IJCRR
Vol 06 issue 10
Section: Healthcare
Category: Research
Received on: 20/01/14
Revised on: 18/02/14
Accepted on: 15/03/14

HONEY PHONOPHORESIS VERSUS LOW INTENSITY LASER THERAPY IN FEMALE GENITAL HERPES

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ABSTRACT

Objective: To compare the efficacy of honey phonophoresis versus low intensity laser therapy in female genital herpes simplex II.

Research Methodology: Forty female patients suffering from genital herpes simplex type II assigned randomly into 2 groups; honey phonophoresis group (A) and low intensity laser group (B). Intensity of pain and serological response were recorded before and after 3 weeks of treatment.

Results: The results of study showed that there were significant differences between both groups post-treatment as p value< 0.05. Percentage of improvement in VAS, IgG, IgM after intervention were 60%, 45%, 8%, respectively for group (A) while for group (B) were 82%, 66%, 56%, Respectively.

Conclusion: The study concluded that low intensity laser was more effective than Honey phonophoresis in the treatment of genital herpes type II.

Keywords: Low intensity laser, genital herpes, honey phonophoresis, serological response, polymerase chain reaction.

INTRODUCTION

Herpes simplex virus type II (HSV-2) gives rise to a variety of clinical disorders and is a major cause of morbidity and mortality worldwide. HSV-2 infections are common in genital area. Genital herpes infections are a major source of morbidity. These infections are responsible for significant health problems, including direct physical discomfort associated with outbreaks, potential complications such as neonatal transmission, and the often devastating psychological effects of a chronic illness[1].

Herpes genitals is characterized by small, grouped, painful vesicles or pustules on an erythematous base, which break and form ulcers in 2-4 days. One of the important characteristics of all herpes viruses is latency. The life cycle of the herpes simplex virus is complex, comprising multiple stages. Following infection, the virus establishes life-long latency in its host and can reactivate at any time as a recurrent infection[2]. There is evidence that latent infection also develops in tissues such as the epithelium of the vagina. The dormant virus then awaits a "trigger" to reactivate it. Triggers may include psychological stress, onset of menses, illness and physical trauma. Many patients experience a burning, tingling or itching sensation (a prodromal) at the location where a lesion later appears[3].

Herpes diagnosis is achieved by assessing the patient's history and physical examination. However, further tests are necessary when HSV infection is asymptomatic, subclinical or atypical, or shows wide expression. The management of herpetic infection is indeed challenging, since none of the different methods of treatment guarantees full remission[4]. Recently a range of infections can be potentially treated with honey.

This can include the common cold, eye infections such as conjunctivitis, as well as Herpes cold sores and genital lesions. Honey has antibacterial, antifungal and antiviral properties. Honey has also considerable anti-inflammatory properties as Anti-inflammatory effects of honey in human plasma were measured[5].

Phonophoresis is actually a combination of ultrasound therapy with topical drug therapy to achieve therapeutic drug concentrations at selected sites in the skin.. Honey had proven to be the best phonophoretic agent for transmission of ultrasound waves as honey is known to contain 17.20% water which is believed to be the best coupling agent in terms of acoustic properties as it reflects only 0.2 % of the sound waves at the water-soft tissue interface[6].

Among treatment options, low-level laser therapy (LLLT) has shown promising clinical results as a longer-lasting suppression therapy. Additionally, it has been shown that this type of phototherapy might have an effect on several immunologic reactions[7-9]. These findings have influenced a number of uncontrolled clinical studies about the effect of low-intensity laser therapy on herpes simplex infection[10,11].

The purpose of this study was to evaluate the efficacy of honey phonophoresis versus low intensity laser therapy in female genital herpes.

PATIENTS AND METHODS

Subjects

Forty female patients had genital herpes simplex infection type II were admitted to dermatology unit at El-Mataria Teaching Hospital, Cairo, Egypt, between July 2012 and September 2013. Age ranged from 25 to 45 years. Patients were free from any other diseases and not under any medications that could affect the immunity and influence the results.

Reasons for exclusions were patients had immunodeficiency disorders, patients had herpes simplex type I (HSV-I), pregnant female, subjects who had diabetes, pre-existing history of dysfunctional bleeding in females, Patients with life threatening disorders as renal failure and myocardial infarction as well as patients with vaginal cancer.

The patients were randomized into two groups of equal number. Group (A); received honey phonophresis for three weeks while Group (B); received low intensity laser therapy for three weeks also.

