

The Synergetic Effect of Alternative Medicine with Acyclovir in the Treatment and Control of Herpes Labialis; HSV1

Kouka Abdelwahab Saadeldin, Mohammad Mustafa Aljafar,
Abdulwahab Abdullah Alghamdi, Morshed Ali Alsawidan, Ali Hassan Almalki,
Fahad Sulaiman Alateeq, Abdulaziz Abdulsalam Alsudairi

Faculty of Medicine, Imam Abdulrahman AlFaisal University, Dammam, Saudi Arabia

ABSTRACT

Background: herpes simplex is a common viral infection of the skin or mucous membranes. The lesions caused by this infection are often painful, burning, or pruritic, and tend to recur in most patients. Short term treatment with acyclovir can accelerate the healing of an acute outbreak, and continuous acyclovir therapy is often prescribed for people with frequent recurrences. While this drug can reduce the recurrence rate by 60-90 percent, it can also cause a wide array of side effects, including renal failure, hepatitis, and anaphylaxis. Safe and effective alternatives are therefore needed. **Aim of the Study:** is to examine and provide evidence on the potent effect of alternative medicine in Herpes treatment and recurrence prevention. **Patients and methods:** 60 Patients were divided into 3 major groups according to the severity of the infection with 7 subgroups split according to the treatment protocol.

Results: among 60 patients with varies severity, recurrence of outbreaks was significantly reduced when a combined therapy was used while 0-10 percent outbreak recurrence rate was observed for a year when alternative therapy was used alone for mild cases.

Conclusion: there is evidence that certain dietary modifications and the use of alternative medicine can be significantly useful for treating active Herpes simplex lesions and preventing recurrences.

Keywords: HSV1, Herpes Labialis, Alternative medicine, Acyclovir.

INTRODUCTION

Herpes virus is an infectious DNA virus belonging to Herpesviridae family that causes latent and lytic infections in a wide range of animals and humans. There are 8 herpesvirus types known to infect humans: herpes simplex viruses 1 and 2 (HSV-1 and HSV-2, aka. HHV1 and HHV2), varicella-zoster virus (VZV, which may also be called by its ICTV name, HHV-3), Epstein-Barr virus (EBV or HHV-4), human cytomegalovirus (HCMV or HHV-5), human herpesvirus 6A and 6B (HHV-6A and HHV-6B), human herpesvirus 7 (HHV-7), and Kaposi's sarcoma-associated herpesvirus (KSHV, also known as HHV-8)⁽¹⁾.

Human herpes viruses may cause infections of the central nervous system during primary infection or following reactivation from a latent state. Especially in immunosuppressed patients, the infection can take a life-threatening course, and therefore early diagnosis of herpesvirus-associated neurological diseases should have high priority⁽²⁾.

Herpes simplex viruses (HSV) are part of the alpha herpes virus subfamily of herpes viruses. There are two types of HSV: type-1 (HSV-1) and type-2 (HSV-2). These viruses are neurotropic capable of infecting the nervous system and causing neurological diseases. Moreover, Herpes viridae family; HSV results in a lifelong infection by establishing latency in the host sensory neurons and replicating in epithelial cells during

primary infection and reactivation. Moreover, HSV results in a lifelong infection by establishing latency in the host sensory neurons and replicating in epithelial cells during primary infection and reactivation⁽³⁾

Unlike many herpes viruses, HSV has low species specificity and a wide host range. It has the unparalleled ability to infect human and nonhuman cells alike⁽⁴⁾. The reason behind this successful story of infection is an accumulation of multiple supporting factors include:

- Possessing several multifunctional HSV glycoproteins to which corresponds an array of HSV entry receptors in the human body and evidence suggests even more unidentified HSV receptors.
- Multiple entry modes. HSV has the ability to enter into host cells by direct fusion with the plasma membrane, or via endocytic pathways. The latter can be pH dependent or independent.
- Multiple spread strategies of HSVs, including: transmission of free virions, movement of HSV along filopodia-like cellular membrane protrusions (surfing) towards the cell body, and lateral cell-to-cell spread.

The virus is spread and transmitted among humans through physical contact and commonly causes localized mucocutaneous lesions^[2]. Oral and ocular lesions are primarily caused by HSV-1 and genital lesions by HSV-2. However, HSV-2

is capable of causing ocular lesions in newborns of HSV-2 infected mothers. In that case, HSV-2 is transmitted to newborns primarily during peripartum period as a result of disrupted membranes, or by direct contact with the mother's vaginal secretions and infected cervix⁽⁵⁾. These viruses are also capable of causing more serious diseases, such as blindness, meningitis, and encephalitis⁽⁶⁾. HSV-1 is a leading cause of viral corneal blindness and viral encephalitis in developed countries⁽⁷⁾.

Herpes simplex labialis, more commonly known as a cold sore, is caused by Herpes simplex virus type-1 (HSV-1). It is a common recurrent disease affecting 40 percent of the population worldwide⁽⁸⁾. After primary infection the virus resides in the associated dorsal root ganglion and establishes a long latency period. This is the period during which the infectious virus cannot be detected with standard virus isolation procedures. External

stimuli such as stress and immunosuppression usually initiate reactivation of the virus from dormancy⁽⁹⁾.

