Comprehensive Primer on Drugs and Diseases in Dermatology

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Disclosures

- L'Oreal
- Valeant
- FitBit
- Genentech
- Menlo
- Sanofi

- Topical Steroids
- Systemic Steroids
- Topical Immunomodulators
- Antihistamines

Steroid Classifications

- Potency classification
  - United States:
    - Class 1 (strongest) → Class 7 (weakest)
      - Traditional
      - No specific definition of classes
    - Super-, high-, moderate-, low-potency
      - Clinical classification in latest edition of Wolverton
- Allergenicity classification
  - Classes A, B, C, D

Warner MR, Camisa C. Topical Corticosteroids. In: Wolverton SE, ed. Comprehensive Dermatologic Drug Therapy. 2nd ed. Saunders, 2007. p.595-624.
Barth-Jones J. Topical Therapy. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology. 8th ed. Wiley-Blackwell. Ch. 75.

Steroid Potencies

- Super-High
  - Clobetasol 0.05%
  - Halobetasol 0.05%
- High
  - Fluocinonide 0.05%
  - Desoximetasone 0.25% (ointment non-allergenic)
- Medium
  - Triamcinolone 0.1%
- Low
  - Desonide 0.05%

What Determines Potency?

- Potency and side effects of TS are related to saturation of the GCRs in different cell types
- What affects the saturation of the GCRs?
  - How many molecules of TS are in the cell
    - Concentration of TS applied
    - Extent and depth of absorption
    - Metabolism and diffusion out of skin
  - How tightly do the TS in the cell bind to the GCR
    - Structure of the TS

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Role of Vehicle in Potency

- Vehicle somewhat affects potency in mid-potency steroids, but not in very weak or strong steroids
- Vehicle effects on potency assume the patient puts it on and it stays on
- With above in mind:
  - Ointments slightly more potent than creams

Potential Adverse Effects

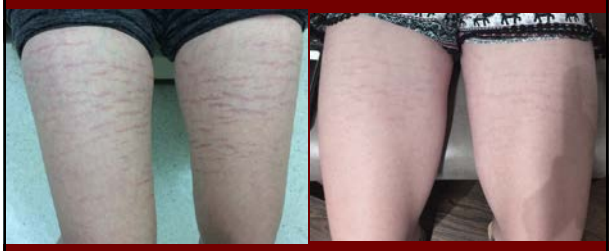
- Systemic:
  - HPA axis suppression and growth retardation
- Local:
  - Epidermal atrophy
  - Glaucoma and Cataracts
  - Striae
  - Allergic contact dermatitis
  - Perioral Dermatitis / Acne

Systemic Adverse Events

- REALLY rare to have clinically meaningful systemic effects
  - Have to put on a lot and have it be absorbed
  - Factors that increase risk:
    - Peds
    - Liver Disease
    - Occlusion

Local Adverse Effects

- Also rare
  - All are reversible except striae, glaucoma, cataracts
    - Be very careful around groin/thigh, breasts (female), axilla, upper/inner arms, in obese patients
    - Safe use on eyelids:
      - Low potency 3x/wk
      - See eye doctor 1-2x/year
      - No hx of glaucoma



Amount to Prescribe

- ALMOST EVERYONE UNDERPRESCRIBES
  - They shouldn't even sell 30 g tubes!

	Twice daily/Four weeks
Face and neck	
Trunk	
One arm	
One leg	
Hands and feet	
Body	

Practical Instructions

- Patient Education
  - Topical steroids are EXTREMELY SAFE for long term use, if used as directed
    - 70% of parents have "steroid phobia"

Practical Instructions

- Avoid continuous use
  - Assume higher potency intermittently is safer and more effective than lower potency continuously
  - However, if prescribe higher potency we risk side effects due to patient overusing if they don't follow intermittent regimen

Practical Instructions

- Thick, Tough Skin:
  - Super-High potency QD M-F
- High risk areas
  - Low potency QD Mon-Thurs
- Everywhere else:
  - Medium potency QD M-F
- Lips (special b/c of risk of perioral)
  - Super-High potency 2 days per week

Steroid Allergy

- Allergy to the active molecule or a vehicle ingredient should be suspected in all patients who don't respond to topical steroids
  - Up to 20% have steroid allergy
  - Of that 20%, 85% have multiple steroid allergies

Brown F, Wilkinson SM. *Effective prescribing in steroid allergy: Controversies and cross-reactions.* Clin Derm 2011 29:287-94.
Basick M, Marot L, Nicolas JF, et al. *Allergic hypersensitivity to topical and systemic corticosteroids: a review.* Allergy 2009 64:978-994

Steroid Allergy

- Can develop after product has been used effectively for a prolonged period or be present on first application
- Difficult to recognize clinically
  - May not respond to steroid
  - May get worse with steroid application
  - May improve initially, then flare when application is interrupted

Steroid Allergy

- In anyone who doesn't respond as expected to initially prescribed topical steroid:
  - Desoximetasone ointment is totally non-allergenic
    - But expensive
  - TAC ointment is rarely allergenic
  - Clobetasol solution is rarely allergenic
    - Can mix into CeraVe (50 ml bottle in 16 oz jar) to make class 4 steroid that is very low allergenicity

Short Term Systemic Steroids

- If they need long term systemic steroids, get someone else involved.
- *Short term* systemic steroids are generally extremely safe and can be combined with topical therapy to significantly improve the quality of life in dermatitis patients with very little additional risk.

