Use of the Beta-Blocker, Pindolol, in the Treatment of Symptomatic Bradycardia

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Background
Beta-blocker medications are commonly used for hypertension, tachyarrhythmias, acute coronary syndrome and heart failure. In recent years, non-selective beta-blockers have been largely replaced by cardio-selective beta-blockers such as metoprolol or bisoprolol. Pindolol exhibits partial intrinsic sympathomimetic activity (ISA), allowing it to become an option in specific clinical situations, such as described in this poster. In the 1980’s and 90’s there was interest in the ISA of pindolol. The potential advantages of this was considered, such as for patients with tachyarrhythmias plus nocturnal bradycardia¹, angina with bradycardia², and was also used to explain a reduction in adverse effects and rebound tachycardia³. ISA activity also appeared to be independent of dose (maximal effect at 2.5mg twice daily)⁴. Since this time, little effort has been put into study of pindolol’s ISA, and its prospective use for bradycardia appears to be primarily via cardiologist expert opinion. A Cochrane review in 2014 on the effects of partial agonist beta-blockers on blood pressure and heart rate, found that pindolol (at doses used for primary hypertension) caused a lower drop in heart rate when compared to other non-selective beta-blockers⁵.

Clinical Features
An 88 year old Caucasian male presented to the emergency department with symptomatic junctional bradycardia, a heart rate (HR) of 30-40 beats per minutes (bpm) and hyperkalaemia (potassium = 6.0mmol/L). Blood pressure was normal, but due to low HR the patient was frequently dizzy and nauseous and became bed-bound secondary to the symptoms. Past medical history and medications are outlined in Table 1.

On admission, hyperkalaemia was corrected using calcium gluconate, insulin and calcium polystyrene sulfonate (Resonium®), reducing to 4.8mmol/L. Despite treatment, the patient remained bradycardic with multiple ‘met calls’ (see Graph 1). Potassium (and other electrolytes) remained stable throughout admission (see Table 2). Despite the prognosis of terminal hepatic cell carcinoma, his quality of life was good and therefore treatment of bradycardia was necessary to allow the patient to return home with the aim to stay out of hospital.

Interventions and Case Progress
A continuous isoprenaline infusion was commenced at a rate of 1 mcg/min, escalating to 3mcg/min, increasing HR to approximately 60bpm, however he also became hypertensive (up to 180mmHg systolic). At stopping isoprenaline, HR dropped and he became symptomatic again. (See Graph 1)
The patient and family were presented with the option of permanent pacemaker (PPM) insertion. The cardiology team felt this a viable option as the patient was physically fit for the procedure, and would allow him to return home to his previous quality of life. While the patient and family considered this, a trial of pindolol, at 2.5mg twice daily, was commenced. The aim was to improve bradycardia, without increasing blood pressure.
Pindolol was co-prescribed to mitigate any potential initial drop in HR, and was ceased shortly afterwards. The patient tolerated pindolol well and over the next 72 hours his HR was a consistent 55-60 bpm. As it appears the intrinsic effect does not increase with dose, he remained on 2.5mg twice daily. See Graph 1 for complete timeline of events, heart rate and systolic blood pressure.

Outcomes
On further discussions with patient and family, PPM insertion was decided to allow for best quality of life. On Day 7 the PPM was inserted and he remained stable with HR approximately 60bpm and blood pressure 130/70mmHg. He was discharged from hospital the next day, remaining on pindolol, with the view for ongoing management (and cessation of pindolol) with a private cardiologist as an outpatient.

Although no record of when pindolol was ceased, in an unrelated admission five months later he was no longer on pindolol and had a consistent heart rate (60-70 bpm).

Table 1: Past Medical History and Current Medications

<table>
<thead>
<tr>
<th>Medication Name and Strength</th>
<th>Dose and Frequency</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinapril 10mg</td>
<td>Half (5mg) orally</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Prazosin 1mg</td>
<td>One orally noche</td>
<td>Hypertension plus benign prostatic hyperplasia</td>
</tr>
<tr>
<td>Methoxy pgy-epitin beta (Mircra) 100mcg</td>
<td>One subcutaneously monthly</td>
<td>Stage 3 Chronic Kidney Disease (CrCl=40ml/min)</td>
</tr>
<tr>
<td>Paracetamol 665mg SN</td>
<td>Two (1330mg) orally BD</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Dexamethasone 4mg</td>
<td>Half (2mg) orally</td>
<td>Hepatic Cell Carcinoma (terminal)</td>
</tr>
</tbody>
</table>

Other Co-Morbidities not currently medically treated:
Type 2 Diabetes Mellitus (Diet Controlled), Dyslipidaemia, Depression, Bladder Cancer (2015), Bowel Cancer (hemicolectomy), Cholelithiasis

No Known Medication Allergies

Table 2: Potassium level throughout admission

<table>
<thead>
<tr>
<th>Day</th>
<th>K+ (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>6.9 (am) 4.8 (pm)</td>
</tr>
<tr>
<td>Day 2</td>
<td>4.5</td>
</tr>
<tr>
<td>Day 3</td>
<td>4.4</td>
</tr>
<tr>
<td>Day 4</td>
<td>4.6</td>
</tr>
<tr>
<td>Day 5</td>
<td>4.4</td>
</tr>
<tr>
<td>Day 6</td>
<td>-</td>
</tr>
<tr>
<td>Day 7</td>
<td>4.7</td>
</tr>
<tr>
<td>Day 8</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Graph 1: Heart Rate and Systolic Blood Pressure Timeline

Graph 2: Heart Rate and Systolic Blood Pressure Timeline

Isoprenaline Infusion
Pindolol 2.5mg BD
PPM insertd

Conclusion
Pindolol’s intrinsic sympathomimetic activity allows the beta-blocker to become a viable option for management of bradycardia in conjunction with elevated blood pressure, as demonstrated in this case.

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References

Figures
1: Heart Rate and Systolic Blood Pressure Timeline
2: Heart Rate and Systolic Blood Pressure Timeline

Table
1: Past Medical History and Current Medications
2: Potassium level throughout admission