Properties of octenidine based products in modern wound management

Dr. Michael Braun
Manager Medical Affairs
Schülke & Mayr GmbH
Properties of octenidine dihydrochloride

- Broad antimicrobial spectrum
- Fast onset of action
- No induction of bacterial resistance
- No protein error
- Long-term effect (24 h remanence)
- Good biological tolerance
Topical antimicrobial agents under specific challenges
Efficacy of topical antimicrobials usually tested *in vitro* according to standard methods, e.g. DIN EN 13727 (quantitative suspension test)

Organic load is simulated by addition of challenging substances (e.g. albumin and / or sheep erythrocytes)

**Questions:**

- How close do these standard methods resemble the wound situation?
- Is the applied amount of challenging substances representative?
- How efficient are different topical antimicrobials under varying conditions?
Patient Characteristics

**Inclusion criteria:**
- Age: min. 18 years
- *Ulcus cruris*
- No underlying infectious diseases (e.g. HIV, hepatitis C)
- No treatment with topical antimicrobials (at least 3 days prior to inclusion)

**Demographic data:**
- Total 30 patients (10 female and 20 male)
- Age 41 to 90 years (mean: 68 years)
Ulcus cruris
Squeezing of foam dressings or NPWT-sponges with a sterile stainless steel garlic or potato press:

- Simple and rapid implementation, sampling during regular dressing changes (at least after 24 h)
- Recovery of exudate is tedious
- Small to medium amount of exudate

Ultrasound suspension (ultrasound assisted wound debridement):

- Sampling requires great effort
- Painful for the patient
- Exudate diluted by the UAW solution (NaCl)
- Large amount of exudate
Protein Content

- Determined with Pierce® BCA Protein Assay Reagent
- Total 29 wound exudate samples:
  - 13 x foam dressing (sampled after 24 hours): Ø 1.85%
  - 11 x UAW suspension: Ø 0.37%
  - 5 x vacuum exudate: Ø 1.00%
- Dilution 1:10 in the lab test ➔ range: 0.04-0.19%
- Standard protein challenges according DIN EN 13727 reflect the clinical reality:
  - “clean conditions”: 0.03%
  - “dirty conditions”: 0.3%
Further Wound Characteristics

Temperature:
- Measured with digital IR thermometer
- Average temperature: 32.4°C ➔ DIN EN 13727: 20°C ± 1°C

pH value:
- Measured with simple pH indicator strips (accuracy 0.5)
- Average pH: 8.2 ➔ not yet defined in the DIN EN 13727
Accompanying Flora

Average germ count in wound exudate: $3.1 \times 10^8$ CFU/ml (2.0 x $10^5$ – $3.4 \times 10^9$ CFU/ml) → high contamination of wound and exudates.

- Staphylococcus aureus / MRSA
- Enterococcus faecalis
- Providencia rettgeri
- Pseudomonas aeruginosa
- Escherichia coli / ESBL
- Corynebacterium striatum
- Streptococcus agalactiae
- Proteus mirabilis
- Acinetobacter spp.
Test design:

- 1 part wound exudate (containing accompanying flora) „spiked“ with 1 part MRSA suspension (ATCC 33592) 1.5 – 5.0 x 10⁸ CFU/ml
- 2 minutes time for equilibration
- Addition of 8 parts antimicrobial solution (1.25 x final concentration, resembling concentration in marketed products):
  - Octenidine dihydrochloride: 0.05% and 0.1%
  - PHMB: 0.04% and 0.1%
  - Chlorhexidine: 0.2%
  - PVP-iodine: 10%
- After observing the defined contact times (15, 30 and 60 s; 2, 5, 15 and 30 min) removal of one part for CFU counting (duplicates)
- Results compared with data using EN 13727 standard challenges
Results
“Clean Conditions“

- 0.05% Octenidine
- 0.1% Octenidine
- 0.04% PHMB
- 0.1% PHMB
- 0.2% Chlorhexidine
- 10% PVP

logarithmic reduction factor (lg RF) vs. contact time

15 sec  30 sec  60 sec  2 min  5 min  15 min  30 min
Results
“Dirty Conditions”

