



Analysis of various treatment modalities of herpetic lesions

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Article History:

Received on: 25 Aug 2020

Revised on: 29 Sep 2020

Accepted on: 07 Oct 2020

Keywords:

Antivirals,
anti-inflammatory,
analgesics,
HSV,
herpes labialis,
herpes gingivostomatitis,
systemic,
topical

ABSTRACT

Herpes Simplex Virus (HSV) is a debilitating infectious disease, often the root cause of all oral herpetic lesions. The oral herpes virus affects the individuals aesthetically, healthwise, and psychologically as well. The aim of the study is to analyze and evaluate the various treatment modalities practiced at the Department of Oral Medicine at Saveetha Dental College and Hospital, Chennai. A total of 64 participants were involved in the study conducted between the period of July 2019 - March 2020. The patients were receiving either of the following treatment: (i) Topical antivirals (ii) Topical anti-inflammatory or analgesics (iii) Systemic antivirals (iv) Systemic antipyretics (v) Supportive therapy if any. The result of the study conducted shows the prevalence of usage of 57% of topical antivirals, 12% of systemic antivirals, 12% of topical anti-inflammatory and analgesics, 13% of systemic antipyretics and 6% of supportive therapy. In conclusion, the topical antiviral drugs prescribed were of high prevalence. However, advising necessary supportive therapy can help in faster healing of the lesions.

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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11iSPL3.3523>

Production and Hosted by

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INTRODUCTION

According to the British Society for Oral Medicine (BSOM) "Oral Medicine is the specialty of dentistry concerned with the oral healthcare of patients with chronic, recurrent and medically related disorders of the oral and maxillofacial region, and with their diagnosis and non-surgical management." (Steele *et al.*, 2015). As the definition goes, oral physicians are experts trained in dealing with conditions pertaining to the orofacial region, helping

the other healthcare workers in diagnosis, treatment planning, and treating the patients via non-surgical therapies. Conditions like potentially premalignant oral epithelial lesions (PPOEL) which are disorders with 16-62% of malignant transformation (Muthukrishnan and Kumar, 2017; Maheswari *et al.*, 2018; Warnakulasuriya and Muthukrishnan, 2018), oral mucosal lesions which are pervasive and affect the quality of life of the individuals (Eg: Herpetic lesions, Recurrent Aphthous Ulcer), with a prevalence rate of 4.1% in Southern part of India (Venugopal and Maheswari, 2016; Chaitanya *et al.*, 2018), vesiculobullous lesions like pemphigus, pemphigoid and their types (Dharman and Muthukrishnan, 2016) and other orofacial painful conditions like primary temporomandibular joint disorders, neuropathic pain are few examples of disorders treated non-surgically and only through medical management by an oral physician.

Herpes Simplex Virus (HSV) is a different type of entity which is the cause of all herpetic lesions present in the body predominantly. HSV are of two types - HSV type 1 and HSV type 2. Of which, the type 1 is usually the one causing orofacial infection.

HSV type 2 is more associated with genital infection. Both types of viruses can establish latent infection within the dorsal root and trigeminal sensory ganglia. Recurrence affecting the same dermatome may occur unpredictably, causing painful recurrent diseases (Whitley and Roizman, 2001; Gupta *et al.*, 2007; Hadigal and Shukla, 2013). Similar to any metastatic carcinoma in the oral cavity with the unknown primary condition present elsewhere in the body (Misra *et al.*, 2015), the herpes simplex virus also has the potential to show both general and oral manifestations primarily being affected by the herpetic virus. When these HSV lesions recur, they tend to be more painful, however, less painful than the neuropathic pain developed in conditions like Postherpetic neuralgia (PHN) which are longer in persistence than any nociceptive pain (Subha and Arvind, 2019).

The identification of the lesion is usually carried out by clinical examination, however, if the lesion is undiagnosed investigations like the Tzanck test, viral culture, polymerase chain reaction (PCR), direct fluorescent antibody testing or serology can be performed. Since the lesions are of soft tissue origin, radiographs like CBCT or CT cannot be used as diagnostic criteria. However, in the case of diseases like PHN or any neuropathic pain caused due to HSV, 3-dimensional imaging like MRI can be suggested (Rohini and Kumar, 2017; Patil *et al.*, 2018).

