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Full Length Article

Iodoacetate and allogenous cartilage particles as models for arthritis induction in equine

Ahmed Elmesiry [a,*], **Magdi Seleim** [b], **David Cullis-Hill** [c]

[a] *Animal Reproduction Research Institute, Agriculture Research Center, 12556 Haram, Giza, Egypt*
[b] *Department of Surgery, Anesthesiology and Radiology, Faculty of Veterinary Medicine, Kafrelsheikh University, 33156 Kafrelsheikh, Egypt*
[c] *Biopharm Pharmaceuticals, 111 Bronte Rd, Bondi Junction, Sydney, 2022 NSW, Australia*

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Abstract Experimental models of osteoarthritis (OA) have been widely developed in different animal species, because of the high incidence of osteoarthritis diseases in humans and animals. To date, no ideal OA animal model has been reported. The present study compare different osteoarthritis models to determine which one is suitable for inducing experimental equine OA. Fifteen donkeys were divided into three equal groups ($n = 5$). The radio carpal joints of the right forelimb of 15 donkeys were injected with 25 mg monoiodoacetate (MIA) (group A), 50 mg allogenous cartilage particles (ACP) (group B), or vehicle solution (group C) over a period of 70 days. Osteoarthritis induction was evaluated weekly through lameness score, carpal circumference, joint flexion angel, synovial fluid analysis (total protein and WBC count), and radiology. Animal were euthanized and joints histopathology were performed at 70 days. Lameness score and joint circumference was increased in both group A and B however joint flexion angel was decreased compared to group C ($p < 0.05$). Osteophytes were observed in MIA injected joints only accompanied with subchondral bone sclerosis. Cartilage damage was observed grossly and histologically in Group A together with synovial membrane fibrosis. Group B had on cartilage damage grossly however histological examination revealed some cartilage surface discontinuity with synovial membrane edema. Injection of monoiodoacetate in the donkey is a successful model to create the acute clinical signs of joint disease as well as cartilage damage. However, allogenous cartilage particles injection need more investigation to be applied.

1. Introduction

In the equine industry, lameness due to joint disease is the most common cause of decreasing the performance in sport horses. Several epidemiologic studies have found that lameness due to joint disease is the most significant factor responsible for inability to race and loss of performance [1,2]. Therefore,

* Corresponding author. Tel.: +20 1062099431.
E-mail address: elmesiry@outlook.com (A. Elmesiry).
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it is important to understand the pathogenesis and medications available to the equine practitioner.

Equine osteoarthritis (OA) may be considered as a group of disorders characterized by a common end stage: progressive degeneration of the articular cartilage together with additional changes in the bone and soft tissues of the joint. This degeneration of the articular cartilage is characterized by local splitting and fragmentation (fibrillation) of articular cartilage. Synovitis and joint effusion are often associated with the disease, and, clinically, the disease is characterized by pain and dysfunction of the affected joint [3].

Animal models are standard research tools for studying the pathogenesis, diagnosis and potential therapeutic intervention of many different diseases. They provide us with information to develop new drugs and moving it toward clinical use. The different types of arthritis models have been previously reviewed [4–7].

Common features of most experimentally-induced osteoarthritis models include the ability to define the type of joint disease, the severity of injury in addition to the time of onset and progression and to relate these events to markers of disease activity [4].

Arthritis-like changes have been induced in the horse by Filipin [8], Amphotericin [9,10], turpentine oil [11], polyvinyl alcohol foam [12], carrageenan [13], complete Freund's adjuvant [14]. Lipopolysaccharide [15], botulinum toxin [16], forced exercise [17], osteochondral fragment-exercise mode [18].

The monoiodoacetate (MIA) arthritis model has been used in rats [19], chickens [20], guinea pigs [21], rabbits [22] and horses [23–25] for assessment of the pathophysiologic process as well as evaluation of the efficacy of therapeutic substances in a controlled environment.

Using cartilage particles to induce osteoarthritis was previously described in dog [26] and rabbit [27]. A combination of intra-articular injection of cartilage particles, arthroscopic partial thickness cartilage defect and exercise were used to create a model of degenerative joint disease in the horse [28]. The fate and effects of surgically implanted osteochondral fragments on the middle carpal joint of horses subjected to exercise were investigated [29].

The donkey is properly the closet animal to the horse, making this species an alternative animal model for studying equine diseases. Few papers reported using of donkey as a model of equine OA [10,11].

In the present study, injections of allogenous cartilage particles (ACP) or monoiodoacetate (MIA) were used to create a model of degenerative joint disease in the donkey. The clinical examination, radiographic, macroscopic appearance, and light microscopy were used to assess the effect of these treatments on healthy cartilage compared to the vehicle control.

2. Material and methods

2.1. Donkeys

The experiment was approved by the Committee on Animal Experimentation at the Kafrelsheikh University, Egypt.

The present study was performed using 15 healthy Egyptian local breed male donkeys weighting from 150 to 200 kg. Animals were housed in indoor stalls and fed on a balanced ration of mixed grain with hay and unlimited water. All donkeys were dewormed with ivermectin (200 mcg/kg; Eqvalan 1.87% Merial Limited. USA).

Prior to inclusion in the study, lameness examination, body condition, radiographs of carpal joints, range of motion of carpal joints (angle of flexion) and evidence of joint effusion were assessed to ensure that all previous variables were within normal limits (baseline measurement).

Donkeys were allowed to acclimatize for 2 weeks prior to the study. During the acclimatization period, the donkeys trained daily to familiarize them to the experimental conditions (investigators, environment, handling, vein puncture and various outcome measures).

2.2. Allogenous cartilage particle solution preparation (ACP)

One local breed donkey weight 150 kg was euthanized, and the articular cartilage was removed from the shoulder, carpal, fetlock, pastern, hock and stifle joints in a biosafety cabinet under aseptic conditions. The pooled cartilage was powdered under liquid nitrogen in a mortar, producing particles as small as 20 mm in diameter (able to pass easy through a 14-gauge needle). These particles were resuspended at a concentration of 50 mg/ml in a physiological saline solution contained amikacin sulfate (50 mg/ml; Amikin 500 mg vial, Bristol Meyer Squiip, Egypt).

2.3. Monoiodoacetate solution preparation (MIA)

MIA (Sodium monoiodoacetate 25 g, ICN, Biomedicals GmBH Thuriger star be 15.Germany) were dissolved at a concentration of 25 mg/ml in a physiological saline solution contained amikacin sulfate (25 mg/ml).

2.4. Study design

The 15 remaining donkeys were divided in to three groups of five. Animals sedated with Xylazine Hcl (1 mg/kg; Rumpon 10%, Bayer animal health. Canada). The skin was aseptically prepared for arthrocentesis of each right radiocarpal joint to obtain synovial sample for baseline analysis. Group A received 25 mg (1 ml solution) of MIA, Group B received 50 mg (1 mL) of ACP and Group C was received the suspended solution (1 mL) without adding cartilage or MIA (Vehicle – Control group) intra-articularly into the right radiocarpal joint using a 14 G needle. These injections were repeated at 7, 14, 21, 28, 35, 42 and 56 days for group B and C however Group A was received a single MIA injection (Fig. 1).

2.5. Outcome measures

2.5.1. Clinical examination

Clinical examinations of right forelimbs were performed weekly from day 0 (baseline) throughout the study period.

2.5.2. Lameness score

Donkeys evaluated for lameness score on a scale 0–5 according to American Association of Equine Practitioners (AAEP) grading system (0: Lameness not perceptible with flexion test, 1: lameness is difficult to observe and is not consistently