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Mini Review

Research Progress on Animal Model of Joint Contracture

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Abstract

Joint contracture is currently one of the very common clinical diseases. The resulting burden of joint contracture is enormous. Now, there are many experimental studies involving joint contracture. Establishing an ideal animal model is of great importance to the further study of joint contracture.

The aim of this review is to summarise the research progress on animal model of joint contracture.

Keywords: Joint contracture; Animal model; Research progress

Introduction

Joint contracture, which is defined as a decrease in both active and passive ranges of motion [1,2], is currently one of the very common clinical diseases. Joint contracture may cause functional disturbances in patients' activities of daily living, decrease movement ability, and impair the joint function, with high incidence [3]. Once joint contracture is established, it is extremely difficult to regain a full range of motion with vigorous and extensive rehabilitation therapy, or even with surgical treatment [4,5]. A variety of reasons can cause joint contracture, of which joint immobilization is the most common one. Joint immobilization is a usefully therapeutic method for a patient who suffered from fracture. It can prevent the displacement of bone and then promote the healing of fracture. What's more, joint immobilization is beneficial to decrease pain and possibly joint damage in the acute phase in inflammatory arthritis [6]. However, many patients finally develop joint contracture due to long-term immobilization. Besides, trauma is one of the important reasons of joint contracture. Intra-articular hematoma fibrosis and adhesions caused by trauma are both factors which can induce and aggravate joint contracture. In addition to joint immobilization and trauma, joint contracture is also a common complication of neurologic conditions including stroke, spinal cord injury, traumatic brain injury, and cerebral palsy [7,8]. Clinically, in view of the severity of contracture, management of an established contracture includes physical therapy and surgical procedures [9]. Nowadays, there are many experimental studies concerning joint contracture. It is important to establish a proper animal model of joint contracture. An ideal animal model can not only be of great importance to the study of the pathogenesis of joint contracture, but also provide a good experimental carrier for the exploration of various therapy methods. At present, animal model of joint contracture can be divided into traumatic animal model and non-traumatic animal model.

Animal Model of Joint Contracture

Traumatic animal model

A model applying plastic plate and metal screw: Hagiwara Y et al. [2] used adult male Sprague-Dawley rats in the experiment investigating the tissue elasticity and the structural characteristics of the anterior and posterior synovial membrane in a rat immobilized knee model. A rigid plastic plate implanted subcutaneously joined the proximal femur and the distal tibia away from the knee joint and was solidly held in place with one metal screw at each end. The knee joint capsule and the joint itself were untouched. Intra-articular structure is not damaged in this model, and hematoma is not formed. Thus we need not consider intra-articular hematoma fibrosis and adhesions when analyzing experimental results. What is more, the immobilization is stable enough for long time immobilization. The drawback of this model may be that infection is likely to be caused. This is a classical traumatic animal model widely used by many researchers. Chimoto E et al. [10] and Onada Y et al. [11] also used adult male Sprague-Dawley rats and similar animal model in their studies concerning the effect of capsule on limiting the range of motion after immobilization and the effect of intra-articular haemorrhage on the joint capsule of immobilized knees, respectively.

A model with cortical windows removed and a Kirschner wire drilling: Monument MJ et al. [12] used skeletally mature New Zealand white rabbits in the experiment investigating whether treatment with a mast cell stabilizer after joint injury would lessen the molecular manifestations of joint capsule fibrosis. A single lateral thigh incision was used to expose the femur and the mobile skin was retracted distally to expose the medial and lateral aspects of the distal femur. Medial and lateral parapatellar arthrotomies were made, taking care to avoid the collateral ligaments. Using an osteotome, 5-mm 2 cortical windows were removed from the non-articular portion of the medial and lateral femoral condyles. The knee was then immobilized at 150° of flexion using a 1.6-mm diameter Kirschner wire, which was drilled through the tibia, passed subcutaneously behind the knee and bent around the femur. Their results indicated that joint capsule fibrosis were significantly elevated in the operated contracture group compared to the non-operated control group, and joint capsule fibrosis in ketotifen-treated groups were significantly reduced compared to the operated contracture group. Through the removal of bone cortex, traumatic intra-capsular hemarthrosis is formed in the model. This model involves both joint immobilization and trauma and is also frequently used by researchers. Hildebrand KA et al. [13,14] also employed skeletally mature New Zealand white rabbits and similar animal model in their studies in order to describe the natural history of motion loss with time and myofibroblast numbers in a rabbit knee model of post-traumatic joint contracture and to evaluate changes in matrix molecules of the joint capsule in a

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Table 1: The advantages and disadvantages of various animal models of joint contracture.

