Not all topical corticosteroids are equal

Dr Kerryn Greive
Not all topical corticosteroids are equal!

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Conflict of Interest: Full time employee of Ego Pharmaceuticals
What will we talk about today?

• Corticosteroids
  – Hydrocortisone and mometasone furoate
• Hydrocortisone
  – Dissolved vs. dispersed
• Mometasone furoate
  – Safety and efficacy
  – Topical delivery to enhance patient compliance
What are corticosteroids?

• Corticosteroids are a class of steroid hormones that are naturally produced in the adrenal cortex.
• Corticosteroids are involved in a wide range of physiologic systems such as stress response, immune response and inflammation.
• Synthetic versions are widely used topically and internally to treat inflammatory conditions such as arthritis, dermatitis and allergic reactions.
What are corticosteroids?

• Corticosteroids act on the immune system by blocking the production of substances that trigger allergic and inflammatory actions

• They control skin cell overgrowth and reduce inflammation

What are corticosteroids?

• Overall, they calm the immune system down, delivering benefits derived from short term vascular changes and limited immunosuppression\(^1\)
  – *While restricted inflammation is beneficial, excessive or persistent inflammation incites tissue destruction and disease*\(^1\)

Before we had corticosteroids...

<table>
<thead>
<tr>
<th>Product</th>
<th>Ingredients</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egosulphyl</td>
<td>Sulphur 10%, Olsum rusci 9%, Salicylic acid 2%</td>
<td>Seborrhoea, dandruff, psoriasis</td>
</tr>
<tr>
<td>Egolotion</td>
<td>Coal tar 2%, Zinc oxide 13.5%, Ethyl alcohol 19.5%, Glycerin 31%</td>
<td>Dry dermatoses, pruritus, eczema, urticaria, insect bites.</td>
</tr>
<tr>
<td>Egopsoryl TA</td>
<td>Allantoin 2.5%, Solution of coal tar B.P 5%, Phenol 0.5%, Sulphur 0.5%</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>Egoderm</td>
<td>Tumenol ammonium 1%</td>
<td>Dermatitis, eczema</td>
</tr>
</tbody>
</table>
Topical corticosteroids

• Over the last 60 years topical corticosteroids have become the cornerstone of treatment for many inflammatory skin conditions

• Over the years, topical corticosteroids have been altered chemically to enhance their selectivity for the glucocorticoid receptor thereby reducing the negative side effects

Topical corticosteroids

- Topical application of corticosteroids produces dramatic suppression of skin diseases in which inflammation is a prominent feature
  - Eczema, infantile eczema, atopic dermatitis, dermatitis herpetiformis, contact dermatitis, seborrhoeic dermatitis, neurodermatitis, psoriasis and intertrigo

Mechanism of action

• Even today we are not 100% sure about the mechanism of action

• The gene-modification model of protein transcription and translation is the leading theory, although it cannot explain all the properties of corticosteroids

Mechanism of action
Gene modification model

• Receptor binding
  – Corticosteroid molecules bind to the specific receptor protein in the cell cytoplasm
  – Build up of steroid-receptor complex in the nucleus
• Synthesis of specific mRNA
  – Steroid-receptor complex binds to certain DNA sequences
  – Induces production of new mRNA based on the new DNA
• Synthesis of protein
  – New proteins produced from the new mRNA including lipocortin, interleukin-1 and lymphokines

From cortisol to super potency

- Modification of both the ring structure and the side chains produced dramatic changes in potency and side effects\(^1\)
  - Increased receptor affinity
    - Fluorination of the position 9
    - Introduction of the unsaturated bond between the first 2 carbon atoms in the A ring
  - Decreased receptor affinity
    - Esterification at position 21
Topical corticosteroids

- Long history of use
- Effective for use on a wide range of dermatoses
- Available in a range of potencies
- But consumers can be concerned about using them
  - *Corticosteroid phobia*
Topical corticosteroids

*Corticosteroid phobia*

• Over 70-80% of patients prescribed topical corticosteroids are fearful of side effects and fail to use them appropriately\(^1,3\)
  - This fear and anxiety is a significant barrier to effective treatment\(^2\)
  - 24% of patients admit to being non-compliant due to their concerns\(^3\)
  - 40% of parents of children with atopic eczema perceive corticosteroid creams as dangerous\(^4\)
    • 20% thought them too dangerous to use on their children\(^4\)

Topical corticosteroids

_Corticosteroid phobia_

• Tachyphylaxis – the alternative definition
  – Does progressive lack of efficacy over time represent gradual loss of steroid receptor function, or
  – The loss of willingness of a patient to apply a messy topical agent?

