinc sulphate in Verruca Vulgaris. Total number of 50 patients will be selected for this study from Dermatology OPD, Krishna Hospital, Karad who will be diagnosed clinically as verruca will be included in to the study valacyclovir and zinc sulphate, both are efficacious in treatment of warts. Valacyclovir was more efficacious therapeutic option than zinc sulphate in treatment of warts.

INTRODUCTION

Warts are usually thin, rugged and hard growths and are close to the rest of the skin in color. These usually will not contribute to complications even where they can be painful on the bottom of the foot. Warts are caused by a kind of human papillomavirus (HPV) infection. It is believed that the virus enters the body by the skin that has infected tissue which has been slightly damaged. Most forms of warts cure in a months to years without medication. A number of options can speed resolution, including salicylic acid applied to the skin and cryotherapy. These typically don't result in significant problems in those who are otherwise healthy. Genital warts are treated differently from other types (Anonymous, 2014a). Oral valacyclovir and zinc sulphate have been utilized in dermatological environments for more than two decades. However it is not commonly considered a primary choice in the treatment of patients with verruca vulgaris, the rise in office visits by wart patients has recently placed a spotlight on the usage of this agent in this patient subgroup. Hence, the study was

done at our tertiary care centre to compare the efficacy and safety profile of valacyclovir vs zinc sulphate in Verruca Vulgaris.

Aim and objectives: To study of oral valacyclovir v/s oral zinc sulphate in the treatment of patients with cutaneous verruca.

Literature review: Greater Celandine's acrid, yellow sap is utilized as a common wart cure (Anonymous, 214b). A solution similar to distilled salicylic acid can be added directly to the wart, albeit in more moderate amounts. One cure for warts in Louisiana includes rubbing the wart with a potato, which is then buried when the "buried potato dries up, the wart is healed" (Webb, 1971). Another treatment close to Twain's is recorded from Northern Ireland where water from a particular well on Rathlin Island has been attributed with the power to cure warts (Ballard, 2009). Traditional hypotheses stated that the virus persisted a lifetime in the body. Nonetheless, experiments utilizing responsive DNA methods have shown that the virus can either be cleared or blocked by

immunological response to rates below what can be assessed by the Polymerase Chain Reaction (PCR) tests. One analysis that examined subclinical HPV genital skin utilizing PCR showed a prevalence of 10% (Scheinfeld and Lehman, 2006). Treatment is only required if it causes symptoms. That may require salicylic acid, cryotherapy, or removal from surgery. Until surgery the skin over-tops the lesion should usually be drained. We go down without further care in only a third or two thirds of cases but that can take a few years. Are growing plantar warts. Very commonly the children and young adults are impacted. Their color usually matches that of the skin (Health Plan of New York, 2007). There may small black dots can appear on the surface. Any or both of these may occur in an environment. They can result in pressure pain so that it can be difficult to move. Around 10% of children and teenagers develop warts at any given time. In infancy, as many as 22% of children contract warts (Silverberg, 2004). Such an treatment is secure, fairly pain-free for most patients and will proceed until the wart recovers. This method is particularly helpful to younger patients, however, diabetic patients and peripheral arterial disease need careful assessment. An exceedingly common concern are plantar warts (verrucae). Reassurance is also the only type of medical therapy needed because most lesions heal naturally over time. There is shortage of support regarding medication effectiveness and sometimes it is confusing.

Gurkan and Ozlu (2015) in a case report summarized that Warts are papillomas caused by the Human Papillomavirus. Although, they can spontaneously resolve, most patients request treatment due to cosmetic concerns or functional impairment. Current treatment options are usually destructive and painful. Zinc is a micronutrient involved in immunologic processes and oral zinc sulphate was reported to be effective in the treatment of warts. The authors reported a 13 year-old girl who had widespread viral warts on both soles. She was receiving systemic corticosteroid therapy for relapse of nephrotic syndrome. Warts were successfully treated with oral zinc sulphate for 3 months without any side effects. The authors concluded that Oral zinc sulphate could be a new treatment option for warts unresponsive to conventional treatments.

MATERIALS AND METHODS

Total number of 50 patients will be selected for this study from Dermatology OPD, Krishna Hospital, Karad who will be diagnosed clinically as verruca will be included in to the study after written and signed consent. Patients will be randomly included in either group A, group B. Before treatment patient will be examined thoroughly using clinical and laboratory measures for any

underlying disease. All previous systemic or topical medications will be stopped at least two months before treatment. Use of concomitant topical or systemic treatment that could affect the outcome of verruca will not be permitted until the end of the study. After baseline evaluation of patient by Visual Analogue Scale (VAS) and Physician Global Assessment (PGA) by investigator, patient will be sent to drug dispenser who will then randomize the patient in group A or B with the help of a randomization table and provide medications as per below. Each patient will have equal chance of getting into either group A or B.