Recurrent HSV-1 lesions usually develop on the lower lip but can also be found on the upper lip, nose, cheek, chin, and eyelid (Figure 1). The resultant epithelial cell death and inflammatory response leads to the characteristic vesicular (sometimes even pustular) and ulceronecrotic lesions. The lesions of herpes labialis tend to occur on the outer third of the lips, and the lower lip is more frequently involved than the upper lip. Lesions on the nose, chin, or cheeks account for less than 10% of cases. Lesions are most often single; "secondary lesions," those appearing one or more days after the first sore, develop in one fifth of cases. HSV1 replicates in ganglia before establishing latent phase.

Figure 1⁽¹⁰⁾

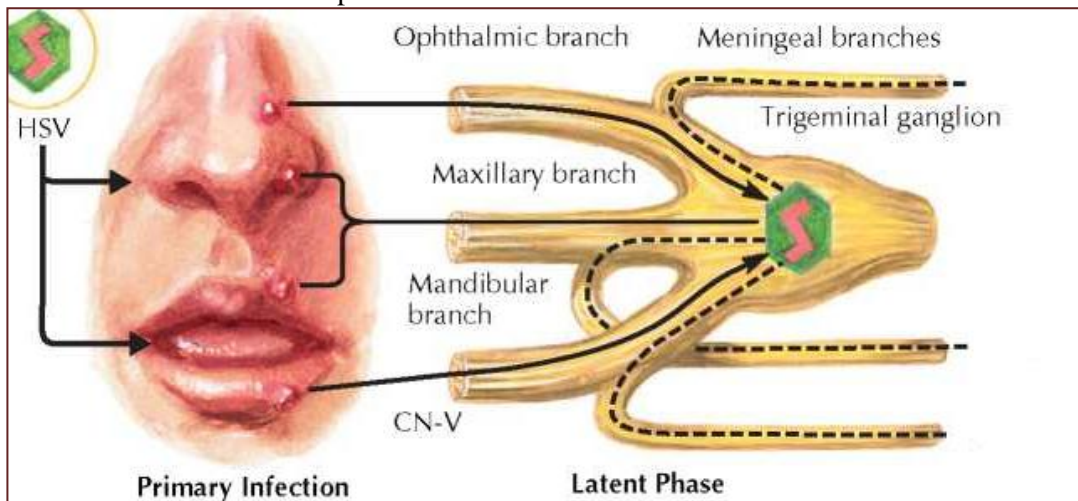


Figure 1: HSV1 enters via cutaneous or mucosal surfaces to infect sensory or autonomic nerve endings with transport to cell bodies in ganglia (Courtesy Salt Lake City/County STD Clinic)

At an active state, symptoms start to develop gradually to reach more painful and contagious phases and hence, stages of Symptoms progression were closely observed and monitored in order to accurately tailor treatment to the specific and right stage – **Figure 2**⁽¹⁰⁾.

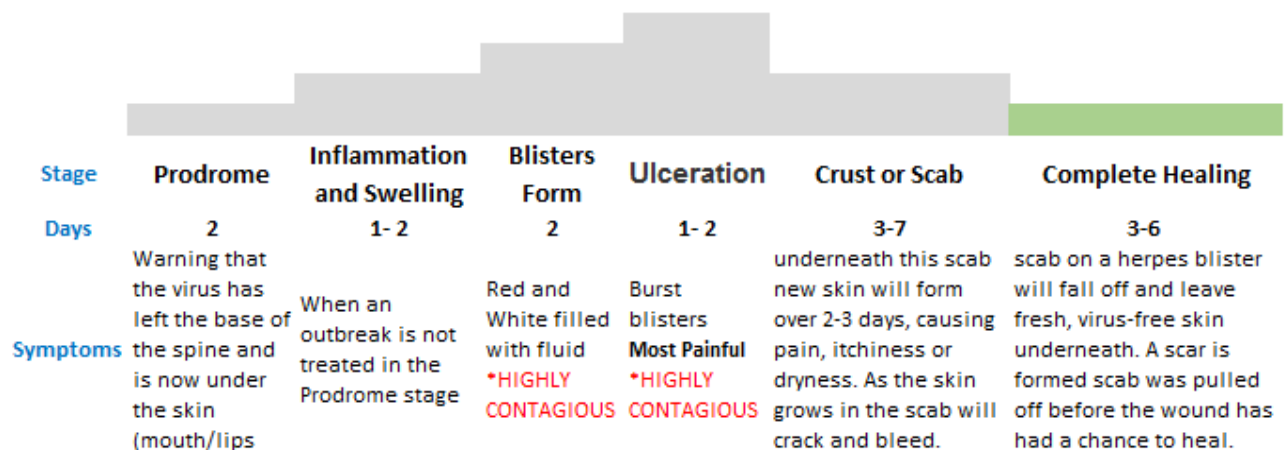


Figure 2: Stages of Oral Herpes- Herpes Labialis- manifested over the course of observation and treatment,*Days vary according to the severity of infection⁽¹¹⁾.

For many, a herpes virus recurrence represents a nuisance; however, for immunocompromised individuals (with HIV, for example) this infection is associated with increased morbidity and mortality⁽¹²⁾. Individuals with severe immunosuppression were excluded from participation in this study.

PATIENTS AND METHODS

A cross-sectional study was carried out at Al Noor Specialist Hospital in Makkah, Saudi Arabia. A representative sample of 60 HSV1 infected patients (18-50 years) of both sexes were included and observed for one year provided that:

- 1- Confirmation of facial or circumoral herpes lesion was completed by a clinician on site.
- 2- Patients of choice were confined to a strict dieting following the treatment protocol.
- 3- Subjects expressed willingness to satisfactorily complete a patient diary for the length of the study (maximum of 21 days).

