Atopic Dermatitis Treatment: The Old, The New, and The Trending

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Speaker Introductions

• Rebecca Flynn is a pediatric nurse practitioner practicing in a specialty pediatric dermatology clinic at Children’s Mercy in Kansas City, Mo. Rebecca has practiced in pediatric dermatology since 2013. She is a dual graduate (bachelor’s and master’s degrees) from the University of Kentucky. She is a member of the PNCB Item Writing Committee, and she has previously presented at NAPNAP national conference in Chicago 2018 and Denver 2017.

• Stephanie Kronberg has worked as a pediatric nurse practitioner at Children’s Mercy Kansas City in the division of dermatology since 2014. She received her master’s degree in nursing from Boston College and her bachelor’s degree in nursing from Bethel University in St. Paul, Minn. Ms. Kronberg is a certified dermatology nurse practitioner, and she is on the Pediatric Nursing Certification Board (PNCB) Exam Committee.

Disclosures

No disclosures to discuss

Learning Objectives

1. Review history, symptoms and non-medication treatments of atopic dermatitis.
2. Describe risks and benefits of traditional medications for patients with atopic dermatitis.
3. Define benefits and adverse effects of newer medications (crisaborole and dupilumab) for treatment of pediatric patients with atopic dermatitis.
4. Identify trending non-pharmaceutical topical treatments as useful or harmful in the treatment of atopic dermatitis.
5. Recognize patients who would benefit from older atopic dermatitis management vs. newer pharmaceutical options.

Diagnostic Criteria Atopic Dermatitis

• Essential Features
  • Pruritus
  • Patterns: Face, neck, extensor (infant) or flexural surfaces
  • Spacing groves/axillae
  • Relapsing history

• Important Features
  • Early age of onset
  • Atopy or Family history
  • Xerosis

• Exclusion of other conditions

2014 Guidelines for Management of Atopic Dermatitis

Case Study #1

What treatment(s) would you initiate for this child with atopic dermatitis?
Atopic Dermatitis Treatment: The Old

Moisturizer

- **Treat Xerosis and Prevent Water Loss**
- 2014 Guidelines- Evidence Level A
  - Decrease disease severity
  - Products
    - Lotion, Cream, Gel, Oil, Balm, Ointment
  - Ideal product
    - Safe, effective, inexpensive
    - Free of: additives, perfumes, fragrances

Moisturizer EBP

- Emollient Prevention of Atopic Dermatitis
- Dermatology and Therapy (2019)- Adverse Effects of Emollient use in Eczema

Bleach Baths

- Effective at decreasing severity of atopic dermatitis.
- Not superior to daily bathing
- Recipe:
  - ¼ cup bleach full bath
  - ⅛ cup bleach to half bath

Wet Wrap Therapy

- Layers of bandages or cotton clothing
  - Medication, Moisturizer, Wet layer, Dry layer
- 1st publication with Atopic Dermatitis- 1987
- Utilize for severe or refractory disease
- Complications:
  - Discomfort, chills, poor acceptance
  - Folliculitis
- Barriers:
  - Time

Wet Wrap Therapy

  - Dryer 5-10 minutes prior to application

https://www.childrensmercy.org/departments-and-clinics/dermatology/wet-wrap-therapy/
Topical Steroids

- **Atopic Dermatitis Guidelines- JAAD (2014)**
  - 1st line use after moisturizers
  - Used > 60 years
  - Used on active rash and to prevent rash
  - Active rash - use 2 x daily until resolved
  - Prevention - Apply 1-2x weekly to common flaring areas
  - 7 classes of potency (VII - Low to I - High)
  - AE - telangiectasia, striae, atrophy
  - Concern Hypothalamic-pituitary-adrenal axis suppression - Very low risk
  - Undertreatment - Topical Steroid Fear

- **Reviewed 490 articles - included 16 international studies**
  - Reason for phobia - #1 - Skin thinning #2 - Affect growth/development
  - 1 incidence of Hypothalamic-pituitary-adrenal axis suppression - Used >100gm Clobetasol / week for 10 weeks - 18 months.
  - Sources of TCS Phobia
    - Top 3 Physician and Healthcare Worker

Topical Calcineurin Inhibitors

- Introduced in 2000
  - Block T-cell pro-inflammatory cytokines
  - Pimecrolimus (Elidel) cream – mild-moderate atopic dermatitis
  - Tacrolimus (Protopic) 0.03%, 0.1% ointment – moderate-severe atopic dermatitis
  - Preferred use:
    - Recalcitrant area
    - Sensitive skin area
    - Steroid atrophy
    - Long-term uninterrupted steroid use
  - AE - Increased risk of secondary infection - hold during acute infection
  - Black box warning

Safety and Benefits

- Sigurjonsdottir, B. et al. (2016). Safety and Efficacy of Pimecrolimus in Atopic Dermatitis: A 5-year randomized trial
  - Topical steroid and Pimecrolimus safe without AE on immune system
  - Similar efficacy (TCS vs PIM)
  - Possible 1st-line treatment - Pimecrolimus

  - 7632 participants enrolled - 26,792 person years reviewed.
  - No skin cancer.
  - No elevation of lymphoma.
  - Unlikely Pimecrolimus increases risk for lymphoma.

