ISSN: 2414-1895 DOI: 10.6919/ICJE.202206_8(6).0018

Advances in Animal Model of Osteomyelitis of Jaw Bone

Peijia Li, Zelin Gao, Shun Tang, Xiuyun Zhang, Wang Zhao, Hui Chen*

School of Stomatology, North China University of Technology Tangshan, Hebei 063000, China

Abstract

Osteomyelitis is an acute or chronic inflammation of bone and its associated tissues due to infection. The disease has the characteristics of difficult treatment, high cost, prolonged course of disease and high disability rate. As the pathogenesis of osteomyelitis is very complex and highly variable, many animal models have been used to study the pathogenesis, diagnosis and treatment of osteomyelitis. Rabbits, rats and mice are often used in the establishment of osteomyelitis model, but dogs, pigs, goats and other large animals are rarely used. However, there is no animal model that can be controlled well. In this study, we searched the current establishment methods of animal models of osteomyelitis, in order to find a better controlled animal model for the study of the occurrence and development of osteomyelitis, and prospected the current research progress of osteomyelitis.

Keywords

Osteomyelitis of the Jaw; Animal Model; Infection; Arterial Injection Model; Biofilm Model.

1. The Model of Rabbit

1.1 Arteriovenous Injection Model

Rabbit is the earliest animal model of osteomyelitis. Rodetm[1] et al. established the rabbit osteomyelitis model in 1885 by directly injecting staphylococcal vein into the rabbit. Since then began the chapter of osteomyelitis in rabbit model. This method can not only control the safety of animals, but also can not simulate the process of human osteomyelitis. Poultsides et al. established a new osteomyelitis model by injecting staphylococcus directly into the femoral artery, but the results showed that high concentration (5x10s colony number) would lead to 100% mortality, and the lower concentration could not achieve stable infection results. This further illustrates the difficulty of establishing this model: even the injection of bacteria at the minimum concentration guaranteed to cause infection will lead to the death of a large number of experimental animals due to systemic inflammatory reactions[2]. Since then, the establishment of animal model of osteomyelitis by direct injection of staphylococcus into arteries and veins has not been satisfactory.

1.2 Local Injection Model

In 1941, Scheman et al. established a reproducible model of chronic osteomyelitis by injecting sodium cohepatolate and staphylococcus directly into the tibial metaphyseal region of rabbit. Sodium cohepatolate caused aseptic necrosis of bone, which was the basis for the progression of osteomyelitis. In the following period of time, this method was verified and developed by a large number of scholars at home and abroad, which laid a foundation and benchmark for subsequent research and became a commonly used modeling method[3]. In 1970, Norden[4] also verified Scheman et al. 's model by studying colony inoculation, and found that no obvious symptoms of osteomyelitis were found when sodium cohepatolate or Staphylococcus were applied alone at 14d or 60d, while 90% of infected tibial bacteria were cultured at 60d and 180d when sodium cohepatolate and Staphylococcus were applied

ISSN: 2414-1895 DOI: 10.6919/ICJE.202206_8(6).0018

simultaneously: Imaging results showed abscess formation, destruction of periosteum, destruction of normal bone structure, and new bone formation.

Domestic scholars tang Hui et al.[5]believed that at least 6×105 CFU staphylococcus aureus should be implanted before obvious signs and bacteriological results of bone infection would appear. Bacteria with 6×105 CFU concentration can not only make the success rate of chronic osteomyelitis model up to 100%.

1.3 Traumatic Osteomyelitis Model

To simulate the clinical common cases of traumatic osteomyelitis, some scholars also make rabbit tibia open fractures secondary osteomyelitis model[6] 42 healthy adult New Zealand white rabbit the self-made stents to open fractures and in right tibial fracture end vaccination standard staphylococcus aureus suspension 0.1 ml3 x 107 cfu induced the occurrence of posttraumatic osteomyelitis, The bacteria were examined by general observation, imaging manifestations, bacteriology and histology.

staphylococcus aureus and sodium cod liver oleate into the medullary cavity after tibial drilling is simple and effective. Zhang Xiaolei et al., in 2012, created a bone defect at the lateral proximal median joint of the rabbit mandible and injected a certain amount of bacterial suspension to obtain an ideal model of chronic suppurative osteomyelitis [7]. Previous studies on osteomyelitis were limited to tibia or fibula, and there were relatively few studies on mandible. Compared with tibia and fibula, mandible is affected by blood circulation, masticatory pressure and teeth. However, the incidence of osteomyelitis of jaw bone has increased significantly in recent years. The success of this experiment has long-term significance for osteomyelitis of jaw bone.