- 0.05% Octenidine
- 0.1% Octenidine
- 0.04% PHMB
- 0.1% PHMB
- 0.2% Chlorhexidine
- 10% PVP

Contact time:
- 15 sec
- 30 sec
- 60 sec
- 2 min
- 5 min
- 15 min
- 30 min

Logarithmic reduction factor (lg RF)
Results
Wound Exudates

Logarithmic reduction factor (lg RF) vs contact time for different antimicrobial solutions:
- 0.05% Octenidine
- 0.1% Octenidine
- 0.04% PHMB
- 0.1% PHMB
- 0.2% Chlorhexidine
- 10% PVP

Contact times: 15 sec, 30 sec, 60 sec, 2 min, 5 min, 15 min, 30 min.
**Summary Antimicrobial Efficacy**

- **Octenidine** shows the best antimicrobial efficacy with full efficacy after 30 (0.1%) resp. 60 seconds (0.05%)

- Followed by 10% **PVP-Iodine** with full efficacy after 60 seconds

- 0.1% **PHMB** reaches full efficacy after 30 minutes, whereas 0.04% **PHMB** does not reach sufficient efficacy even after 30 minutes

- 0.2% **Chlorhexidine** reaches full efficacy after 15 minutes
12.30. Wound-Conditioning in Pressure Ulcer Patients: Negative Pressure Wound Therapy and Octenidine-Containing Wound Irrigation Solution – *in-vitro* Results and Clinical Outcome

J. MATIASEK (VIENNA, AUSTRIA)
Multicenter multinational randomised controlled clinical trial

Effectiveness and tissue compatibility of a 12 weeks treatment of chronic venous leg ulcers with an octenidine based antiseptic

Prof. Wolfgang Vanscheidt, M. D. ¹, Prof. Keith Harding, M. D. ², Luc Téot, M. D., Ph. D. ³, Jörg Siebert, Ph. D. ⁴

¹ Paula-Modersohn-Platz 3, 79100 Freiburg, Germany
² CARDIFF University, Wound Healing Research Unit, Heath Park, CF14 4XN Wales, United Kingdom
³ Hôpital Lapeyronie, 371, Avenue du Doyen Gaston Giraud, 34295 Montpellier Cedex 5, France
⁴ Schülke & Mayr GmbH, Robert-Koch-Straße 2, 22851 Norderstedt, Germany
Aim of the study

- Evaluation of tolerability and safety of octenisept® in the treatment of chronic venous leg ulcers
- Does octenidine prevent the healing of venous leg ulcers?
Study design

- International (GER, FRA, HUN, UK), multicenter (15 centres), double-blind, randomised controlled clinical study
- November 2007 – March 2009

- 126 patients included, randomised into 2 groups
- Group 1 (n = 60): octenidine dihydrochloride / phenoxyethanol (octenisept®)
- Group 2 (n = 66): Ringer-Solution
Inclusion criteria

- > 18 years, locally infected ulcer of the lower limb
- CVI Grade C₆ (CEAP Classification)
- Proved diagnosis of CVI
- Duration ≥ 4 Weeks ≤ 2 Years
- Wound area after debridement ≥ 2 cm² und ≤ 20 cm²
- 2 of 9 infection criteria according to Cutting & White (2005) fulfilled
  - Abscess, cellulitis, exudation, rubor, torpid granulation pain, tenderness, pocketing at base of wound or wound breakdown, bridging of the epithelium or soft tissue, and abnormal smell
Exclusion Criteria

- Duration $\leq 4$ Weeks $\geq 2$ Years
- Compression therapy contraindicated
- Hypersensitivity against octenidine
- Preceding or concomitant therapy with topical or systemic drugs
Course of the study

- Demographic data
- Physical examination
- Topical rinsing of ulcer area
- Dressing changes (min. 1 / week, max. 3 / week)
- Basic therapy: Compression therapy with elastic bandages and foam dressings
- Rinsing of ulcer area at least 1 / week
Planimetry and wound assessment

- Tracing and planimetry after debridement
- Wound assessment according to “Cutting & White”-criteria before debridement
Scaling of efficacy and tolerability