This is hospital based double-blinded, controlled trial in patients attending Dermatology OPD of Krishna Hospital, Karad. Duration of study was two years. A total of 50 subjects will be enrolled in study from Department of Dermatology OPD, Krishna Hospital, Karad, after meeting the inclusion and exclusion criteria. Half of them will receive Oral valacyclovir (1000 mg day⁻¹) and the other half will receive oral zinc sulphate (400 mg day⁻¹).

Patients are free to withdraw from participation in study at any time without prejudice to further treatment. Patient who will discontinue from study will always be asked for the reasons of discontinuation and presence of any adverse event and if possible, assessed by the investigator and all adverse events will be followed up.

Drugs and dosage: Patients will be divided into two groups: Group A, the selected patients (25) will be given oral valacyclovir (1 g day⁻¹) according to the need and tolerability of patient.

Group B, the selected patients (25) will be given oral zinc sulphate (400 mg day⁻¹) according to the need and tolerability of patient. Patient will be asked to follow up regularly for both the groups to assess safety and efficacy. All the patients will be followed up throughout the course of the treatment for any adverse drug reactions particularly adverse effects related with psychiatric side effects. Percentage different adverse reaction seen during the course of the treatment will be noted.

RESULTS AND DISCUSSION

A hospital based comparative study was conducted to compare the efficacy and safety profile of valacyclovir vs. zinc sulphate in treatment of Verruca Vulgaris. The present study was carried out with following two groups of 25 patients each:

Group A, oral valacyclovir (1 g day⁻¹) was given to the patients. Group B: Oral zinc sulfate (400 mg day⁻¹) was given to the patients. As seen in Table 1, in Group A, the most common type of wart was common and plantar (24% each) followed by palmar (16%), flat (12%), genital (12%), periungual (8%) and filliform (4%). In Group B,

Table 1: Distribution of patients according to type of wart

Types of wart	Group A		Group B		p-value
	N	Percentage	N	Percentage	
Common	6	24	7	28	>0.05
Plantar	6	24	4	16	
Palmar	4	16	5	20	
Flat	3	12	3	12	
Genital	3	12	3	12	
Periungual	2	8	3	12	
Filliform	1	4	0	-	
Total	25	100	25	100	

Table 2: Distribution of patients according to number of warts

Number of warts	Group A		Group B		p-value
	N	Percentage	N	Percentage	
0-4	14	56	17	68	>0.05
5-9	8	32	5	20	
10-15	3	12	3	12	
Total	25	100	25	100	
Mean±SD	4.88±3.84	4.48±4.15			

Table 3: Comparison of Serum Urea values between groups

Serum Urea (mg%)	Group A		Group B		p-values
	Mean	SD	Mean	SD	
Baseline	32.00	6.18	30.24	5.95	>0.05
Visit 2	33.32	7.53	30.98	6.23	>0.05
Visit 4	33.84	7.90	31.08	6.59	>0.05
p-value	>0.05		>0.05	-	-

Table 4: Comparison of number of warts between groups

Number of warts	Group A				Group B				p-values
	Mean	SD	Mean of diff	Diff%	Mean	SD	Mean of diff	Diff%	
Baseline	4.88	3.84			4.48	4.15			>0.05
Visit 1	4.76	3.84	0.12	2.5	4.48	4.15	0	0	>0.05
Visit 2	4.24	3.77	0.68	13.9	4.32	3.87	0.16	3.57	>0.05
Visit 3	3.76	3.41	1.12	22.9	4.08	3.80	0.4	8.9	>0.05
Visit 4	3.12	3.31	1.76	36.1	3.88	3.64	0.6	13.4	>0.05
Visit 5	2.20*	3.29	2.68	54.91	3.36	3.07	1.12	32.8	>0.05
p-values	>0.05	-	-	>0.05	-	-	-	-	-

the most common type of wart was common (28%) followed by palmar (20%), plantar (16%), flat (12%), genital (12%) and periungual (12%).

As seen in Table 2, in Group A, the number of warts in 14 (56%) patients was in the range of 0-4 while 8 (32%) and 3 (12%) patients had warts in the range of 5-9 and 10-15, respectively. In Group B, the number of warts in 17 (68%) patients was in the range of 0-4 while 5 (20%) and 3 (12%) patients had warts in the range of 5-9 and 10-15, respectively. The mean number of warts was comparable between the groups (4.88±3.84 vs. 4.48±4.15).