1.4 The Model of Biofilm

Li Yunfei et al. [8] implanted drug-loaded nano-biomimetic bone to treat rabbit osteomyelitis and achieved good efficacy. Wu Wei et al. [9] studied the therapeutic effect of degradable sustainedrelease antibiotic carriers on chronic osteomyelitis by establishing a rabbit model of chronic femoral osteomyelitis, and found that calcium sulfate and nano-hydroxyapatite carriers had better effects and had good application value.

2. The Model of Rat

2.1 Local Injection Model

After Rissing et al. successfully constructed a reproducible animal model of rat osteomyelitis in 1985, rats became one of the most commonly used animal models of osteomyelitis. In Rissing's study, rats were injected with 5% sodium cod liver olate and staphylococcus aureus suspension in the proximal tibial metaphysis. The results show that this model can construct chronic osteomyelitis, and can cultivate a large number of stable pathogenic bacteria from the lesion area in a long period of time [10].

There are few reports on animal models of rat osteomyelitis in China. Chen Lianyuan [11-15] et al reported the simulated Shen Lin method [16] by placing cotton balls soaked with Staphylococcus aureus into the medullary cavity of the proximal tibia of rats, and then injecting 5% sodium cod liver oilate into the medullary cavity. One week later, cotton balls were removed for modeling of osteomyelitis. However, this method has the disadvantage that cotton balls need to be removed after one week of modeling.

2.2 Biofilm Model

Lucke et al. created a rat model in 2016 by simulating intramedullary needles. In order to mimic the human disease process, other promoters that can cause osteomyelitis are not used. It was found that acute destructive osteomyelitis can occur with 100 colonies, and sterile Kirschner wires can simulate foreign body implantation and biofilm formation in vivo. This model has since been validated and replicated by other researchers. In addition, bacterial implantation and intramedullary fixation were used to seal the nail hole with bone cement and bone wax to establish the model.

ISSN: 2414-1895 DOI: 10.6919/ICJE.202206_8(6).0018

Hao Jianhua et al. prepared a rat tibial osteomyelitis bone defect model by absorbing Staphylococcus aureus with gelatin sponge [18], and established a rat osteomyelitis bone defect model that is easy to replicate, simple to operate, low test cost and in line with the clinical pathogenesis process.

In the past, the osteomyelitis model was made by directly adding bacteria into the borehole, which was obviously different from the clinical pathogenic factors, and the amount of bacterial suspension was not easy to control, and it was easy to cause the death of model animals. However, bacterial biofilm was the most common cause of osteomyelitis in clinical practice. Staphylococcus aureus (STAPHYlococcus aureus) was used to make Kirschner needles with bacterial biofilm. Eighteen healthy SD rats were selected, and kirschner needles with staphylococcus aureus biofilm were inserted into the tibia of SD rats. Building closely observing animals after operation state and incision healing, imaging and pathological examination after 4 weeks to observe the bone infection, aseptic take building site discharge for bacterial culture, parallel mass spectrometry to identify whether the inoculation of bacteria for the production of bacterial biofilm, and rat serum inflammatory factors before and after the detection of building, building successful indicators for evaluating osteomyelitis model. Results & CONCLUSIONS: All 18 rats were consistent with the characteristics of osteomyelitis, and showed different degrees of pus, dead bone, dead cavity and new bone formation. After modeling, serum inflammatory factors such as procalcitonin, tumor necrosis factor α and interleukin 10 were significantly increased ($P<0.05$); Staphylococcus aureus was identified as the bacterium formed after culture of rat secretions. The above results confirmed that the rat model of osteomyelitis can be successfully made by kirschner wire implantation of the rat tibia with STaphylococcus aureus biofilm, and it is closer to the clinical incidence of osteomyelitis.

Sodnom-IshB et al made a 4mm diameter perforation defect in the mandibular bone of rats in 2021 and inoculated with staphylococcus aureus injection (20μl1×107CFU/ml). The successful establishment of rat jaw osteomyelitis model provides a new choice for clinical jaw osteomyelitis animal model. Compared with rabbits, rats also have the advantages of cheap price and simple operation.

