

Concentrated heat therapy in herpes simplex attacks – current data and practical considerations

Study discussed:

The use of concentrated heat prevents recurrence of herpes labialis under real life conditions – results of a prospective, double-arm, acyclovir or Herpotherm® treatment observational cohort study
(Wohlrab et al. 2013)

Application and tolerability of Herpotherm® in the treatment of genital herpes
(Schlippe et al. 2013)

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Principles behind local hyperthermia

Local hyperthermia is a promising, physical therapeutic approach. It involves brief application of concentrated heat to a highly localised area of skin. The temperature at the application site is approx. 51 °C. The short period of application means that there is usually no risk of damage to the skin. Application of concentrated heat for a few seconds is, however, sufficient to activate various physiological processes at the treatment site. As a practical consideration, it is important that the treatment site should be heated rapidly and evenly. This prevents damage to the skin and ensures that the temperatures achieved are effective. The study discussed here used a patented medical device, Herpotherm®, to deliver this controlled heat transfer. Some practical experience has been gained in using the device for the treatment of local reactions to insect bites/stings. To illustrate the potential of local hyperthermia and its advantages over existing treatment options, an open label study was performed for the purpose of quantifying the effects of this treatment for this indication.

Heat transfer and mechanism of action

Heat energy is transferred from the Herpotherm® medical product by a process of thermal conduction. Thermal convection and radiation are negligible. The precise biological mechanism of action of this original treatment method has not yet been clarified, but is the subject of ongoing research. Previous findings and theories on the physiological effects of this treatment were discussed by a panel of experts at a workshop on concentrated heat therapy*. These are as follows:

- Possible activation of mast cells: Histamine provocation tests with subsequent application of local hyperthermia suggest an effect on mast cells.

- Possible activation of TRPV1 receptors*: These nerve receptors are activated at temperatures over 40 °C. There is a post-acute antipruritic, analgesic and vasodilatory effect.
- Possible induction of heat shock proteins: Some of these proteins are involved in antigen presentation and can activate various types of lymphocyte.
- Possible denaturation/inhibition of reproduction: Some pathogens (e.g. the herpes virus) and toxins are heat labile.

Method of application and technology used

When activated, the patented Herpotherm® medical device generates a temperature of approx. 51 °C, and maintains this temperature for 3 seconds. The device ensures controlled heating of the heating module by internally linking temperature and time controls (time-heat constant) and is regulated by a software-controlled microprocessor. Heat transfer is via a ceramic pad. Ceramic is resistant to disinfectants and abrasion during cleaning. To use the device, the contact surface is pressed gently onto the skin, before pressing the start button. An LED lights up once the device attains the treatment temperature and is extinguished when the device switches off automatically after 3 seconds.

Areas of application

- Application of concentrated heat is an established treatment for herpes labialis and herpes genitalis attacks.
- The objective in treating a herpes infection is to prevent an acute attack by applying treatment when the first symptoms appear.

* June 5, 2013, MW Office GmbH; Prof. Dr. Ulrich Mrowietz, Prof. Dr. Johannes Wohlrab, Prof. Dr. Ulf Darsow, Dr. Gerrit Schlippe

* transient receptor potential cation channel subfamily V member 1

Application of local concentrated heat versus topical acyclovir for the treatment of herpes labialis attacks – results of a pilot study under real-life conditions

Johannes Wohlrab, Franziska Voß, Christian Müller, Lars C Brenn; Clinical, Cosmetic and Investigational Dermatology 2013;6 263–271

Background

Herpes labialis is caused by infection with herpes simplex virus type 1, which, in the European population, has a seroprevalence in excess of 90%. Treatment generally involves the use of the antimetabolite drug acyclovir, starting from the prodromal period. This inhibits virus replication, but has no direct effect on the prodromal symptoms burning, itching and swelling. Local concentrated heat can reduce these symptoms.