_Professor Steven Feldman_
Topical corticosteroids

*Corticosteroid phobia*

- Fear of treatment is an understandable response to misinformation, much of which comes from trusted sources.\(^2\)

- Steroid phobia may be accentuated by\(^1\):
  - The media
  - The misconception that topical corticosteroids are analogous to anabolic steroids or oral steroids

- Parents are most afraid of\(^1\):
  - Systemic absorption causing effects on growth and development
  - Skin thinning

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Topical corticosteroids

*Corticosteroid phobia – skin thinning*

• Using healthy subjects skin thinning can be induced using¹:
  – Twice daily application
  – Potent and super potent corticosteroids
  – For 6 weeks
  – A return to normal skin thickness was seen 4 weeks after treatment stopped

Topical corticosteroids

*Corticosteroid phobia – skin thinning*

- Adults with atopic dermatitis\(^1\)
  - Treated for 20 weeks
  - Once a day
  - Potent corticosteroid
  - No evidence of skin atrophy seen

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Topical corticosteroids

Corticosteroid phobia – skin thinning

• Skin thinning is well documented for super potent corticosteroids
  – but rare for moderate to high potency corticosteroids *if they are used appropriately*¹,²
    • Hydrocortisone – mild
    • Mometasone furoate - potent

Topical corticosteroids

Corticosteroid phobia – growth effects

• A long term study
• Examined the effect of mild to moderate topical corticosteroids used for 3-10 years in children
• Moderate to severe atopic dermatitis
• No evidence of adrenal suppression in these children

Topical corticosteroids

Corticosteroid phobia – growth effects

• Adult height
• Subjects developed atopic dermatitis before 5 years of age, continuing into adulthood
• Severe enough to need specialist care
• Adult height was not significantly different from controls
  – Any growth impairment that did occur in childhood was considered temporary and reversible

Topical corticosteroids

Corticosteroid phobia

• When used appropriately topical corticosteroids present a well tolerated and effective means of reducing the body's destructive inflammatory processes\(^1\)

• The vast majority of adverse events for topical corticosteroids occur from inappropriate selection and application\(^1\)

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Topical corticosteroids

Corticosteroid phobia

• Although skin thinning and systematic effects can develop very occasionally, the concern expressed by people using them is out of proportion to the evidence of harm.¹

• When skin damage occurs it is in the context of inappropriate use outside of a supervised treatment program.²

• Overall topical corticosteroids have very few side effects if used correctly.²

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Topical corticosteroids
Hydrocortisone and mometasone furoate

• Since 1951 when hydrocortisone was first marketed, many corticosteroids have been marketed with increasing potency.
• With increased potency came increased side effects, until the development of mometasone furoate.
• With mometasone furoate this connection was broken.
  – High potency corticosteroid with the safety of hydrocortisone.
Topical corticosteroids
Hydrocortisone and mometasone furoate

• Hydrocortisone has been available for many decades, and is often overlooked as an option for cortico-responsive dermatoses, despite its long history of safe usage.

