What hypoglycemia does to the heart: Impact of nocturnal hypoglycemia on cardiac repolarization in diabetic children

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Background

Hypoglycemia is the most common and most feared complication of insulin treated diabetes. Though mostly asymptomatic, nocturnal hypoglycemia can be fatal in rare cases: sudden nocturnal death is more frequent in diabetic patients than in others. It is postulated that hypoglycemia related QTc prolongation contributes to cardiac arrhythmia and can even lead to dead in bed syndrome.

Objective

To evaluate the influence of nocturnal hypoglycemia on QTc in children with type 1 diabetes.

Patients and methods

In 25 (11f, 14m) children with type 1 diabetes continuous glucose monitoring was performed for 5 days, and simultaneously, Holter ECG (Schiller) was recorded during each night.

Magnesium, Calcium and Potassium levels were measured once at the start of the observation period.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>13.5</td>
<td>8.1-17.5</td>
</tr>
<tr>
<td>DM duration (y)</td>
<td>5.79</td>
<td>0.5-13.25</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.8</td>
<td>6.3-12.9</td>
</tr>
</tbody>
</table>

All subjects had normal cardiac findings in clinical examination/echocardiography and normal values for potassium, calcium and magnesium.

No patient was under medication knowing to affect cardiac function or repolarization.

Nocturnal hypoglycemia was defined as any sensor glucose measurement below 3.7 mmol/l for at least 15 minutes during documented nighttime.

Mean QTc was calculated by the Bazett formula for every period of nocturnal hypoglycemia and compared to a period of the same duration preceding hypoglycemia.

Results

41 episodes of nocturnal hypoglycemia were documented, 33 of them with ECG recording.

Nocturnal hypoglycemia episodes lasted 15 to 365 min (mean 96min), in 48% (16/33 episodes) nadir was below 3.0 mmol/l.

No relevant cardiac arrhythmia was observed.

Mean QTc during hypoglycemia was significantly longer compared to normoglycemia

![Fig 1: Study design](image1)

<table>
<thead>
<tr>
<th></th>
<th>Before hypoglycemia</th>
<th>During nocturnal hypoglycemia</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc ms (mean, sd)</td>
<td>404 (+/-15)</td>
<td>412 (+/-18)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

![Tab 1: Patient characteristics](image2)

The change in QTc was NOT dependent on age, HbA1c, diabetes duration, nadir or duration of hypoglycemia.

However, the QTc lengthening seemed to be more pronounced in subjects with lower magnesium levels (p= 0.04).

Conclusion

We could document a QTc lengthening and thereby potentially arrhythmogenic effect of nocturnal hypoglycemia in otherwise healthy children with diabetes.

The QTc change was not clinically relevant in our study population but could be in predisposed subjects or in the face of co-medication. In such risk patients, nocturnal hypoglycemia should be avoided even more aggressively.

![Fig 3: QTc before and during nocturnal hypoglycemia](image3)

We thank Medtronic for providing 2iPro2 and Enlite sensors.