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Pressure algometry and thermal sensitivity for assessing pain sensitivity and effects of flunixin meglumine and sodium salicylate in a transient lameness model in sows

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ABSTRACT

Sow lameness can result in decreased animal health and productivity, and is a significant animal welfare concern. Swine producers and veterinarians lack objective assessment tools to detect lameness. Objectives of this study were to evaluate pressure algometry (PA) and thermal sensitivity (TS) as objective assessment tools for changes in pain sensitivity associated with lameness and to assess analgesic drugs for mitigating lameness pain. Twelve mixed parity crossbred sows were anesthetized and injected with Amphotericin B in the distal interdigital space of both claws of one hind leg to induce transient lameness. Sows were randomly assigned to one of three analgesic treatment groups: (1) Sodium Salicylate (SS; 35 mg/kg per os q.12 h+0.04 ml/kg IM q.24 h sterile saline), (2) Flunixin meglumine (FM; 2.2 mg/kg IM q.24 h), or (3) Control (C; 0.04 ml/kg IM q.24 h sterile saline). All sows received each treatment over three trials with two-wk wash-out periods between trials. Forty-eight h post-induction, analgesic treatments were administered daily for four consecutive d. Pain sensitivity was assessed with PA and TS on each hind leg on d−1, d+1 and d+6 relative to induction (d0). Proc Glimmix of SAS 9.2 was used to analyze the difference between sound (S) and lame (L) legs on each trial day, with a simple effect comparison used to analyze effect of analgesia treatment on d+6. As predicted, S and L legs did not differ on d−1 (P=0.56) and less pressure was tolerated on L legs on d+1 ($P<0.001$) (Raw Means in kilograms of force: d−1 L 7.2±0.2; d−1 S 7.4±0.2; d+1 L 2.1±0.2; d+1 S 7.7±0.2 kgf). A simple effect comparison of d+6 revealed no differences between FM and C (p=0.90), FM and SS (p=0.17), or SS and C (p=0.07). The TS latency of S versus L legs differed on all trial days (d−1 p=0.02, d+1 $p<0.0001$, d+6 $p<0.01$) over all trials. (TS Raw means (s): d−1 L 7.3±0.6; d−1 S 9.1±0.6; d+1 L 3.3±0.2; d+1 S 6.8±0.6; d+6 L 6.0±0.6; d+6 S 8.4±0.7 s), including lame and sound days. In conclusion, these results support PA as an objective non-invasive method for

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measuring pain sensitivity in sows induced with transient lameness. Sodium salicylate or flunixin meglumine did not reduced pain sensitivity as measured by PA from d+1 to d+6 in this model of induced transient lameness.

1. Introduction

Sow lameness negatively impacts animal welfare, decreases productivity and is a major reason for culling. (Stalder et al., 2004; Anil et al., 2008). In a survey of US swine producers, lameness was the second most common reason for culling sows, accounting for 9–15% (Anil et al., 2005). However, lameness estimates based on primary reasons for culling may be too conservative. Knauer et al. (2007) found that 23% of on-farm diagnoses leading to culling were inaccurately reported, and lameness was identified as a significant risk factor for sows that died or were euthanized on farm (Jensen et al., 2010). Furthermore, lameness presents significant animal welfare concerns due to chronic pain and impaired mobility.

For effective diagnosis and treatment, swine producers and veterinarians need non-invasive and reliable tools to detect sow lameness. Gait or locomotion scoring has traditionally been used for assessing degrees of lameness, and implemented into farm assurance assessment protocols (Main et al., 2000). Changes in gait score have also been used for assessing the effectiveness of pain mitigating interventions (Mustonen et al., 2011). D'Eath (2012) found subjective gait scoring of sows was associated with good to fair inter-observer agreement overall, but was poorest for mild gait abnormalities. In particular, swagger of the rear end while walking was pronounced in older sows that appeared otherwise normal, presenting an ambiguous association between gait score and lameness at higher parities. Furthermore, farmers were found to underestimate lameness when compared to other assessors, but agreement improved when a assessors were asked to discriminate between fewer categories (lame versus sound, rather than a five-point scale). Hence, there is a need for more robust and objective tools for assessing lameness in sows.