Measurement of pain associated with HSV-II as well as laboratory measurement of (HSV-II) IgG, IgM were conducted for all patients before the starting treatment as a first record and after three weeks of treatment as second record. The experimental protocol was explained in details for every patient before starting the initial assessment, and a written consent form was signed by each patient before starting. All patients were instructed to report any side effects during the treatment.

Measurement procedures

A) Measurement of pain

Intensity of pain was measured by visual analogue scale (VAS). A VAS is usually a horizontal line, 100 mm in length, anchored by the verbal descriptors "No pain" and" Worst pain imaginable". Measurement was conducted by asking the patient to place a vertical mark on the line below which indicate how she feel pain at the time of assessment. The VAS score was determined by measuring in millimeter from left hand end of the line to the point that patient marked and was represented by a number from total ten [12.]Fig (1).

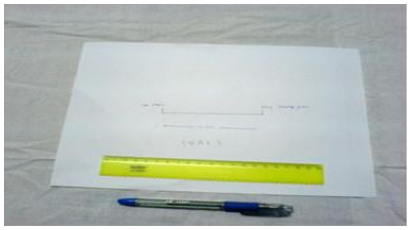

Figure (1): Visual Analogue Scale (VAS)

b) Laboratory Assessment

Serological Response and polymerase chain reaction

ELISA reader and ELISA washer equipment were used for laboratory assessment of (HSV-II) IgG and (HSV-II) IgM. Stat fax-2700 and BioTek- ELx808 were used for analysis of HSV-II IgG and HSV-II IgM **Fig (2,3).**

Figure (2): (BioTek- ELx808)

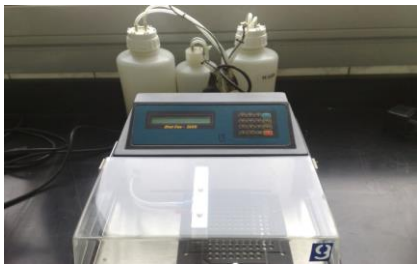

Figure (3): (stat fax-2600)

Treatment Procedures

Honey Phonophoresis Treatment

Nonius, sonopuls 434, S. No. 03-202 type 1463.900 is a therapeutic US device manufactured by Enraf Holland. The Enraf nonius machine delivered the ultrasound wave, with a frequency of 1-3 MHz. Sonopuls 434 has a digital screen for time and intensity. It allows either pulsed or continuous mode

Honey phonophoresis group received honey phonophoresis for 5 minutes; once daily for 3 weeks. Honey was the ultrasound coupling medium and was obtained from the National Research Center. The treated area was divided into zones which are approximately 1.5 times the area of the ultrasound treatment head, and then treat for 1 minute per zone, Frequency was 1.0 MHz, intensity was 1 w/cm^2 pulsed waves [13].

Figure (4):, ultrasound device

Figure (5): The honey

Low intensity Laser Treatment

Patients in the laser group received low-intensity laser therapy by an infrared diode laser with a wave length 905nm, intensity 0.2 mw, frequency 100 Hz and enegy 20 mJ per cm^2 for 100 seconds once daily for 3 wk at the site of original lesion. Protective glasses were worn during application of laser to avoid permanent eye damage resulting from direct exposure to laser beam[14].

Fig.(6): laser probe

Statistical procedures

Mean, the standard deviation and the standard error were calculated for all patients. Paired t-test used to compare within each group to detect level of significance in each group. Unpaired t-test was used to detect significance level between two groups. The statistical package for social science (SPSS) was utilized for data analysis and the level of significance was set at the 0.05 level .

RESULTS

Data concerning age, VAS, IgG, IgM had been collected at the beginning of the study. Follow up evaluation of VAS, IgG, IgM, variables had been performed after three weeks of treatment. As shown in table (1), there were no statistical significant differences (P>0.05) observed between both groups concerning age, VAS, IgG, IgM, before intervention.

Table 1: Statistical analysis of age & clinical variables (VAS, IgG, IgM) of patients between both groups before intervention

	Group A	**Group** B	**P value**
Age (years)	32.5±6.08	33.2±6.43	0.726*
VAS	8.90±1.11	8.95±1.05	0.885*
IgG (Eu/ml)	12.45±2.41	12.80±2.62	0.664*
IgM (Eu/ml)	7.30±2.84	8.00±2.12	0.384*

P-value=Probability level,*Non-Significant (P>0.05).