Dosing of Systemic Steroids

- No particular dosing regimen supported over others with comparative trials
- Typically start at 40 mg/day and taper over 3-4 weeks.
  - Example:
    - 40 mg qam x 3, 20 mg qam x 3, 10 mg qam x 15
  - Point of taper is to prevent rebound.
    - Significant adrenal suppression does not happen in less than a month.

Dosing of Systemic Steroids

- Intramuscular triamcinolone
  - This vs oral prednisone is controversial
  - However:
    - Oral taper
      - 40 mg po x 7 + 20 mg po x 7 + 10 mg po x 7 = 490 mg
      - 490 mg x 70% absorption = 343 mg
    - IM injection
      - 40 mg IM = 40 mg
      - 40 mg TAC = 50 mg prednisone = almost 90% reduction

Side effects with *short term* systemic steroids

- Primary issues are:
  - Psychological
    - Mean, irritable, rarely even psychotic
  - Weight gain
    - Due to increased appetite
  - Menstrual irregularity
    - Not a common problem

Side effects with *short term* systemic steroids

- Osteoporosis does not happen
- Avascular necrosis of the femoral head does not happen
- Short term bump in glucose of diabetics is common

How often can pulses be safely repeated long term?

- With minimal to no risk?
  - IM triamcinolone: 4x per year x many years
  - Prednisone: 2-3x/year x many years
- With low risk?
  - 8-10 injections of IM triamcinolone
  - Prednisone: unknown
    - In these situations, must consider the risk/benefit ratio.
    - There is risk, but is it lower than the risk of moving on to chronic methotrexate or mycophenolate?

Carson TE. Is Bone Mineral Density Testing Indicated with Long-Term IM Triamcinolone Acetonide Therapy? Practical Dermatology, 12/08.

Topical Calcineurin Inhibitors

- You need to know four things:
  - Except in REALLY rare situations, these are extremely safe
  - They cause intense burning and this will prevent patients from using them
  - They are not as strong as steroids
  - They are expensive

TCIs are REALLY safe

- Numerous studies have shown no increased lymphoma risk.
  - Almost impossible to definitively prove there is no risk, but if there is, it is infinitesimal.
- There is no increased skin cancer risk
- Systemic absorption is basically zero
  - Exception is Netherton Syndrome

TCIs cause burning

- Both pimecrolimus and tacrolimus cause burning via substance P and calcitonin gene related peptide release
  - This is what capsaicin does
  - Explains both why they burn and why they work better for itch than you would expect
  - Tell patients that if they are *really lucky*, when they start using it, it will feel the way your tongue feels when you eat a hot pepper
  - It will progressively get less severe

Comparison to topical steroids

- Tacrolimus 0.1% ointment is roughly equivalent to a high-to-mid potency steroid
- Pimecrolimus cream is roughly equivalent to a mid-to-low potency steroid

TCIs are not that expensive

- Tacrolimus 0.1% ointment
  - 30 gm tube = $74
  - 60 gm tube = $140
  - 100 gm tube = $227
- Pimecroliums 1% cream
  - 30 gm tube = $272
  - 60 gm tube = $523
  - 100 gm tube = $890

www.goodrx.com accessed on 5.12.15

Anti-histamines

- They don't work very well for most types of itch, including itch of atopic dermatitis
- Sedating antihistamines are useful for night-time itch that keeps the patient up at night
  - Mainly b/c of sedation, not itch relief
- Non-sedating useful for histamine mediated itch

Sedating Anti-histamines

- Start low and titrate up
- Diphenhydramine
  - Start at 25 mg qhs, titrate up as needed to 100 mg qhs
    - Max 300 mg/day in adults
    - Careful of anti-cholinergic effects
- Hydroxyzine
  - Same as diphenyhydramine, except:
    - Max dose is 600 mg/day
    - Consider starting at 10 mg qhs

Non-sedating anti-histamines

- Effectiveness increases with increasing dose, side effects do not
  - Start at high dose, titrate back if working
    - Loratadine 30 mg bid
    - Fexofenadine 360 mg bid
    - Cetirizine 20 mg bid
  - Cetirizine works best, but about 1 patient in 6 gets sedated with it

References

- Wolverton SE. Comprehensive Dermatologic Drug Therapy, 3rd ed.
  - Chapter 12: Systemic corticosteroids
  - Chapter 28: Antihistamines
  - Chapter 40: Topical Corticosteroids
  - Chapter 44: Topical calcineurin inhibitors