AN IMPROVED METHOD FOR ECG RECORDING IN CONSCIOUS DOGS AND MONKEYS: PERICARDIAL LEAD PLACEMENT

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Introduction

Assessing the effects of new chemical entities on cardiovascular function is an essential component of nonclinical safety evaluation. Regulatory guidelines advocate the use of telemetry to evaluate drug effects on the cardiovascular system of animal including electrocardiogram (ECG) waveforms. Currently, standard method is to place ECG electrodes subcutaneously and the ECG signals have a suboptimal signal mainly due to movement artifacts. In order to improve and optimize the ECG signal and minimize movement artifacts, a model for continuous monitoring of the ECG in conscious, unrestrained animals by placing ECG electrodes on the pericardium was evaluated.

Methods

Dogs and monkeys were pre-medicated with atropine, an analgesic (banamine 1mg/kg im, or butorphanol 0.1 – 0.05 mg/kg subcutaneously), and an antibiotic. Anesthesia was induced with propofol (6 mg/kg intravenously) for dogs and with ketamine (10 mg/kg, im) for monkeys. Anesthesia was maintained using isoflurane (2-4%). Heart rate, respiratory rate, ECG, indirect blood pressure, pulse oximetry and end tidal CO_2 were monitored continuously throughout the procedure. Positive pressure ventilation was performed during the thoracotomy. Animals were placed in right lateral recumbency with the left hindleg being rotated upward and laterally to expose the femoral triangle. Briefly, for ECG electrodes placement, coils were made at the ends of the ECG electrodes and were sutured to the pericardial surface at the base (close to left atrium for dog and right atrium for monkey) (negative) and the apex (positive) of the heart in dog or monkey. The ECG waveforms obtained from pericardial leads in conscious dogs and monkeys were evaluated for ECG signal quality and the occurrence of arrhythmias using EMKA ECG-Auto computer software. ECG waveforms were recorded beat by beat continuously for approximately 24 hours prior to surgery using surface electrodes and at approximately 1, 2 and 3 months after surgery via telemetry in conscious dogs and monkeys. The ECG quality was compared to those obtained in dogs and monkeys using standard subcutaneous ECG electrodes placement (base-apex).

Objectives

The objective of this study is to develop a method to improve the quality of the ECG waveform by surgical placement of electrodes on the pericardium (pericardial leads) in conscious dogs and monkeys.

Results

- Implantation of pericardial electrodes significantly improved ECG signal to noise ratio with a more stable baseline, less movement artifacts, bigger R amplitude, and more stable T wave morphology.
- The R wave amplitude ranged from 7-10 mV and 2-10 mV (vs 0.7-7 mV and 0.8 -3.2 mV in subcutaneous lead) for dogs and monkeys, respectively.
- Approximately 93.6% of the recorded ECG data from the pericardial leads could be analyzed as compared to approximately 72.1% from the subcutaneous lead in dogs; while , approximately 94.8% of the recorded ECG data from the pericardial lead could be analyzed as compared to approximately 55.5% from the subcutaneous lead in monkeys.
- The placement of pericardial leads did not lead to an increased incidence of arrhythmias in conscious dogs or monkeys.

Figure 1: Pericardial vs Subcutaneous Comparison in NHP using 24-Hour ECG Waveforms

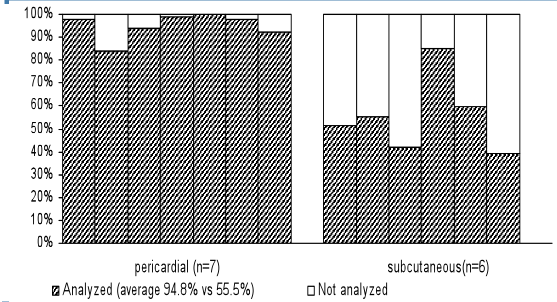

Figure 2: Pericardial vs Subcutaneous Comparison in Dog using 24-Hour ECG Waveforms

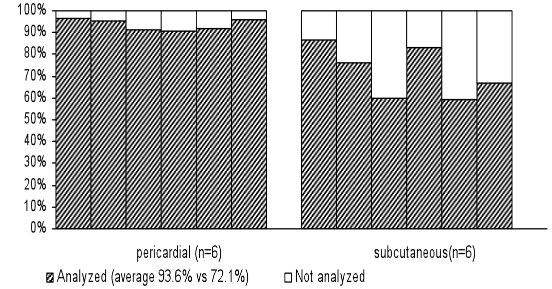

Figure 3: Representative ECG waveforms from Dog and NHP using Pericardial or Subcutaneous Electrodes Placement

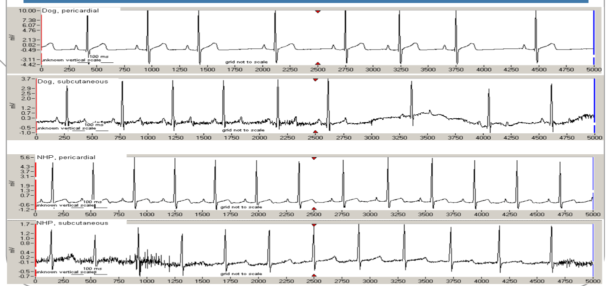

Table 1: Number of Arrhythmia Incidence in Animals Before and After Pericardial ECG Electrodes Placement (24-Hour Intervals)

Animal ID Species	Timepoint	Lead placement	VPC	JEC	APC	2°AVB
5183910 dog	pre-surgery	skin	NAD*	42	1	123
	post-surgery					
	1 month	pericardial	NAD	NAD	NAD	117
	2 months	pericardial	1	5	1	141
	3 months	pericardial	NAD	5	4	76
5199280 dog	pre-surgery	skin	1	181	NAD	989
	post-surgery					
	1 month	pericardial	NAD	2	NAD	422
	2 months	pericardial	NAD	18	NAD	422
	3 months	pericardial	NAD	321	2	1326
5207207 dog	pre-surgery	skin	NAD	69	6	NAD
	post-surgery					
	1 month	pericardial	NAD	5	1	NAD
	2 months	pericardial	4	60	7	NAD
	3 months	pericardial	NAD	45	12	NAD
124-432 Monkey	pre-surgery	skin	2	NAD	NAD	NAD
	post-surgery					
	1 month	pericardial	3	NAD	NAD	NAD
	2 months	pericardial	NAD	NAD	NAD	NAD
	3 months	pericardial	7	NAD	NAD	NAD
124-715 Monkey	pre-surgery	skin	1	NAD	NAD	NAD
	post-surgery					
	1 month	pericardial	1	NAD	NAD	NAD
	2 months	pericardial	2	NAD	NAD	NAD
	3 months	pericardial	1	3	NAD	NAD
124-878 Monkey	pre-surgery	skin	1	NAD	NAD	NAD
	post-surgery					
	1 month	pericardial	1	NAD	NAD	NAD
	2 months	pericardial	1	1	5	2
	3 months	pericardial	1	NAD	NAD	NAD

VPC: ventricular premature complex; JEC: junctional escape complex; APC: atrial premature complex; 2°AVB: second-degree atrioventricular block. *NAD: No arrhythmia detected. Dog 5207207 had a short non-sustained atrial tachycardia episode at 1 month post-surgery.

Conclusions

Surgical placement of ECG electrodes on the pericardium is considered to be a safe and optimal method for continuous ECG monitoring in conscious dogs and monkeys.

References

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