

## VALACYCLOVIR IN THE MANAGEMENT OF HERPETIC GINGIVOSTOMATITIS AND HERPETIC LABIALIS: CASE REPORT AND REVIEW OF LITERATURE

Virender Gombra<sup>1\*</sup>, Mandeep Kaur<sup>2</sup>, Shamimul Hasan<sup>3</sup>, Arpita Rai<sup>4</sup>

<sup>1,3,4</sup>Assistant Professor, <sup>2</sup>Associate Professor, Department of Oral Medicine and Radiology, Faculty of Dentistry, Jamia Millia Islamia.

**\*Corresponding Author:**

Email: vgombra@jmi.ac.in

### ABSTRACT

Acute herpetic gingivostomatitis (AHGS) is the primary manifestation of herpes simplex-I (HSV-I) infection which causes painful vesicles and ulcers on gingiva and palate. AHGS commonly involves the immobile mucosa of the oral cavity. Recurrent painful oral infections can also occur in immunocompromised and HIV positive patients causing discomfort. Recurrent symptomatic and asymptomatic herpetic labialis may occur because of reactivation of latent virus in sensory ganglia. The objective of this paper is to discuss cases of acute herpetic gingivostomatitis and herpetic labialis and evaluate the effect of valacyclovir in the management of herpetic infections.

**Keywords:** Acute herpetic gingivostomatitis, Herpetic labialis, Valacyclovir.

### INTRODUCTION

Herpetic gingivostomatitis is a viral infection caused by herpes simplex virus (HSV) of the herpetoviridae family. <sup>(1)</sup> HSV is a double-stranded DNA virus which is a type of human herpes virus (HHV). The herpetic simplex infections are caused by HSV-1 and HSV-2. Orofacial infections are mostly associated with HSV-1, whereas lower body infections are usually associated with HSV-2. <sup>(2)</sup> The monthly frequencies of recurrence are 0.33 in genital HSV-2 infections, 0.12 in orolabial HSV-1 infections, 0.020 in genital HSV-1 infections and 0.001 in oral HSV-2 infections. <sup>(3)</sup> The recurrences are more when HSV-1 is oral and HSV-2 is genital. <sup>(4)</sup> Acute HSV infections occurs at two peaks, one at the age of 6 months to 5 years and other at 20 years of age. <sup>(2)</sup>

The virus causes chronic latent infection after inoculation along the sensory nerves such as trigeminal ganglion. Extraneuronal latency within the epithelium may result in recurrent lesions. The incubation period range is few days to three weeks. Severity of the lesion is related to the virulence of HSV and the host's immunity. Virions remain latent in asymptomatic HSV infection with minimal epithelial destruction and infect adjacent epithelial cells with inflammatory response in symptomatic infections. <sup>(1)</sup> The predisposing factors include stress, fever, extremes in temperature, ultraviolet radiation, immunosuppression or trauma. Asymptomatic shedding of HSV in saliva may cause transmission of virus. <sup>(5)</sup> Virus infection causes acantholysis of intermediate and basal cells leading to vesicle formation. <sup>(6)</sup> After onset of symptoms, peak viral load occurs at 48 hrs, with no virus detected beyond 96 hrs. HSV type 1 may cause asymptomatic infection or acute herpetic gingivostomatitis (AHSG)

as primary infection whereas recurrent infection results in herpetic labialis. <sup>(7)</sup>

AHGS and herpetic labialis are self-limiting lesions. Acyclovir is conventional pharmacotherapy advised for acute painful and severe recurrent infections. Valacyclovir is altered form of acyclovir with good gastrointestinal absorption and better oral bioavailability. <sup>(2)</sup>

### CASE REPORT 1

A 24 years old female patient reported with lesions in the mouth with inability to brush, chew and take liquid diet. Patient gave history of fever 4 days back followed by lesion in mouth and throat. On examination submandibular lymph nodes were palpable, mobile and tender. Gingiva was erythematous with multiple shallow ulcers on hard palate (Figure-1). Diagnosis of AHGS was given. Valacyclovir 1000 mg twice /day was prescribed for 3 days along with acetamenophen-500mg T.D.S. with local anaesthetic agents, Benzylamine mouth rinse three times /day and soft diet. After 3 days, relief in pain and improvement of lesion was observed (Figure-2) and same medication was given for two days which resulted in complete resolution of the lesion.



**Figure: 1**



Figure: 2



Figure: 4

## CASE REPORT 2

A 41 years old female patient reported with tingling sensation, irritation followed by lesion on upper lip from last 2 days. Clinically, tender vesicular lesions of upper lip and vermilion border were present (Figure-3). There was previous history of such lesions on same site since 10 years. The lesions ruptured after 4-5 days leaving painful ulceration, which persisted for 10-15 days. A diagnosis of recurrent herpetic labialis was given. Valacyclovir 2 g B.D. was prescribed for one day with a topical anaesthetic agent. Patient reported with resolved lesions after 3 days. (Figure-4)



Figure: 3

## DISCUSSION

In primary oral HSV-1, prodromal symptoms of fever, followed by mouth lesions with submandibular and cervical lymphadenopathy are usually seen. The mouth lesions consist of painful vesicles on a red, swollen base which heals within 10 to 14 days. Symptoms of tingling, pain, itching, and burning precedes in 60% of herpetic labialis lesions. Herpetic labialis may appear as clusters of vesicles on the lip which subsequently ulcerate and form a crust. Re-epithelization of lesions may take a week.

