Empagliflozin significantly attenuates QTc prolongation in rats due to sotalol

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Anti-Diabetic Pharmacotherapy

Introduction:
Sotalol (SOT) is a Class 3 antiarrhythmic drug and commonly used for various arrhythmia treatments. However, it can prolong QT interval and lead to malignant arrhythmias. Empagliflozin is a selective SGLT-2 inhibitor used in the treatment of Type 2 diabetes and has been shown to have positive effects on cardiovascular outcomes. Since the effect of empagliflozin (EMPA) on potassium channel activation is not yet known, there is no recommendation for the concomitant use of these drugs.

Purpose:
In this study, we aimed to evaluate possible protective effects of empagliflozin in sotalol induced QT prolongation.

Materials and methods:
Twenty-four male Wistar Alba rats were randomized into four groups. The first (control) group (n: 6) received only serum physiologic (1ml) via orogastric gavage (OG). The second (EMPA) group (n: 6) received EMPA (10 mg/kg) via OG. The third (SOT) group (n: 6) received SOT(80 mg/kg) via OG. The fourth (EMPA+SOT) group (n: 6) received EMPA (10 mg/kg) and SOT (80 mg/kg) via OG. Under anesthesia; PR, QT intervals and heart rate (HR) were measured and QTc value was also calculated at second hour on lead II using electrocardiogram (ECG).

Results:
In the SOT group; QT intervals, T wave durations and QTc values were found to be statistically longer than the control group, whereas HR was found to be lower than the control group (p < 0.01). In the EMPA+SOT group; QT intervals, T wave durations and QTc values were significantly lower and HR was significantly higher compared to the SOT group (p <0.001, p<0.01, p<0.001, p<0.001 respectively) (Table)

Conclusion:
In the present study, we detected that EMPA significantly ameliorates SOT induced QT prolongation. In addition to this, we have also shown that EMPA can be used safely with SOT in clinical practice. With more clinical trials, the routine use of EMPA may be suggested to prevent QTc prolongation in diabetic patients receiving SOT. Finally, our study indicates that EMPA can effect on potassium channels.

### Table

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>EMPA</th>
<th>SOT</th>
<th>EMPA+SOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR duration (ms)</td>
<td>54,8±4,7</td>
<td>56,1±5,5</td>
<td>59,6±4,5</td>
<td>57,7±3,2</td>
</tr>
<tr>
<td>QT duration (ms)</td>
<td>81,6 ± 5,9</td>
<td>73,9 ±8,1</td>
<td>123,5±7,7</td>
<td>83,7 ±6,8</td>
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<tr>
<td>HR (bpm)</td>
<td>332,0 ± 18,3</td>
<td>296,4±29</td>
<td>211,3±24,3</td>
<td>266,3±13,7</td>
</tr>
<tr>
<td>QTc</td>
<td>191,54 ±10,5</td>
<td>163,9±18,5</td>
<td>231,6±22,1</td>
<td>176,1±11,6</td>
</tr>
<tr>
<td>T duration</td>
<td>42,3±4,7</td>
<td>49,5±6,2</td>
<td>65,2±7,0</td>
<td>50,6±4,9</td>
</tr>
</tbody>
</table>

Table: PR, QT, QTc, T durations and heart rate for all groups in 2nd hour a: Control vs Sotalol; P<0,001, b: EMPA+SOT vs SOT; P <0,001, c: EMPA+SOT vs SOT; P <0,01