As seen Table 3, the mean Serum Urea in Group A at baseline visit was 32.00±6.18 mg% while mean Serum Urea values was 33.32±7.53 and 33.84±7.90 mg% at 2nd visit and 4th visit, respectively. There was no significant difference within the groups as per ANOVA test (p>0.05). The mean Serum Urea in Group B at baseline visit was

30.24±5.95 mg% while mean Serum Urea values was 30.98±6.23 and 31.08±6.59 mg% at 2nd visit and 4th visit, respectively.

As seen in Table 4, the mean number of warts in Group A at baseline and 1st visit was 4.88±3.84 and 4.76±3.84, respectively while mean number of warts was 4.24±3.77 and 3.76±3.41 at 2nd and 3rd visit, respectively. The mean number of warts was 3.12±3.31 and 2.20±3.29 at 4 and 5th visit, respectively. The mean number of warts were significantly lesser in 5th visit as per ANOVA test (p<0.05). The mean number of warts in Group B at baseline and 1st visit was 4.48±4.15 while mean number of warts was 4.32±3.87 and 4.08±3.80 at 2nd and 3rd visit, respectively.

As seen in Table 5, there was statistically no significant reduction in Physician Global Assessment (PGA) Score of patients in Group B during 1st, 2nd and 3rd visit while there was statistically significant

Table 5: Comparison of PGA Score of patients in Group B before and after treatment

PGA score	Group B		p-values
	Mean	SD	
Baseline	4.04	0.89	-
Visit 1	4.04	0.89	>0.05
Visit 2	4.04	0.89	>0.05
Visit 3	3.56	1.00	>0.05
Visit 4	3.24	0.60	<0.05
Visit 5	2.96	0.35	<0.05

reduction in PGA Score during 4 and 5th visit. The disease severity was significantly reduced in patients in Group B during 4 and 5th visit as per ANOVA test ($p < 0.05$).

A hospital based comparative study was conducted to compare the efficacy and safety profile of valacyclovir vs. zinc sulphate in verruca. The present study was carried out with following two groups of 25 patients each:

- Group A: oral valacyclovir (1 g day⁻¹) given to patients
- Group B: oral zinc sulfate (400 mg day⁻¹) given to patients

Warts are healthy epithelial spreads triggered by Human Papillomavirus (HPV). The >200 types of HPV have been reported (Cubie, 2013). Common warts are the most common type of warts in children and adults (Bernard *et al.*, 2010). Methods may be a therapeutic alternative, helping to modulate and allow the immune system to recognize and protect against this virus. INF is a major component of the Th1 response which regulates the expression of antigen MHC I. Zinc deficiency reduces with INF. There are also other pathways by which zinc helps improve the immune system and combat numerous bacterial and viral infections.

Bangash and Sethi (2012) conducted a randomized control trial of 45 patients in determining the oral Zinc Sulphate effectiveness in the treatment of natural recalcitrant warts; Zinc sulphate (600 mg day⁻¹) was given to 45 patients for 2.5 months and 62.2% improvement was seen. The 5% of the patients experienced side-effects in the form of nausea, vomiting, abdominal pain. In compassion the current study, Zinc sulphate (400 mg day⁻¹) was given to 25 patients for 2.5 months and 32.8% improvement was seen. No side effects were seen. The disparity in result could be due to larger doses of zinc sulphate used in Waqas, etc., study.

Mohamed *et al.* (2016) studied oral zinc sulphate in recalcitrant warts in 40 patients. Zinc sulphate (600 mg day⁻¹) was given to 40 patients for 3 months and 87% improvement was seen. 10% of the patients experienced side-effects in the form of nausea, vomiting,

diarrhoea. In compassion, the current study included 25 patients. Zinc sulphate (400 mg day⁻¹) was given to 25 patients for 2.5 months and 32.8% improvement was seen. No side effects were seen. The disparity in result could be due to longer duration of study and larger doses of zinc sulphate used in Al-Gurari, etc., study.

Tandeter and Tandeter (2005) in a case study reported of the unexpected effect of valacyclovir, A 30 year old male had genital herpes with plantar warts. And seen that valacyclovir is effective in treating palmar warts and plantar warts completely. No side effects were seen with the drug.

Pitfalls of the study: The treatment duration in our study was shorter as compared to other studies. Low doses of drugs were used. Valacyclovir, if given in larger doses and for longer duration may be efficacious in other types of warts.

CONCLUSION

Verruca, also known as warts are benign skin growths that are caused by human papilloma virus. It is usually seen in children and teens and people with a weak immune system. We compared the efficacy and safety profile of valacyclovir and zinc sulphate in treatment of verruca. It was noted that valacyclovir and zinc sulphate, both are efficacious in treatment of warts. Valacyclovir was more efficacious therapeutic option than zinc sulphate in treatment of warts. Valacyclovir was more efficacious in treatment of palmar-plantar warts. Zinc sulphate was more efficacious in treatment of flat warts, common warts.

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