Since lameness is associated with changes in pain sensitivity, including allodynia and hyperalgesia, pressure algometry (PA) is one candidate as an objective tool to quantify sow responses. Mechanical nociceptive threshold (MNT) repesents the amount of pressure that is tolerated prior to a withdrawal response, indirectly signaling discomfort. Devices to quantify changes in MNT have been developed and applied to different species of animals, including livestock (cattle: Whay et al., 1998; Dyer et al., 2007; Heinrich et al., 2010; sheep: Ley et al., 1989; Stubsjøen et al., 2009; swine: Sandercock et al., 2009; Fosse et al., 2010; Di Giminiani et al., 2012). Devices used to quantify MNT values have typically been practical only in laboratory conditions, but inexpensive hand held pressure algometry devices are marketed for human patients. Although vulnerable to variable rates of application by handlers versus automated, laboratory-based devices, Janczak et al. (2012) concluded hand held PA produced reliable and stable results when applied to healthy (presumably non-painful) piglets that were restrained in a sling. Effectiveness of PA for identifying lameness in sows has not been explored.

Changes in pain sensitivity can also be determined by tolerance of animals to thermal (versus mechanical) stimuli. The thermal sensitivity (TS) test quantifies latency for a withdrawal response to precise, focused radiant heat, and is most commonly applied to laboratory rodents in the plantar test (Hargreaves et al., 1988; Chen et al., 1999). Researchers modified the concept for application to livestock (cattle: Pinheiro Machado et al., 1997; Veissier et al., 2000; Herskin et al., 2003; Tapper et al., 2011; sheep: Nolan et al., 1987; swine: Jarvis et al., 1997; Herskin et al., 2009). However, effectiveness of TS for identifying lameness in sows has not been explored.

Due to the variable nature of hyperalgesia and allodynia associated with chronic pain, validation of tools for sow lameness requires assessment in known painful and non-painful states (Weary et al., 2006; Vinuela-Fernandez et al., 2007; Millman, 2013). Hence, use of lameness induction models is a more robust approach and requires fewer experimental subjects than use of sows presenting with naturally occurring clinical lameness. Amphotericin B-induced lameness models produce a predictable, reproducible and moderate-severity synovitis that is transient in duration. Injecting Amphotericin B into the synovial joint has been shown to produce a temporary acute localized synovitis by inducing the synovial cells to produce and secrete cytokines, which triggers a local inflammatory response within the joint. Amphotericin B can induce acute lameness in cattle (Kotschwar et al., 2009) and horses (Hulten et al., 2002; Marttinen et al., 2006; Bussieres et al., 2008). Karriker et al. (2013) showed that Amphotericin B injected into the distal interdigital space of the claw induced a transient lameness in sows, with the most severe changes in gait score occurring 24 h post injection and return to normal gait score occurring 7 d post injection.

The use of non-steroidal anti-inflammatory drugs may provide analgesic effects against the localized synovitis induced by Amphotericin B. Currently, no FDA-approved analgesics are approved for swine. Schulz et al. (2011) found that flunixin meglumine (FM) was effective in providing analgesia for steers with Amphotericin B-induced transient lameness. Welsh and Nolan (1995) found repeated administration of FM over three days reduced nociceptive thresholds in sheep with foot-rot to within the same range as in matched healthy sheep. Hence, FM may be beneficial for mitigating lameness pain in sows. Sodium salicylate (SS) is widely available for producers and inexpensive, but has not been explored as an analgesic for mitigating lameness pain. Coetzee et al. (2007) showed that SS attenuated the cortisol response associated with castration pain in calves.

The objectives of this study were to evaluate PA and TS for quantifying changes in pain sensitivity associated with