• Today we will look at what can be achieved with hydrocortisone and mometasone furoate
Topical corticosteroids

*Potency ranking*

- **Mild**
  - *Hydrocortisone (0.5 / 1.0%)* & *Desonide (0.05%)*
- **Moderate**
  - Clobetasone butyrate (0.05%) & Betamethasone valerate (0.02/0.05%)
  - Methylprednisolone aceponate (0.1%) & Triamcinolone acetonide (0.02%)
- **Potent**
  - Betamethasone dipropionate (0.05%) & Betamethasone valerate (0.1%)
  - *Mometasone furoate (0.1%)* & Triamcinolone acetonide (0.1%)
- **Very / Super Potent**
  - Betamethasone dipropionate (0.05% OV)
  - Clobetasol propionate (0.05%)
Scheduling

• Topical hydrocortisone
  – 1% is Pharmacist Only, S3
  – 0.5% is Pharmacy Only, S2
  – Customer can largely self select

• Topical mometasone furoate
  – Prescription Only, S4
  – Learned intermediary
Hydrocortisone

*What is it?*

- Hydrocortisone is a mild potency corticosteroid\(^1\)
- Hydrocortisone is produced naturally by the adrenal cortex\(^2\)
  - Important point for those looking for ‘natural’ solutions
- Introduced as a medicine in 1951\(^3\)

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Hydrocortisone

*Safety*

- Hydrocortisone is considered to be the safest of all corticosteroids
  - Reflected in its OTC status
Hydrocortisone

Efficacy

• Approved for use on a wide range of corticosteroid responsive dermatoses including:
  • Eczema and dermatitis

Hydrocortisone

Efficacy

• Approved for use on a wide range of corticosteroid responsive dermatoses including:
  • Itching and rash from cosmetics or jewellery

Watch strap reaction  Adhesive plaster reaction  Reaction to nickel stud

Hydrocortisone

**Efficacy**

- Approved for use on a wide range of corticosteroid responsive dermatoses including:
  - Anogenital itch
Hydrocortisone

Efficacy

• Approved for use on a wide range of corticosteroid responsive dermatoses including:
  • Sunburn

Images from http://www.dermnetnz.org/reactions/sunburn.html
Hydrocortisone

*Efficacy*

- Approved for use on a wide range of corticosteroid responsive dermatoses including:
  - Insect bites

Images from http://www.dermnetnz.org/arthropods/bites.html
Hydrocortisone
Most appropriate for...

- Mild disease\(^1\)
- Disease on more permeable or thinner\(^1\) skin such as the face, the flexures and the genitals
- For areas where maceration is common, i.e. the axilla\(^1\)
- Maintenance therapy once control of the flare has been gained\(^1\)

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Hydrocortisone

*Perception*

- Most commonly used topical corticosteroid¹
- Considered as a strong or very strong corticosteroid by about a third of users²
  - Misunderstanding contributes to fear
- Need to reassure users that hydrocortisone is
  - Gentle, mild and natural

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Hydrocortisone

State of the active

- Hydrocortisone in topical products will be in one of two states
  - Dispersed
  - Dissolved
- The state of the hydrocortisone will have a major impact on how rapidly the active is delivered to the site of action
Hydrocortisone
State of the active

• Dispersed
  • Fine particles of hydrocortisone are suspended uniformly through the product
  • The hydrocortisone must dissolve into the skin lipids before it can become available to the skin
Hydrocortisone
State of the active

- Dissolved
  - Hydrocortisone is present in free molecular form
  - The hydrocortisone is immediately available to the skin from the product

- This difference between dissolved and dispersed can be observed using the vasoconstrictor assay.
Hydrocortisone
*Visualized using vasoconstriction*

- The vasoconstrictor assay is a human bioassay that allows us to visualize the rate and extent of deliver of a corticosteroid from a base into the skin
  - Based on the skin blanching response to corticosteroids
    - The release of the steroid from the formulation followed by its penetration through the stratum corneum and viable epidermis into the dermis produces the characteristic vasoconstrictor effect
Hydrocortisone
*Visualized using vasoconstriction*

- Validated against clinical response
  - Potency by clinical response equals potency by vasoconstrictor
- First use by Stoughton in 1972
- Now used by the FDA to compare the rate and extent of delivery of topical corticosteroids

Hydrocortisone
*Dissolved or Dispersed*

**Vasoconstriction**

A dissolved 1% hydrocortisone cream shows significantly more vasoconstrictor activity than a dispersed 1% hydrocortisone cream.

**Comparative Results of Vasoconstriction Trial**

(Area under the curve as left)

The preparations were applied at these times (days).

