Rabbit is suitable for establishing an animal model of rhino-sinusitis

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Abstract

BACKGROUND: Using experimental animals to simulate diseases of human being is the basis of studying etiology and treatment of the diseases, so the diseases of nasal cavity and sinus need suitable experimental animals as models.

OBJECTIVE: To observe the regional anatomy of rhino-sinus in rabbits and its performance through CT imaging, and to discuss the feasibility of applying a rabbit model to the study of animal rhino-sinusitis.

METHODS: Routine coronal and axial scanning images of rhino-sinus of New Zealand rabbits were performed through Discovery CT750 HD. The rhino-sinus anatomy was then observed.

RESULTS AND CONCLUSION: The nasal septum is located on both sides of the nasal cavity. The lateral wall of rabbit nasal is composed of maxillary turbinate, middle turbinate, the inside of the middle turbinate and inferior turbinate. The maxillary sinus cavity is the largest one and ethmoid sinus, sphenoid sinus and frontal sinus are relatively much smaller. All these sinuses are paired and symmetrical. The rhino-sinus in rabbit is displayed clearly in CT scan. The anatomical location of rabbit is similar to that of human; however, the maxillary sinus of rabbit is greater than that of human correspondingly, which is suitable for operating and applying to surgical anatomy and imaging analysis. The rabbit model of rhino-sinus can be applied to simulate human rhino-sinusitis.

Subject headings: sinusitis; paranasal sinuses; nasal cavity; models, animal

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INTRODUCTION

The pathogenesis of chronic sinusitis, a common and frequently occurring disease of otolaryngology, remains uncertain. Numerous doctors have performed multilevel studies of the occurrence, development, and various treatment interventions of rhino-sinusitis. However, these studies are limited by many factors. Since the last century, many scholars have been devoted to the research of rhino-sinusitis in animal models. The researches have become a hotspot research all over the world. Many scholars have successfully established the animal model of rhino-sinus. The anatomical location of rabbit is similar to that of human, and the maxillary sinus is the largest and most important sinus in rabbit, which is suitable for operation. Rabbit is feasible to be used as animal model to research rhino-sinusitis. The rabbit model of rhino-sinusitis is accepted by most scholars. However, the rhino-sinus in rabbit has not yet to be observed in CT and anatomical images.

An advanced GE gemstone CT, which can offer high-definition images of the rhino-sinus in rabbit with a low scanning dose, is used in this study. This tool operates under a new gem spectroscopy and volumetric spiral dynamic 500-row technology. Analysis of the CT images can reflect the feasibility and advantages of employing rabbit as an animal model to study rhino-sinusitis.

Depending on the study, CT is valuable experimental tool and measure for sinusitis[1-15]. Through observing the regional anatomy of rhino-sinus in rabbit and its CT imaging performance, we can confirm the feasibility of applying a rabbit model to the study of animal rhino-sinusitis.

MATERIALS AND METHODS

Design
Basic research of an animal model.
Time and setting
This study was conducted in the Central Laboratory of Affiliated Hospital of Qingdao University in China from May to October 2013.

Methods

Animals
Fifteen experimental New Zealand white rabbits were purchased from the Animal Feeding Laboratory of Qingdao Food and Drug Administration (certificate number of production SCXK(Lu)2009007). No gender restriction of rabbits was applied. The weight of rabbits ranged from 2.5 to 3.0 kg. The rabbits were fed in the Animal House of Affiliated Hospital of Qingdao University. The air of animal room was circulated, with a humidity of 40%–60% at 30–32 ℃. Diseases and deaths were not found after a week. This experiment was abided by ethical issues in animal experimentation.

Main reagents and equipment are listed as follows:

<table>
<thead>
<tr>
<th>Related drugs and instrument</th>
<th>Source</th>
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<tbody>
<tr>
<td>Midazolam injection</td>
<td>Jiangsu Nhwa Pharmaceutical Co., Ltd., China</td>
</tr>
<tr>
<td>Ketamine hydrochloride injection</td>
<td>Jiangsu Hengrui Medicine Co., Ltd., China</td>
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<tr>
<td>Lidocaine hydrochloride injection</td>
<td>Shandong Hualu Pharmaceutical Co., Ltd., China</td>
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<td>CT</td>
<td>GE</td>
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Methods
Preparation of experimental rabbits
The rabbits were anesthetized through an intramuscular injection with 30 mL/kg ketamine and an intravenous injection with 10% midazolam (10 mL).

Morphology of rabbit rhino-sinus observed by CT
The rabbits were then fixed on frames for CT scanning. The coronal and axial positions of the rhino-sinus in rabbit were scanned by Discovery CT750 HD, with an interlayer spacing of OM to 166.1 mm, a thickness of 2.5 mm, a window width of 3 000 Hu, and a window level of 600 Hu. The rabbits with rhino-sinus lesions were excluded.