Exclusion Criteria:

1. Patients had history of past or present immunosuppressive condition, either due to a disease or immunosuppressive medication.
2. Patients had signs of disseminated HSV illness; history of use of - unprescribed /advised in the protocol of the study -oral or topical antiviral agents within 10 days of entry into the study and/or at first study visit
3. Pregnancy or lactation.

60 patients were divided into 3 groups with respect to severity with subgroups according to the selected treatment protocol:

Group A: Patients diagnosed with HSV1 with mild symptoms with the following subgroups:

A1: Diet change *with no drug administration orally or topically.

A2: No dieting or lifestyle limitation and Acyclovir cream applied topically on the lips area.

Group B: Patients diagnosed with HSV1 with moderate severity of symptoms, divided into the following subgroups:

B1: Diet change *with no drug administration orally or topically.

B2: No dieting or lifestyle limitation and Acyclovir cream applied topically.

B3: No dieting or lifestyle limitation and 200 mg Acyclovir tablets administered orally three times daily x 5d.

Group C3: Patients diagnosed with HSV1 with relatively severe manifestation divided into the following subgroups:

C1: Strict diet* and lifestyle change. 400 mg Acyclovir tablets administered orally three times daily x 5d + Acyclovir cream was applied locally on the blisters.

C2: No dieting or lifestyle limitation. 400 mg Acyclovir tablets administered orally three times daily x 5d + Acyclovir cream was applied locally on the blisters.

Methods

Self-administered questionnaire in Arabic language was conducted by the researchers in order to collect data from 60 patients attending dermal clinics. It included demographic data, outbreak history, lifestyle and social factors such as: age of first onset, Type of Herpes diagnosed and diagnostic test used (Physical examination only, Living cell culture, PAP smear, others), symptoms manifested during lesion formation (sharp pains, itching, ...etc.), frequency and average duration of outbreak occurrences, patients treatment history, nutrition habits, potential and accidental stress factors involves, possible stimulus preceding Prodrome and noticeable progression of the symptoms in the past.

Diagnosis, repetitive admission and outbreaks history data was also pulled from the file of the patients and a re-diagnosis was done through physical examination and Type-Specific blood tests to confirm infection and possible future HSV2 outbreaks in patients with no symptoms.

Medication

- 1- Acyclovir 5% cream for topical application
- 2- Acyclovir 200 and 400 tablets for oral administration

- 3- Panthenol 5% on the perioral area

Life Style changes

Patients were advised to avoid HSV recurrences triggers, such as:

- Extreme physical conditions: Physical (Sun/UV light exposure), overexposure to wind, cold, wet, heat, and sweating.
- Emotional Stress.
- Smoking

Patients were also advised to go a regular stress relieving exercises like walking, Yoga...etc.

Dietary changes

Selective dietary regimen was followed with accordance to the below:

Lysine/Arginine ratio:

- Avoid low-lysine, high-arginine food intake : such as chocolate, nuts, oats, wheat products, protein supplements

- Divert to high Lysine/Arginine ratio food: fruits like apples, figs, Apple, Dietary products, particularly gelatin-free Yogurt and all kind of meat.

Table 1 illustrates dietary sources of lysine (mg/serving), arginine levels (mg/serving) of these same foods, as well as the arginine: lysine

ratio; which was handed out to the selected patients for reference with accordance to the data from *Agricultural Handbook by U.S. Department of Agriculture* which was handed out to the patients.

Table 1: Ratio of Lysine to Arginine in Certain Foods, the list below was printed and handed out to patients confided to dietary restriction in the treatment protocol⁽¹³⁾.

Transcribed and calculated using data from *Agricultural Handbook, 1-23, U.S. Department of Agriculture*.

	Weight (g)	Lys (mg)	Arg (mg)	Ratio Lys/Arg
Margarine	14.1	9	3	3.000
Plain Yogurt	227	706	237	2.979
Fruit Yogurt, lowfat	227	810	272	2.978
Plain Yogurt, skim	227	1160	391	2.967
Plain Yogurt, lowfat	227	1060	359	2.953
Swiss Cheese	28	733	263	2.787
Gruyere Cheese	28	768	276	2.783
Edam Cheese	28	754	273	2.762
American Cheese Spread	28	427	155	2.755
Gouda Cheese	28	752	273	2.755
Whey, dry, sweet	7.5	77	28	2.750
Blue Cheese	28	526	202	2.604
Provolone Cheese	28	750	290	2.586
Papaya	454	76	30	2.533
Brie Cheese	28	525	208	2.524
Camembert Cheese	28	501	199	2.518
Parmesan Cheese	28	937	373	2.512
Parmesan Cheese, grated	5	192	77	2.494
Gjetost Cheese	28	231	93	2.484
Goat Milk	244	708	291	2.433
Brick Cheese	28	602	248	2.427
Muenster Cheese	28	606	250	2.424
Beets	136	72	30	2.400
Limburger Cheese	28	475	198	2.399
Tilsit Cheese	28	578	241	2.398
Port du salut Cheese	28	563	235	2.396
Processed Swiss Cheese	28	696	293	2.375
Cream Cheese	28	192	81	2.370
Mozzarella Cheese, part s	28	699	295	2.369
Processed American Cheese	28	623	263	2.369
Mozzarella Cheese	28	559	236	2.369
Neufchatel Cheese	28	253	107	2.364
Butter	14.1	9	4	2.250
Colby Cheese	28	561	254	2.209
Monterey Jack Cheese	28	578	262	2.206
Cheshire Cheese	28	551	250	2.204
Cheddar Cheese	28	588	267	2.202
Buttermilk	245	679	309	2.197
Skim Milk	245	663	302	2.195
Half and Half Cream	242	568	259	2.193
Sherbet	193	171	78	2.192
Condensed Milk, sweetened	306	1920	876	2.192
Chocolate Milk	250	629	287	2.192