The treatment of choice for all kinds of herpes simplex infections is the administration of Acyclovir (ACV). Acyclovir was introduced in the 1980s and has become the first line of therapy for HSV infections. They can be administered either topically or systemically. However, the long term use of ACV can lead to resistance of viral strains (Whitley and Roizman, 2001; Vadlapudi *et al.*, 2013). Other antiviral drugs that have similar effects like ACV are valacyclovir and famciclovir.

The study aims to evaluate the different treatment modalities practiced for the orofacial herpetic lesions in the Chennai population.

MATERIALS AND METHODS

A total of 64 participants were taken into the study randomly to avoid bias in the study. The participants of the study attended the Oral Medicine clinic at Saveetha Dental College and Hospital in Chennai between the duration of July 2019 to March 2020.

Two researchers were involved in the study - one researcher had more than 30 years of experience in the field, whereas the second researcher had fewer than 5 years of experience. The participants' nec-

essary data was retrieved through the institutional archival software for cross-references and grouped accordingly.

The study population involved a) Patients with primary or recurrent herpetic lesions related only to the oral cavity. b) Patients treated at the institution by the institutional doctors. c) Patients with regular medications and follow-up.

Patients with any other viral diseases causing ulcerations in the oral mucosa, without proper history and irregular follow-up, or patients allergic to the drugs prescribed at the institution were excluded from the study.

The patients were grouped into categories as (i) Topical antivirals (ii) Topical anti-inflammatory or analgesics (iii) Systemic antivirals (iv) Systemic antipyretics (v) Supportive therapy if any. It is made sure that the participants were receiving medications from one of the above-listed categories.

Prior to starting the study, ethical approval (SDC/SIHEC/2020DIASDATA/0619-0320) was obtained from the Institutional Scientific Review Board.

Statistical evaluation of the study was done with the help of SPSS software version 20.0. A parametric independent t-test was performed between the four treatment groups, and the statistical efficacy of the prescribed drugs was determined. Frequency distribution was performed for the demographic data of the population, types of herpetic lesions and various modalities followed at the institution.

RESULTS AND DISCUSSION

The data were grouped according to the age of the population, the gender of the population, and the treatment modality - topical or systemic antivirals, systemic antipyretics, topical analgesics and anti-inflammatory, and supportive therapy if any.

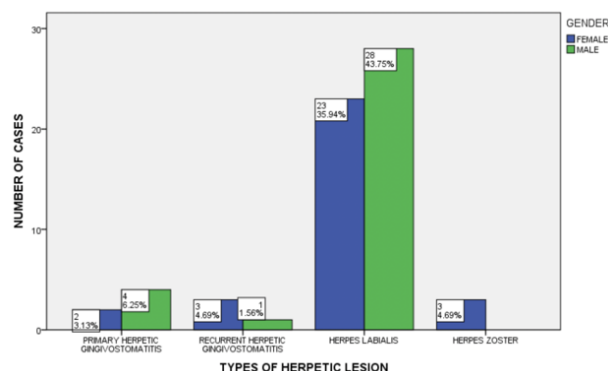


Figure 1: Bar chart showing the association between types of herpetic lesions and gender

Table 1: The overall individual frequency and percentage of the gender, age, types of herpetic lesions and treatment modalities

