Assessment of non-invasive telemetric blood pressure and electrocardiogram measurement in conscious dogs

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Introduction

Implanted radio telemetry to monitor a range of fundamental cardiovascular parameters, including blood pressure, is the gold standard method for cardiovascular safety pharmacology assessment in freely moving unrestrained animals. Blood pressure, however, is rarely included in repeat dose toxicology studies. Methods are available to acquire blood pressure from dogs using minimally invasive direct methods such as ear artery puncture (McMahon et al, 2007), via an implanted miniature telemetry device (McMahon et al, 2010) or non-invasively via oscillometric cuff systems (Mitchell et al, 2010). These foregoing methods have limitations such as need for restraint and surgery that may preclude wide-spread use, thus a non-invasive method for acquisition of ambulatory blood pressures with acceptable precision is required.

Objectives

To evaluate the veracity of a non-invasive (NI) telemetry system for detecting changes in blood pressure (BP), heart rate (HR) and electrocardiogram (ECG) in ambulatory dogs.

Methods

All animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Laboratory Animals.

Male beagle dogs were acclimatised (over 3 days) to the jackets required for NI telemetry monitoring and on study test days were prepared with ECG leads, tail cuff and jackets (Fig. 1). Ambulatory BP and Lead II ECG data were simultaneously acquired from an invasive telemetry (IT) system (Data Sciences International, USA) and a NI system (EMKA Technologies, France) for 2h predose and 24h post oral dosing with vehicle (n=5), minoxidil (1 mg/kg, n=4) and L-NAME (10 mg/kg, n=5) on separate days. Dogs were 1.4 to 3.8 years and had a weight range of 11.5 to 15.2 kg.

For NI BP the tail-cuff was programmed to inflate at 3 minute intervals and raw BP amplitude measured during each inflation/deflation cycle using a detection algorithm to calculate systolic, diastolic and mean BP. Values for BP (mean, systolic, diastolic and pulse), HR, RR, PR, QRS, QT and QTcL interval were continuously recorded using both telemetry methods. Group mean and standard error of the mean (SEM) are reported, each data point is the mean over a 30 minute collection period. Clinical observations, food consumption and body weights were also recorded. A Dunnett's t-test was run for each telemetry method separately, comparing the treatment (minoxidil or L-NAME) with vehicle with P<0.05 taken to indicate significance.

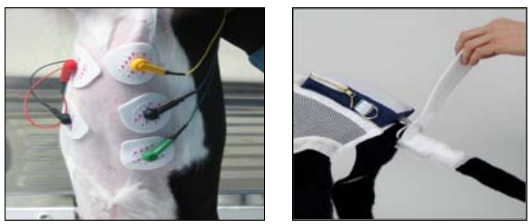

Figure 1. Position of ECG Electrodes and tail-cuff for the Non-Invasive Telemetry System

Results

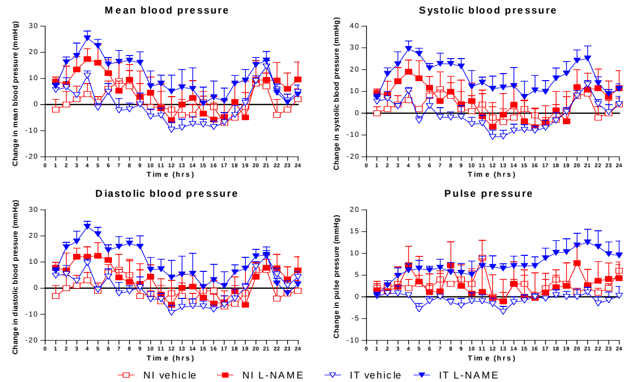

Figure 2. Effect of L-NAME on blood pressure parameters via implanted telemetry (IT) and non-invasive telemetry (NI)

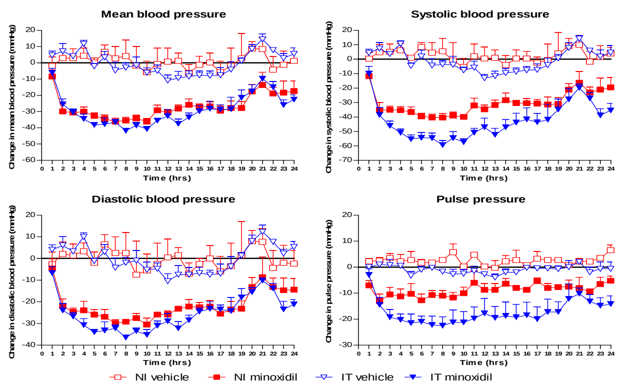

Figure 3 . Effect of minoxidil on blood pressure parameters via implanted telemetry (IT) and non-invasive telemetry (NI)

Results

For IT system statistically significant increases in BP and pulse pressure were apparent with L-NAME, where as for the NI system increases in BP were of shorter duration and reduced magnitude (Fig. 2). For both systems statistically significant decreases in heart rate, with associated changes in ECG intervals, were apparent with L-NAME (data not shown). For NI and IT systems, statistically significant reductions in BP and PP and increases in heart rate (data not shown), with associated ECG interval changes were apparent with minoxidil (Fig. 3). Statistically significant (p<0.0001) correlations were found between all parameters for both blood pressure and ECG intervals (Fig. 4).

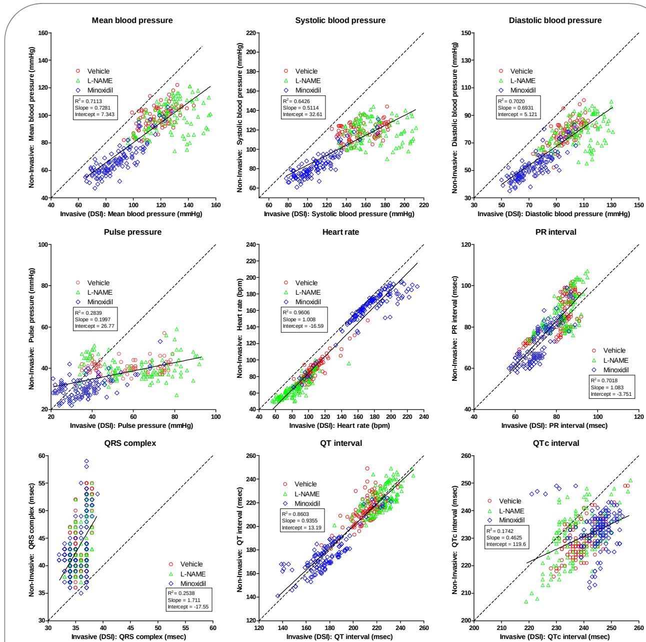

Figure 4. BP and ECG parameter correlation between IT and NI systems, n=300 data points. Dotted line is the line of unity.

Discussion and Conclusions

The non-invasive method described the magnitude and duration of a BP depressor response caused by minoxidil but performed less well in characterising a pressor response produced by L-NAME. The reason for this difference is not known, however, it maybe due to comparisons between a central measure (IT system) versus and peripheral measure (NI system), differential effect of L-NAME on peripheral versus central vascular bed though no evidence supporting this could be found or a lack of method sensitivity. For ECG the results were comparable with those previously reported in the conscious dog (Prior et al, 2009).

The data in this study demonstrates that the non-invasive oscillometric cuff method can be used in freely moving conscious dogs to monitor changes in blood pressure, however, further work is required to assess the NI method's ability to detect increases in blood pressure and assess its sensitivity range.

References

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