DEVELOPMENT OF AN IN VITRO METHOD TO STUDY PENILE RESISTANCE VESSELS USING MYOGRAPHY

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Relaxation of penile arteries is one of three main events leading to erection, which also include relaxation of trabecular tissue and decreased venous outflow (reviewed by Simonsen *et al*., 2002). The aim was to use small vessel wire myography as a model in which to study pharmacological targets in genital resistance vasculature. Dorsal and cavernous penile arteries (DPA and CPA, internal diameters 182±3 and 164±3μm, respectively) were isolated from male New Zealand White rabbits (2.5-3.5 kg, n=31) at necropsy. Isometric tension measurements were recorded in response to noradrenaline (NA), the α_1-adrenoceptor agonist, phenylephrine (PE) and to the α_2-adrenoceptor agonist, UK-14,304 (UK) in the absence and presence of rauwolscine (α_2 antagonist) and prazosin (α_1 antagonist). NA, PE and UK all produced concentration-dependent contractions of both DPA and CPA (Table 1). UK was 37-54 and 10-14 fold more potent than NA and PE in DPA and CPA, respectively ($P<0.001$). However, UK behaved as a partial agonist in both tissues relative to NA and PE (Table 1). In addition, the slopes (n_H) of the UK concentration-effect curves were significantly shallower than those estimated for NA and PE.

At low concentrations of UK ($3x10^{-8}$M), rauwolscine produced complete, concentration-dependent inhibition of the contractile response in both tissues (pIC_{50}=8.37±0.05 and 8.77±0.22 in DPA and CPA, respectively, $P>0.05$ n=5-8). In contrast, prazosin ($1x10^{-9}$-$1x10^{-6}$M) only produced 66.3±6.8 and 65.9±12.5% inhibition of the response to $3x10^{-8}$M UK in DPA and CPA, respectively (n=5-6).

Remarkably, in DPA, prazosin did completely reverse the contraction induced by a higher concentration of UK ($3x10^{-5}$M) in a concentration-dependent manner (pIC_{50}=8.16±0.10, n=8) whereas rauwolscine ($1x10^{-9}$-$1x10^{-6}$M) only produced partial inhibition under these conditions (55.7±9.2%, n=7). In CPA, prazosin and rauwolscine antagonised $3x10^{-5}$M UK with similar potency and produced partial inhibition (77.8±9.9 and 63.3±4.8%) at the highest concentration tested ($1x10^{-6}$M, n=5).

In conclusion, this study demonstrates the utility of myography in investigating pharmacological properties of genital resistance vessels. In addition, the higher potency of UK compared to NA and PE and the potent antagonism by rauwolscine of a low concentration of UK indicates the involvement of α_2-adrenoceptors in both DPA and CPA. However, the lower intrinsic activity (E_{max}) of UK compared to NA and PE and the apparent increase in potency of prazosin relative to rauwolscine when tested against a higher concentration of UK suggests that α_1-adrenoceptors are also involved, although this requires further investigation.

Table 1 Parameters (mean±s.e.mean) obtained by fitting individual (n=6-11) NA, PE and UK-14,304 concentration-effect curves in DPA and CPA to the Hill equation.

CPA	NA	PE	UK	DPA	NA	PE	UK
E_{max} (g)	0.96	0.93	0.49		2.01	1.56	1.10
(s.e.mean)	*(0.03)*	*(0.04)*	*(0.01)*		*(0.04)*	*(0.03)*	*(0.03)*
pEC_{50}	6.28	6.12	7.85		5.85	5.70	6.86
(s.e.mean)	*(0.02)*	*(0.01)*	*(0.07)*		*(0.06)*	*(0.03)*	*(0.04)*
n_H	1.27	1.15	0.58		1.34	1.85	0.61
(s.e.mean)	*(0.07)*	*(0.04)*	*(0.06)*		*(0.18)*	*(0.16)*	*(0.04)*

Simonsen *et al.*, (2002). *J. Vas. Res.*, **39**, 283-303