USE OF VASCULAR ACCESS BUTTONS (VABs) IN RODENT TELEMETRY SAFETY STUDIES.

Matt Skinner
Vivonics Preclinical Ltd, Biohub at Alderley Park, Cheshire, UK, SK10 4TG

Introduction: Various options exist when intravenous dosing is required in rodent cardiovascular safety studies. Restraint and placement of a temporary catheter in the tail vein may be the most straightforward method, but this is unsuitable for longer duration infusions and stress-induced cardiovascular changes may mask effects caused by the test item. Implantation of catheters requires surgery and has other welfare issues including use of harnesses and permanent single housing. We recently assessed vascular access buttons (VABs) (Instech Ltd) which offer some advantages over traditional techniques.

Methods: *Surgery:* Thirteen male rats were implanted with telemetry transducers (Datasciences Inc) for recording of ABP and ECG using standard methods and analgesic regimens. Following recovery, rats underwent a second separate surgery in which the left femoral vein was catheterised. The intravenous catheter was tunnelled to an incision on the animal's back and the catheter connected to the underside of a VAB. The skin was then sutured around the VAB. The animals were recovered and welfare checks made daily for 7 days post-surgery. Buprenorphine and metacam were administered at the time of VAB surgery and metacam was also administered for 2 days after.

Methods (cont): *Catheter patency:* The intravenous catheter was flushed, via the VAB, every day after implantation to maintain patency (0.1mL heparinised saline (100IU/mL)). The catheter was maintained for dosing and not blood sampling.

Housing: Animals were returned to group housing 1-2 days after implantation of the VAB. Animals were fit for use on an investigatory safety pharmacology study 5-9 days after implantation of the VAB. On study days, animals were moved to single housing for dosing and telemetry recording (see below) but were returned to group housing at the end of the recording periods (22-24h post start of dose).

Intravenous dosing: On each dosing day, the VAB was connected to an infusion pump via a magnetic VAB tether kit approximately 0.5h prior to the start of intravenous dosing. Only light, transient restraint was required to make the connection. No restraint was applied during intravenous dosing. Intravenous doses of 15 and 60min duration were administered during the study.

Results: *Surgery:* All thirteen animals recovered well from the catheter and VAB implantation. Daily checks were performed and the VAB wound site of some animals required cleaning periodically during the first few days post-surgery.

Catheter patency: No problems with catheter patency were encountered but the catheter moved to an extravascular position after 2 doses in one rat and this animal could not be used for further dosing.

Fig. 1

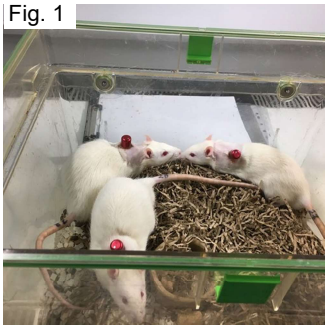

Fig. 1 Group housed rats with VABs on non-dosing day

Fig. 2

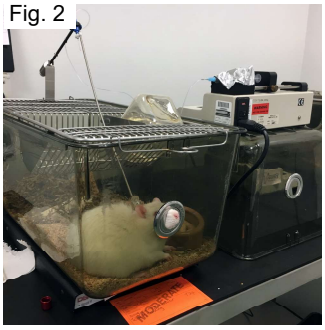

Fig. 2 Singly housed rat during infusion and telemetry recording

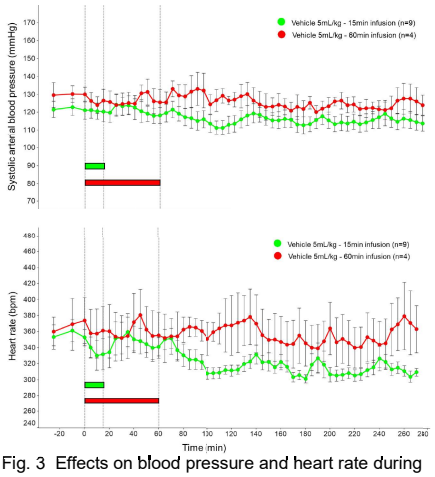

Fig. 3 Effects on blood pressure and heart rate during intravenous infusion of vehicle using VABs. Bars and lines indicate infusion times.

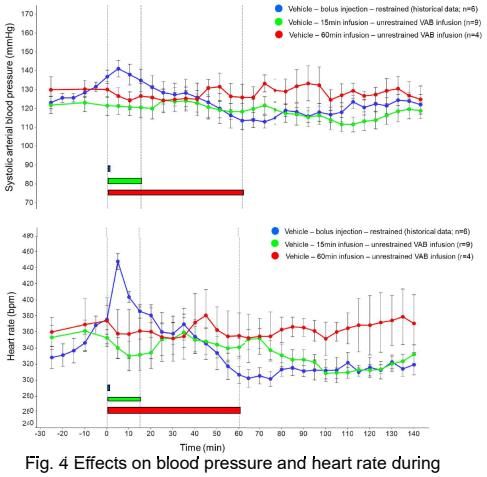

Fig. 4 Effects on blood pressure and heart rate during intravenous infusion of vehicle using VABs compared to restraint and tail vein method. Bars and lines indicate infusion times.

Intravenous dosing: Fifteen and sixty minute infusions were administered during the course of the safety pharmacology study. There were no notable changes in arterial blood pressure and heart rate before, during or after the infusion caused by the dosing technique (Fig. 3). This is in contrast to techniques involving restraint in which clear stress-induced increases in cardiovascular parameters are seen (Fig. 4).

Conclusion: VABs can be used in telemetered rats to allow intravenous infusion of test items without causing stress-induced cardiovascular responses. This technique will be useful in safety investigations when trying to detect acute effects of intravenously administered test items. Use of VABs is also a welfare refinement since it allows group housing of animals during recovery and non-dosing periods.