La patologia infiammatoria genitale

Alessandro Borghi
Dipartimento di Scienze Mediche, Sezione di Dermatologia e Malattie Infettive
Università degli Studi di Ferrara
Direttore: Prof. Monica Corazza
lichen sclerosus: prima scelta

2012

- clobetasolo propionato (CP) 0.05% unguento / crema

The recommended and accepted first-line treatment is the very potent topical corticosteroid clobetasol propionate 0.05%\(^5\)\(^6\)–\(^8\) (Strength of recommendation B; quality of evidence 2++; see Appendix for definitions).

The very potent topical steroid, clobetasol propionate 0.05%, was found to be significantly more effective than placebo in treating genital lichen sclerosus
corticosteroidi alternativi

- **metilprednisolone furoato 0.1% crema**

- **triamcinolone acetonide 0.1% unguento**

- **metilprednisolone aceponato 0.1% crema**

- **idrocortisone 0.1% unguento, betametasone dipropionato 0.05% unguento**
corticosteroidi alternativi

MMF 0.1% unguento in trattamento di fase acuta 12 settimane

- 5/settimana per 4 settimane
- a dì alterni per 4 settimane
- 2/settimana per 4 settimane

147 pazienti affette da VLS

- 113 pazienti (80.7%) responsive (responder)
- ↓ significativa dei sintomi, anche nelle non responder
- buona tollerabilità
**Implications for research.** The current evidence is limited, and further studies are required to fill in gaps in knowledge. First, we need RCTs determining the potency and regimen (e.g., frequency and duration of application) of topical corticosteroids that have adequate therapeutic efficacy but with the least desirable adverse effects (e.g., infections and atrophy).
potenza
RCT: CP vs MMF

First randomized trial on clobetasol propionate and mometasone furoate in the treatment of vulvar lichen sclerosus: results of efficacy and tolerability

A. Virgili, A. Borghi, G. Toni, S. Minghetti and M. Corazza

Clobetasolo propionato 0.05% unguento

VS

Mometasone furoato 0.1% unguento

in trattamento di fase acuta 12 settimane

- 5/settimana per 4 settimane
- a dì alterni per 4 settimane
- 2/settimana per 4 settimane
RCT: CP vs MMF

clobetasolo propionato 0.05% unguento

vs

mometasone furoato 0.1% unguento

efficacia
sicurezza
aderenza e soddisfazione
risultati

Active treatment phase (ATP)
Topical corticosteroid applied on a tapering regimen for 12 weeks
Number of patients entering the study = 54

**Clobetasol propionate (CP) 0.05% ointment**
Number of patients = 27

**Mometasone furoate (MMF) 0.1% ointment**
Number of patients = 27

**Drop-out**
- n = 2 patients
- n = 1 patient

**Results at the end of ATP with CP**
- Responders = 24 (88.9%)
- Nonresponders = 1 (3.7%)
- GSS75 = 16 (59.3%)
- GOS75 = 10 (37.0%)
- GSS50 = 21 (77.8%)
- GOS50 = 21 (77.8%)

**Results at the end of ATP with MMF**
- Responders = 24 (88.9%)
- Nonresponders = 2 (7.4%)
- GSS75 = 18 (66.7%)
- GOS75 = 13 (48.2%)
- GSS50 = 21 (77.8%)
- GOS50 = 22 (81.5%)
risultati

- tollerabilità del trattamento:

  non effetti collaterali legati alla terapia
In conclusion, these results provide evidence that MMF is as effective as CP in the treatment of VLS; consistent with this, MMF could represent an effective alternative to CP as a first-line treatment for the disease.
posologia
There are no randomized controlled trials providing evidence that a once- or twice-daily application of any one specific corticosteroid is the most effective, or documenting that one regimen is superior to another.
RCT: continuo vs tapering

mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung

in trattamento di fase acuta 12 settimane

<table>
<thead>
<tr>
<th>continuativo</th>
<th>VS</th>
<th>tapering</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/settimana per 12 settimane</td>
<td></td>
<td>5/settimana per 4 settimane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a di alterni per 4 settimane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2/settimana per 4 settimane</td>
</tr>
</tbody>
</table>
RCT: continuo vs tapering

mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung

continuativo vs tapering

- continuativo: 5/settimana per 12 settimane
- tapering: 5/settimana per 4 settimane, a dì alterni per 4 settimane, 2/settimana per 4 settimane

- efficacia
- sicurezza
- aderenza
Enrolment
Number of patients assessed for eligibility = 67

Excluded
n = 3 patients not meeting inclusion criteria

Active treatment phase
Number of patients entering the study = 64

Week 0
Allocation
Mometasone furoate 0.1% ointment in tapering regimen
(group A)
Number of patients (ITT population) = 32

Week 0
Allocation
Mometasone furoate 0.1% ointment 5 days per week for the entire treatment duration
(group B)
Number of patients (ITT population) = 32