The greater the area under the curve, the greater the vasoconstriction.
Hydrocortisone

Safety

• Category A for pregnancy and breastfeeding
  • Safe for use in pregnancy¹
  • Safe for use in breastfeeding²

• Children
  • Can be administered as an OTC to children from 2 years
  • No limits if under medical supervision

1. In M. Drugs in Pregnancy. Melbourne, Australia: The Royal Women’s Hospital Pharmacy Department; 2006.
Hydrocortisone

Summary

• Long history of use, since 1951
• Safe
  • OTC
  • Suitable for children, pregnancy and breast feeding
• Effective
  • Approved for use for a wide range of dermatosis from eczema to sunburn
  • Dissolved hydrocortisone results in faster delivery of the active to the skin
Mometasone furoate

What is it?

- Potent topical corticosteroid
- Topical mometasone furoate has been available worldwide for over 20 years
- Available as an ointment, a (fatty) cream, and a lotion
- Now also available as a hydrogel
Mometasone furoate

- Mometasone furoate is:
  - a synthetic corticosteroid and is related to the naturally occurring cortisol
  - a synthetic 16\(\alpha\)-methyl analogue of beclomethasone
Mometasone furoate

*Potency vs. efficacy*

- Traditionally the more potent a corticosteroid is, the more side effects associated with it
  - Topical
  - Systemic
- Mometasone furoate has been able to break that connection through clever molecular design
Mometasone furoate

*Potency vs. efficacy*

- It is the chlorine molecules attached to the mometasone furoate molecule that are responsible for making it:
  - As potent as betamethasone
  - As safe as hydrocortisone
Mometasone furoate

Safety

• Topical mometasone furoate has minimal potential for systemic effects due to:
  – Very high lipophilicity so it binds very strongly with its receptor in the skin
  – Limited cutaneous penetration\(^1\), with less than 1% passing from the skin to the systemic circulation
  – Liver rapidly metabolizes any absorbed material

Mometasone furoate

Safety

• A human study
• Application of 10g/day of mometasone furoate 0.1% ointment
  – under occlusion
  – 20 hours a day
  – for 5 days
• Only 0.00076% of the total administered dose was excreted in the urine as mometasone furoate or its metabolites.¹

Mometasone furoate

Safety

• Another study found that 0.7% of mometasone furoate 0.1% ointment was systemically absorbed after an 8-hour contact time with no occlusion\(^2,3,4,5\)
  – 94% of the total dose remaining on the skin unabsorbed with approximately 1.6% diffusing into the skin.\(^2\)

• Under the same conditions mometasone furoate cream has been found to have a percutaneous absorption of 0.4%.\(^6\)
Mometasone furoate

Safety

• Any mometasone furoate that does reach systemic circulation:
  – has a low resorption rate and,
  – undergoes rapid biotransformation in the liver,
  – resulting in minimal or no systemic side effects.4

Mometasone furoate

Safety - Children

• The use of mometasone furoate 0.1% once daily has been documented in a number of studies in children from 7 months to 12 years old, with moderate to severe dermatitis involving at least 15% of the body surface area.
  – Duration of treatment was usually only for 3 weeks, but up to 6 weeks in one study.
• No skin thinning was observed in these studies
• No change in plasma cortisol levels, where this was monitored.

1. Prescribing Information. Zatamil. Mometasone furoate. Date of TGA approval: 10/05/2012
Mometasone furoate

Safety - Children

• In general, mometasone furoate was well tolerated.
  – Local reactions were minor, eg. stinging occurred in few patients.

• Mometasone appears to be safe in young children and may have less effect on the HPA axis than other corticosteroids of similar strength
  – Care should be taken that application sites in infants and young children are not occluded with tightly fitting nappy’s or plastic pants.
Mometasone furoate

Safety – Pregnancy

• Category B3\(^1\)
  – There are no adequate and well controlled studies of the teratogenic effects of mometasone furoate in pregnant women.
    • Should be used with caution during pregnancy and only if the potential benefit to the patient outweighs the potential risk to the foetus.
    • Potent corticosteroids should not be used on pregnant patients in large amounts or for prolonged periods of time.