Nonfat Milk, dry	120	3440	1570	2.191
Lowfat Milk, 2%	244	644	294	2.190
Evaporated Milk	126	681	311	2.190
Ice Cream	133	381	174	2.190
Whole Milk	244	637	291	2.189
Whole Milk, dry	128	2670	1220	2.189
Nonfat Milk, dry, instant	68	1890	864	2.188
Ice Milk	131	409	187	2.187
Whipping Cream, heavy	238	387	177	2.186
Evaporated Milk, skim	128	763	349	2.186
Whipping Cream, light	239	411	188	2.186
Ice Cream, rich	148	327	150	2.180
Mango	300	85	39	2.179
Whipped Cream, pressurize	60	152	70	2.171
Apricot	114	103	48	2.146
Coffee Cream	15	32	15	2.133
Apple	150	17	8	2.125
Ricotta Cheese	246	3290	1550	2.123
Ricotta Cheese, part skim	246	3320	1570	2.115
Pear, dried	175	116	56	2.071
Eggnog	254	758	378	2.005
Applesauce, unsweetened	244	24	12	2.000
Crabapple, slices	110	28	14	2.000
Loquat	16	2	1	2.000
Apple, dried	64	37	19	1.947
Pear	180	23	12	1.917
Apricot, dried	35	89	49	1.816
Cottage Cheese, creamed	210	2120	1190	1.782
Cottage Cheese, Lowfat 2%	226	2510	1410	1.780
Cottage Cheese, dry	145	2020	1140	1.772
Fig, dried	189	228	131	1.740
Fig	65	19	11	1.727
Human Milk	246	168	105	1.600
Avocado	272	189	119	1.588
Salmon	85	1550	1000	1.550
Swordfish	85	1550	1000	1.550
Haddock	85	1480	961	1.540
Smelt	85	1380	897	1.538
Snapper	85	1600	1040	1.538
Pollock	85	1520	989	1.537
Eel	85	1440	938	1.535
Catfish	85	1420	925	1.535
Anchovy, in oil, drained	20	531	346	1.535
Whitefish	85	1490	971	1.535
Tuna, in water	165	4480	2920	1.534
Cod	85	1390	906	1.534
Flat fish, flounder and s	85	1470	959	1.533
Mackerel	85	1450	946	1.533
Shark	85	1640	1070	1.533
Carp	85	1390	907	1.533
Pike	85	1500	979	1.532
Herring	85	1400	914	1.532
Sardines, in oil, drained	24	542	354	1.531
Bass	85	1380	902	1.530
Perch	85	1450	948	1.530
Bluefish	85	1560	1020	1.529
Halibut	85	1620	1060	1.528

The Synergetic Effect of Alternative Medicine...

Tomato	123	41	27	1.519
Turnips	130	47	31	1.516
Tomato juice	243	54	36	1.500
Soybean sprouts	70	386	266	1.451
Canadian Style Bacon	454	7370	5100	1.445
Wild pheasant	371	7470	5240	1.426
Pork Spareribs	454	4730	3340	1.416
Tomato paste	262	282	200	1.410
Liver cheese	28	334	237	1.409
Chicken, dark meat, w/o s	109	1860	1320	1.409
Chicken, light meat w/o s	88	1730	1230	1.407
Chicken neck	79	298	212	1.406
Summer sausage	23	318	228	1.395
Pineapple	155	39	28	1.393
Pork leg	454	7550	5530	1.365
Pork loin chop	151	1950	1430	1.364
Pork Shoulder	454	7140	5240	1.363
Potato	150	190	140	1.357
Chicken breast	181	2500	1870	1.337
Cream of Mushroom soup	244	127	95	1.337
Turkey noodle soup	244	212	159	1.333
Celery	120	32	24	1.333
Chicken drumstick	110	1160	872	1.330
Potato, baking	202	283	214	1.322
Beef Flank steak	454	7270	5500	1.322
Chicken gumbo	244	161	122	1.320
Chicken noodle soup	241	219	166	1.319
Beef Round steak	454	7320	5550	1.319
Beef noodle soup	244	261	198	1.318
Vegetable w/beef soup	244	344	261	1.318
Cream of Asparagus soup	244	112	85	1.318
Porterhouse steak	454	6560	4980	1.317
Beef T-bone steak	454	6330	4810	1.316
Beef Sirloin steak	454	6880	5230	1.315
Knockwurst	68	634	482	1.315
Beef Rib roast	454	6050	4600	1.315
Beef Short ribs	454	5430	4130	1.315
Beef Chuck roast	454	6900	5250	1.314
Beef Tenderloin	454	6990	5320	1.314
Persimmon	200	55	42	1.310
Squash, summer	130	85	65	1.308
Chicken leg	231	2470	1890	1.307
Chicken, light meat	116	1920	1470	1.306
Ham, boneless	454	6750	5170	1.306
Chicken canned, boned	142	2500	1920	1.302
Turkey, dark meat	152	2620	2020	1.297
Cream of chicken soup	244	215	166	1.295
Chicken heart	6.1	79	61	1.295
Turkey, light meat	180	3540	2740	1.292
Bratwurst, ckd	85	910	706	1.289
Turkey, canned boned	142	3040	2360	1.288
Italian sausage, ckd	67	1020	792	1.288
Pork sausage	28	252	196	1.286
Wild quail	405	6660	5180	1.286
Chicken thigh	120	1310	1020	1.284
Chicken, dark meat	160	2150	1680	1.280