	Animal model of joint contracture					
	Traumatic animal model			Non-traumatic animal model		
	A model applying plastic plate and metal screw	A model with cortical windows removed and a Kirschner wire drilling	A model applying Kirschner wire and resin	A model applying plaster cast	A model applying wooden splint	A model applying steel mesh and T-shirt
Advantages	Stable enough for long time immobilization.	Stable enough for long time immobilization.	Easy to control the flexion angle.	Simple and clinically coincident.	The immobilization method is easy to carry out.	Light material and low cost; would not limit or interfere negatively with animal development.
Disadvantages	Infection is likely to be caused.	Intraarticular structure is easy to be damaged; infection is likely to be caused.	Difficult to maintain.	Difficult to control the degree of the tightness; difficulty in the animal's locomotion.	Instable and difficult to maintain for a long time.	Not be stable enough for long time immobilization.

rabbit model of chronic joint contracture.

A model applying Kirschner wire and resin: Hayashi M et al. [15] used adult Japanese white rabbits in the experiment for the sake of exploring an effective method for contracture prevention. For external fixation, two 1.5-mm-diameter Kirschner wires were inserted into the greater trochanter of the femur, and another was inserted into the distal part of the tibia. These three wires were then connected to each other by a 1.8-mm-diameter Kirschner wire using dental resin, fixing them externally so as to hold the knee at 45º of flexion. Nagai M et al. [16] took similar method to fix knee flexion of approximately 140º ± 5º in male Wistar rats to study the contributions of biarticular myogenic components to the limitation of the range of motion after immobilization of rat knee joint. Intra-articular structure is not damaged in this model, and flexion angle is easily controlled. But the deficiency is that the model is difficult to maintain.

Non-traumatic animal model

A model applying plaster cast: Okita M et al. [17] and Nakano J et al. [18] used the same animal model in their experiments. Okita M et al. adopted the model to study the effects of reduced joint mobility on sarcomere length, collagen fibril arrangement in the endomysium, and hyaluronan in rat soleus muscle. Nakano J et al. used the model to evaluate the contributions of biarticular myogenic components to the limitation of the range of motion after immobilization of rat knee joint. They employed male Wistar rats and had the rats' bilateral ankle joints fixed in full planter flexion by plaster casts, the soleus muscles being immobilized in shortened position. Kojima S et al. [19] used male Wistar rats in their experiment to clarify temporal effects on restrictions to range of motion and the histopathological changes of joint components after joint immobilization in a rat knee-contracture model. Plaster casts were extended from the pelvic girdle to the ankle joint, with the hip joint at maximal extension, the knee joint at maximal flexion, and the ankle joint at maximal plantar flexion. The cast area was exposed from the distal ankle to the foot to confirm the absence of swelling and congestion. Plaster immobilization is a simple and clinically coincident technique. Nevertheless, this resource involves a series of complicating factors at the same time. First of all, it is difficult to control the degree of the tightness. If we fix the plaster too tightly, edema in the distal extremity of the immobilized segment, osteofascial compartment syndrome may be caused; On the contrary, if we fix the plaster too loosely, it is not easy to maintain the model. What's more, difficulty in the animal's locomotion resulted from the heavy weight of the cast must be taken into consideration.

A model applying wooden splint: Okazaki R et al. [20] used male Japanese white rabbits in their experiment to study the sequential changes in transforming growth factor TGF-β1 concentration in synovial fluid and mRNA expression of TGF-β1 receptors in chondrocytes after immobilization of rabbit knees. The right lower extremity from the proximal thigh to the distal end of the limb was tied with fiberglass casting tape to a straight wooden splint. The right knee joint of the rabbits was securely immobilized in full extension. This immobilization method is easy to carry out. And yet, the device may be instable and difficult to maintain for a long time.

A model applying steel mesh and T-shirt: Benedini-Elias PC et al. [21] used female Wistar rats in their experiment to determine the morphology of shortened soleus and plantaris muscles. They used a special immobilization device with light material. The device is divided into two parts: the lower part and the upper part. The lower part, divided into anterior and posterior sections, is made of stainless steel mesh covered with adhesive tape. The lower part is joined with staples to the upper part, which is similar to a T-shirt made of viscolycra fabric. To maintain the quality and position of the device, a tape was fixed around the animal's abdomen between the shirt and the stainless steel mesh. In addition, two 0.5-cm strips were placed on the upper parts of both shoulders acting like suspenders. The merits of this device lie in the light material and low cost, but it may not be stable enough for long time immobilization.

Summary

So far, many researchers have simulated joint contracture from multiple perspectives with animal model, providing various reference models for the study of joint contracture. Each animal model has its advantages and disadvantages (Table1). We now require an ideal animal model which has high similarity to human joint contracture. To sum up, ideal animal model should have following conditions: (1) The anatomical and physiological characteristics of selected animals must be similar with that of humans, so the animals can reproduce the objective laws of joint contracture. (2) The animal model should have high repeatability and be easy to control. (3) The management of the model should have less interference factors, shorter cycles and lower cost. (4) The model must provide a reference for the clinical treatment of joint contracture. An ideal animal model can provide a convenience for the further study of joint contracture, shortening the study period.

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