\(^1\) Prescribing Information. Zatamil. Mometasone furoate. Date of TGA approval: 10/05/2012
Mometasone furoate

Safety – Breastfeeding

• Systemically administered corticosteroids are secreted into breast milk but the quantities are too low to have a deleterious effect on the infant.

• It is not known if topically applied mometasone will be absorbed in sufficient quantities to produce detectable levels in breast milk.
  – Use with caution during breastfeeding
  – Temporary cessation of breastfeeding during treatment may also be considered.
Mometasone furoate

**Efficacy**

• The efficacy of mometasone furoate has been tested:
  – in a variety of skin conditions
  – against a number of other corticosteroids
# Mometasone furoate compared with hydrocortisone

**Potent vs. mild**

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bressinck R <em>et al</em>¹</td>
<td>Psoriasis</td>
<td>MF: 47% in 21 days HC: 12% in 21 days</td>
<td>No diff. in plasma cortisol hematolgy, blood chemistry, urine analysis, blood pressure or body weight. 3 AE for MF, 1 for HC.</td>
</tr>
<tr>
<td>(15g/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vernon HJ <em>et al</em>²</td>
<td>Childhood atopic dermatitis</td>
<td>MF: 95% in up to 6 wks HC: 75% in up to 6 wks</td>
<td>No diff in plasma cortisol level. No skin atrophy in either group. 3 reports of stinging for MF.</td>
</tr>
<tr>
<td>(MF once/day; HC twice/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz HI <em>et al</em>³</td>
<td>Psoriasis, bilateral paired comparison</td>
<td>38% of subjects responded equally to MF and HC MF: 60% in 43 days HC: 38% in 43 days</td>
<td>1 had mild skin thinning at both MF and H treatment sites. After 6 weeks 1 case of telangiectasia in MF. No other signs of cutaneous skin atrophy.</td>
</tr>
</tbody>
</table>

Mometasone furoate 
*compared with methylprednisolone aceponate*

Potent vs. moderate

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kecskes A <em>et al</em> 17 (0.1% MpA Ointment 0.1% MF Ointment)</td>
<td>UVB induced erythema 3 MED of UVB radiation followed by application of topical steroid.</td>
<td>MF: Total erythema suppression 15/20 Partial suppression 4/20 No suppression in 1 case. MA Total erythema suppression 17/20 Partial suppression 3/20</td>
<td>No data</td>
</tr>
</tbody>
</table>

## Mometasone furoate compared with clobetasone butyrate

**Potent vs. moderate**

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominguez L et al (^1) (MF once/day; CB twice/day)</td>
<td>Variety of dermatoses</td>
<td>No significant difference between MF and CB but those treated with MF improved faster. Patient evaluations rated MF as sig. better than CB. MF: 93% markedly improved or cleared after 21 days CB: 88% markedly improved or cleared after 21 days</td>
<td>No AE for MF; 3 AE for CB</td>
</tr>
<tr>
<td>Rafanelli A et al (^2) (MF once/day; CB twice/day)</td>
<td>Atopic dermatitis</td>
<td>MF worked faster than CB. From the 4th day of treatment MF was significantly better than CB. MF: 50% in 21 days CB: 6.7% in 21 days</td>
<td>Plasma cortisol remained within normal at all times. No skin alterations, atrophy or AE reported.</td>
</tr>
</tbody>
</table>

1. Dominguez L et al: Comparison of the safety and efficacy of mometasone furoate cream 0.1% and clobetasone butyrate cream 0.05% in the treatment of children with a variety of dermatoses. *Cur Ther Res* 48(1): 128-133. 1990
### Mometasone furoate compared with triamcinolone acetonide