Goose, domesticated	320	4010	3150	1.273
Pork and beef sausage	13	141	111	1.270
Bologna, beef and pork	28	250	198	1.263
Peach, dried	130	151	120	1.258
Black bean soup	247	415	331	1.254
Bean w/ frankfurters soup	250	415	331	1.254
Peach	115	20	16	1.250
Corned Beef, brisket	454	5100	4100	1.244
Pastrami	28	375	302	1.242
Bologna, beef	28	254	205	1.239
Frankfurter, beef	45	389	314	1.239
Ground beef, regular	113	1560	1260	1.238
Cream of celery soup	244	73	59	1.237
Ground beef, lean	113	1670	1350	1.237
Chicken liver	32	35	352	1.236
Duck liver	44	624	505	1.236
Turkey liver	102	1540	1250	1.232
Mortadella	28	358	291	1.230
Goose liver	94	1160	943	1.230
Plum	5.5	90	74	1.216
Green beans	110	97	80	1.213
Chicken back	177	1090	900	1.211
Beef smoked, chopped	28	467	386	1.210
Pork Bacon	454	2900	2400	1.208
Beef, dried	28	673	557	1.208
Brotwurst	28	323	268	1.205
Polish sausage	28	315	262	1.202
Salami, hard	10	182	152	1.197
Bologna, pork	28	341	285	1.196
Chicken wing	90	698	585	1.193
Braunschweiger	28	258	217	1.189
Duck, domesticated	287	2610	2210	1.181
Lentil sprouts	77	548	470	1.166
Lettuce, romaine	56	58	50	1.160
Lettuce, iceberg	75	60	52	1.154
Caviar, black and red	16	293	254	1.154
Cauliflower	100	108	96	1.125
Vienna sausage	16	127	113	1.124
Liver	113	1570	1420	1.106
Guava	112	21	19	1.105
New England Clam Chowder	244	251	229	1.096
Cream of potato soup	244	83	76	1.092
Spinach	55	98	90	1.089
Kale	67	132	123	1.073
Chicken rice soup	241	251	234	1.073
Kielbasa	28	286	267	1.071
Frankfurter, beef and por	45	407	382	1.065
Whole Egg	50	410	388	1.057
Egg White	33	206	195	1.056
Whole Egg, dried	5	155	147	1.054
Watermelon	160	99	94	1.053
Cabbage, chinese	70	62	59	1.051
Corn	154	210	200	1.050
Sweet potato	130	105	100	1.050
Turnip greens	55	54	52	1.038
Abalone	85	1090	1060	1.028
Oysters	84	444	433	1.025

The Synergetic Effect of Alternative Medicine...

Clams	180	1720	1680	1.024
Scallops	85	1060	1040	1.019
Banana	175	55	54	1.019
Asparagus	134	194	192	1.010
Oat flakes	48	583	579	1.007
Mayonnaise	185	1400	1400	1.000
Vegetarian vegetable soup	241	99	99	1.000
Beet greens	38	20	20	1.000
Endive	50	32	32	1.000
Leeks	124	97	97	1.000
Pumpkin	245	96	96	1.000
Shrimp	85	1500	1510	0.993
Crab	85	1350	1360	0.993
pea soup w/ham	253	696	703	0.990
Lima beans, cooked	170	765	775	0.987
Egg Yolk	17	189	193	0.979
Okra	100	82	84	0.976
Broccoli	88	124	128	0.969
Chicken gizzard	37	465	484	0.961
Strawberries	149	37	39	0.949
Collards	186	140	72	0.931
Minestrone soup	241	183	198	0.924
Carrots	110	44	48	0.917
Dates	83	50	55	0.909
Peppers, sweet	100	38	42	0.905
Radish	45	16	18	0.889
Watercress	104	172	200	0.860
Swiss chard	36	36	42	0.857
Eggplant	82	42	50	0.840
Tomato soup	244	51	61	0.836
Cabbage, common	70	40	48	0.833
Wheat germ	180	1330	1790	0.743
Peas, green	146	463	625	0.741
Brussels sprouts	88	130	178	0.730
Tangerine	116	27	37	0.730
Orange	180	62	85	0.729
Onions, green	100	4	6	0.667
Mushrooms	70	48	72	0.667
Cucumber	104	22	36	0.611
Wheat granules	28.4	101	169	0.598
Corn grits	242	68	114	0.596
Snails	85	1250	2100	0.595
Wheat, shredded	23.6	79	133	0.594
Wheat flakes	33	101	171	0.591
Cream of wheat	251	98	166	0.590
Pistachios, shelled	128	1640	2790	0.588
Corn, puffed	28.4	65	112	0.580
Wheat, puffed	12	49	85	0.576
Squash, winter	205	902	1590	0.567
Bran flakes	47	177	314	0.564
Elderberries	145	38	68	0.559
Plantain	148	89	160	0.556
Oats, puffed	28.4	175	320	0.547
Oatmeal	234	78	147	0.531
Cashews	160	246	470	0.523
Chestnuts, fresh	160	246	470	0.523

