Early Treatment for Alopecia Areata Prevention (ETAAP)

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EBM Hair Update 15th May 2019
Good to be Back [1]!
HAIR DISORDERS
AN EVIDENCE BASED UPDATE

Programme & Abstracts

Thursday, 11 May 2006
Holywell Park, Loughborough

Kindly sponsored by:

Proceeds from the day will be donated to the UK Dermatology Clinical Trials Network
“Leaving alopecia areata untreated is a legitimate option for many patients”

“Spontaneous remission occurs in up to 80% of patients with limited patchy hair loss of short duration (< 1 year).”
“If there is no hair regrowth and there is less than 50% hair loss, discuss the option of watchful waiting with no current treatment needed”
<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Proportion with spontaneous regrowth</th>
<th>Risk of developing chronic AA</th>
<th>Risk of developing AT or AU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solitary stable patch of AA ≤6 months duration</td>
<td>87%</td>
<td>15%</td>
<td>6%</td>
</tr>
<tr>
<td>Solitary stable patch of AA ≥6 months but ≤12 months</td>
<td>55%</td>
<td>65%</td>
<td>50%</td>
</tr>
<tr>
<td>Solitary stable patch of AA ≥12 months duration</td>
<td>0</td>
<td>100%</td>
<td>45%</td>
</tr>
<tr>
<td>Multiple patches within 6 months of initial presentation</td>
<td>65%</td>
<td>55%</td>
<td>15%</td>
</tr>
<tr>
<td>Aged 0–6 years at initial presentation</td>
<td>0</td>
<td>100%</td>
<td>45%</td>
</tr>
<tr>
<td>Aged 6–12 years at initial presentation</td>
<td>60%</td>
<td>40%</td>
<td>18%</td>
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AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis.

Alopecia areata: A long term follow-up study of 191 patients

Antonella Tosti, MD, Sara Bellavista, MD, and Matilde Iorizzo, MD
Bologna, Italy

• Contacted 16-23 years later

• Significant tendency for AA to worsen with time
  • 19% with mild disease (<50% area) had AT / AU at follow-up
  • 93% with AU still had extensive disease (AT / AU) at follow-up
  • 3% with extensive disease (AT / AU) were disease free at follow-up

(J Am Acad Dermatol 2006;55:438-41.)
Poor Prognosis in AA

- Extensive disease
- Long disease duration
- Onset before puberty
- Atopy
- Associated autoimmune disease
- Nail disease
- Positive FH
SRFT Hair Clinic
(2013 – present)
[n=1883]

522 AA pts with >30 % AT/AU
Impact on the NHS

**STANDARD TREATMENT PATHWAY**

- Topical / Intralesional Steroids
  - DPC
  - Dithranol
- Systemic Steroids
  - PUVA
  - Ciclosporin
  - MTX
  - (JAKi / Others)

- Multiple unsuccessful treatments
  - Clinic visits
  - Treatment / monitoring costs

- Estimated cost for DPC + wig treatment in Glasgow = £1500 per patient / year

*(Phillips R, Holmes S. WCHR Abstract 2019)*
Significant Psychological Impact

The diagram illustrates the psychological impact scores for different conditions and measures. The scores are categorized into two groups: 

- DLQI (Dermatology Life Quality Index)
- PHQ9 (Patient Health Questionnaire 9)
- GAD7 (Generalized Anxiety Disorder 7)

Scores are compared for two thresholds: <10 and >10. The graph uses different colors to represent different conditions:

- Blue: FPHL
- Red: AA
- Green: LPP
- Purple: FFA

The percentage distribution is shown for each condition pair, illustrating the impact on psychological well-being.
Significant Psychological Impact

The bar chart shows the percentage of scores across different psychological impact scores for DLQI, PHQ9, and GAD7. The scores are categorized into two groups: <10 and >10. The chart indicates a significant psychological impact with higher scores in the categories >10 for DLQI, PHQ9, and GAD7.
## Alopecia Areata Priority Setting Partnership (PSP)