| Characteristics of the study population | | Frequency | Percentage |
|--|---|-----------|------------|
| Age | 0-10 years | 1 | 1.6 |
| | 11-20 years | 1 | 1.6 |
| | 21-30 years | 11 | 17.2 |
| | 31-40 years | 19 | 29.7 |
| | 41-50 years | 16 | 25.0 |
| | 51-60 years | 11 | 17.2 |
| | Above 60 years | 5 | 7.8 |
| | Total | 64 | 100.0 |
| Gender | Female | 31 | 48.4 |
| | Male | 33 | 51.6 |
| | Total | 64 | 100.0 |
| Types of herpetic lesions | Primary herpetic gingivostomatitis | 6 | 9.4 |
| | Recurrent herpetic gingivostomatitis | 4 | 6.3 |
| | Herpes labialis | 51 | 79.7 |
| | Herpes zoster | 3 | 4.7 |
| | Total | 64 | 100.0 |
| Systemic antipyretics | Ibuprofen | 3 | 4.7 |
| | Paracetamol | 13 | 20.3 |
| | Total | 16 | 25.0 |
| Topical analgesics and anti-inflammatory | Lidocaine gel | 10 | 15.6 |
| | Chlorhexidine gluconate gel | 2 | 3.1 |
| | Benzydamine mouth rinse | 2 | 3.1 |
| | Total | 14 | 21.9 |
| Systemic antivirals | Famciclovir | 3 | 4.7 |
| | Acyclovir | 9 | 14.1 |
| | Total | 12 | 18.8 |
| Topical antivirals | Penciclovir | 7 | 10.9 |
| | Acyclovir | 50 | 78.1 |
| | Total | 57 | 89.1 |
| Supportive therapy | Avoid hot and spicy food, advised constant hydration | 4 | 6.3 |
| | Avoid hot and spicy food, denture wearing for 5 days and constant hydration | 2 | 3.1 |
| | Tablet zincovit for 2 weeks | 2 | 3.1 |
| | Total | 8 | 12.5 |

The results of the study showed that, of the 64 participants, 31 were female participants, and 33 were male, and the highest prevalence of male patients were seen in herpes labialis condition (43.7%). In female patients, 35.9% of the highest prevalence was evident in herpes labialis condition. The X-axis shows the various types of herpetic lesions, and Y-axis denotes the number of cases. The association between female (Blue) and male (green) among the types of herpetic lesions was found to

be statistically not significant with a p-value of 0.97 >0.05 (chi-square test) (Figure 1). Analysing the age of the population, the highest prevalence was seen in the age group 31-40 years, where 16 (25%) patients were present with herpes labialis. The X-axis shows the age and Y-axis denotes the number of cases. The association between types of herpetic lesions - primary herpetic gingivostomatitis (red), recurrent herpetic gingivostomatitis (purple), herpes labialis (yellow) and herpes zoster (grey)

Table 2: The statistical analysis of the treatment modalities

| Types of Drugs | Gender | Total (n) | Mean | p |
|--|--------|-----------|------|-------|
| Systemic antipyretics | Female | 10 | 1.90 | 0.041 |
| | Male | 6 | 1.67 | |
| Topical analgesics and anti-inflammatory | Female | 9 | 1.56 | 0.05 |
| | Male | 5 | 1.20 | |
| Systemic antivirals | Female | 5 | 1.80 | 0.53 |
| | Male | 7 | 1.71 | |
| Topical antivirals | Female | 27 | 1.85 | 0.27 |
| | Male | 30 | 1.90 | |

$p > 0.05$ - statistically not significant, but clinically significant. $p = 0.05$ - statistically significant. $p < 0.05$ - statistically significant.

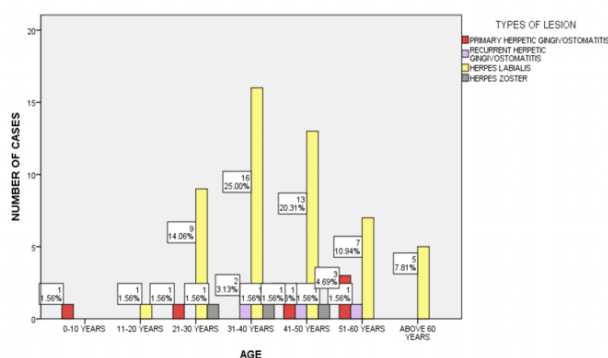


Figure 2: Barchart showing the association between types of herpetic lesions and age

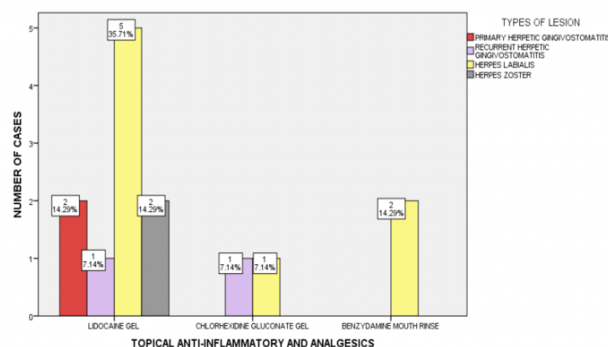


Figure 4: Barchart showing the association between types of herpetic lesions and topical anti-inflammatory and analgesics