Results of group A(honey phonophoresis group)

As shown in table (2) the mean value, standard deviation and p value of VAS, IgG, IgM, for group A pre and after intervention. The results showed highly significant difference as p value <**0.05.**

Table 2: Statistical analysis of clinical variables (VAS, IgG, IgM,) of patients for group A before and after intervention

	Pre	**Post**	**P-Value**
VAS	8.90±1.11	3.50±1.46	0.00*
IgG (Eu/ml)	12.45±2.41	6.80±2.72	0.00*
IgM (Eu/ml)	7.30±2.84	5.20±1.90	0.026*

Results of group B (Laser group)

As shown in table (3) the mean value, standard deviation and p value of VAS, IgG, IgM, for group B pre and after intervention. The results showed highly significant difference as p value <**0.05.**

Table 3: Statistical analysis of clinical variables (VAS, IgG, IgM) of patients for group B before and after intervention

	Pre	Post	P-Value
VAS	8.95±1.05	1.65±0.81	0.00*
IgG (Eu/ml)	12.80±2.62	4.25±1.86	0.00*
IgM (Eu/ml)	8.00±2.12	3.50±1.31	0.000*

Comparative analysis of VAS, IgG, IgM between both groups after intervention

As shown in table (4) the mean value, standard deviation and p value of VAS, IgG, IgM between both groups. The results showed highly significant difference as regard to VAS, IgG, IgM, as (p value <0.05). Percentage of improvement in VAS, IgG, IgM, after intervention were 60%, 45%, 8%, respectively for group A while for group B the percentage of improvement in VAS, IgG, IgM, after intervention were 82%, 66%, 56%, Respectively. Fig (7)

Table 4: Statistical analysis of clinical variables (VAS, IgG, IgM) between both groups after intervention

	Group A	Group B	P-Value
VAS	3.50±1.46	1.65±0.81	0.00*
IgG (Eu/ml)	6.80±2.72	4.25±1.86	0.002*
IgM (Eu/ml)	5.20±1.90	3.50±1.31	0.003*

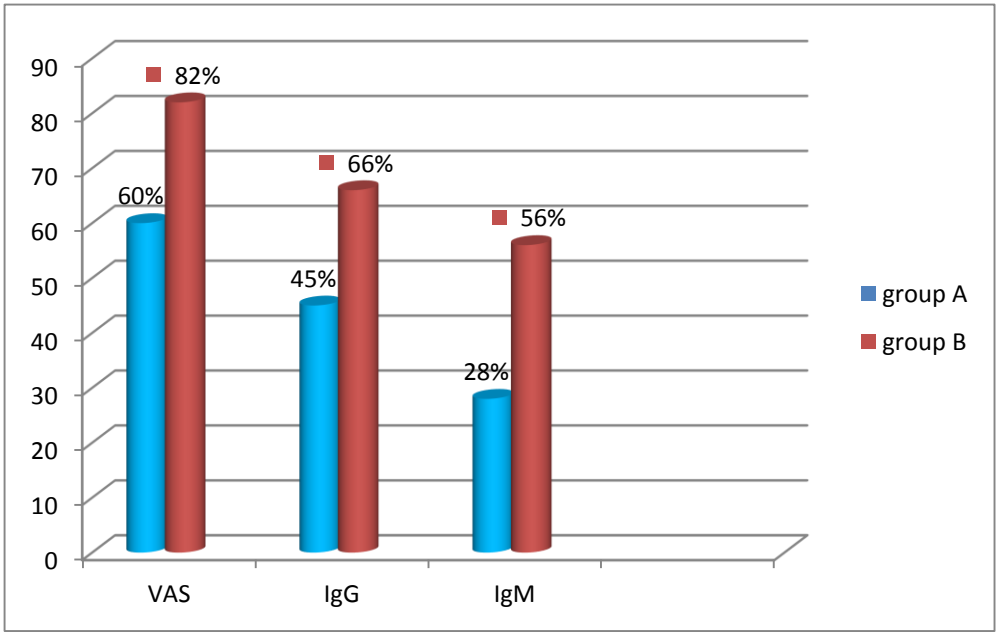

Fig (7): Percentage of improvement of VAS, IgG, IgM in both groups after intervention

DISCUSSION

In the present study, effects of honey phonophoresis versus low intensity laser on female herpes simplex virus type II were investigated.

According to results of this study, there were significant decrease in pain intensity after treatment with honey phonophoresis for group A. The efficacy of honey phonophoresis may be attributed in partly to anti-inflammatory, acidity, anti-osmotic and antibacterial effects of honey and also to efficacy of ultrasound for enhancement of delivering the honey as well as physical effects of ultrasound.