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<th>Rank</th>
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<td>2</td>
<td>Are immunosuppressant therapies (e.g. methotrexate; mycophenolate mofitil) better than placebo in the treatment of alopecia areata?</td>
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<td>3</td>
<td>In alopecia areata, are biological therapies (including janus kinase (JAK) inhibitors and anti-cytokine therapies) more effective than placebo in causing hair regrowth?</td>
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<td>4</td>
<td>Are psychological interventions helpful in alopecia areata?</td>
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<td>5</td>
<td>Can progression of alopecia areata be prevented by early diagnosis and treatment?</td>
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<td>Do certain foods, vitamins or nutritional supplements improve hair regrowth in alopecia areata?</td>
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<td>What can be learnt about alopecia areata from other autoimmune conditions?</td>
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(MacBeth et al. Br J Dermatol 2017)
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Lessons from other Immune-Mediated Inflammatory Disorders (IMID)

Aggressive early intervention in RA, Crohn’s disease & MS:

Reduce tissue damage and longer-term complications

Induces disease-free remission

(Girolomoni et al. J Dermatol Treat 2015)
Is there any Evidence that Early Treatment effects Prognosis in AA?
“There is no good trial evidence that any treatment provide long-term benefit to patients with alopecia areata, alopecia totalis and alopecia universalis.”
Clinical Observation: Better Outcomes with Early Treatment?

• 68 Pt with chronic AA treated with systemic therapy and followed for 2-7 years
• Rates of AT/AU = 17.6% [Expected rate 45% based on Ikeda data]
• Rationale to treat chronic AA to prevent AT/AU (Cranwell et al. Aus J Dermatol 2018)

• Shorter duration between disease onset and treatment commencement
• “good” prognosis in children <10yrs old with “early onset” AA (Suh et al. Ann Dermatol 2014)

• Treatment with pulsed systemic corticosteroids for extensive AA
• more effective, and less likely to relapse, when started within 1 year of disease onset compared with treatments commenced later on (Yang et al. Ann Dermatol 2013)
Clinical Observation: AA Recurring at Previously Affected Sites

If previously affected skin is more susceptible to future attack = Argues for aggressive early treatment to prevent more extensive scalp involvement

(Li & Sinclair. Aus J Dermatol 2016)
Is there Any Biological Rationale for Early Treatment?

As there is no tissue damage in AA
Alopecia Areata – Bulb IP Collapse
Positive feedback loop in AA

(From Divito and Kupper. Nat Med 2014)
As has been proposed in Psoriasis, it is conceivable that stimulation of a small region of AA-predisposed skin results in an immune reaction that leads to the development of lesions at local and distant body sites.

(Girolomoni et al. J Dermatol Treat 2015)

• Disease recrudesce in susceptible tissue
  • Ongoing immune dysfunction / Sub-clinical inflammation?
  • Incomplete IP restoration?
  • “Molecular scar”

(Girolomoni et al. J Dermatol Treat 2015)
Testing the Hypothesis

Early treatment can prevent disease progression in AA
A Successful Early Treatment Strategy in AA would:

• Target those most likely to benefit from early treatment

• Improve Q of L & Reduce social stigmatisation

• Modify the disease course
  ➢ Achieving prolonged medication-free remission

• Cost-effective management strategies
Early Treatment for Alopecia Areata Prevention (ETAAP)

Possible Trial Design....

“Classic”
Single intervention vs. placebo given early in disease course

“Pragmatic”
Early intervention (of whatever type) vs. deferred treatment
Early Treatment for Alopecia Areata Prevention (ETAAP)

Feasibility work...

- Target population and barriers to recruitment
  - Early case identification
  - Acceptability of interventions
- Preferred outcome measures
- Power calculation
- Potential economic impact
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Feasibility work...

• Target population and barriers to recruitment
  ➢ Early case identification
  ➢ Acceptability of interventions
• Preferred outcome measures
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• Potential economic impact

...eventually Leading to a Clinical Trial
ETAAP: Progress

• Building the Team
  • Dermatologists / Patient / GPwSI / (Qualitative researcher) / Statistician

• Seeking advice
  • University of Manchester Primary Care Academic Unit
  • NIHR Research Design Service (RDS)
  • UK-DCTN

• Secured Funding
  • Alopecia UK

• Ethics
  • NIHR Portfolio adoption

• PUBLISH RESULTS
EHRS 2020
18th - 20th June 2020, Sheffield, UK

19TH EUROPEAN HAIR RESEARCH SOCIETY MEETING

SHEFFIELD
City of Steel & Nature

Save the Date
18th - 20th June 2020
Sheffield, UK

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