Photodynamic therapy (PDT) of cervical intraepithelial neoplasia

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Photodynamic therapy of cervical intraepithelial neoplasia: Is it past, reality or future?
PHOTODYNAMIC THERAPY

Use of a photo-sensitizer (PS) to aid in the diagnosis (fluorescence) or treatment of cancer cell (radical oxygen)
PHOTODYNAMIC THERAPY

Application  Accumulation  Therapy
Photosensitiser
Photosensitizers

- **Porphyrrins**
  - Photofrin (PF) - intravenous
  - "Aminolevulinic acid (ALA)" - local
  - Protoporphyrin IX (PpIX)

- **Chlorins**
  - m-Tetrahydroxyphenyl chlorin (mTHPC)
  - Benzoporphyrin derivative mono-acid (BPD)
  - Tin ethyl etiopurpurin (SnET2)

- Phtalocyyanines
Material and methods

Medline was searched

9 studies was:
1. 2 studies local application with (ALA) drug light interval 1.5h-5h
   1 study local application with (ALA) drug light interval 1.5h-5h, a randomised, double-blind, placebo-controlled trial

2. 2 studies local application with (ALA) drug light interval 8h-24h
   1 study local application with (DHE) drug light interval 8h-24h

3. 3 studies intravenous application (PF)

In all studies was include non pregnant women with age 18-62yrs

6 studies looked HPV destruction
## Results

<table>
<thead>
<tr>
<th>Method</th>
<th>Cure rate %</th>
<th>HPV eradication</th>
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<tbody>
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<td></td>
<td>(number of patients)</td>
<td></td>
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<tr>
<td>Local application</td>
<td></td>
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<tr>
<td>Drug light interval 1,5h-5h</td>
<td>16% (51)</td>
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<td>(3 studies)</td>
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<tr>
<td>Local application</td>
<td>91% (31) (ALA)</td>
<td>73-80%</td>
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<tr>
<td>Drug light interval 8h-24h</td>
<td>68% (22) (DHE)</td>
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<td>(3 studies)</td>
<td>83% (53) (total)</td>
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<td>Intravenous application</td>
<td>92% (192) (Photofrin)</td>
<td>72-80%</td>
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<td>(3 studies)</td>
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Conclusion

- High cure rate (83%) was observed with local drug application – illumination time interval in studies with more than 8h
- ALA (91%) was more effective than DHE (68%)
- High cure rate (92%) with Intravenous application of Photofrin was observed in all 3 studies.
- Local and iv sensitizer application are very good for specific HPV eradication (75%)

- No side effects (skin phototoxicity) with local application
- Further larger, well designed studies are needed with local application and longer time interval
PHOTODETECTION
Fluorescence image and white light image of the cervix uteri after the application of 5% acetic acid.
Application of 10mg HAL in 10ml 0.9% NaCl solution on the cervix during 3 hrs.
CIN II x20, HAL 0.5%, 180 min application

glande endo-cervicale

exocol CIN II

stroma
Advantages to treat CIN with PDT

- Outpatient clinic
- Specificity (drug, light)
- Tailored to the shape of the cervix
- No stromal destruction (stenosis, cervix insufficiency)
- Cell death by apoptosis (no inflammation, no scarring)
- Specific HPV destruction (tetrapyrrrol)
- Repeatable

- In young women with open fertility planning
PDT may become also reality in developing countries because:

- Sensitizer (Hypericin) from St. Johns Wort (cultivated in own garden like ancient Chinese and Egyptian, for skin cancer treatment)
- Light applicator (LED)
  Can be developed (with batteries)
Merci
Haem Biosynthesis

5-ALA synthase

Uptake of exogenous 5-ALA

Cycline + succinyl CoA

5-ALA

5-ALA

Feedback control

Mitochondria

Coprotoporphyrinogen IX

Protoporphyrinogen IX

5-ALA

5-ALA

Cytoplasm

Ferrochelatase

Lower rate in tumour cells

Higher rate in tumour cells

Protoporphyrin IX

Coproporphyrinogen III

Porphyrinogen

Uroporphyrinogen III

Protoporphyrinogen IX

Coproporphyrinogen III

Feedback control

Fe^{2+}

Cytoplasm

PBG Deaminase

Uroporphyrinogen

Protoporphyrin IX

Coproporphyrinogen

Protoporphyrinogen