Hans-Christian Stahl
cand. Dr. sc. hum.

Fach/Einrichtung: Public Health / Universitätsklinikum Heidelberg
Doktorvater: Prof. Dr. med. Rainer Sauerborn, Dr. P.H.

**Clinical and Health Economic Evaluation of Wound Debridement and Moist Wound Care in Chronic Cutaneous Leishmaniasis Ulcers in Afghanistan**

Part I: Randomized Clinical Trial
Background
A proof of principle phase IIa trial with 113 patients from Kabul showed that bipolar high-frequency (HF) electro-thermo-debridement (ETD) of cutaneous leishmaniasis (CL) ulcers and subsequent moist wound treatment (MWT) closed 85% of all L. tropica lesions within 60 days.

Methods
We performed a three-armed, randomized, phase IIb clinical trial in Mazar-e-Sharif. L. tropica- or L. major-infected CL patients received intradermal SSG (Group I); HF-ETD followed by MWT with 0.045% DAC N-055 (Group II); or MWT with 0.045% DAC N-055 in basic crème alone (Group III). The primary outcome was the complete epithelialisation before day 75 of treatment.

Findings
87 patients enrolled in the trial were randomized into group I (n=24), II (n=32) and III (n=31). The per-protocol analysis of 69 (79%) patients revealed complete epithelialisation before day 75 in 23 (100%) patients of group I, in 15 (65%) patients of Group II, and in 20 (87%) patients of Group III (p=0.004). Wound closure times were significantly different between all regimens in a pair-wise comparison (p=0.000039). Re-ulcerations occurred in four (17%), three (13%) and seven (30%) patients of Group I, II or III, respectively (p=0.312).

Interpretation
Treatment of CL ulcers with bipolar HF-ETD followed by MWT with 0.045% DAC N-055 or with DAC N-055 alone caused more rapid wound closure than the standard IL SSG therapy, the latter only in the per-protocol analysis. This result merits further exploration in the light of our current knowledge of the in vivo biochemistry of chlorite.

Trial registration
Clinicaltrials.gov identification number NCT00996463

Part II: Health Economic Evaluation
Background
Clinical results need to be complemented with health economic evaluations to help decision makers and health care managers to allocate resources efficiently towards evidence based and appropriate treatments, especially in the context of poor populations and neglected diseases such as cutaneous Leishmaniasis.

Methods

A decision analytical model was used to analyse the cost-effectiveness of two wound care regimens with DAC N-055 (Group II and III) versus IL SSG (Group I) parallel to the clinical trial in cutaneous Leishmaniasis patients. Costs were collected from a societal perspective. Effectiveness was measured in wound free days. Baseline parameters, sensitivity ranges and parameter distributions were defined on the basis of the patient level data collected during the trial. Final outcome was the incremental cost-effectiveness ratio of the different regimen under study and a budget impact analysis in the context of Afghanistan.

Findings

Average baseline costs per patients were 11 US$ for intra-dermal antimony (Group I), 16 US$ for wound debridement and subsequent moist wound care (Group II) and 25 US$ for moist wound care alone (Group III) in patients with a single chronic CL ulcer elicited by L. tropica or L. major. The incremental societal budget impact analysis estimated additional costs of 0.765 Million US$ and 2.3 Million US$ for Group II and Group III regimens compared to Group I, respectively. The incremental baseline cost-effectiveness ratio of Group II versus Group I was 0.09 US$ and Group III versus Group I 0.77 US$, Group III versus Group II and very cost-effective according to WHO CHOICE criteria. Within a Monte-Carlo probabilistic sensitivity analysis Group II was cost-effective in 80% of the cases starting at a willingness-to-pay of 80 cent per wound free day.

Interpretation

Based on the clinical and health economic results moist wound treatment with DAC N-055 with prior electro-thermo-debridement of crusted chronic CL ulcers covered by biofilms and infiltrated with L. tropica or L. major parasites is an effective and efficient treatment option in the context of Afghanistan. The baseline results are robust against the probabilistic sensitivity analysis.