**Table 1: Diagnosis of HSV infection**

History and clinical picture	Appearance of the lesions correlating with history
Viral culture	Obtained from the base of vesicles with swab. Culture sensitivity is seen in 50% of patients.
PCR	More sensitive method and detects asymptomatic viral shedding.
Tzanck test	Scraping of the floor of vesicle shows multinucleated giant cells microscopically.
Serology	Elevated IgM titers in primary infection Raised IgG titers several weeks later.
Direct fluorescent antibody testing	Detects 80 percent of HSV cases. Its sensitivity is 40-77 percent for AHGS.

(4, 5)

Treatment (table-2, 3) is generally symptomatic and antiviral therapy instituted immediately can significantly reduce the duration and severity of the lesions.

**Table 2: Treatment for Primary herpetic gingivostomatitis**

Advised	Rest, soft diet and adequate fluid intake.
Avoid	smoking and drinking alcohol
Topical anesthetics, analgesics, and antipyretics	Rinsing with 2% lidocaine or 20% Benzocaine before each meal. Elixir of diphenhydramine hydrochloride, 12.5 mg/5ml and benzydamine hydrochloride mouth wash.
analgesic/antipyretic agent	Acetaminophen – 500mg – t.d.s. for 3-5 days.
Antiviral drugs	Acyclovir- 15 mg per kg five times/day for 7 days in young children Valacyclovir- 1000mg twice for 5days Famcyclovir – 500 mg twice for 5days

(5, 8)

**Table 3: Treatment for herpetic labialis**

Sunscreen application	
Topical anaesthetic agents	1.8% Tetracaine cream upto 6 times/day
Topical antiviral agents	5% Acyclovir cream 3% Penciclovir cream- 3 to 6 times /day 10% docosonal
Systemic antiviral drugs in severe lesions	Acyclovir- 400mg qid for 5 days Valacyclovir- 2 g bid for 1 day

(5, 9)

The oral acyclovir has low bioavailability and needs frequent dosing. Valacyclovir is the l-valyl ester of acyclovir which rapidly converts to acyclovir after oral administration by intestinal and liver valacyclovirase. Its mechanism of action, antiviral spectrum and resistance are the same as those of acyclovir.<sup>(7)</sup> Valacyclovir gets rapidly converted to acyclovir after oral administration via intestinal and hepatic metabolism, resulting in serum levels that are three to five times greater than those achieved with oral acyclovir and approximate those achieved with intravenous acyclovir administration.<sup>(10)</sup> Adverse effects of valacyclovir include GI disturbances, headache, rash, hallucinations, confusion, and nephrotoxicity.<sup>(8)</sup>

Valacyclovir is safe and effective in HSV infections.<sup>(3)</sup> Valacyclovir oral suspension is also well tolerated by 3 months old child to 11 years old age. It is not recommended for infants less than 3 months of age because of less clearance in this age group.<sup>(7)</sup> Valacyclovir is safe and causes less resistance on long term administration such as recurrent HSV infections in immunocompromised and HIV positive patients.<sup>(11)</sup>

## CONCLUSION

Primary herpetic gingivostomatitis is an acute painful infection of oral cavity. Recurrent herpetic labialis can cause irritation in lip region with discomfort and is unaesthetic. Valacyclovir, a prodrug of acyclovir with better bioavailability should be preferred over acyclovir in acute and recurrent oral HSV infections because of better compliance of valacyclovir by patients and early resolution of painful lesions.

## REFERENCES

1. Pithon, M. M. & Andrade, A. C. D. V. Primary herpetic gingivostomatitis in an adult patient using an orthodontic appliance. *Int. J. Odontostomat* 2010; 4(2):157-160.
2. Ajar AH, Chauvin P J, Acute Herpetic Gingivostomatitis in Adults: A Review of 13 Cases, Including Diagnosis and Management. *J Can Dent Assoc* 2002; 68(4):247-51.
3. Wu JJ, Brentjens MH, Torres G, Yeung-Yue K, Lee P, Tying SK..Abstract-Valacyclovir in the treatment of herpes simplex, herpes zoster, and other viral infections.*J Cutan Med Surg*.2003 Sep-Oct; 7(5):372-81. Epub 2003 Sep 24.(accessed 15may2015)

4. Richard P. Usatine, and Rochelle Tinitigan, Non genital herpes simplex virus, *Am Fam Physician*. 2010 Nov 1;82(9):1075-1082
5. GreenbergMS,Glick M, Ship JA. *Burket's Oral Medicine*.Eleventh edition.2008. BC Deckerhamilton.
6. *Pathogenesis of herpes simplex viruses infection*. virology-online.com/viruses/HSV2.htm (accessed 15 May 2015).
7. Kimberlin DW, JacobsRF, WellerS,van der Walt JS, HeitmanCK,ManCY,Bradley JS. Pharmacokinetics and Safety of Extemporaneously Compounded Valacyclovir Oral Suspension in Pediatric Patients from 1 Month through 11 Years of Age.*Clinical Infectious Diseases* 2010; 50:221–8.doi: 10.1086/649212 (accessed 16 May 2015)
8. Sankar V, TerézhalmyGT.*Herpetic Infections: Etiology, Epidemiology,Clinical Manifestations, Diagnosis, and Treatment*.Crest® Oral-B® at dentalcare.com Continuing Education Course 6May 2010.<https://www.scribd.com/doc/140394900/Herpes-pdf> (accessed 16 May 2015).
9. LaskarisG.*Treatment of Oral Diseases. A concise textbook*.2005. ThiemeVerlag.
10. Safrin, S., in: Katzung, B.G. (Eds.). *Basic and Clinical Pharmacology*, 10th edition. Mc Graw Hill, New York 2007, pp.790-818.
11. Tying ST, BakerD, Snowden W.*The Journal of Infectious Diseases* 2002;186(Suppl 1):S40–6.