Rice, puffed	14	38	73	0.521
Yams	200	89	191	0.466
Pumpkin seeds & squash	140	2530	5570	0.454
Garlic	3	8	19	0.421
Macadamia nuts	134	434	1200	0.362
Blackberries	145	17	49	0.347
Blueberries	145	17	49	0.347
Onions, mature	160	90	262	0.344
Grapes, slip skin	153	13	42	0.310
Grapes, adherent skin	160	24	78	0.308
Peanuts	144	1450	5050	0.287
Peanut butter	15	176	613	0.287
Coconut, shredded	80	118	437	0.270
Almonds	142	946	3540	0.267
Rutabaga	140	55	207	0.266
Pecans	108	315	1190	0.265
Sesame seeds	150	1240	4990	0.248
Hickory nuts	15	70	298	0.235
Brazil nuts	140	757	3350	0.226
Tahini	15	82	378	0.217
Grape juice	253	25	119	0.210
Tangerine juice	247	17	84	0.202
Pine nuts	28	256	1330	0.192
Orange juice	248	22	117	0.188
Hazelnuts	135	459	2480	0.185
Walnuts	100	466	2520	0.185

2. Sugar intake:

In some cases, ingestion of even small amounts of refined sugar appears to trigger an exacerbation. Restriction of refined-carbohydrate intake should, therefore, be considered on a case-by case basis.

3. Packaged, Processed and Junk food avoidance.

4. Vitamin C: 250-500 mg ascorbic acid per day for 7-10 days.

5. Antiviral and antibacterial natural Food: food that contain organosulfur compounds such as Garlic, onion...etc.

6. Topical Zinc treatment (Zinc monoglycerolate (n=102))

7. Cotton saturated with vitamin E oil (20,000-28,000 IU per ounce) was placed over it for 15 minutes

8. Apple cider vinegar application on the sores.

Treatment protocol

Alternative medicine treatment includes all of the Dietary and life style changes mentioned above.

The study was done after approval of ethical board of University of Dammam, and an informed written consent was taken from each participant in the study.

RESULTS

Groups and subgroups classification, treatment protocol, complications and recurrence data are explained in **Table 2**

Clinical findings

Patients with mild cases responded immediately to Acyclovir cream in the prodrome stage and symptoms didn't manifest in 70% of the patients. When Prodrome phase passed undetected, 1-2 days later usually the symptoms proceed to the next phase when a blister is formed and painful stages would follow. 5% Acyclovir cream was very beneficial in the early stages.

Group A: manifestation of HSV1 - referred to as "cold sores" - lesion varied from a single blister to a cluster on-and slightly around -the lips.

- Subgroup A1: when alternative medicine was used (Diet and lifestyle changes only without the use of medication (Acyclovir), 60% of the patients with mild symptoms (max of 1-2 blisters during the outbreak)had a 6-8 days full cycle recovery time while 40% had it up to 10 days before the lips could completely restore a normal healthy state.

- Subgroup A2: when only topical Acyclovir was applied, phases were accelerated and 70% of patients have fully recovered in 6-8 days when treated in the prodromal phase; failing to detect the prodromal phase resulted in a slowdown in the healing process up to 10 days.

Group B: manifestation of HSV1 - referred to as “cold sores” –75% of the patients experienced multiple outbreaks all over and around the lips while 25% had the virus extended to the nasal area (in and around the nose).

- Subgroup B1: Alternative medicine alone (Homeopathic therapy + diet and life style changes) resulted in a slow progress in the healing process at first, frequent application throughout the day of lemon balm and Apple Cider Vinegar was done locally on the sores then a pickup was observed as of end of weeks 2 – however atopic eczema around the mouth was observed as well as multiple outbreaks during the first week of treatment.

- Subgroup B2: Only Acyclovir 5% cream was used and applied in the Prodrome stage when detected for 43% of the patients, however multiple outbreaks took place for all patients and a perioral dermatitis was observed on 56% of females – a further medical intervention was called for on day 5.

- Subgroup B3: a dose of 200 mg three times daily x 5d was provided to all patients. Symptoms started to reside at the end of day 2 and recovery cycle was shortened to 9-11 days, however, a local intervention for skin lesions was needed.

Group C: manifestation of HSV1 –lesions manifested in form on multiple blisters on the lips, inside and outside the nose and on eyelids for some patients, outbreaks were recurrent and aggressive, also a history of recurrence was recorded in the patients’ files.

- Subgroup C1: a combination of Diet and life style change coupled with the oral administration of 400 mg three times daily x 5d ,Topical Acyclovir Ointment for the eyes -30% of the cases had eyelids infection- and Acyclovir cream was also locally applied on the Lips and nose ; made significant effect in the prodrome phase only which was only detected in 23% of the patients , while natural remedies were used for symptomatic relief instead for the rest of the patients when Prodrome’s passed undetected and the blisters already popped out).

- Subgroup C2: Same drug dosage and forms as C1, excluding alternative medicine and life style change.

C1 subgroup has not only have a shortened episode but also the recurrence rate was minimized to 1 cases vs. 2 cases in C2 after the first 3 months only one case of recurrence taking effect (mild symptoms)afterwards for a full year vs. 3 cases (outbreaks on lips and nose) in C2 .