Week 12
Dropout
n = 1 patient

Week 12
Dropout
n = 3 patients

Results at the end of the ATP within group A
Responders = 27 (84%)
Nonresponders = 4 (12%)
GSS 75 = 22 (69%)
GOS 75 = 15 (47%)
GSS 50 = 23 (72%)
GOS 50 = 24 (75%)

Results at the end of the ATP within group B
Responders = 25 (78%)
Nonresponders = 4 (12%)
GSS 75 = 20 (62%)
GOS 75 = 9 (28%)
GSS 50 = 22 (69%)
GOS 50 = 21 (66%)
risultati

- tollerabilità del trattamento:
  
  non effetti collaterali legati alla terapia
risultati

- aderenza al trattamento:

mometasone furoato 0.1% ung vs mometasone furoato 0.1% ung

relative risk: 2.14 (95% confidence interval 0.20–22.34)

$\rho = 0.60$
Our findings seem to indicate strongly that both tapering and continuous application of MMF have similar efficacy and tolerability in treating active VLS, with both well tolerated and effective in improving the symptoms and signs of the disease. No significant differences in patient adherence to the two study protocols were found. In conclusion, these results confirm the usefulness of topical potent corticosteroids in the ATP of VLS, and provide evidence that they can be administered equally well in a continuous or tapering regimen.
formulazione

Mometasone furoate in the treatment of vulvar lichen sclerosus: could its formulation influence efficacy, tolerability and adherence to treatment?

Monica Corazza, Annarosa Virgili, Giulia Toni and Alessandro Borghi

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Responders, n (%)</th>
<th>Patients treated with MMF cream (group A)</th>
<th>Patients treated with MMF ointment (group B)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate 0.1% crema vs Mometasone furoate 0.1% ointment</td>
<td>16 (59.26)</td>
<td>29 (78.38)</td>
<td></td>
<td>.09</td>
</tr>
<tr>
<td>GSS75, n (%)</td>
<td>12 (44.44)</td>
<td>25 (67.57)</td>
<td></td>
<td>.06</td>
</tr>
<tr>
<td>GOS75, n (%)</td>
<td>11 (40.74)</td>
<td>17 (45.95)</td>
<td></td>
<td>.67</td>
</tr>
<tr>
<td>GSS50, n (%)</td>
<td>21 (77.78)</td>
<td>30 (81.08)</td>
<td></td>
<td>.74</td>
</tr>
<tr>
<td>GOS50, n (%)</td>
<td>19 (70.37)</td>
<td>30 (81.08)</td>
<td></td>
<td>.31</td>
</tr>
</tbody>
</table>
Our findings indicate that MMF in ointment formulation is more effective in treating active VLS, especially in improving symptoms, in comparison with MMF cream. Both formulations were well tolerated and no significant differences in patient adherence and satisfaction with the treatment were found.

In conclusion, based on these results the ointment vehicle seems to optimize the therapeutic action of potent corticosteroids and thus could be preferable to the cream for the treatment of VLS.
Implications for research. …one of our secondary outcomes, “duration of remission or prevention of subsequent flares,” should be included in future RCTs
About 60% of patients experience complete remission of their symptoms.\textsuperscript{60,61} Others will continue to have flares and remissions; they are advised to use clobetasol propionate 0.05% as required.
...a lungo termine?

1. terapia reattiva
2. terapia protratta

- metilprednisolone aceponato 0.1% crema
- idrocortisone 0.1% unguento
- betametasone dipropionato 0.05% unguento

12 mesi

Vulvar lichen sclerosus in postmenopausal women: a comparative study for treating advanced disease with clobetasol propionate 0.05%.

Diakomanolis ES1, Haidopoulos D, Syndos M, Rodolakis A, Stefanidis K, Chatzipapas J, Michalas S.

clobetasolo propionato per 6 mesi vs al bisogno
...a lungo termine?

1. terapia reattiva
2. terapia protratta
3. terapia proattiva

MMF 0.01% unguento, 2 applicazioni /settimana per 12 mesi
Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study

A. Virgili, S. Minghetti, A. Borghi and M. Corazza

mometasone furoato 0.1% ung per 12 settimane (ATP)

responders
RCT: MMF proattiva

**Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study**

A. Virgili, S. Minghetti, A. Borghi and M. Corazza

---

**responder**

12 mesi

**MMF 0.01% unguento, 2 applicazioni / settimana**

**vs**

**crema base, 1 applicazione / die**

**vs**

**vitamina E, 1 applicazione / die**
risultati

**Active treatment phase (AP)**
- Mometasone furoate 0.1% ointment, 12 weeks
- n = 27 patients

**Withdrawals**
- n = 2 patients
- Pregnancy, n = 1 patient
- Lost to 12-week visit, n = 1 patient

**Maintenance phase (MP)**
- Number of patients randomized = 25

**Week 0**
- Vitamin E pure oil, once daily
  - n = 9 patients
  - Relapse, n = 4 patients
  - Drop out, n = 1 patient

- Mometasone furoate 0.1% ointment, twice weekly
  - n = 8 patients
  - Relapse, n = 4 patients