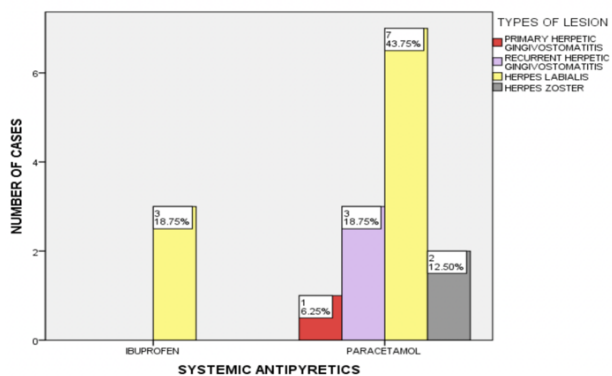


Figure 3: Barchart showing the association between types of herpetic lesions and systemic antipyretics

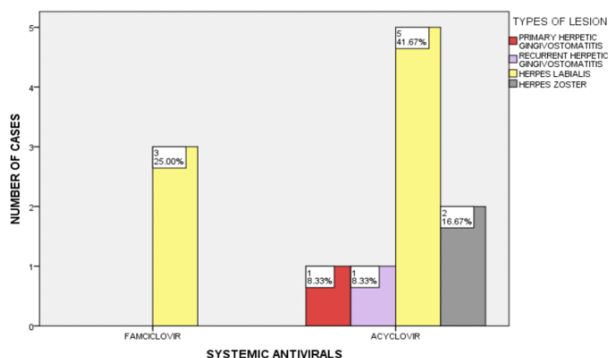


Figure 5: Barchart showing the association between types of herpetic lesions and systemic antivirals

among the age group was found to be statistically not significant with a p-value of 0.48 > 0.05 (chi-square test) (Figure 2). On comparing the two systemic antipyretics prescribed, it is observed that paracetamol was widely advised for all types of herpetic lesions. The X-axis shows the systemic antipyretics and Y-axis denotes the number of cases. The association between types of herpetic lesions - primary herpetic gingivostomatitis (red), recurrent herpetic gingivostomatitis (purple), herpes labialis (yellow) and herpes zoster (grey) among the sys-

temic antipyretic group - ibuprofen and paracetamol were found to be statistically not significant with a p-value of 0.52 > 0.05 (chi-square test) (Figure 3). In Figure 4, the topical anti-inflammatory and analgesics were observed, and it states that lidocaine gel was prescribed more to the patients. The X-axis shows the topical anti-inflammatory and analgesics, and Y-axis denotes the number of cases. The association between types of herpetic lesions - primary herpetic gingivostomatitis (red), recurrent

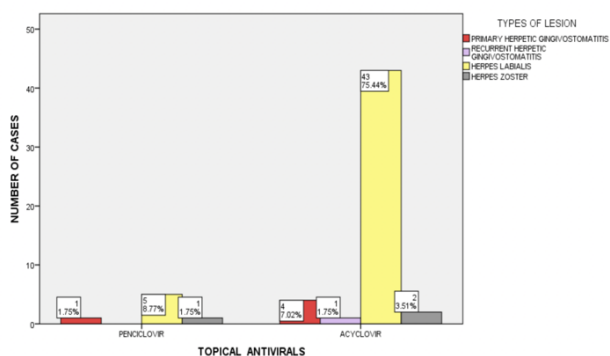


Figure 6: Barchart showing the association between types of herpetic lesions and topical antivirals

