Antioxidant treatment of Smith-Lemli-Opitz syndrome (SLOS) and retina function determined by electroretinography

Kimberly Christnacht MD Candidate; Ellen R Elias MD

Introduction
Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive disease caused by a defect in cholesterol metabolism, resulting in cholesterol deficiency, elevated 7-dehydrocholesterol (7DHC) and progressive retinal degeneration. SLOS may be mild, moderate or severe based on serum levels of cholesterol, 7DHC and clinical characteristics. Phototransduction is abnormal in SLOS, likely due to high levels of 7DHC in cell membranes of photoreceptors, free radical formation and retina cell death. Cholesterol and antioxidant supplementation may protect against SLOS retinopathy.1,2,3

Methods
IRB approval was obtained prior to conducting the study. 9 Patients with SLOS were prospectively enrolled. Data presented is from 2008-2022. 2008 – present patients were treated with cholesterol and Antioxidants- first AQUADEKS, and more recently DEKAs Plus via liquid or capsule.

Cholesterol supplementation was adjusted based on patient body weight and 7DHC levels

Results
In Mild patients:
- There were decreased amplitudes, but rods improved towards normal values (Figure 4).
- Increased implicit time improved in 2 of 3 patients but remained mildly abnormal (Figure 5).

In Moderate patients:
- Decreased amplitudes improved from moderate to mild towards normal values in 3 of 4 patients (Figure 6).
- Implicit times remained within normal ranges in 3 of 4 patients (Figure 7).

In Severe patient:
- There were mild to moderate decreased amplitudes in rods which improved over time (Figure 6).
- Implicit times remained within a normal range (Figure 7).

Discussion
This study allows us to objectively follow retinal function for patients with a known degenerative pigment retinopathy.

Over time as patients continue to take antioxidants there is a stabilization if not an improvement in rod function.

Future research is needed to determine which particular antioxidants are most impactful and the most optimal doses.

Future studies will analyze oxysterol levels to see if antioxidants help decrease levels of oxysterols and their damaging effects.

Conclusions
Treatment of SLOS with cholesterol and antioxidants is associated with improvement of retina function determined by electroretinography.

Further study of antioxidants and retina function may someday help treat other diseases that result in retinal degeneration.

Purpose
The purpose of this study was to determine the effect of treatment with cholesterol and antioxidant/vitamin (DEKAS Plus and AQUADEKS) supplementation on the retina function in patients with SLOS by electroretinography (ERG).

Table 2. Cholesterol averages and ranges of patients in Mild, Moderate, and Severe Cohorts at time of first ERG.

<table>
<thead>
<tr>
<th>Serum Cholesterol</th>
<th>Mild±SD</th>
<th>Moderate±SD</th>
<th>Severe±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>144.88±3.67</td>
<td>129.10±10.16</td>
<td>165.0±14.26</td>
<td>64±10.16</td>
</tr>
<tr>
<td>Serum 7DHC</td>
<td>3.44±0.33</td>
<td>3.5±1.96</td>
<td>6±1.2</td>
</tr>
<tr>
<td>Serum 8-DHC</td>
<td>1.72±0.01</td>
<td>4.77±0.75</td>
<td>8.8±1.2</td>
</tr>
<tr>
<td>Sterol Ratio (%)</td>
<td>0.5±0.3</td>
<td>2.4±0.4</td>
<td>3.3±0.8</td>
</tr>
</tbody>
</table>

Table 2. Serum cholesterol, 7DHC, and 8-DHC levels in Mild, Moderate, and Severe Cohorts at time of first ERG.

Supplement Facts
DEKAs Plus contains:
- 7-dehydrocholesterol (7DHC) - 100 mg
- Phytosterols - 50 mg
- Phytol - 50 mg
- Erythritol - 250 mg
- Squalene - 10 mg

A baseline ERG under anesthesia was performed according to ISCEV standards when possible.

Repeat ERG’s were performed a minimum of one year after initial treatment.

In Mild patients:
- There were decreased amplitudes, but rods improved towards normal values (Figure 4).
- Increased implicit time improved in 2 of 3 patients but remained mildly abnormal (Figure 5).

In Moderate patients:
- Decreased amplitudes improved from moderate to mild towards normal values in 3 of 4 patients (Figure 6).
- Implicit times remained within normal ranges in 3 of 4 patients (Figure 7).

In Severe patient:
- There were mild to moderate decreased amplitudes in rods which improved over time (Figure 6).
- Implicit times remained within a normal range (Figure 7).

Figure 4. 0 dB Scotopic Flash B wave amplitude over time for patients in Mild cohort.

Figure 5. 0 dB Scotopic Flash B wave implicit time over time for patients in Mild cohort. It should be noted that findings less than 52 ms are normal values.

Figure 6. 0 dB Scotopic Flash B wave amplitude over time for patients in Moderate and Severe cohort. It should be noted that findings less than 52 ms are normal values.

Figure 7. 0 dB Scotopic Flash B wave implicit time over time for patients in Moderate and Severe cohort. It should be noted that findings less than 52 ms are normal values.

The authors have no financial or proprietary interest in any of the materials presented. Support by The Pediatric Clinical Translational Research Center at the Children’s Hospital Colorado and Colorado Clinical and Translational Sciences Institute Grant number UL1RR025750.

Literature Cited