Concentration-dependent effects of sunitinib on LVP and ECG parameters in guinea-pig Langendorff perfused isolated hearts

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INTRODUCTION:

The tyrosine kinase inhibitor sunitinib, used as an anticancer drug, has been clinically associated with QT prolongation. It has also been shown to increase action potential duration in dog Purkinje fibres from 6.7 µM at the pacing frequency of 1 Hz.

Left ventricular dysfunction has also been reported in patients during chemotherapy with sunitinib.

The aim of the present work was to check if the guinea-pig Langendorff perfused isolated heart could detect the effects of sunitinib on electrocardiogram and left ventricular pressure parameters.

MATERIALS AND METHOD:

Spontaneous beating guinea-pig Langendorff perfused isolated hearts were perfused with Kreb's solution, oxygenated and warmed at 37 ± 1°C, at a constant perfusion pressure of 55 ± 5 mmHg.

After an equilibration period and a 10 min vehicle superfusion, sunitinib was perfused at three increasing concentrations (0.3, 2 and 10 µM) for 15 minutes per concentration.

The following parameters were measured: developed pressure, maximal rate of contraction (Max dP/dt), maximal rate of relaxation (Min dP/dt), heart rate, PR interval, QRS interval, QT interval, QTc interval (Fridericia) (n=3).

RESULTS

Conclusion: The guinea-pig Langendorff perfused isolated heart is useful to detect acute cardiotoxicity of sunitinib and would therefore be useful to detect direct adverse effects of tyrosine kinase inhibitors on contractility and ECG parameters.