New aspects in prophylaxis of ophthalmia neonatorum (Credé prophylaxis)

The problem
There are two reasons for the replacement of silver nitrate in the prophylaxis of ophthalmia neonatorum by other antimicrobial agents:
- the locally irritating potency of silver nitrate [1], which can cause reversible neonate conjunctivitis, the so-called argentum catarrh [2] and
- the changing etiology of ophthalmia neonatorum.

In Germany, S. aureus with a prevalence of 30–35% ranks first in the etiology of ophthalmia neonatorum, followed by S. epidermidis (10–15%), E. coli (5–15%), C. trachomatis (5–13%), β-hemolyzing streptococci (5–10%), S. pneumonia (1–6%) and other pathogens [3]. At the Austrian consensus meeting, the prevalence of S. aureus was given as 37% and of chlamydia even as 34% [4]. Owing to the lack of activity of silver nitrate against C. trachomatis in vitro [2] and in neonates [5], a new, well tolerated and effective antiseptic with a broad spectrum of activity against the relevant microorganisms including C. trachomatis and responsible viruses is required.

Reasons for the necessity of prophylaxis against ophthalmia neonatorum

In the US, the incidence of ophthalmia neonatorum is about 1.6% or less. In some African countries, it is as high as 23% and every year between 1000 and 4000 new-borns go blind as a result of ophthalmia neonatorum [6]. In Germany, the sexually transmitted infections of pregnant women can be attributed to N. gonorrhoea to 0.1–0.5% (risk of eye affection by infected mothers for neonates is 30–40%), for T. pallidum < 0.01% (with ~ 50% infection risk), C. trachomatis 2–12% (with 8–43% infection risk) and for HSV 1 and 2 (in USA) ~ 1% (with max. 1–2% infection risk) [2, 3].

When Credé prophylaxis was stopped, the increase in gonococcal infections was, for instance, in Canada 8-fold (1955), in New York 15-fold (1957), in Denmark 3-fold (1985), in Kenya 5-fold (1986) and in South Africa 6-fold (1986) [3]. These findings again confirm the efficacy of silver nitrate against gonococci.

Because chlamydial infections are on the rise and gonococci constitute a persistent risk, an effective broad spectrum antiseptic is required for prophylaxis. This is of particular importance, since untreated gonococcal infections can be deleterious for the eye and untreated chlamydial infection can impair vision as well, e.g. from scarring, and in isolated cases even lead to blindness. As an alternative a general screening for pregnant women by way of vaginal smear could be performed. However, for logistic and financial reasons this is not feasible, particularly because the detection of gonococci and chlamydia calls for a high input in laboratory technology. The practice of only taking vaginal smears if clinical symptoms are present is not safe, quite apart from the costs and the lack of laboratories in undeveloped regions.

Current developments
In the light of the deficiencies and risks of silver nitrate, in 1969 in the USA the silver nitrate solution was replaced by 0.5% erythromycin and 1% tetracycline. In 1989 this recommendation was renewed by the CDC [7]. Nevertheless, the local application of systemic antibiotics is problematic, in particular because of the risk of development of antimicrobial resistance. In addition, erythromycin in 0.1% dilution was still ineffective against C. trachomatis strain D in vitro over 15 min [2].

PVP-iodine seems to be the best alternative to replace silver nitrate, because of its wide spectrum of action that includes some virus species and due to its good tolerance in the antiseptically effective dilution of 1.25%. Gram positive as well as gram negative germs are killed within 30 s, C. trachomatis is destroyed within 30 s as well by just 0.06% PVP-iodine (Table 1). In the same dilution of 1.25%, PVP-iodine also inactivates HSV 1 and 2, Echo and strain-related Coxsackie viruses to a greater extent than silver nitrate [8]. This complies with the study of Isenberg et al. [9] on 3,117 newborns in Kenya in which erythromycin and silver nitrate were less effective than 2.5% PVP-iodine.

Table 1. Microbiocidal efficacy (log reduction ≥ 5) of Beta-isodona in aqueous dilution in quantitative suspension test (unpublished data)

<table>
<thead>
<tr>
<th>Test strain</th>
<th>PVP-iodine content (%)</th>
<th>0.2% Albumin load</th>
<th>Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N. gonorrhoeae</td>
<td>1.25</td>
<td>+</td>
<td>15</td>
</tr>
<tr>
<td>S. aureus, E. coli, P. aeruginosa</td>
<td>0.5</td>
<td>+</td>
<td>30</td>
</tr>
<tr>
<td>C. trachomatis strain D</td>
<td>0.025</td>
<td>–</td>
<td>30</td>
</tr>
</tbody>
</table>

1 Sauerbrei and Wutzler, unpublished data [2].
The local tolerance of 1.25% PVP-iodine is much better than of tetracycline, as demonstrated by cell growth from peritoneal explants in vitro [10].

There is also no systemic risk, when one drop of PVP-iodine 1.25% is administered to each eye. The iodine quantity mathematically given is an applied total amount of 68.75 μg iodine. By comparison, 11 maternal milk contains 86 ± 65 μg iodine and 11 industrial pre-infant food approx. 100 μg iodine. The recommended alimentary intake of iodine is 50 μg iodine/d for up to 4 months of age [2]. In a controlled blinded study with PVP-iodine eye antisepsis in adults just before ophthalmological surgery, the real absorption rate ranged between 0.8 and 2.4% of the total applied iodine amount [2]. At the moment we are assessing these data in newborns.

Whereas the application of 2.5% PVP-iodine solution caused pronounced burning for more than 30 min, a 1% solution was tolerated almost without pain [11]. For practical purposes, we do not recommend an aqueous solution of PVP-iodine, but an isoosmolaric solution with the following contents [12]:

- povidone iodine
  (low molecular with a K-value of < 18) 0.125 g
- sodium chloride 0.08 g
- disodium hydrogen phosphate x 12 H2O 0.025 g
- water for injection ad 10 g.

**Conclusion**

Given the status of the present knowledge PVP-iodine 1.25% as isoosmolaric solution is the antiseptic of choice for Crédé prophylaxis. It must be administered as soon as possible after birth, at the latest by the first hour after delivery. A careful mechanical cleansing of the eyelid should be carried out, followed by one drop in the conjunctival sac of each eye with no subsequent rinsing. To avoid any risk of contamination, the solution must be prepared for a once-only application.

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**References**


**Key words:** Ophthalmia neonatorum, Crédé prophylaxis, neonatal conjunctivitis, antibiotic prophylaxis, prophylactic agents.

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Neue Aspekte zur Prophylaxe der Ophtalmia neonatorum (Credé prophylaxis)

Nach derzeitigem Stand der Wissenschaft ist PVP-Jod 1,25% als isoosmolare Lösung das Antiseptikum der Wahl für die Credésche Prophylaxe. PVP-Jod ist die beste Alternative zu Silbernitrat, weil es ein breites Keimspektrum abdeckt und besser verträglich ist.

Empfohlene Rezeptur:

- Povidone iodine (Low molecular with a K-value of <18) 0.125 g
- sodium chloride 0.08 g
- disodium hydrogen phosphate X 12 H₂O 0.025 g
- water for injection ad 10 g