Deissl and Frenkel,[14] reported that IgM antibodies appear early in the course of an infection which is demonstrating IgM antibodies in patient's serum which indicates recent infection and Fatahzadeh and Schwartz,[15] demonstrated that IgG antibodies are predominantly involved in the secondary antibody response. In this study Immunological assays (ELISA) was used for detection of the presence of anti-bodies of the virus (IgG and IgM) and reflected the efficacy of application of honey phonophoresis by their highly significantly decrease after treatment.

Previous studies agreed with this study and support the efficacy of honey therapy in the treating genital herpes simplex type II. Al-Waili;[16] investigated the effect of raw honey, topically applied, on recurrent attacks of herpes lesions, labial and genital, and compared this with the effect of Acyclovir cream and he was concluded that topical honey application is safe and effective in the management of signs and symptoms of recurrent lesions, of labial and genital herpes. Honey is capable of reducing the associated symptoms by means of reducing inflammation.

Honey has been shown to have antibacterial effects owing to its high osmolarity and low pH . Its low water activity inhibits microbial growth, particularly bacterial growth. When applied topically to wounds, water is drawn away from the wound by osmosis, helping to dry the infected tissue and inhibiting bacterial growth[17,18]. Kwakman *et al*;[19] have reported on the role of sugar, hydrogen peroxide, methylglyoxal, and bee defensin-1 in the antibacterial properties of honey. In their study they show that the antibacterial effects of honey are reduced after the combined neutralization of these factors.

Also the results of this study, showed that there were significant differences as regard to VAS, IgG, IgM, in group B (low intensity phonophoresis group) after intervention. This confirm the efficacy of low intensity laser therapy, this attributed to analgesic, anti-inflammatory and biostimulating effects of low intensity laser therapy.

Previous studies agreed with this study and support the efficacy of low intensity laser therapy in the treating genital herpes simplex type II. Some studies confirmed the benefit of Low Level Laser Therapy in decreasing pain, improving wound healing compared to other treatment modalities like acyclovir[20]. Donnarumma et al; [21] have postulated a mechanism of action that laser irradiation "acts in the final stage of HSV-1 replication by limiting viral spread from cell to cell and that laser therapy acts also on the host immune response unblocking the suppression of pro-inflammatory mediators induced by accumulation of progeny virus in infected epithelial cells.

Sanchez *et al*;[22] demonstrated that among treatment options, low-level laser therapy (LLLT) has shown promising clinical results as a longer-lasting suppression therapy. Patients were symptom free for 17 months following initial treatment for recurrent simplex lesions with the laser. Schindl and Neumann[23] found similar results in their LLLT study for the laser in delaying reoccurrence of the herpetic lesion outbreaks. The median recurrence-free interval in the laser-treated group was 37.5 wk (range: 2–52 wk) and in the placebo group 3 wk (range: 1–20 wk). Vélez-Gonzalez et al [45] also discovered delays in reoccurrence of lesions after laser therapy.

Marrotti *et al* [24] used a 660 nm wavelength laser, energy density of 120 J/cm², output power of 40 mW, during two minutes on spot and 4.8J of energy per spot on four spots. After 24 hours, the patients returned and then 3.8J/cm² and 15mW were applied to their lesions (the total dose was 0.6J). The same procedure was repeated after 72 hours and one week after. There were no significant side effects and herpetic lesions healed faster.

De Carvalho RR *et al*;[25] reported a significant decrease in dimension of herpes labialis lesions and inflammatory edema using low level laser therapy. The reduction in pain level and monthly recurrences did not reach statistical significance

To the best of our knowledge, there is no study compare the effect of honey phonophoresis versus low intensity laser therapy in treatment of herpes simplex type II. The results of this study showed that there were significant differences between honey phonophoresis and low intensity laser therapy after the treatment duration. Percentage of improvement in VAS, IgG, IgM, after intervention were 60%, 45%, 8%, respectively for group A while for group B the percentage of improvement in VAS, IgG, IgM, PCR after intervention were 82%, 66%, 56%, respectively. The limitations of our study were no control group included and no period of follow-up. Further studies including control group and follow-up are needed to further validate our findings.

CONCLUSION

The study concluded that low intensity laser was more effective than honey phonophoresis in the treatment of genital herpes type II.