DISCUSSION

HSV-1 is ubiquitous, with a seroprevalence of about 60 to 85% in the adult population ⁽¹⁴⁾. Acute HSV-1 infection most commonly occurs in children and young adults as a gingivostomatitis, pharyngitis, or tonsillitis and is readily transmitted through oral secretions ⁽¹⁵⁾. Reactivation of latent infection generally presents as oral-facial disease (cold sores) ⁽¹⁶⁾.

It’s important to mention that treatment was most effective when initiated during the prodromal stage (itching, tingling, or painful sensation in the area where their recurrent lesions will develop. The prodrome often precedes lesions by a day or two. During this time, it is best to assume virus is active and, therefore, can be spread through close contact ⁽¹⁷⁾.

In this study, we have closely observed and monitored the different stages of HSV1 symptoms manifestations on the 60 patients provided the previous understanding of the virus latency and invasion mechanism.

It’s important to mention that treatment was most effective when initiated during the prodromal stage.

- Antiviral chemotherapy – Acyclovir in this case - offers clinical benefits to most symptomatic patients and is the mainstay of management. Counseling regarding the natural history of genital herpes, sexual and perinatal transmission, and methods to reduce transmission is integral to clinical management.

- Dietary restriction was based on the below evidence :

~ The proteins synthesized by HSV contain more arginine and less lysine than proteins synthesized by host cells, and arginine is required for HSV replication. In tissue culture, lysine antagonized the growth-promoting action of arginine on HSV. These observations raise the possibility that increasing either absolute lysine intake or the ratio of lysine-to-arginine

intake would be of value for the prevention and treatment of Herpes simplex infections⁽¹⁸⁾.

Sugar intake:

Ingestion of large amounts of refined carbohydrates impairs certain parameters of immune function. In rats, the addition of sucrose to the diet (10- 20% of energy) caused a dose-dependent reduction in the capacity to produce antibodies⁽¹⁹⁾. In healthy humans, acute ingestion of 75 g of glucose significantly depressed cell-mediated immune function after 30 and 60 minutes⁽²⁰⁾. Although the relationship between refined-carbohydrate intake and susceptibility to Herpes simplex has not been investigated, many patients have observed that herpetic lesions recur when they eat too many sweets.

-Ascorbic acid has been shown to inactivate a wide range of viruses in vitro, 21 including Herpes simplex virus, and to enhance immune function. Reference to this was a double-blind trial, patients with Herpes simplex outbreaks received 200 mg ascorbic acid and 200 mg water-soluble flavonoids (apparently from citrus) three times daily for three days or a placebo. Randomization was not specified. The mean time until remission of symptoms was 57-percent shorter in the active-treatment group than in the placebo group (4.2 versus 9.7 days;P<0.01) Treatment was most effective when initiated during the prodromal stage.²⁶ The importance of flavonoids as a component of this treatment is uncertain, although several different flavonoids have demonstrated antiviral activity against HSV-1 in vitro^(21,22).

-Antiviral herbs : Garlic, Ginger, Astragalus and Licorice root

-Zinc : 25 mg of zinc sulfate with 250 mg of vitamin C taken by mouth every day can prevent cold sore outbreaks altogether in some people and reduce the duration of symptoms to one day in others. Topical preparations that contain 0.01% to 0.025% zinc sulfate produce similar effects.

Group A:

A1 subgroup applied ice patches and topical preparations that contain 0.01% to 0.025% zinc sulfate twice a day with ingestion of 250 mg Vit. C , this protocol did not only have the same recovery rate of Acyclovir but also inhibited the recurrence when patients followed dietary modifications as a life style for at least 6 month during which 47 percent of subgroup A2 had

recurrent outbreaks driven by stress factors (cold , sunlight , hormonal,...etc.)

Group B:

B1&B2 subgroups have responded to the treatment similarly in the first 10 days then healing in other words applying topical Acyclovir had no superior benefit over dietary and alternative medicine treatment. 29% of B1and 31% of B2 developed mild perioral dermatitis and Atopic Eczema who we represcribed a non-steroidal anti-inflammatory creams which suggested an impaired skin immune function following the skin lesions and cracks around the mouth during the multiple outbreaks.

B3 Subgroup :subjects were prescribed a 200 mg capsule three times daily x 5d had their symptoms subsided in 6-7 days with total recovery in 10-14 days with no recurrence for 3 month, however 36% of the patients suffered a recurrence in month 6 with a single outbreak triggered by a strong Flu.

Group C:

C1&C2 subgroups: subjects were prescribed a400 mg tablet Acyclovir tablets three times daily x 5d.

72% patients fromC1 subgroup were confined to strict dieting and life style changes did not suffer reoccurrence for a year.

33% of C2 suffered recurrence with less severe symptoms in 2-6 months and repeated the same medication course, another 50% suffered an outbreak in Month 7- 11.

For both subgroups: Symptoms began to subside by day 5 and patients were monitored for recurrence as explained.

54% of the subjects suffered Nausea and vomiting throughout the course of treatment.

The use of alternative medicine has made a significant improvement to Core sore symptoms when applied locally and gradually when a selective dietary plan .

CONCLUSION

The Studied selective alternative medicine provided a potent synergic antiviral effect with Acyclovir in the treatment of Herpes Labialis in part due to the antiviral effect and another part due to antioxidant and the significant immune boosting power that can keep outbreaks under control strong enough to suppress the recurrence evidenced by a comprehensive detailed study on a variety of infected patients.