herpetic gingivostomatitis (purple), herpes labialis (yellow) and herpes zoster (grey) among the topical anti-inflammatory and analgesics group - lidocaine gel, chlorhexidine gluconate gel and benzydamine mouth rinse was found to be statistically not significant with a p-value of $0.53 > 0.05$ (chi-square test). Systemic antivirals and topical antivirals were described in Figure 5 and Figure 6 respectively. It states that acyclovir both systemic (14.1%) and topical (78.1%) application showed a higher prevalence than systemic famciclovir or topical penciclovir. These were prescribed widely in all types of herpetic lesions. In Figure 5, X-axis shows the systemic antivirals and Y-axis denotes the number of cases. The association between types of herpetic lesions - primary herpetic gingivostomatitis (red), recurrent herpetic gingivostomatitis (purple), herpes labialis (yellow) and herpes zoster (grey) among the systemic antivirals group - famciclovir and acyclovir were found to be statistically not significant with a p-value of $0.097 > 0.05$ (chi-square test). In Figure 6, X-axis shows the topical antivirals and Y-axis denotes the number of cases. The association between types of herpetic lesions - primary herpetic gingivostomatitis (red), recurrent herpetic gingivostomatitis (purple), herpes labialis (yellow) and herpes zoster (grey) among the topical antivirals group - penciclovir and acyclovir was found to be statistically significant with a p-value of $0.049 < 0.05$ (chi-square test).

The overall individual frequencies and percentages of the study population are seen in table 1. 51.6% of the male population is affected, which is higher than the female population at 48.4%. 29.7% of the population affected with herpetic lesions are present between the age group 31-40 years. 79.7% of the population were present with herpes labialis, and only 4.7% of the study population had herpes zoster which is caused by Varicella zoster virus in the

human body. 25% of patients were advised systemic antipyretics, 21.9% of the patients were under topical anti-inflammatory and analgesics, 18.8% of the patients were under systemic antivirals, and 89.1% of them were advised topical antiviral drugs.

Apart from prescribing drugs, certain patients were advised supportive therapies. The supportive therapies include a) Avoidance of any hot and spicy food. b) Restricted to wear dentures for a shorter period of time. c) Vitamin supplements like tablet zincovit. All the above mentioned supportive measures were either advised alone or in combination with the other therapies. Prevalence of 12.5% of patients was advised supportive therapies during the treatment.

Improper maintenance of oral hygiene can enhance the recurrence of the herpetic lesions, and thus proper maintenance of oral hygiene was emphasized to minimize the recurrence rate of herpetic lesions. (Choudhury, 2015; Subashri and Maheshwari, 2016).

The effectiveness of the prescribed medications was described in table 2 detailedly. Of 64 patients, 57 (89.1%) of the patients were advised topical antiviral drugs, namely acyclovir and penciclovir. Though clinically significant, the statistical efficacy of the drugs was not significant. On the other hand, the topical anti-inflammatory and systemic antipyretics, 21.9% and 25% respectively were administered in patients and showed both clinical and statistical significance.

You *et al.* (2015) conducted a study in the Chinese population, first of its kind in China with inosine pranobex versus acyclovir in the treatment of recurrent herpes labialis infection. Similarly, in 2017 Semprini A did a study comparing 90% Kanuka honey versus 5% acyclovir for the treatment of HSV - herpes labialis in the community setting. He found that the efficacy of the kanuka honey was greater in comparison with acyclovir for herpes labialis (Semprini *et al.*, 2017). Precautions from the usage of medications have to be taken, as the drugs used for curing can cause ill-effects, and hence cautious administration of drugs is mandatory (Muthukrishnan *et al.*, 2016).

From the current study, it is understood that the topical acyclovir was predominantly prescribed to patients with herpetic lesions. However, there was no statistical significance seen between the systemic and topical antiviral groups. These medications were proven to be effective clinically though. The systemic antipyretics prescribed like paracetamol and ibuprofen, and topical anti-inflammatory and analgesics were proven to be both clinically and statistically significant.

The limitation of the study is that like oral mucositis, and oral herpetic lesions also have a severe physical and mental disability during the treatment prompting interventions either to prevent such occurrence or treat them (Chaitanya, 2017). Necessary precautionary measures have to be followed to avoid future recurrences.

CONCLUSION

Topical antiviral drugs were prescribed majorly than any other drugs in the study. The healing of the herpetic lesions was, however, seen to be faster in patients consuming systemic antipyretics and topical anti-inflammatory drugs along with topical antivirals than the administration of topical antiviral drugs taken alone. However, additional measures like avoidance of hot and spicy foods, etc., paved the way for faster and better healing of the lesion. This study can also be carried forward to check for other placebo trials as a treatment modality for oral herpetic lesions.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

Funding Support

The authors declare that they have no funding support for this study.

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