**Potent vs. potent**

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medansky RS et al(^1) (MF 0.1% cream once/day; 0.1% TA cream twice/day) (MF 0.1% ointment once/day; 0.1% TA ointment twice/day)</td>
<td>Psoriasis</td>
<td>Improvement at 3 weeks: MF: 54% TA 51%</td>
<td>No difference in rate or type of adverse reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improvement at 3 weeks: MF: 60% TA 37%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MF better than TA</td>
<td></td>
</tr>
<tr>
<td>Swinehart et al(^2) (MF 0.1% lotion once/day; 0.1% TA lotion twice/day)</td>
<td>Scalp Psoriasis</td>
<td>Marked improvement of complete clearance achieved in: MF: 77% TA: 62%</td>
<td>No difference in rate or type of adverse reactions</td>
</tr>
</tbody>
</table>

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Mometasone furoate compared with betamethasone valerate

*Potent vs. potent*

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
</table>
| Vanderploeg DE et al\(^1\) (MF once/day; BV twice/day) | Scalp Psoriasis | MF: 85% at 21 days  
BV: 70% at 21 days  
MF significantly better | 8 AE for MF; 10 AE for BV |
| Svensson A et al\(^2\) (MF once/day; BV twice/day) | Psoriasis | No diff between MF and BV at 4 weeks, but MF sig better at 8 weeks. | 3 AE for MF; 4 AE for BV |
| Viglioglia P et al\(^3\) (MF once/day; BV twice/day) | Variety of Dermatoses | MF: 93.6% at 21 days  
BV: 96.5% at 21 days  
No significant diff. | No side effects reported, *no skin atrophy seen*. |
| Rajka G et al\(^4\) (MF once/day; BV twice/day) | Allergic contact dermatitis | MF was significantly more effective, particularly after the first week of treatment. | *No suppression of plasma cortisol levels.*  
8 AE for MF; 2 AE for BV |

# Mometasone furoate compared with betamethasone dipropionate

*Potent vs. potent*

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Efficacy Results</th>
<th>Safety Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bjerring P&lt;sup&gt;1&lt;/sup&gt; (UVB radiation: BD 0.05% cream MF 0.1% cream)</td>
<td>UVB induced erythema</td>
<td>At 5, 12 and 24 hours after application, MF was significantly better at reducing inflammation than BD</td>
<td>No data</td>
</tr>
<tr>
<td>Marchesi E <em>et al</em>&lt;sup&gt;2&lt;/sup&gt; (MF ointment once/day; BD ointment twice/day)</td>
<td>Atopic dermatitis</td>
<td>No significant difference between MF and BD after three weeks</td>
<td>No systemic or local reactions seen.</td>
</tr>
<tr>
<td>Peharda V <em>et al</em>&lt;sup&gt;3&lt;/sup&gt; (MF ointment once/day; BD ointment twice/day)</td>
<td>Psoriasis vulgaris</td>
<td>No significant difference between MF and BD after four weeks 85% cured or had good to moderate improvement for both MF and BD</td>
<td>MF: 1 mild atrophy, 2 irritation BD: 4 mild atrophy, 2 irritation</td>
</tr>
<tr>
<td>Kelly JW <em>et al</em>&lt;sup&gt;4&lt;/sup&gt; (MF cream once/day; BD cream twice/day. Up to 12 weeks)</td>
<td>Variety of dermatoses</td>
<td>No significant difference between MF and BD in mean percentage improvement</td>
<td>No difference seen in HPA axis function.</td>
</tr>
</tbody>
</table>

Mometasone furoate

Overview of safety

• The risk to benefit ratio of any topical steroid must be a consideration in prescribing
• The studies examining topical mometasone furoate have demonstrated that mometasone furoate is safe for the treatment of steroid responsive dermatoses in both children and adults.
• The majority of studies on both adults and children have used a once a day for 3 weeks application regimen, with minimal side effects.
Mometasone furoate

*Overview of safety*

- A few cases have been noted in the literature of severe side effects, but these are very rare and have been associated with patient abuse or long term use of topical mometasone furoate.
  - Very few cases of sensitization or allergy have been reported to mometasone furoate despite its worldwide availability for over 20 years.