Observation of the regional anatomy of rhino-sinus in rabbits
We removed their dorsal midline for leather, regularly disinfected, and then towel[16-17]. The rabbits were anesthetized by injecting 0.5% lidocaine. Then, a 3–5 cm dorsal midline incision was made longitudinally. Their subcutaneous tissue and periosteum were separated. On the left side approximately 0.5 cm at the center line of the nasal cavity post, we opened a hole with a diameter of approximately 3 mm in the anterior wall of maxillary sinus using a grinding drill and observed the structure, size, mucous membrane, and anatomic relations of the rabbit maxillary sinus by nasal endoscopy with a diameter of 2.7 mm. The contralateral maxillary sinus was observed following the same procedure. Finally, the lips of the rabbits were chain sawed along the dorsal midline (2 mm) starting from the bottom. The nasal cavity, nasal septum, sinus, middle turbinate, and nasal mucous membrane structure of the rabbits were then observed.

Main outcome measures
Rhino-sinus morphology in rabbits was observed.

RESULTS
Quantitative analysis of experimental animals
All rabbits were included in the final analysis.

Anatomical observation of rhino-sinus structure of rabbits
The rabbit nose consists of maxillary bone, ethmoid bone, and nasal bone. A large dark-red structure can be found at each lateral wall of the nasal cavity. This structure looks like a "coil" and is referred to as the inferior turbinate. A reddish uplift structure can be found at the post of the inferior turbinate. This structure looks like a three-layer ladder and is referred to as the middle turbinate. These structures are in substantially longitudinal direction. The maxillary sinus is divided into two or three parts with different sizes and then disconnected. The maxillary sinus-ostium is the inner wall of the maxillary sinus and is the contact channel between the nasal cavity and the maxillary sinus, which is the largest and most important sinus in rabbits. Ethmoid sinus, located in the posterior side post higher side of the maxillary sinus, consists of many small air cells similar to those in human. The mucosa of the ethmoid sinus is thinner than that of the maxillary sinus. The position of each ostium of the sinus of rabbit is similar to that of human (Figure 1).

Imaging observation of rhino-sinus structure of rabbits
The bilateral nasal cavity, sinus and nasal bone are shown clearly in the CT scans. The nasal septum is located on both sides of the nasal cavity as the human beings. The turbinate structure is visible at the lateral nasal, and a low-density mass shadow can be observed at both sides in front of lateral wall of the nasal cavity. The anatomical area of the maxillary sinus is shallow, and the sinus cavity with longitudinal elliptic shape is the largest. The ethmoid sinus is in the posterior high side of the maxillary sinus and consists of many air cells. Sphenoid and frontal sinuses are small (Figure 2).

DISCUSSION
Research background of animal models of rhino-sinusitis
The regeneration of the maxillary sinus mucosa was first studied by Knowlton and McGregor[18] in 1928 by using dog as an animal model. Hiding[19] was the first to introduce rabbit as an animal model of rhino-sinusitis in 1941. Since then, rabbits have become the main animal model used to research rhino-sinusitis. In 1998, Bomer et al[20] first proposed to establish a rat model of acute rhino-sinusitis.
Since then, acute rhino-sinusitis, chronic rhino-sinusitis, and the erosion of fungal rhino-sinusitis in rabbit models have been successively reported in China[21-22]. In recent years, domestic and international scholars[23-24] have attempted to improve existing technology to establish animal models of rhino-sinusitis and have indicated that an ideal animal model of rhino-sinusitis should have the following characteristics[25-30]: (1) the rhino-sinus should have no direct damage when establishing its animal model; (2) the clinical process of human chronic rhino-sinusitis should be stimulated when establishing an animal model of rhino-sinusis; (3) the rhino-sinusitis of the animal model should have the ability to invade other sinuses; (4) the model has staging and classification of signs in inflammation pathologically[31-32]; (5) the process is simple and easy to be implemented.

Although dog has a larger sinus cavity than rabbit, which is easy to operate major surgical procedures[31], scholars rarely employ dog in studies because of feeding problems, lacking of relating reagents and many other relating factors. Rat is excluded because of its small rhino-sinus, which is hard to operate. Rabbit is the most ideal animal model because the structural and physiological functions of its rhino-sinus are similar to those of human. In addition, rhino-sinus in rabbit is suitable for operation[33], and the CT image of the rhino-sinus in rabbit is clear and easy to be observed. Therefore, most scholars prefer to use rabbit as the animal model in rhino-sinusitis research. Many scholars have reported several times the successful application of rabbit models[34-44]. The observation and research of the rhino-sinusitis of rabbit through CT are feasible and necessary[45-46].

Nasal anatomy and CT features in rabbits
The present study is similar to the research of Kelemen[47]. Kelemen found that the nasal cavity of rabbit, similar to human beings through macroscopic and microscopic observations. The nasal cavity of rabbit is divided into the left and right chambers by the nasal septum. The nasal septum is formed by quadrilateral cartilage, vomer, and ethmoid bone vertical plates. A three-tier, pale-red, terraced structure exists beside the lateral nasal wall, which is equivalent to the middle turbinate of human. The anterior structure is called the maxillary turbinate, and posterior structure that in post is called the inside turbinate. A large, “coil-like,” dark-red structure exists on the lateral wall of the
nasal cavity. This structure is equivalent to the inferior turbinate of human, and its function is to humidify and warm air. We obtained basic similar conclusions.