REFERENCES:

1. **John Carter and Venetia Saunders(2007).** *Virology, Principles and Applications.* John Wiley & Sons. ISBN 978-0-470-02386-0.
2. **UtaMeyding-Lamadé and Cornelia Strank(2012).** Herpesvirus infections of the central nervous system in immunocompromised patients, *TherAdvNeurolDisord.*, 5 (5): 279–296.
3. **Akhtar J and Shukla D(2009):** Viral entry mechanisms: cellular and viral mediators of herpes simplex virus entry. *FEBS J.*, 276(24):7228-7236.
4. **Spear PG and Longnecker R(2003):** Herpesvirus entry: an update. *J Virol.*, 77(19):10179-10185
5. **Jacobs RF (1998) :** Neonatal herpes simplex virus infections. *Semin Perinatol.*, 22(1):64-71.
6. **Connolly SA, Jackson JO, Jardetzky TS, Longnecker R(2011):** Fusing structure and function: a structural view of the herpesvirus entry machinery. *Nat Rev Microbiol.*, 9(5):369-381.
7. **Shoji H, Azuma K, Nishimura Y, Fujimoto H, Sugita Y and Eizuru Y(2002):** Acute viral encephalitis: the recent progress. *Intern Med.*, 41(6):420-428.
8. **Higgins CR, Schofield JK, Tatnall FM and Leigh IM(1993):**Natural history, management and complications of herpes labialis. *J Med Virol.*, 11:22-26.
9. **Jones C(2003):**Herpes simplex virus type 1 and bovine herpesvirus 1 latency. *ClinMicrobiol Rev.*,16:79-95.
10. **<http://aibolita.com/infectious-diseases/40850-herpes-labialis.html>**
11. **WWW.MD-HEALTH.COM**
12. **Huber MA(2003):** Herpes simplex type-1 virus infection. *Quintessence Int.* ,34:453-467
13. **Whitby MC (1988):** The Agricultural Handbook , U.S. ,Department of Agriculture, 1-23
14. **Nahmais A J, Lee F K, Beckman-Nahmias S (1990):** Sero-epidemiological and -sociological patterns of herpes simplex virus infection in the world. *Scand. J. Infect. Dis.* , 69:19–36
15. **Glezen W P, Fernald G W, Lohr J A (1975):** Acute respiratory disease of university students with special reference to the etiologic role of Herpesvirus hominis. *Am. J. Epidemiol.*, 101:111–121.
16. **Bader C, Crumpacker C S, Schnipper L E, Ransil B., Clark J. E.,Arndt K, Freedberg I (1978):** The natural history of recurrent facial-oral infection with herpes simplex virus. *J. Infect. Dis.*, 138:897–905
17. **<http://www.ashasexualhealth.org/stdsstis/herpes/oral-herpes/>**
18. **Griffith RS, DeLong DC, Nelson JD(1981):** Relation of arginine-lysine antagonism to Herpes simplex growth in tissue culture. *Chemotherapy*, 27:209-213.
19. **Nalder BN, Mahoney AW, Ramakrishnan R, Hendricks DG(1972):** Sensitivity of the immunological response to the nutritional status of rats. *J Nutr.*,102:535-541.
20. **Bernstein J, Alpert S, Nauss KM, Suskind R (1977):**Depression of lymphocyte transformation following oral glucose ingestion. *Am J Clin Nutr.*,30:613.
21. **Terezhalmay GT, Bottomley WK, Pelleu GB(1978):** The use of water-soluble bioflavonoid-ascorbic acid complex in the treatment of recurrent herpes labialis. *Oral Surg Oral Med Oral Pathol.*,45:56-62.
22. **Middleton E Jr(1984):** The flavonoids. *TIPS.*, 5:335- 338.

Table 2 illustrates the details of the groups' subdivision, methods, observation and results obtained:

	Group A		Group B			Group C	
	Group A1	Group A2	Group B1	Group B2	Group B3	Group C1	Group C2
Severity	Mild		Moderate			Relatively Severe	
No of Patients	10	8	7	11	11	7	6
Manifestation	Lips only		Multiple blisters on and around Lips and inside nose			Multiple blisters on and around Lips , inside nose and around eyes (skin of the eyelids)	
Diet Change	Yes	No	Yes	No	No	Yes	No
Lifestyle Change	Yes	No	Yes	No	No	Yes	No
Acyclovir Administration	No	Yes	No	Yes	Yes	Yes	Yes
Acyclovir route of Administration	NA	Topical	NA	Topical	Oral	Combined (Oral + Topical)	
Acyclovir Dosage	NA	Applied 2x /day	NA	Applied 2x /day	200 mg three times daily x 5d	400 mg PO three times daily x 5d Acyclovir cream Acyclovir ointment for the eyes	
Complications	None	None	29 % Atopic eczema+ perioral Dermatitis		None	None	None
Recurrent Outbreaks during treatment	No	No	Yes	Yes	None	None	None
Recurrent Outbreaks after treatment	None In a year	13% After 1 month	28% after 1 month , another 28% in month 3 then 0% till end of year 1	18% after 2 month and another 36% after month 5	36% after 6 month	14% after 2 month then 14% with a mild lip blister in a year	33% After 2-6 months and another 50% in Month 7-11