

Poster Communications: Effects of changes in blood pressure and heart rate on indices of cardiac contractility

L. Mooney^{1,2}, S. Currie¹, S. J. Coker¹, M. Skinner²

1. Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom. 2. Global Safety Assessment, AstraZeneca, Macclesfield, United Kingdom.

View other abstracts by:

- [Mooney, L](#)
- [Skinner, M](#)
- [Currie, S](#)
- [Coker, SJ](#)

Recently several drugs have been found to adversely affect cardiac contractility and there is a need to assess these risks in routine safety pharmacology studies. Left ventricular (LV) dP/dt_{max} and the QA interval (QAI, the interval between the onset of the Q wave of the ECG and the beginning of the rise in the following arterial blood pressure pulse) are used as indices of cardiac contractility, however, these have been reported to be influenced by changes in cardiac loading and heart rate. The aim was to determine the influence of heart rate and blood pressure (BP) on LVdP/dt_{max} and QAI in the anaesthetised guinea pig. Male Dunkin-Hartley guinea pigs (510-650 g) were anaesthetised with fentanyl (50 µg kg⁻¹ s.c.) followed by sodium (Na) pentobarbital (50-60 mg kg⁻¹ i.p.). The trachea was cannulated for ventilation with room air (7-8 mL kg⁻¹, 60 strokes min⁻¹) and ECG, arterial BP, and LV pressure (LVP) were recorded. BP was increased using phenylephrine (0.02 and 0.07 µmol kg⁻¹) and decreased by Na nitroprusside (0.17 and 0.34 µmol kg⁻¹) infused i.v. for 5 min each dose (n = 6). In a separate group of animals heart rate was increased via a pacing clip attached to the right atrial appendage and decreased by stimulation of the right vagus

nerve (n = 4). Phenylephrine increased mean BP from 48 ± 3 mmHg to a peak of 62 ± 2 mmHg with the first dose and 81 ± 8 mmHg with the second dose ($p < 0.05$, two-way ANOVA plus Dunnett's test). LVdP/dtmax (2462 ± 371 to 2839 ± 285 and 3118 ± 342 mmHg sec⁻¹) and QAI (40 ± 2 to 44 ± 2 and 46 ± 2 msec) also increased. Heart rate was unchanged. Na nitroprusside decreased mean BP from 48 ± 3 to 30 ± 3 mmHg with the first dose and to 26 ± 3 mmHg with the second dose. Both LVdP/dtmax and QAI also decreased (2462 ± 371 to 1947 ± 258 and 1800 ± 149 mmHg s⁻¹, and 40 ± 2 to 35 ± 3 and 34 ± 3 msec, respectively). Heart rate increased with the second dose of Na nitroprusside (258 ± 7 to 281 ± 8 beats min⁻¹). Cardiac pacing and vagus nerve stimulation achieved a range of heart rates from 139 ± 4 to 321 ± 2 beats min⁻¹. At heart rates < 160 beats min⁻¹ LVdP/dtmax was 1295 ± 31 mmHg s⁻¹. This increased as heart rate increased peaking at 2860 ± 158 mmHg s⁻¹ at heart rates of 220-249 beats min⁻¹. As heart rate increased towards 310 beats min⁻¹ LVdP/dtmax decreased to 1532 ± 14 mmHg s⁻¹. QAI and BP were unchanged throughout. In conclusion, LVdP/dtmax and QAI were both altered by changes in BP, and LVdP/dtmax by changes in heart rate. These parameters have limitations as reliable indices of cardiac contractility and care should be taken in their interpretation when simultaneous changes in heart rate and/or BP occur.