  - Topical calcineurin - used in flares
  - Topical Tacrolimus - preferred option for maintenance/ prevention of flares
  - 7 million individuals evaluated - No evidence of lymphoma
  - Black box warning not justified.
Phototherapy

- First reported as a dermatologic treatment in 1925, first used for treatment of atopic dermatitis in 1948
- Mechanism: photo-immunosuppression and immunomodulation
- There are multiple forms of light therapy - NB/UVB is most common for atopic dermatitis
- Second line treatment after failure of emollients, topical steroids, and TCI
- Barriers: local availability, travel time, missed school/work, insurance coverage, cost, skin type, history of skin cancer
- Risks/side effects: sun damage, skin aging, and skin cancer

Case Study #2

An 18-month-old child is experiencing an acute flare on arms and legs. Which of the following are part of the treatment plan? Select all that apply.

Atopic Dermatitis Treatment: The New

Crisaborole (Eucrisa) Ointment

- PDE4 inhibitor that suppresses production of proinflammatory cytokines
- Mild to moderate atopic dermatitis in children 2 and older
- Adverse effects: Application site pain (stinging and burning)
  - Pain may be more common in older individuals; worst on day 1
  - May apply emollient first, anti-pruritic ointment such as Pramoxine, start treatment at younger age, or numb area before application
  - Does not have the safety risks of topical steroids and topical calcineurin inhibitors
- Studies show improvement in pruritus, improvement in disease severity, and reduction in AD signs/symptoms (erythema, excoriation, lichenification)

Dupilumab (Dupixent)

- First and only biologic for patients ages 12 and older with moderate to severe atopic dermatitis (approved for adults in 2017 and age 12+ in 2019)
- Human monoclonal antibody that targets IL-4 and IL-13
- No lab screening or monitoring!
- Side effects:
  - Conjunctivitis and keratitis
  - Injection site reaction
  - Cold sores on mouth/lips
  - May influence response again parasitic infections – treat pre-existing parasite infections prior to starting
**Dupilumab (Dupixent)**

- Subcutaneous injection administered every 2 weeks
- Dosing:
  - Adolescents less than 60 kg: 400 mg loading dose followed by 200 mg every other week
  - Adolescents over 60 kg and all adults: 600 mg loading dose followed by 300 mg every other week
- Also FDA approved for treatment of moderate to severe asthma in age 12+, and for chronic rhinosinusitis with nasal polyps in adults

**Dupilumab Adolescent Data**

- 16 week randomized, double-blinded trial
- 251 patients ages 12-17
- Efficacy and safety of dupilumab similar to those in adults
- Results:
  - 42% achieved significant improvement in lesion extent and severity
  - 37% achieved significant itch reduction
  - 24% achieved clear to almost clear skin

**Dupilumab Pediatric Data**

- Children <12
  - Case series of 6 patients (average age of 10.8 years) with average IGA of 4 (severe) and average BSA of 55% - after 8 months, all patients had an average IGA of 1.5 and average BSA of 25%
  - Multicenter retrospective review of off-label use in pediatrics showed similar treatment response and similar adverse events compared to adult/adolescent trials
- Access: Requires prior authorization and appeal when used under the approval age of 12
- Some insurance companies require failure of immunosuppressant, phototherapy, and/or certain topicals
- Pediatric dosing is under investigation - pediatric clinical trials used dosing of 2-4 mg/kg/dose

**Who is a good candidate for Dupilumab?**

- Patients with moderate to severe atopic dermatitis who are...
  - unable to tolerate or have contraindications to other systemic immunosuppressant
  - unresponsive to other systemic therapies
  - transitioning off methotrexate or cyclosporine after large cumulative doses
- Example from CMH Derm:
  - Adolescent with mod-severe AD since age 7, affecting face and body, history of treatment with variety of topical steroids, TCIs, Eucrisa, and started PO methotrexate in order to get dupilumab approval
  - Adolescent with history of ALL (in remission), moderate to severe diffuse AD, history of eczema herpeticum and multiple bacterial infections requiring hospitalization, NBUVB treatment, allergic to methotrexate and not good candidate for cyclosporine due to renal insufficiency