- The side effect profile of mometasone furoate in topical preparations has been shown to be on par with that of topical hydrocortisone 1%.
Mometasone furoate

Overview of efficacy

• Mometasone furoate in topical treatments is highly efficacious, for treating a broad range of steroid responsive dermatoses.
  – Eczema, Dermatitis, Psoriasis etc

• A once a day application regimen is not only as efficient as the twice a day topical steroids, it is also more patient friendly, resulting in greater treatment compliance.
Mometasone furoate

*Overview of efficacy*

- An application duration of 3 weeks is sufficient to clear the majority of dermatoses
  - Many conditions clear in less than 3 weeks.
- Mometasone furoate is equally as effective as betamethasone dipropionate
  - As safe as hydrocortisone
Mometasone furoate

which product form for which concern?

• Ointment
  – Occlusive delivery systems like ointments produce greater cutaneous hydration and improved penetration\(^1\)
  – But can be messy, sticky and non-absorbptive

• Lotion
  – Makes treating scalp conditions easier. Very thin product and come with a tip applicator
  – Less ideal for the rest of the body

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Mometasone furoate

which product form for which concern?

• Cream
  – Mometasone cream is a ‘fatty cream’ with ointment like properties.
  – Contains titanium dioxide to make it white, so can be somewhat residual.

• Hydrogel
  – Vehicle selection, especially the use of gels, may improve patient compliance

Hydrogels

• What is a hydrogel?¹
  – A low residue gel with a high water content that is free of acetone, alcohol or other harsh solvents
  – An ingredient with humectant properties is typically added to a hydrogel
  – Water based, so non-greasy

• While an alcohol based gel can be drying, a hydrogel based on water with humectants can provide moisturising properties.

¹ Trookman NS, Rizer RL, Ho ET et al. Moisturising advantages of desonide hydrogel in treating atopic dermatitis. Cutis. 88:7-12, 2011.
Hydrogels

• Hydrogels are¹:
  – Easy to apply
    • Smooth and light
  – Suitable for use on multiple body areas
    • Including hirsute limbs
  – Comfortable to wear under clothing
    • Not greasy or residual, dry quickly
  – Quickly absorbing and dry clear
    • Optimal for visible areas of skin

Hydrogels
Simplified therapy

• Hydrogels have the advantage of possibly replacing the use of multiple formulations
  – They can be used anywhere on the skin and hairy areas such as the scalp
• Having a single product could provide:
  – A versatile simplified treatment option for some patients
  – Result in improved compliance with treatment1

Mometasone furoate Hydrogel

• What is mometasone furoate hydrogel?
  – 0.1% mometasone furoate in a hydrogel
  – No alcohol, no surfactants
  – Contains hexylene glycol as the humectant moisturiser
  – Contains hydroxypropylcellulose to form a barrier on the skin
Mometasone furoate Hydrogel - moisturising

• More than 40% reduction in transepidermal water loss 6 hours after application

• Using mometasone furoate hydrogel treats the inflammation and helps hydrate the skin
Summary of the patient benefits of mometasone hydrogel

• Effective, once daily topical therapy for corticosteroid responsive dermatoses
• Could replace the use of multiple formulations in some patients
• Acceptable, soothing, non-greasy, easy to apply, non-irritating vehicle for application to the skin
  – Comfortable to use under clothing, clear finish
• Potentially improving patient compliance due to the patient preferring the hydrogel vehicle
Mometasone furoate

*which product form for which concern?*

- **Ointment / Cream**
  - Best for large areas of dry skin
  - Non-facial areas due to visibility of base
- **Lotion**
  - Best for use on the scalp
- **Hydrogel**
  - Visible areas of skin i.e. hands and face
  - Great for hairy limbs
Mometasone furoate

Summary

• Potent corticosteroid
  – As effective as betamethasone dipropionate
  – As safe as hydrocortisone
• Ideal for first line treatment
  – Then step down to hydrocortisone
• Available in a range of forms, including a hydrogel
Topical corticosteroids

How to use them?