Objective

To compare the effect of treatment with antiviral agents and local hyperthermia on prodromal symptoms and quality of life in acute herpes labialis attacks.

Method

- Prospective, controlled, open label, multicentre, non-interventional cohort study.
- Participants: 103 pharmacy customers aged from 18 to 72 with acute symptoms; 72% female.
- Two study arms: i) concentrated heat at a temperature of approx. 51 °C for 3 seconds several times a day using the certified medical device Herpotherm® (n = 51) or ii) acyclovir (n = 52).
- Documentation: symptoms and effect on quality of life measured using a numeric analogue scale (0 to 9) over a period of 7 days and final evaluation of efficacy and tolerability.

Results

- Both treatments led to an improvement in symptoms and quality of life.
- During the treatment period, the average symptom score for all symptoms was significantly lower in participants in the concentrated heat arm (figure 1A).
- Hyperthermia was significantly superior from day 2 and a 50% reduction in symptoms was attained two days earlier.
- The average duration of illness was 2.3 days for Herpotherm® vs. 4.5 days for acyclovir.
- 53% of patients receiving hyperthermia treatment rated the treatment outcome as very good, compared to 12% of patients treated with acyclovir (figure 1B).
- In both study arms, tolerability was rated as good or very good by more than 90% of participants.

Summary

Local hyperthermia provided more effective relief of the prodromal symptoms burning, itching and swelling and better quality of life than acyclovir. Symptoms improved significantly more quickly, the average duration of illness was shorter and patient satisfaction was higher.

Summary based on the original study:

The use of local concentrated heat versus topical acyclovir for a herpes labialis outbreak: results of a pilot study under real life conditions
Johannes Wohlrab, Franziska Voß, Christian Müller, Lars C Brenn
Clinical, Cosmetic and Investigational Dermatology 2013;6 263–271

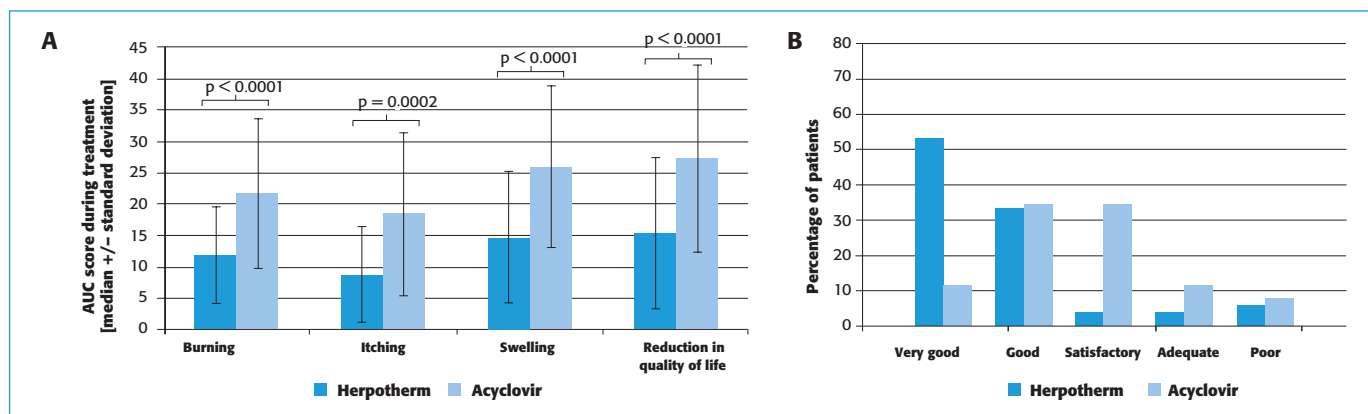


Figure 1: **A** Symptom (area under the curve [AUC]) score over the period of treatment with local hyperthermia and acyclovir. **B** Patient evaluation of treatment outcome

Application and tolerability of Herpotherm® in the treatment of genital herpes

Gerrit Schlippe, Werner Voss, Lars Christian Brenn; *Clinical, Cosmetic and Investigational Dermatology* 2013;6 163–166

Background

Herpes genitalis is usually caused by infection with herpes simplex virus type 2, or in some cases type 1. Type 2 is less prevalent than type 1, but prevalence is still up to 60%. As with herpes labialis, asymptomatic periods may be followed by acute attacks generally lasting 5–10 days. Until now, treatment has generally involved the systemic or topical use of antivirals. Because concentrated heat has proven effective in treating herpes labialis, we wished to investigate the use of this approach for treating herpes genitalis.

