Long Acting Somatostatin Analogue (Lanreotide) therapy in Congenital Hyperinsulinism – Pharmacokinetics and long term follow up study

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Background

• Congenital hyperinsulinism (CHI) causes severe hypoglycaemia in children.
• Diazoxide and daily octreotide injections are first and second-line of treatment for CHI respectively.

Objective and hypotheses

• To evaluate the efficacy, safety and pharmacokinetics of long acting somatostatin analogue (Lanreotide) therapy in CHI patients.

Methods

• Patients >6 months of age either on high dose diazoxide (causing side effects), or daily octreotide were started on 30mg Lanreotide every 4-weeks.
• Children >3 years of age had Paediatric Quality of Life (PedsQL) with Strengths and Difficulties questionnaires (SDQ) and continuous glucose monitoring (CGMS) pre- and 1-year post-Lanreotide.
• Plasma Lanreotide concentrations measured by radioimmunoassay (>3 years of age) at different time points after first dose and subsequently prior to each dose for 6 months.

Results

• 31 children were commenced on Lanreotide and 5 had to stop treatment. Out of 26 children, 18 were on daily octreotide and 8 on diazoxide.
• Pharmacokinetic data on 21 children showed highest median value (25th-75th interquartile range) of Lanreotide concentration was 14.93ng/ml (4.39-31.6) at +4 hours of 1st dose (figure 1).
• The median values (25th-75th interquartile range) prior to 2nd, 3rd, 4th, 5th, 6th and 12th doses were 0.88ng/ml (0.66-1.32), 1.09ng/ml (0.89-1.35), 1.21ng/ml (0.87-1.49), 0.79ng/ml (0.67-1.55), 1.35ng/ml (1.19-1.86) and 1.44ng/ml (1.08-2.18) respectively (figure 2).
• PedsQL showed significant change in total health and psychosocial score and significant reduction in overall stress in the SDQ after 1-year post-Lanreotide (p<0.05).
• CGMS on 15 children showed significant reduction in hypoglycaemic episodes after 1 year of therapy (p=0.012) (figure 3).

Conclusion

• This study demonstrates lanreotide is safe and effective alternative to diazoxide and octreotide therapy in CHI patients with a significant improvement in blood glucose control and quality of life.
• There is cumulative effect in Lanreotide concentration after each dose. Our 2.5 years follow-up data shows no adverse effects on growth.
• However also to note that not all patients with CHI will response to Lanreotide and they need close monitoring when assessing the response of Lanreotide.

% Pre-Lanreotide % Post-Lanreotide

<table>
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<tr>
<th>Blood glucose</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>N</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Below 3.5 mmol/l</td>
<td>4.7</td>
<td>4.4</td>
<td>1.7</td>
<td>2.3</td>
<td>15</td>
<td>0.012</td>
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<td>Within 3.5-7.8 mmol/l</td>
<td>81.7</td>
<td>11.9</td>
<td>87.3</td>
<td>10.8</td>
<td>15</td>
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<tr>
<td>Above 7.8 mmol/l</td>
<td>13.6</td>
<td>10.9</td>
<td>11.0</td>
<td>9.1</td>
<td>15</td>
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Authors have nothing to disclose