PHARMAKOKINETIC OF ANTIMYCOTICS INTO THE EYE

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THREE WAYS OF DRUG ADMINISTRATION IN OCULAR MYCOTIC INFECTION

• topical drops: highest drug level on ocular surface     
  → best for keratomycosis
• topical intravitreal injection: highest drug level intraocular 
  → best for endophthalmitis
• systemical: only moderate or poor penetration into the eye 
  → only supportive in ocular infection, highest possible dosis necessary
TOPICAL ADMINISTRATION
OF EYE DROPS

example

- Tobramycin-eyedrops 0.3 %
- person of 50 kg body weight 150 g systemical
  → 0.3 %
- normal dosis 150 mg

- systemical side-effects avoided
## TOPICAL ADMINISTRATION OF EYE DROPS

Molecular weights of antimycotics

<table>
<thead>
<tr>
<th>Antimycotic</th>
<th>Dalton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flucytosin</td>
<td>129.09</td>
</tr>
<tr>
<td>Fluconazol</td>
<td>306.3</td>
</tr>
<tr>
<td>Voriconazol</td>
<td>349.32</td>
</tr>
<tr>
<td>Miconazol</td>
<td>416.12</td>
</tr>
<tr>
<td>Ketoconazol</td>
<td>531.44</td>
</tr>
<tr>
<td>Pimaricin</td>
<td>665.75</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>924.1</td>
</tr>
<tr>
<td>Nystatin</td>
<td>926.11</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>1.093.50</td>
</tr>
</tbody>
</table>

Corneal epithelium permeable for drugs up to 500 D

Lit.: Maurice, DM 1960; Benson, H 1974
PHARMAKOKINETICS OF AMPHOTERICIN B INTO THE RABBIT EYE

- eye drops 0.5%: poor corneal penetration if epithelium present, moderate penetration into non-epithelialized cornea (Behrens-Baumann et al. 1987)
- intravitreal injection (10 µg): half-life time in phakic, candida-infection, aphakic and vitrectomized aphakic eye 9.1, 8.6, 4.7 and 1.4 days (Doft et al. 1985)
- intravenous injection (1 mg/kg body weight): 0.13 µg/ml in the aqueous humour after 24 h (Green et al. 1965)
PHARMACOKINETICS OF AMPHOTERICIN B INTO THE HUMAN EYE

- intracameral, -vitreal injection (7.5 µg):
  no exact data available, good tolerability
  (Pflugfelder et al. 1988, Behrens-Baumann 1991,
  Chapman et al. 1998)

- intravenous (0.6 mg/kg body weight, 2 patients):
  serum 0.6 and 1.5, *aqueous humour* 0.24 and 0.1,
  *vitreous humour* 0.23 und 0.1 µg/ml, resp.
  (Fisher et al. 1983)
PHARMACOKINETICS OF FLUCONAZOLE INTO THE RABBIT EYE

- eye drops (0.2 %): *aqueous humour* in non-debrided 1:2, in debrided cornea 1:8 using serial dilution test (Behrens-Baumann et al. 1990), in non-debrided 1.6, in debrided cornea 9.4 µg/ml (Yee et al. 1997)
- intravitreal injection: no data available
- intravenous (25 mg/kg/day for 14 days): *vitreous humour* 15.7 (peak) and 9.8 µg (trough) (Walsh et al. 1989)
PHARMACOKINETICS OF FLUCONAZOLE INTO THE HUMAN EYE

- oral dose (200 mg): *aqueous humour* $3.7 \pm 2.17 \, \mu g/ml$
  
  (Aust et al. 1995)

- oral dose (400 mg): *vitreous humour* $15 \, \mu g/ml$
  
  (Urban et al. 1982)
PHARMAKOKINETICS OF VORICONAZOLE INTO THE HUMAN EYE

- oral dose (2 x 400 mg): 53 % and 38 % of the plasma level in *aqueous humour* (1.13 ± 0.57 µg/ml) and *vitreous humour* (0.85 ± 0.31 µg/ml) in vitrectomized eyes (Haviprasad et al. 2004)

- intravenous (dosis not mentioned): *aqueous and vitreous* level 1.52 µg/ml and 1.12 µg/ml postmortem in a patient with septicemia (C. guilliermondii) (Breit et al. 2005)
LITERATURE