Objective

To investigate the suitability of local hyperthermia for the treatment of genital herpes with reference to use, acceptance and reduction in pain and herpes symptoms.

Method

- Monocentric, open label study carried out at a Russian gynaecology practice.
- 31 participants aged between 23 and 49 with acute symptoms.
- Two study arms: i) concentrated heat at approx. 51 °C for 3 seconds using the patented medical device Herpotherm® as sole therapy (n = 10) or ii) in combination with acyclovir (n = 21).
- Symptoms were recorded over the course of 5 individually arranged consultations.
- Symptoms were clinically evaluated by the physician and improvement was subjectively assessed by the patient.

Results

- At the beginning of treatment (second consultation), 90% of patients had blisters, 77% ulcers and 3% crusting (figure 2A).
- At the third consultation (2–3 days), only 9% still had blisters.
- At the fourth consultation (3–18 days), 97% of patients were symptom-free.
- Patients self-assessed that symptoms started to recede immediately in 67% of cases both with sole therapy and combination therapy (figure 2B).
- Treatment outcomes were assessed by the physician as good in 90% and satisfactory in 10% of cases.
- No intolerance was observed and treatment was not discontinued in any patients.

Summary

The results show that concentrated heat therapy can also be used effectively in genital herpes. This treatment option was assessed by both physicians and patients as an alternative to antiviral drugs. Comparison with literature data on other treatment options showed a very rapid reduction in pain and herpes symptoms. Combination therapy did not offer any additional therapeutic value.

Summary based on the original study:

Application and tolerability of Herpotherm® in the treatment of genital herpes
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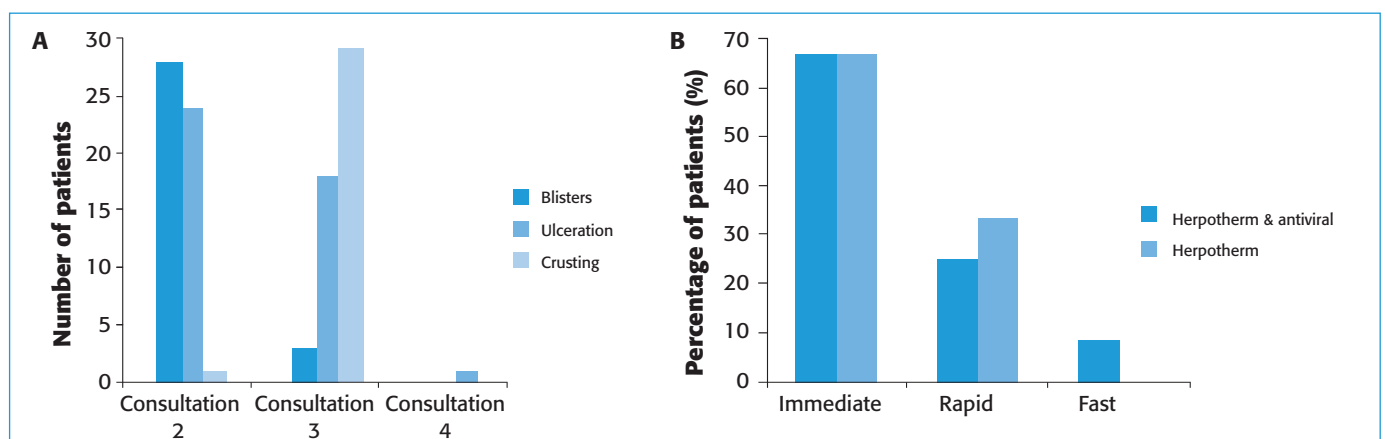


