Highly Predictive Objective Measurement of OA Joint Pain in Rat Using Bioseb Automated Dynamic Weight Bearing System

Harun Rashid[1], Joe Cornicelli[2], Alan Young[3] and Rana Samadfam[1]

1. Charles River Montreal, Quebec, Canada, 2. Charles River Wilmington, Massachusetts, USA, 3. Charles River Harlow, ESSEX, UK

1 Introduction

Osteoarthritis (OA) is often associated with chronic debilitating joint pain. Similar pain has been reported in animal models of OA. However, most pain measuring techniques in animal are subjective in nature where reflex responses upon stimulation with nociceptive stimuli are measured. The purpose of the present study was to provide a highly reproducible objective joint pain measuring technique in the mono-iodoacetate (MIA)-induced OA model in rats.

2 Method

Rats are injected with a single intra-articular injection of MIA (3mg/25uL) into the right knee joint. Dynamic weight bearing (DWB) patterns by different limbs and tail are quantified using the BioSeb automated DWB system.

The system consists of an arena box with a pressure-sensitive sensor mat on the bottom and an attached high-resolution camera on the top. The rat can move freely inside the arena box. The system automatically calculates the weight borne by each limb and the tail. DWB data are calculated by normalizing as percent of total body weight borne by each limb and tail. Joint pain is indicated by reduction in weight bearing by the MIA-injected right hind limb.

A two-minute recording is done for each rat. Analysis of dynamic weight bearing data is done off-line using the BioSeb software.
Effects of drugs on MIA-induced joint pain were evaluated at different time points post MIA injection.

3 DWB Time-course in MIA Rat

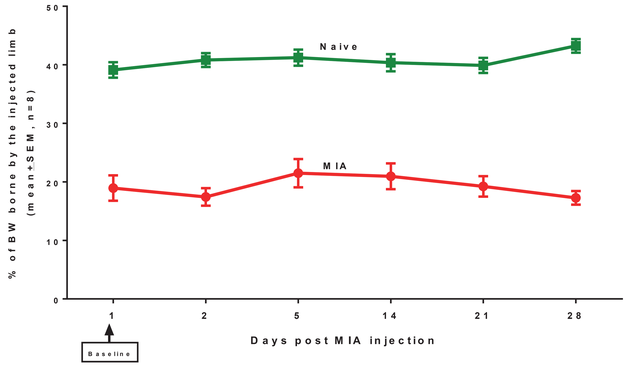

Figure 1: MIA caused significant dynamic weight bearing deficits in the injected limb compared with that in the control naive rats from Day 1 to Day 28 post injection. Once daily oral gavage from Day 2-28 with 0.3 mg/kg of Dexamethasone (Dexa) reversed the weight bearing deficits in MIA rats.

4 Effects of Analgesics

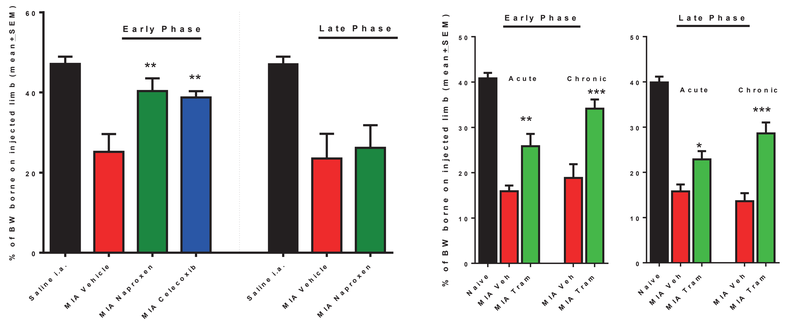

Figure 2: Naproxen (30 mg/kg, PO) and Celecoxib (40 mg/kg, PO) were effective only in the early phase of the MIA model following 3 days of BID dosing, suggesting NSAID-insensitivity of the late phase. Tramadol (60 mg/kg) significantly reversed the weight bearing deficits in both early and late phase of the rat MIA model following 3 days of BID dosing.

5 Model Reproducibility

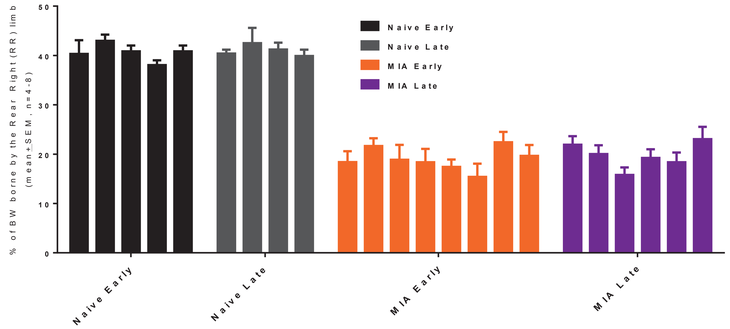

Figure 5: Control %RR weight bearing data for Naïve (or saline-injected), MIA Early (Day 1-5) and MIA Late (Day 18-24) Phase. Overall, similar level of weight bearing deficit was observed in early and late phase.

6 Conclusion

- Reliable and reproducible objective measurement of OA joint pain could be done in rat MIA model using the BioSeb DWB system.
- The window of weight bearing deficit in MIA rats is well enough to assess effects of analgesics at any time point from week1 to week4.
- Early phase of the model is more sensitive to NSAIDs compared with the late phase while analgesics such as tramadol and morphine works both in early and late phase.
- Finally, repeat dosing is often required for optimal efficacy in the rat MIA model using the DWB endpoint.