Peter H Andersen
Department of Dermatology
Marselisborg Hospital
P.P Orumsgade 11
DK-8000 Ärhus C.

Title:
Treatment of recurrent herpes labialis (cold sores) using trans-cutaneous electrical nerve stimulation

Purpose:
To investigate if recurrent attacks of herpes labialis may be prevented or the severity diminished using trans-cutanneous electrical nerve stimulation (TCNS).

Panellist:
29 otherwise healthy volunteers with more than 7 recurrent attacks pr year of cold sores and positive HSV cultivation, were included.

Materials & Methods:
The investigation was planned as a randomised double blind cross-over study. After one observation attack where no TCNS was offered subjects were randomised. The following episode of cold sores were TCNS treated (active / placebo). After the first treatment period panellists initially receiving placebo were given active treatment or vice versa. However, it was soon clear that this set-up was impossible, since most of the panellist immediately knew if the pen was active. Therefore, most included patients were initially given placebo. To record symptoms panellists were supplied with a diary card and as soon as a cold sore episode was suspected time was noted and prodomal symptoms graded: itch, stinging and pain. This was done as soon as the first symptoms develop and routinely three times daily. When a clear blister had developed the subjects were allowed to initiate standard systemic aciclovir treatment (200 mg x 5, for 5 days). After the initial attack patients are supplied with equipment to perform TCNS (placebo / active) and a new diary card. At the next two HSV episodes TCNS were started as soon as prodomal symptoms developed and diary cards were filled out.

Effect parameters:
Due to the limited numbers going through all 3 observations period the statistical calculations were modified and performed "semi-quantitative". It was not possible to select any single primary efficacy Parameter. Therefore a overall estimation was performed in each case diving the panellists in 3 groups. No difference between active versus placebo. Active > placebo or placebo > active. In the cases were panellists failed to complete the entire study active was compared to run in periods.

Results:
A total of 29 panellists were included. Three newer reported back after the initial enrolment. 18 panellist were observed during the first observation outbreak and one treatment period (active/placebo) and 8 complete totally. Of the 18 patients 3 were given active treatment. In this group all had better results in active period than in observation period. Of the 8 completing all 3 periods 7 were better in active period and in one panellist there were no difference between periods ($p<0.01$).

Discussion:
A disappointingly low number completed the study, which overall reduced the statistical strength of our conclusion. However, even though we only managed to complete a small group of patients, it seem as if electrical stimulation of a Herpes Labialis episode may diminish symptoms; both in terms of symptom severity and disease duration, but blisters always developed after the prodomal period.

A total of 15 episodes of pen-dysfunction developed and we therefore had to redo the active period in these cases. This lead to high numbers of drop-outs in this period. Today it is clear, that it was not a sound decision to change from a random order of active versus placebo to a predetermined form. However, there was no way the study could have been completed double blind, since the patients immediately knew it the pen was active.

The patients included all had very active Herpes Labialis, and it is a known fact from pharmaceutical studies that this group often needs more active treatment. Therefore, when we can show effect it this group of patients, it is likely that people with less severe disease activity may gain even more. In the present experiment no visible damage was noted in the skin after treatment, and besides a tingling effect when stimulation was performed on the lips no side effects were observed. However it is important to realise that this experiment can not stand alone. Further tests may document safety profile, possible side effects and effect verification.

Project location and responsible:
The investigation is performed at Marselisborg hospital, department of dermatology, Ärhus, Denmark. Peter H. Andersen, MD will be project responsible. Furthermore Sanne K. Hansen MD will perform some of the clinical controls.

References:

1. Omura Y. Treatment of acute or chronic severe, intractable pain and other intractable medical problems associated with unrecognised viral or bacterial infection: Part I. Acupunct Electrother Res. 1990;15:51-69.

2. Morcos R, Seidah NG, Lazure C, Chretien M. [Endorphins 1989: neuroendocrine aspects]. Rev Neurol Paris. 1989;145:747-63.

3. Rawat B, Genz A, Fache JS, Ong M, Coldman Aj, Burhenne HJ. Effectiveness of transcutaneous electrical nerve stimulation (TENS) for analgesia during biliary lithotripsy. Invest Radiol. 1991;26:866-9.