Scaling of efficacy

- Verbal five point scale— „very good“ to „worse than first visit“

Scaling of tolerability

- Doctor and patient via verbal scale
  “very good” to “very bad”
Results

Wound Surface Area Visit (V 1) until end of study (V 6)

![Bar chart showing wound surface area progression from V1 to V6]

- Octenisept®
- Ringer solution

20.05.2014 | Topical antimicrobials – Dr. Michael Braun | Schülke & Mayr GmbH | Seite 26
### Patients with complete wound closure

(100% within 12 weeks)

<table>
<thead>
<tr>
<th></th>
<th>octenisept®</th>
<th>Ringer solution</th>
<th>Chi²-Test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n)</td>
<td>%</td>
<td>Total (n)</td>
</tr>
<tr>
<td>Total responder</td>
<td>15/49</td>
<td>30.6</td>
<td>16/50</td>
</tr>
<tr>
<td>Responder split by size of target ulcer at Visit 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 6 cm²</td>
<td>9/26</td>
<td>34.6</td>
<td>13/29</td>
</tr>
<tr>
<td>&gt; 6 cm²</td>
<td>6/23</td>
<td>26.1</td>
<td>3/21</td>
</tr>
<tr>
<td>Responder split by duration of target ulcer at visit 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 6 months</td>
<td>8/27</td>
<td>29.6</td>
<td>12/28</td>
</tr>
<tr>
<td>&gt; 6 months</td>
<td>7/22</td>
<td>31.8</td>
<td>4/22</td>
</tr>
<tr>
<td>Responder split by size and duration of target ulcer at visit 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 6 cm² and ≤ 6 months</td>
<td>7/19</td>
<td>36.8</td>
<td>9/20</td>
</tr>
<tr>
<td>≤ 6 cm² and &gt; 6 months</td>
<td>2/7</td>
<td>28.6</td>
<td>4/9</td>
</tr>
<tr>
<td>&gt; 6 cm² and ≤ 6 months</td>
<td>1/8</td>
<td>12.5</td>
<td>3/8</td>
</tr>
<tr>
<td>&gt; 6 cm² and &gt; 6 months</td>
<td>5/15</td>
<td><strong>33.3</strong></td>
<td>0/13</td>
</tr>
</tbody>
</table>

Patients with complete wound closure (100% within 12 weeks)
Conclusion

- Excellent tolerability of octenisept®
- The octenisept® group developed clearly less adverse events (17% vs. 29%)
- Overall healing rates are equal in both groups
- With larger ulcers (≥ 6 cm²) and ulcers of longer duration (≥ 6 months) healing rates with octenisept® are significantly higher than with Ringer-solution (33% vs. 0%)
Efficacy and cost-effectiveness of octenidine wound gel in the treatment of chronic venous leg ulcers in comparison to modern wound dressings

Gilbert Hämmerle¹ & Robert Strohal²

¹ Department of Nursing, Federal County Hospital, Bregenz, Austria
² Department of Dermatology and Venereology, Federal Academic Teaching Hospital, Feldkirch, Austria
octenilin® wound gel study

Questions:
- Reduction of bioburden in comparison to silver
- Potency to stimulate wound healing compared to modern wound-phase adapted dressings
- Combination with modern wound-phase adapted dressings (sandwich dressing) useful

Study team:
- Prim.Univ.-Doz.Dr.Strohal, Dept. of Dermatology and Venereology, Acad. Teaching Hospital Feldkirch, Austria (Principal Investigator)
- DGKP G. Hämmerle, Federal Hospital of Bregenz, Austria, (Investigator)
- Prof. Dr. M. Mittlböck, Med. Univ. Vienna, Austria (Statistics)
Study characteristics

- **Design**: open-labeled, prospective, controlled, mono-center, clinical study
- **Cohort**: 44 patients/49 venous ulcers
- **Age**: median: 66.2 years (38 to 87-years), non significant distribution
- **Gender**: 31 males/13 females, non significant distribution
Study design