**Up and Coming Treatment**

- One size fits all? No. New medications are more targeted.
- Examples:
  - Tralokinumab: anti-IL-13 (Phase III)
  - Nemilizumab: anti-IL-31 (Phase II)
  - JAK inhibitors (e.g. baricitinib, upadacitinib) (Phase III)
  - Oral PDE4 inhibitor (Apremilast) (Phase II)
  - Neurokinin-1 antagonists (Phase II)
  - Histamine 4 receptor antihistamines (Phase II)

**Case Study #4**

This 6-year-old child has mild focal atopic dermatitis. She has used hydrocortisone ointment in the past, but parents prefer to avoid topical steroids. Which treatment would be most appropriate?
Case Study #5

This 13-year-old adolescent has poorly controlled, diffuse atopic dermatitis. Previous treatment includes long-term treatment with topical steroids and tacrolimus ointment. She has a history of liver disease. What is the next best treatment option?

Atopic Dermatitis Treatment: The Trending

The Aron Regimen

- Recipe:
  - Betamethasone valerate 0.1% cream: 15 gm
  - Mupirocin cream: 22 gm
  - Vanicream: 226 gm

- Instructions: Apply 4 times daily to all affected areas on face and body x 3 weeks, then follow up consultation
- The frequency of application is gradually decreased to 3 times daily, 2 times daily, and once daily

Three features

1. Dilute topical steroid and apply more frequently
2. Antimicrobial
3. Simple regimen

Three features

- 116 patients, children and adults, were treated with a compounded antimicrobial, steroid, and moisturizer (CASM) with average follow up period of 49 days
- Results:
  - 80% of patients had improved severity
  - Decrease in mean severity of 1.4 points on 6-point scale
  - Average decrease in BSA affected of 23%
“Mommas of other babies with eczema, I need help! My baby’s eczema started when he was 8 weeks old and has just gotten progressively worse! I have tried EVERYTHING! I cut out dairy and eggs from my diet, and his eczema got worse. He is allergic to Vaseline. Other than using steroid creams (which I don’t want to do we can’t keep him from breaking out. It’s heartbreaking and I want to help him!”

"Cut out gluten"
"Start him on a probiotic and buy a Hazelwood necklace"
"Give him a milk bath in breastmilk, and use breastmilk lotion"
"Steroids will cause more glucose in his body, which feeds bad bacteria. I would highly recommend detox with a 60-day elimination diet. I can almost promise you that he’ll start feeling better."

"This may sound nutty but personally I would rub butter on it and also Emu oil…seemed to work for me!"

"It may be a reaction to vaccines"
"Try CBD oil!"

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• AAP released a new clinical report in 2019 to replace 2008 clinical report
• Not enough evidence to support maternal dietary restrictions during pregnancy or lactation (unchanged from 2008 report)
• No short- or long-term advantages for exclusive breastfeeding beyond 3-4 months for prevention of atopic disease (unchanged from 2008) - however longer breastfeeding duration may protect against wheezing and asthma (*changed from 2008)
• No conclusions about role of breastfeeding in preventing/delaying food allergies (unchanged from 2008)
• Lack of evidence that partially or extensively hydrolyzed formula prevents atopic disease (*changed from 2008)
• No evidence that delaying introduction of allergenic foods beyond 4-6 months prevents AD (unchanged from 2008)

©2020 Alternative Treatments for Atopic Dermatitis (2019)
• Herbal Treatment
  • Indian Pennywort, walnut, turmeric
• Vitamin E
• Amino Acids
• Melatonin
• Sandalwood oil
• Honey

©2020 “Natural Oil” Moisturizer (2019)
• Olive oil
  • May induce inflammation
  • No antibacterial effects on skin
  • May include allergic contact dermatitis
• Coconut oil
  • Anti-inflammatory effects
  • Anti-bacterial effects
  • Decreases TEWL (water loss).
  • Low concern for allergic contact dermatitis
• Sunflower oil
  • Improves skin barrier dysfunction
  • Decreases inflammation
  • No concern for allergic contact dermatitis

©2020 Cannabis and Cannabinoid Treatment in Atopic Dermatitis
• Endocannabinoid System of skin (2018)
  • Anti-cancer, Anti-inflammatory, anti-bacterial, anti-analgesic
  • Atopic Dermatitis- Inflammation, Immune Response, Epidermal barrier function
  • No substantiated research trials
• JADA (2017): Promising role relating to “itch”
  • Cream applied 2 x daily with Atopic Dermatitis
  • Endocannabinoid cream- Palmitoylethanolamide (PEA)
  • Anti-inflammatory
• Secondary Cannabinoid Smoke Indoor (2019)
  • Exposure 83% increase odd adverse health outcomes for children
Conclusion

- Old Practices remain true and tested
- New practices are breaking the barrier in skin and eczema treatment
- The internet is not always a reliable source if you like evidence-based practice
- Alternative treatments have the power to make improvements if you believe

Resources