• With corticosteroids more is not better
  – No point putting on a thick layer instead of a thin layer
    • Absorbs better from a thin layer
    • Avoid the use of the phrase “use sparingly” as it can be alarming and confusing and lead to minute amounts being applied
    • Better to say “apply enough to cover the affected area”
  – No point applying them more than the instructions say
    • Will just increase the chances of side effects
  – If dosing once daily, application in the morning is best
    • Mimics the circadian secretion of cortisol

3. Bewley A. Expert consensus: a time for a change in the way we advised our patients to use topical corticosteroids. BJD. 158:917-20. 2008
Topical corticosteroids

*Fingertip unit*

- Harder to explain correct topical application than it is to explain correct oral dosage
- The ‘fingertip unit’ (FTU)\(^1\)
  - The amount of cream/ointment delivered from a 5mm diameter nozzle, applied from the distal skin crease to the tip of the patients index finger
  - Same principle for a hydrogel

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1. Bewley A. Expert consensus: a time for a change in the way we advised our patients to use topical corticosteroids. BJD. 158:917-20. 2008
Topical corticosteroids

*Fingertip unit*

- Automatically corrects for body size\(^1\)
  - For an adult one FTU is about 500mg

<table>
<thead>
<tr>
<th>Area of skin to be treated (adults)</th>
<th>Approximate size (in adult hands)</th>
<th>FTU’s each (adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A hand and fingers (front and back)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>A foot (all over)</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Front of chest and abdomen</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Back and buttocks</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Face and neck</td>
<td>5</td>
<td>2.5</td>
</tr>
<tr>
<td>An entire arm and hand</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>An entire leg and foot</td>
<td>16</td>
<td>8</td>
</tr>
</tbody>
</table>

1. Bewley A. Expert consensus: a time for a change in the way we advised our patients to use topical corticosteroids. BJD. 158:917-20. 2008
Topical corticosteroids
Which product to recommend?

• Ointments, Creams, Lotions, Hydrogel?
  – The right vehicle may play an important role in patient adherence\(^1\)

• There's one vehicle that works better than all the others, and that’s the one that the patient is prepared to use

Professor Steven Feldman

Topical corticosteroids
Which product to recommend?

• Characteristics important to patients, in order:\textsuperscript{1}
  – How well it absorbs
  – Ease of application
  – Side effects
  – Suitability for use on multiple body areas
  – How it smells

• Delivery vehicle preference has a significant effect on compliance:\textsuperscript{1}
  – Gels over ointments, creams and oils

Topical corticosteroids
Which product to recommend?

• Hydrocortisone
  – First line treatment for mild to moderate corticosteroid responsive dermatoses
  – Can be used as step down treatment once control of a flare has been obtained using stronger corticosteroids
  – Can be used for self management due to OTC status
  – Choose a dissolved form of hydrocortisone for optimal drug delivery
Topical corticosteroids
Which product to recommend?

• Mometasone furoate
  – First line treatment for moderate to severe corticosteroid responsive dermatoses
    • Once control is gained the patient can step down to hydrocortisone
  – Next step for non-responsive mild to moderate corticosteroid responsive dermatoses
  – Choose a product form that will suit the patient and the condition for optimal compliance
Conclusions

_Corticosteroids_

• Topical corticosteroids help moderate an overresponsive immune system
  – Reduces tissue destruction and disease from persistent inflammation
• 60 years of corticosteroid research has given us a range of active options of varying potencies
• Effective for a range of inflammatory skin conditions
Conclusions

**Hydrocortisone**

- Long history of use, since 1951
- Safe, gentle, OTC
  - Suitable for children, pregnancy and breast feeding
- Effective
  - Approved for use for a wide range of dermatoses from eczema to sunburn
- Using dissolved hydrocortisone will increase the speed of action, getting faster resolution for the patient
- Naturally produced by the adrenal cortex
Conclusions

*Mometasone furoate*

- Potent corticosteroid
  - As effective as betamethasone diproprionate
  - As safe as hydrocortisone
- Ideal for first line treatment
  - Then step down to hydrocortisone
- Available in a range of forms, including a hydrogel
Conclusions

Corticosteroids

• Talking with patients about how to best apply corticosteroids will increase compliance
• Talking with patients about the safety and efficacy of corticosteroids will reduce fear
• Selecting the product to match the patient’s needs, lifestyle and personality will increase compliance and ultimately therapeutic outcomes
Thank you