**Arm 1**
- **n**: 17
- **Primary**: foam dressing
- **Secondary**: foam dressing Ag, alginate, 2x alginate Ag, Hydrogel

**Arm 2**
- **n**: 17
- **Primary**: octenilin® Gel
- **Secondary**: 1x alginate foam dressing

**Arm 3**
- **n**: 15
- **Primary**: octenilin® Gel Adaptic®
- **Secondary**: suction gauze (Vliwazell®)

Visit days (V/d): 0 - 3 - 5 - 12 - 26 - 42
dressing change every 3-5d
Cleaning: saline (infected wounds: antiseptic solution)

**Study period**: 42 d

All venous ulcers at the lower extremities
(subgroup locally infected wounds)
### Wound healing

#### Healing of 9 ulcers (18%) before or at the last visit (d 42)

<table>
<thead>
<tr>
<th>Hydrogel + Active Dressing (Arm 2)</th>
<th>Hydrogel Alone (Arm 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V4 (d26) - grh</td>
<td>V3 (d12) - he</td>
</tr>
<tr>
<td>V4 (d26) - kap</td>
<td>V3 (d12) - mb</td>
</tr>
<tr>
<td>n = 2 (11%)</td>
<td>V4 (d26) - gm</td>
</tr>
<tr>
<td></td>
<td>V5 (d42) - ge</td>
</tr>
<tr>
<td></td>
<td>V5 (d42) - sth</td>
</tr>
<tr>
<td></td>
<td>V5 (d42) - sb</td>
</tr>
<tr>
<td></td>
<td>V5 (d42) - bro</td>
</tr>
<tr>
<td></td>
<td>n = 7 (47%)</td>
</tr>
</tbody>
</table>

No early healing of ulcers in the first arm (without hydrogel, just active dressings)
Reduction of bioburden

not significant

amount of bioburden [%]

Arm 1
Arm 2
Arm 3

V0 V1 V2 V3 V4 V5
Perception of the Dressing

Arm 1

- p = 0.0001 significant (better)

Arm 2

- p = 0.0001 significant (better)

Arm 3

- p = 0.6406 not significant
Tolerability

\[ p = 0.8771 \]
not significant

\[ p = 0.0117 \]
significant (better)

**Arm 1**

```
Visit Percentage [%]
0 20 40 60 80 100
1 2 3 4 5
```

**Arm 2**

```
Visit Percentage [%]
0 20 40 60 80 100
1 2 3 4 5
```

**Arm 3**

```
Visit Percentage [%]
0 20 40 60 80 100 120
1 2 3 4 5
```
### Calculation of costs

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>not infected</td>
<td>infected</td>
<td></td>
</tr>
<tr>
<td>Costs Material</td>
<td>23,04 €</td>
<td>25,81 €</td>
<td></td>
</tr>
<tr>
<td>Costs Patient</td>
<td>322,62 €</td>
<td>361,31 €</td>
<td></td>
</tr>
<tr>
<td>Total Costs</td>
<td>5716.- €</td>
<td>5615.- €</td>
<td></td>
</tr>
<tr>
<td>Average per patient</td>
<td>336.- €</td>
<td>330.- €</td>
<td>244.- €</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Day 26</th>
<th>entire period</th>
<th>Day 12</th>
<th>Day 26</th>
<th>Day 42</th>
<th>entire period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>24,85 €</td>
<td></td>
<td>20,34 €</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>198,79 €</td>
<td>347,89 €</td>
<td>81,37 €</td>
<td>162,74 €</td>
<td>264,46 €</td>
<td>284,80 €</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

20.05.2014 | Topical antimicrobials – Dr. Michael Braun| Schülke & Mayr GmbH | Seite 37
On average Group 1 ist the most expensive (mainly due to costs of Ag-dressings in infected wounds). Next is Group 2. The most cost-effective group is Group 3 considering the average costs per patient.

The costs for individual dressing changes are minor between the groups. When treating non-infected wounds, Group 2 is the most expensive treatment.

Cost effectiveness is achieved mainly by quicker wound healing.
Conclusions

- Treatment of venous ulcers with and without local signs of infection by octenilin® alone + simple secondary dressings
- Dressing change every 3-5 days

- Significant faster wound healing
- More pleasant perceptions by the patient
- Better tolerability
- Fast and effective removal of bioburden
- Best cost efficiency
Thank you very much for your attention!

Dr. Michael Braun
Manager Medical Affairs
Schülke & Mayr GmbH