Journal of Equine Veterinary Science 35 (2015) 105–110

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

Clinical Evaluation of Intra-articular Administration of Stanozolol to Manage Lameness Associated With Acute and Chronic Osteoarthritis in Horses

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ARTICLE INFO

Article history:
Received 22 October 2014
Received in revised form 1 December 2014
Accepted 3 December 2014
Available online 9 December 2014

Keywords:
Stanozolol
Lameness
Horse
Joint
Osteoarthritis

ABSTRACT

Poor data could be found in the literature on the effects of intra-articular (IA) administration of stanozolol in horses affected by osteoarthritis (OA). To verify the clinical effects of IA stanozolol in acute and chronic cases of OA in horses, a clinical double-blinded trial involving 60 client-owned horses was performed. Veterinary practitioners selected horses, all showing clinical signs of acute or chronic OA, diagnosed in a single joint. After lameness evaluation and synovial fluid collection, the clinicians administered one to four (acute cases) or one to six (chronic cases) weekly IA doses of 5 mg of stanozolol or placebo. Positive result was considered a grade 1 improvement in lameness scored according to the American Association of Equine Practitioner scale. The characteristics of the synovial fluid were also evaluated. Of the 60 horses included in the study, 31 were affected by acute OA and 29 by chronic OA. Horses were treated blindly with placebo. The overall outcomes were positive in 82.50% of cases. Lameness disappeared completely in 15 of 21 (acute) and 11 of 19 (chronic) animals, and there was a significant reduction after two and four treatments, in the acute and chronic cases, respectively. Improvement in the physical characteristics of the synovial fluid sampled was evident after the third treatment. Stanozolol injected IA at a dose of 5 mg significantly resolved lameness in affected joints. Stanozolol could be considered a safe option for the treatment of horses suffering from OA.

1. Introduction

Osteoarthritis (OA) is one of the most prevalent and debilitating diseases affecting horses, with a notable economic impact on the equine industry [1–3]. Numerous treatment methods (physical, biological, and pharmaceutical) have been advocated either to prevent OA or to minimize clinical signs of pain (lameness), reduce joint deterioration, and prolong the competitive career of athletes. Acute or chronic synovitis and capsulitis are commonly treated with intra-articular (IA) medications [4]. An increased number of IA medications and treatment options are available on the market today, with therapies focused on providing symptom-modifying and/or disease-modifying effects [5,6], to decrease inflammation in the damaged joint by acting on both synoviocytes and chondrocytes [7,8].

Stanozolol is a synthetic derivative of testosterone. Its properties include anabolic and/or androgenic activity [9], probably associated with its affinity for androgenic and, at lower doses, glucocorticoid receptors [10]. It has been demonstrated that stanozolol induces in vitro upregulation of osteoblast proliferation, collagen synthesis through transforming growth factor-b1 activity [11], chondrocyte secretion of insulin-like growth factor-1 [12], and, in rats,

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http://dx.doi.org/10.1016/j.jevs.2014.12.003

growth plate chondrocyte proliferation [13]. Moreover, it reduces NO production [12]. By increasing the production of collagen and other fundamental elements of the cartilage matrix, stanozolol stimulates the cartilaginous tissue [14], as indicated by the latest histological studies and clinical reports.

Stanozolol has been used to treat sheep with OA induced by bilateral surgical medial meniscectomy [15]. In that study, a protective effect of IA stanozolol was observed in animals treated with 1 mg of the drug after 3 and 9 months compared with animals not been treated at all or animals administered placebo.

Published reports on the clinical IA use of stanozolol in horses for the treatment of articular diseases, to our knowledge, are limited to a recent citation concerning the benefits of its use for the treatment of subchondral bone pain [16] and a report on 60 clinical cases of articular diseases [17].

A product containing stanozolol has been recently licensed in Italy for IA use in horses. The dosage of the drug was established with a previous pharmacokinetic study (N. Romagnoli, personal communication, 2013). Anecdotal reports refer to positive results obtained in clinical practice in Italy and in the UK especially in some difficult cases.

This report aims to assess the ability of stanozolol to produce clinical and/or disease-modifying effects in horses affected by acute or chronic OA when administered IA and to monitor for any adverse effects. This trial design is a field multicenter double-blinded study. Our hypothesis was that American Association of Equine Practitioner (AAEP) scale lameness scores would improve by at least one degree after adequate treatment.

2. Materials and Methods

The care and handling of the animals were in accordance with the provisions of the European Economic Community Council Directive 86/609, adopted by the Italian Government (D.L. 27/01/1992 n° 116).

2.1. Animals

Client-owned horses were selected for the inclusion in a multicenter study by equine veterinarian practitioners across Italy. The practitioners involved contacted the owners and requested the participation of their horses in the trial.

Horse owners signed an informed consent for the inclusion in the study and committed to strictly following the rules of the experimental design; they were asked to agree that the designated individual would be administered the treatment blindly as prescribed.

Horses were selected and enrolled in this study on the basis of the following inclusion criteria. (1) Horses must not be destined to the food chain; they must be in activity and aged between 2 and 20 years, with no distinction in sex or breed and weighing 250–650 kg. (2) Horses were required to be lame and show signs of joint pain attributed to aseptic acute or chronic OA in one joint only. (3) Horses had to be healthy other than the lameness from OA in one joint; no gross anatomic abnormalities must be detected on the affected limb.

Horses were excluded from the study on the basis of several criteria. (1) Horses with lameness caused by joint disease in more than one joint. (2) Horses subjected to local or systemic administration of Nonsteroidal anti-inflammatory drugs, glycosaminoglycans, hyaluronic acid, corticosteroids, or other antiarthritic drugs in the 15 days preceding the study. (3) Horses that had received anabolic drugs in the 30 days before the inclusion visit. (4) Lactating or pregnant mares, stallions during the reproductive period, horses with systemic diseases or infectious septic arthritis, specifically those with signs of hepatic or renal pathologies or tumors.

Postinclusion removal from the study cohort could be decided (1) for any horse that failed to conform to the inclusion criteria during the study period, specifically if the correct prescription and treatment duration were not respected; (2) occurrence of serious adverse effects caused by the drug; and (3) if the owner withdrew the horse from the study without any motivation necessary.

Because of economic constraints, only 60 horses were enrolled in the study.

2.2. Tested Product

Each phial contains 5 mg of micronized stanozolol, 1.50 mg of polysorbate, 3.70 mg of sodium chloride (NaCl—salt), 10 mg of NaH_2PO_4, and phosphoric acid in 1 mL of water to pH 6.6.

The placebo phials contain the same preparation without the tested drug (1.50 mg of polysorbate, 3.70 mg of NaCl, 10 mg of NaH_2PO_4, phosphoric acid in 1 mL of water to pH 6.6).

2.3. Double-Blinded Procedure

Stanozolol and placebo were formulated and packed with an identical physical appearance and distributed in identical code-labeled containers. A coin toss randomly assigned the horses to treatment, either with stanozolol or placebo. Blinding of both the veterinary investigators and the horse owners was maintained throughout the study. The coding information was confidentially stored until the conclusion of the trial.

2.4. Participating Veterinarians

Selected veterinarians who agreed to participate in the study signed a bilateral endorsement letter in which, as investigators, they declared to follow the scheduled protocol of the random double-blinded study. The veterinarians must compile the required forms and log books as described in the protocol. They were provided with a package with phials containing stanozolol or placebo.

2.5. Procedures

Every owner agreed with the conditions and signed the informed consent. The horses were clinically evaluated by