After observing the anatomical structures and CT images, we confirmed that the maxillary sinuses are the primary nasal sinuses of rabbit and are located in the front of the rhino-sinus. A natural ostium in the medial wall of the maxillary acts as the contact channel between the nasal cavity and the maxillary sinus. The area near the ostium is considered as the osteomeatal complex in rabbit\(^{[49]}\), which is similar to that of human. The ethmoid sinus is located in the rear of the maxillary sinus. These results are consistent with previous research\(^{[49]}\). However, previous scholars only observed the CT image of rabbit rhino-sinus; studies on the anatomy of rabbit rhino-sinus compared with CT imaging are lacking. In the present study, we confirmed that the rhino-sinus in rabbit could have a clear and easy-to-observe CT image. After analyzing the CT images, we verified the feasibility and advantages of using rabbit as an animal model of rhino-sinusitis. The use of animal model may help us further understand the pathogenesis of human diseases related to the nasal cavity, paranasal sinuses, nose, and eyes. The model presented in this study may be used to study the etiology of rhino-sinusitis and may serve as a reference for clinical diagnoses and treatments.

Marks\(^{[50]}\) found that numerous collective lymph nodes exist in the floor of the nasal cavity in rabbit. The functions of these nodes are unclear, but may be equivalent to the adenoid in human. Vomeronasal organ is located at the bottom of the septum and is involved in pheromone detection. A large serous and mucus gland called nasal gland can be found in the inferior maxilla. This study, however, did not observe this aspect, which needs to be further studied.

In addition, studies on the initial factor chronic dacryocystitis referred, many researchers\(^{[51-52]}\) believe that the tear duct blockage is important virulence factor for dacryocystitis, they were trying to seek a suitable animal model, owing to the great similar nose histological structures beween rabbit and human\(^{[53-54]}\), and facilitating observation of the rabbit nasal and endoscopic surgical procedures, cheap, easying to get and feed, a variety fields of rabbit lacrimal study, so we concluded that rabbit is an ideal animal to choose for basic research, such as nose-eye correlated diseases.

In conclusion, animal models of rhino-sinusitis have gradually been established and improved successfully by many scholars in recent years\(^{[54-55]}\). The rabbit model of rhino-sinusitis has been the successful animal model of rhino-sinusitis accepted by most scholars and applied to numerous basic studies\(^{[54-60]}\). We can confirm the feasibility of applying a rabbit model to the study of animal rhino-sinusitis through this study. With the study expanding into the molecular and genetic levels, many related laboratory reagents and antibodies have been developed successfully to provide the necessary conditions for establishing the rabbit model of rhino-sinusitis. In our future studies, we will conduct sectional imaging anatomy analysis on the established rabbit model of rhino-sinusitis to obtain accurate data.

It is a great advantage that the anatomy and imaging studies of the rabbit’s rhino-sinusitis to establish animal models of rhino-sinusitis. Firstly, it is helpful to observe the inflammatory changes and occurrence of pathogenic dynamic evolution of remodeling about the rhino-sinusitis, mucosa and bone wall with time going on. Secondly, it is benefit to study chronic sinusitis on pathophysiology, histopathology, and pathology. Finally, under the transmission electron microscope, it is also able to observe the dynamic ultrastructural changes of maxillary sinus mucosa, expecting a better understanding of human chronic nasal-sinusitis pathogenesis. Furthermore, the correlation treatment of rabbit sinusitis can be developed. In a word, the successful establishment of animal models of rhino-sinusitis gives great help to clinical diagnosis and treatment of eye-related diseases and provides deep understanding to many basic research references and its targeted therapy and further research.

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兔适合构建鼻窦炎动物模型

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文章特点在于从兔鼻腔鼻窦解剖结构与CT影像学对比性研究证实兔可作为鼻窦炎动物模型的良好选择。但未构建鼻窦炎动物模型,仅从正常兔鼻腔鼻窦解剖学研究进行分析,需进一步实验支持结果。

关键词: 实验动物; 组织构建; 鼻窦炎; 动物模型; 解剖; CT; 兔; 鼻腔; 鼻窦

文章亮点：文章特点在于从兔鼻腔鼻窦解剖结构与CT影像学对比性研究证实兔可作为鼻窦炎动物模型的良好选择。但未构建鼻窦炎动物模型,仅从正常兔鼻腔鼻窦解剖学研究进行分析,需进一步实验支持结果。

文章结论：兔鼻中隔将鼻腔分为左、右两个腔,鼻腔外侧壁由上颌鼻甲、中间鼻甲、内侧鼻甲、下甲组成。以上颌窦窦腔最大,筛窦、蝶窦相对较小,以上颌窦解剖部位与人类相似且窦腔较大便于操作,具有动物实验模型建立的可行性,适用于鼻窦炎动物模型建立,可应用于模拟人类鼻窦炎的研究。