**Introduction**

- The bladder vasculature has become an area of focus in the quest to understand the pathophysiology of bladder dysfunction and LUTS. Hypoperfusion-induced hypoxia can produce bladder dysfunction (1,2) and enhancing perfusion can ameliorate dysfunction in experimental studies (3).
- Vascular smooth muscle tone is regulated via noradrenaline acting at α₁-adrenoceptors to cause vasoconstriction. There are 3 cloned subtypes of α₁ adrenoceptor (α₁A, α₁B and α₁C), and the functional phenotype of the α₁ receptor, the α₁Aα₁α1̂-adrenoceptor (4).
- Which functional subtype regulates vasoconstriction of the superior vesical artery supplying the porcine bladder is currently unknown.
- The aim was to classify the α₁-adrenoceptor subtype mediating vasoconstriction of the porcine superior vesical artery.

**Methods**

- Sections (~4mm) of porcine superior vesical artery (SVA) (internal diameter ~1mm) were isolated from 6-month old pigs and mounted on stirrups in tissue baths containing gassed Krebs-bicarbonate solution at 37°C.
- Developed tension of the circular smooth muscle was recorded via force transducers connected to a PowerLab using LabChart software.
- Contraction to noradrenaline, phenylephrine and the α₁A-adrenoceptor selective agonist A-61603 were recorded. Concentration-response curves to phenylephrine were obtained in the absence and presence of α₁-adrenoceptor antagonists silodosin and RS-100329 (α₁A-selective), BMY-7387 (α₁B-selective) and prazosin (α₁D-selective).
- Developed tension of the circular smooth muscle was recorded via force transducers connected to a PowerLab using LabChart software.
- Control experiments without antagonists were performed to correct for time dependent changes in tissue sensitivity.

**Results**

**Responses of SVA to agonists**

- Noradrenaline, phenylephrine and A-61603 caused concentration-dependent contractions of the SVA (Fig. 1). A-61603 was more potent, with the relative potency of agonists A-61603 > phenylephrine ≥ noradrenaline (Table 1).

<table>
<thead>
<tr>
<th>Agonist</th>
<th>n</th>
<th>Potency (pEC₅₀)</th>
<th>Maximum Response (g/mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-61603</td>
<td>6</td>
<td>7.33±0.15</td>
<td>1.71±0.11</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>9</td>
<td>5.83±0.20</td>
<td>1.76±0.14</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>6</td>
<td>5.79±0.15</td>
<td>2.14±0.11</td>
</tr>
</tbody>
</table>

*Data is mean ± SEM. **p<0.01 vs phenylephrine & noradrenaline (ANOVA plus Tukey).*

**Effect of antagonists**

- The α₁A-selective antagonist BMY7378, at relatively high concentrations up to 30µM, failed to antagonise responses to phenylephrine (Fig. 2A). However the α₁D-selective antagonists RS-100329 and silodosin produced rightward shifts of phenylephrine curves, at 10nM and 30nM (p<0.01 vs control) (Fig. 2B) and 1nM and 10nM (p<0.05 vs control) (Fig. 2C). Maximal responses to phenylephrine were not significantly affected by RS-100329 or silodosin and the pKᵦ estimates were 8.48±0.25 and 9.47±0.18, respectively.
- Prazosin shifted phenylephrine concentration-response curves without significantly affecting the maximal response, and with a relatively low affinity (pKᵦ) of 8.63 and pKᵦ estimate of 8.02±0.06 (Fig. 2D & E).

**Conclusion**

- Sections (~4mm) of porcine superior vesical artery (SVA) (internal diameter ~1mm) were isolated from 6-month old pigs and mounted on stirrups in tissue baths containing gassed Krebs-bicarbonate solution at 37°C.
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**References**

2. Gopi et al. (2013) J.Urol. 190: 1116-1122