REFERENCES

1. Lavoie SR, Kaplowitz LG. Management of genital herpes infection. Semin Dermatol. 1994 Dec;13(4):248-55.
2. S Faro; A review of famciclovir in the management of genital herpes; Infect Dis Obstet Gynecol. 1998; 6(1): 38–43.
3. Siegel MA. Diagnosis and management of recurrent herpes simplex infections. J Am Dental Assoc 2002; 133:1245-1249.
4. Fiddian AP, Yeo JM and Stubbings RF, (2006) :"Successful treatment of herpes simplex with topical acyclovir". Br. Med. . (Clin. Res. Ed.), 286:1699-1701.
5. Armon TT, (2009): "the use of honey in the treatment of infected wounds". Trop. Doct; 10:91.
6. Sanya AO and Oluseye KA (2000): Relative transmissivity of local substitutes for the manufacturer's ultrasonic transmission medium. J Nig Soc Phys 2000; 10(2): 23-25.
7. Ohta, A, Abergel, RP, Uitto, J: Laser modulation of human immune system: inhibition of lymphocyte proliferation by a gallium-arsenide laser at low energy. Lasers Surg Med 1987 7:199–201.
8. Yu, W, Chi, L, Naim, JO, Lanzafame, RJ: Improvement of host response to sepsis by photobiomodulation.Lasers Surg Med 1997b 21:262–268.
9. Schindl, A, Schindl, M, Schindl, L: Successful phototherapy with low intensity laser irradiation of a chronic radiation ulcer in a patient with lupus erythematosus and diabetes mellitus. Br J Dermatol 1997a 137:840–841.
10. Haichenberger-Wildner, I, Michels, H: Laserstrahlen bei Herpeserkrankungen. Med Cosmetol 1981 11:142–144,
11. Landthaler, M, Haina, D, Waidelich, W: Behandlung von Zoster, postzosterischen Schmerzen und Herpes simplex recidivans in loco mit Laser-Licht. Fortschritte Med 1983 101:1039–1041.
12. Cork RC, Isaacc IG and El-Sharydah AR, (2004): "A comparison of the verbal rating scale and the visual analog scale for pain assessment". The Internet Journal of Anaesthesiology, 8(1):227-236.
13. Pfister WR and Hsieh DS, (2007): Permeation enhancers compatible with transdermal drug

delivery systems. Part II. System design considerations. Pharm Tech: 14(10):54-60.

14. Deissl LP and Frenkel NS, (2006): "Herpes simplex virus amplicon: Cleavage of concatameric DNA is linked to packaging and involves amplification of the terminally reiterated a sequence". J. Virol., 57:933.
15. Fatahzadeh MS and Schwartz RA, (2007): "Human herpes simplex. ". Clinical and Experimental Dermatology, (32):625-630.
16. Al-Waili NS, (2004): Topical honey application vs. acyclovir for the treatment of recurrent herpes simplex lesions. Medical Science Monitor, 10(8), 94-98
17. Molan PC (1992) The antibacterial activity of honey. The nature of the antibacterial activity. Bee World 73: 5–28.
18. Booth S (2004) Are honey and sugar paste alternatives to topical antiseptics? Journal of Wound Care 13(1): 31–3.
19. Kwakman PH, te Velde AA, de Boer L et al (2010) How honey kills bacteria FASEB J 24(7): 2576–82
20. Tunér, J., Hode, L.: Low Level Laser Therapy - clinical practice and scientificbackground, 1999, ISBN 91-630- 7616-0.
21. Donnarumma G, De Gregorio V, Fusco A, Farina E, Baroni A, Esposito V, Contaldo M, Petruzzi M, Pannone G , Serpico R. Inhibition of HSV-1 replication of laser diodeirradiation: possible mechanism of action. Int J Immunopathol Pharmacol. 2010 Oct-Dec;23(4);1167-76.
22. Sanchez PJM, Femenias JLC, Tejeda AD, Tuner J. The Effect of 670-nm Low Laser Therapy on Herpes Simplex Type 1. Photomedicine and Laser Surgery. ahead of print. 0.1089/pho.2011.3076. Online Ahead of Print: November 2, 2011.
23. Schindl A, Neuman R. Low-intensity laser therapy is an effective treatment for recurrent herpes simplex infection. Results from a randomized double-blind placebocontrolled study. J Invest Dermatol. 1999: 113 (2): 221-223
24. Marotti J, Aranha AC, Eduardo Cde P, Ribeiro MS.Photodynamic therapy can be effective as a treatment for herpes simplex labialis. Photomed Laser Surg. 2009;27(2): 357-63.
25. De Carvalho RR, de Paula Eduardo F, Ramalho KM, Antunes JL, Bezinelli LM, de Magalhães MH, et al. Effect of laser phototherapy on recurring herpes labialis prevention: an in vivo study. Lasers Med ScI 2010;25(3):397-402