- Cold cream, once daily
  - n = 8 patients

**Week 26**
- Vitamin E oil, once daily
  - n = 5 patients
  - Relapse, n = 1 patients

- Mometasone furoate 0.1% ointment, twice weekly
  - n = 7 patients
  - Relapse, n = 0 patients

- Cold cream, once daily
  - n = 4 patients

**Week 52**
- Vitamin E ointment once daily
  - Total completed trial = 4
  - Total relapses = 5
  - Total drop out = 0
  - 5 (56%)

- Mometasone furoate 0.1% ointment, twice weekly
  - Total completed trial = 7
  - Total relapses = 0
  - Total drop out = 1
  - 0

- Emollient cream once daily
  - Total completed trial = 3
  - Total relapses = 5
  - Total drop out = 6
  - 5 (63%)
risultati

**MMF 0.01% unguento, 2 applicazioni /settimana**

vs

**crema base, 1 applicazione / die**  \( p = 0.0128 \)

vs

**vitamina E, 1 applicazione / die**  \( p = 0.0204 \)

recidiva

\[ RR = 0.0951 \quad (95\% \, CI \, 0.0177 \,– \, 0.5106) \]
In conclusion, these results provide evidence that maintenance treatment with mometasone furoate 0.1% ointment twice weekly may play an important role in clinical practice and could represent the treatment of choice in the challenging long-term management of VLS.
RCT: MMF vs CP proattiva

Clobetasol propionate vs. mometasone furoate in 1-year proactive maintenance therapy of vulvar lichen sclerosis: results from a comparative trial

M. Corazza, A. Borghi,* S. Minghetti, G. Toni, A. Virgili

CP 0.05% unguento vs MMF 0.1% unguento

responder responder

mantenimento

12 mesi

CP 0.05% unguento vs MMF 0.1% unguento

2 applicazioni / settimana
risultati

$p = ns$

tra T0 e T12

efficacia della proattiva nel mantenimento

CP vs MMF

non differenze tra corticosteroidi
The study results provide evidence that proactive treatment with either CP 0.05% ointment or MMF 0.1% ointment is an effective, safe and reliable therapy for the long-term prevention of relapse in VLS previously treated with topical corticosteroid.
Cure is not usually the aim of treatment but improvement of symptoms (75–95%) after 3 months or at its best reversals of signs (20%) (1+/A).
Clearance in vulvar lichen sclerosus: a realistic treatment endpoint or a chimera?

A. Borghi,* A. Virgili, S. Minghetti, G. Toni, M. Corazza

studio retrospettivo su 196 pazienti trattate per 12 settimane

sintomi = 0

segni = 0

segni e sintomi = 0

<table>
<thead>
<tr>
<th>Patients (n.)</th>
<th>Treatment regimen (12-week duration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>0.1% of MMF ointment once daily, at tapering regimen, as previously described(^1,2)</td>
</tr>
<tr>
<td>52</td>
<td>0.1% of MMF ointment once daily for five consecutive days per week</td>
</tr>
<tr>
<td>27</td>
<td>0.05% of CP ointment once daily, at tapering regimen, as previously described(^1,2)</td>
</tr>
<tr>
<td>21</td>
<td>0.1% of MMF ointment and 0.05% of tretinoin cream, for five consecutive days per week</td>
</tr>
<tr>
<td>17</td>
<td>0.025% of tretinoin cream once daily, every other day</td>
</tr>
</tbody>
</table>
(i) 165 pz sintomatiche al baseline ⟷ $\text{GSS} = 0$ in 78 pz (47.3%)

(ii) 187 pz che hanno completato la terapia ⟷ $\text{GOS} = 0$ in 40 pz (21.4%)

(iii) 165 pz sintomatiche al baseline ⟷ complete clearance in 23 pz (13.9%)

(iv) 59 pazienti con dispareunia ⟷ 18 pz (30.5%) risoluzione del sintomo
In conclusion, a 12-week topical treatment, although highly effective in ameliorating both symptoms and objective changes, is unlikely to induce a complete cure of VLS. As a result, a relevant part of the patients labelled as responders are not actually clear of the disease, and this may account for a divergence between physicians’ and patients’ perspectives regarding treatment outcome and satisfaction.
memoranda

- corticosteroidi **potenti** e **ultra-potenti** pari efficacia e tollerabilità nella terapia di attacco ➔ **prima linea terapeutica**

- posologia **continuativa** e **tapering** pari efficacia e tollerabilità nella terapia di attacco

- **unguento maggiore efficacia** di crema

- terapia **corticosteroidea proattiva** efficace e sicura nel **mantenimento** a lungo termine
memoranda

- clearance obiettivo difficile da raggiungere in 12 settimane