Figure 2: **A** Clinical symptom score at consultations 2–4 (medical evaluation). **B** Point at which symptoms started to recede according to patient (n = 18)

Discussion of the study results

In accordance with practical experience, previous studies on local hyperthermia have indicated high efficacy against the prodromal symptoms of herpes attacks.* At the temperatures used, permanent changes/damage to skin or denaturation of skin proteins would be expected to require minutes or hours of exposure and cannot occur with the short hyperthermia application times used here. This is in keeping with the high level of tolerability observed in these studies. Treatment options for the indications investigated were previously limited. Although, if used early, topical antivirals (for cold sores) or systemic antivirals (for genital herpes) do reduce the duration of symptoms, they rarely prevent an attack. Early use of Herpotherm® is able to prevent or at least significantly attenuate recurrent herpes. People for whom treatment with antivirals is potentially contraindicated may also benefit from non-drug based treatment with concentrated heat.

Expert recommendations for practice

After use, the practitioner should wait for approx. 10 seconds before assessing whether prodromal symptoms have subsided completely or have merely been reduced. To maximise the efficiency of heat transfer to the skin when using Herpotherm®, care needs to be taken to ensure good skin contact. Due to its poor thermal conductance, a thin layer of air between the heating surface and the area being treated may affect energy transfer. The effect is likely to be limited to the treatment site only. The device should therefore be placed precisely on the affected area of skin. The earlier the device is used, the more effective it is in treating symptoms, but later use also generally provides some therapeutic benefit. Its small size and availability for immediate use mean that the device can always be carried to allow immediate use. This is an advantage for people who suffer from regular recurrences of their herpes and wish to intervene at the first sign of prodromal symptoms in order to prevent an attack. People with sensitivities, pregnant women, children and people with allergies gain particular benefit from this non-pharmacological therapy.

Herpotherm®

Heat in excess of 42 °C activates the thermal/capsaicin receptor TRPV1. Pain receptors also carry the TRPV1 protein. Consequently, as well as being activated by mechanical pain stimuli such as bites and stings, they are also activated by high temperatures or capsaicin. Capsaicin has long been used as a topical analgesic. By activating TRPV1, capsaicin initially triggers a painful burning sensation followed by hypersensitivity, which is primarily the result of neurogenic inflammation. This is then followed by the neurons becoming insensitive to heat, capsaicin, and other stimuli (Szallasi A, Blumberg PM., Vanilloid [Capsaicin] receptors and mechanisms. *Pharmacol Rev.* 1999; 51:159–212). Since TRPV1 is also activated by heat, it seems reasonable to assume that heat application using Herpotherm® may trigger the same processes in nerves as capsaicin, and could therefore also lead to desensitisation of the neurons, and thus moderate herpes attacks. Mechanical stimuli such as heat and cold can cause cells to become so stressed that they die off. This causes these cells to release stress proteins such as HMGB1 and heat shock proteins. These proteins then enable the immune system to initiate a response to the stimulus. The objective of such an immune response may include, for example, removing dead tissue and damaged cells. This reaction could also prevent a herpes attack.

* Schlippe G et al. Dovepress Clinical, Cosmetic and Investigational Dermatology 2013;6; 163–166 and Wohlrab et al. 2013

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Brief profile of Dr. Schlippe

Dr. Gerrit Schlippe is a medical dermatology specialist and lead author of the study on genital herpes. She is responsible for research, validation and publications in the skin physiology/medical test methodologies field at Dermatest, a dermatology research company.



Sources & links

Herpes labialis study:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3821542/>

Herpes genitalis study:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3681267/>

User information for non-specialist users:
www.herpotharm.de