BIOLOGIC THERAPY: A NEW OPTION FOR TREATMENT JUVENILE IDIOPATHIC ARTHRITIS

DR TON THAT HOANG
INTRODUCTION

• JIA is the most common chronic rheumatic inflammatory disease of childhood. If not successfully treated, it can lead to severe disability.

• Juvenile idiopathic arthritis (JIA) is a collective term for arthritides that are diagnosed before the age of 16 years. Diagnosis requires disease duration of at least 6 weeks and the exclusion of other causes of arthritis.
### Classification of JIA

Based on symptoms presented during 1st 6 months of ds -

1. Systemic onset JIA (10-15%)
2. Oligo-articular JIA (50%)
   - a. Persistent oligo-articular JIA
   - b. Extended oligo-articular JIA
3. Polyarticular JIA (RF negative) (15-20%)
4. Polyarticular JIA (RF positive) (≤5%)
5. Psoriatic arthritis (5-10%)
6. Enthesitis related arthritis (5-10%)
7. Undifferentiated arthritis (10-15%)
Principles of management

• Two major trends :
  • “Window of opportunity”: literature suggests that treating inflammatory disease early and aggressively to ‘switch off’ the immune process leads to better longterm.
  • “Treat to target”: This concept has arisen in the era of biological agents, when treatment goals have become more ambitious and patient outcomes vastly improved.
Principles of management (cont…)

• **The first treatment:**
  - Anti-inflammatory drugs: NSAIDs, Steroids
  - Classical DMARDs: Methotrexate, Sulfasalazine, Hydroxychloroquin

• **But:**
  - 30% patients response to NSAIDs.
  - 50% patients nonresponse to Methotrexate (*)

Side effects of Corticosteroids
Biologic therapies

• Biologic therapies: are treatments which utilise either monoclonal antibodies or soluble cytokine receptors, to specifically target individual components of the immune system(*)

• Biologics should not be used unless a patient is intolerant to, or has failed optimised treatment with MTX; this is defined as 15mg/m2 given subcutaneously once-weekly for at least 3 months; higher doses have no evidence to suggest increased efficacy (**) 


History of biologic agents

• Biologic agents: “bench to bedside” medicine.
• Biologic agents are approved by FDA for treatment JIA
  • Anti TNF-α: Etanercept (1999), Adalimumab (2008)
  • Anti IL-1: Anakinra
  • Anti IL-6: Tocilizumab (2011)
  • Rituximab
  • Abatacept
Comparison of treatment response, remission rate and drug adherence in polyarticular juvenile idiopathic arthritis patients treated with etanercept, adalimumab or tocilizumab

Honeff et al, Arthritis & Therapy (2016) 18:272

**Background**: Treatment response, remission rates and compliance in patients with polyarticular juvenile idiopathic arthritis (polyJIA) treated with adalimumab, etanercept, or tocilizumab were analyzed in clinical practice.

**Methods**: 

- Treatment response, remission rates and compliance in patients with polyarticular juvenile idiopathic arthritis (polyJIA) treated with adalimumab, etanercept, or tocilizumab were analyzed in clinical practice.

- 236 patients started adalimumab, 419 etanercept and 74 tocilizumab, with differences in baseline patient characteristics
Improvement in patients using etanercept, adalimumab or tocilizumab according to the ACRpedi30

Fig. 1 Improvement in patients using etanercept, adalimumab or tocilizumab according to the Pediatric American College of Rheumatology (PedACR)30/50/70 and 90 criteria
Improvement in patients following etanercept, adalimumab or tocilizumab treatment according to Juvenile Disease Activity Score 10 at baseline compared with the last observation.

Fig. 2 Improvement in patients following etanercept, adalimumab or tocilizumab treatment according to Juvenile Disease Activity Score (JADAS)10 at baseline compared with the last observation on a study drug.
Rates of Juvenile Disease Activity Score (JADAS)10 remission and minimal disease activity in patients taking etanercept, adalimumab or tocilizumab

**Fig. 3** Rates of Juvenile Disease Activity Score (JADAS)10 remission and minimal disease activity in patients taking etanercept, adalimumab or tocilizumab
## Table 2 Rates and reasons for discontinuation

<table>
<thead>
<tr>
<th>Details</th>
<th>Etanercept cohort</th>
<th>Adalimumab cohort</th>
<th>Tocilizumab cohort</th>
<th>Adalimumab versus etanercept</th>
<th>Tocilizumab versus etanercept</th>
<th>Tocilizumab versus adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuations, n (%)</td>
<td>207 (49.4)</td>
<td>142 (60.4)</td>
<td>23 (31.1)</td>
<td>1.57 (1.03; 2.41); 0.037</td>
<td>0.20 (0.09; 0.45); &lt;0.001</td>
<td>0.13 (0.06; 0.29); &lt;0.001</td>
</tr>
<tr>
<td>Inefficacy, n (%)</td>
<td>50 (11.9)</td>
<td>52 (22.0)</td>
<td>9 (12.2)</td>
<td>1.65 (0.88; 3.08); 0.118</td>
<td>0.34 (0.11; 1.00); 0.050</td>
<td>0.20 (0.07; 0.60); 0.004</td>
</tr>
<tr>
<td>Remission, n (%)</td>
<td>54 (12.9)</td>
<td>22 (9.3)</td>
<td>2 (2.7)</td>
<td>0.78 (0.43; 1.40); 0.404</td>
<td>0.12 (0.02; 0.79); 0.27</td>
<td>0.16 (0.02; 1.05); 0.056</td>
</tr>
<tr>
<td>Intolerance, n (%)</td>
<td>15 (3.6)</td>
<td>15 (6.4)</td>
<td>2 (2.7)</td>
<td>2.28 (1.03; 5.04); 0.042</td>
<td>0.84 (0.18; 4.01); 0.826</td>
<td>0.37 (0.08; 1.79); 0.216</td>
</tr>
</tbody>
</table>

Details: Hypersensitivity (5), uveitis (3), vasculitis (1), lymphoma (1), infections (4)\(^b\), impetigo (1)\(^b\), elevated transaminases (1), neuropsychiatric (4)\(^b\), neutropenia (1)\(^b\)

Others*, n (%) | 88 (16.0) | 53 (22.4) | 10 (13.4) | 1.21 (0.74; 1.96); 0.443 | 0.27 (0.10; 0.72); 0.009 | 0.22 (0.08; 0.60); 0.003 |

*Analyses weighted by an inverse probability of treatment estimated by a generalized propensity score. \(^a\)Infections included pneumonia and soft tissue infections; neuropsychiatric included headache, nausea, aggressiveness, anxiety, and vertigo. \(^b\)Beta regression coefficient for continuous variables. CI confidence interval, OR odds ratio for categorical variable.
Conclusions

- Adalimumab/etanercept/tocilizumab showed comparable efficacy toward polyJIA.
- Tolerance was acceptable.