Combination $T_3/T_4$ therapy in paediatric patients with autoimmune hypothyroidism unresponsive to $T_4$ therapy alone

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Introduction

- We do not fully understand why some hypothyroid patients complain of persistent symptoms despite normalisation of TSH with levothyroxine therapy.
- Recent evidence in adults suggests that polymorphism in deiodinase 2 enzyme could lead to lower level of $T_3$ in some tissues and persistence of symptoms.
- A combination therapy with $T_3/T_4$ may improve symptoms especially psychological well-being, mood and memory in such patients.
- Combination therapy is used in adults but rarely in children.

Results

Case 1:
- 14 year old female diagnosed with autoimmune hypothyroidism
- Patient complained of low mood, poor memory and tiredness, affecting her school performance despite normalisation of TSH
- Transient symptomatic relief only, with increasing doses of levothyroxine ($T_4$) to maximum 125 micrograms
- Other baseline investigations unremarkable
- Liothyronine ($T_3$) was added in after 2 years of levothyroxine, with significant improvement of her symptoms

<table>
<thead>
<tr>
<th>Patient</th>
<th>At diagnosis</th>
<th>On $T_4$ treatment</th>
<th>On $T_3/T_4$ treatment</th>
<th>Current treatment</th>
<th>Tiredness, memory and concentration</th>
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<tbody>
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<td>75 OD 10 TDS</td>
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<tr>
<td>Case 2</td>
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<td>13.4 0.86 1.5</td>
<td>9.4 0.46 1.5</td>
<td>75 OD 10, 20 BD</td>
<td>Improved</td>
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Case 2:
- 12 year old female diagnosed with autoimmune hypothyroidism
- Continued to have low mood and lethargy despite increasing doses of levothyroxine to 150 micrograms
- Other baseline investigations unremarkable
- $T_3$ was added to her therapy after nearly 3 years with good effect and patient-reported improvement in mood and energy levels

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Patient comments:

Before combination treatment

“She feels excessively tired throughout the day though she has had a good night’s sleep. She has missed a lot of school due to this and generally feels like lying down most of the time. This is very unlike H who is normally a very academic, active young lady.”

On combination treatment

“[She] is doing much better on her combined $T_4$ and $T_3$ now. Her energy levels are much improved. She is coping very well with her daily routine and is able to do a lot more physical activity.”

“Overall [she] says that although she is not 100%, she is better than when she was on [Levothyroxine] only and would not like to go back to this.”

Conclusion

- Our paediatric patients with autoimmune hypothyroidism showed a good symptomatic response to $T_3/T_4$ combination treatment after a limited response to $T_4$ alone.
- Both patients opted to continue combination treatment despite increased frequency of dosing.
- Prospective paediatric RCT is required comparing $T_4$ and $T_3/T_4$ combination therapy to identify the subset of patients who may benefit.

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