3. Modeling Results and Conclusions of Animal Models

Results & CONCLUSIONS: All 18 rats were consistent with the characteristics of osteomyelitis, and showed different degrees of pus, dead bone, dead cavity and new bone formation. After modeling, serum inflammatory factors such as procalcitonin, tumor necrosis factor α and interleukin 10 were significantly increased ($P<0.05$); Staphylococcus aureus was identified as the bacterium formed after culture of rat secretions. The above results confirmed that the rat model of osteomyelitis can be successfully made by kirschner wire implantation of the rat tibia with STaphylococcus aureus biofilm, and it is closer to the clinical incidence of osteomyelitis.

Sodnom-IshB et al made a 4mm diameter perforation defect in the mandibular bone of rats in 2021 and inoculated with staphylococcus aureus injection (20μ/1×107CFU/ml). The successful establishment of rat jaw osteomyelitis model provides a new choice for clinical jaw osteomyelitis animal model. Compared with rabbits, rats also have the advantages of cheap price and simple operation.

4. Expectation

Recent advances in experimental and clinical studies of osteomyelitis have significantly improved our understanding of the pathophysiology of osteomyelitis, including the mechanisms of bacterial adhesion, biofilm formation, intracellular infection, and bone destruction. However, further research is needed on histopathological changes that clearly date infection, and a better understanding of pathophysiology will facilitate the development of new therapeutic strategies for this devastating disease. A significant advance in the treatment of osteomyelitis has been local administration, which improves treatment effectiveness and minimizes side effects of systemic administration of large doses of antibiotics. However, none of the materials used for local drug delivery can fully meet clinical

ISSN: 2414-1895 DOI: 10.6919/ICJE.202206_8(6).0018

needs. New transfer materials with appropriate mechanical properties, low exothermic response, controlled release of antibiotics and resorbable scaffolds to promote bone regeneration need further research.

In surgical treatment, it is still a difficult problem to determine the resection range of the infected lesions, and solving this problem is of great significance in reducing recurrence and speeding up follow-up recovery. Clinicians and scientists are working together to develop more effective osteomyelitis prevention, early diagnosis and innovative treatment strategies, such as biofilm disruptors and immunotherapies. At the same time, in recent years, many new technologies have been used for the treatment of osteomyelitis, such as hyperbaric oxygen, electromagnetic therapy and other physical therapy, as well as the growth factor and gene therapy mentioned later to promote the treatment of osteomyelitis to a certain extent, but its safety, effectiveness, controllable, promotion still need to be confirmed by further research.

References

[1] RodetA.Etudeexperimentalesurl'osteomyeliteinfectieuse.

[2] Lazaros,A,Poultsides,etal.Novelmodelforstudyinghematogenousinfectioninanexperimentalsettingofimplant-relatedinfectionbyacommunity-acquiredmethicillin-resistantS.aureusStrain[J].JournalofOrthopaedicResearch,2008,26(10):1355-1362.

[3] Theproductionofexperimentalosteomyelitis[J].AmericanJournalofOrthodonticsandOralSurgery,1942,28(6):B383.

[4] NordenCW.ExperimentalOsteomyelitis.I.ADescriptionoftheModel[J].JournalofInfectiousDiseases,1970,122(5):410-418.

[5] Tang Hui, XU Yongqing, Ma Tao, et al. Effects of total injection amount of drug-resistant Staphylococcus aureus on the formation of infectious bone defects in rabbits [C]/ Proceedings of the 6th Western Orthopaedic Forum and Guizhou Orthopaedic Annual Conference. Physical Disability Rehabilitation Professional Committee of PLA,2010.

[6] Chu L T. Establishment of rabbit animal model of osteomyelitis after tibial trauma [D]. Nanjing University, 2012. (in Chinese with English abstract).

[7] Zhang Xiaolei, Shen Juxiang, XIE Zhijian. Rabbit mandibular animal model of chronic pyogenic osteomyelitis establish [J]. Chinese journal of experimental animals, 2012, 20 (3) : 74-77, 3. DOI: 10.3969 / j.i SSN. 1005-4847.2012.03.016.

[8] Li Yunfei, Fang Taolin, Dong Jian. Repair of bone defect by vancomycin-loaded nano-hydroxyapatite in rabbits with methicillin-resistant Staphylococcus aureus chronic osteomyelitis [J]. China's tissue engineering research and clinical rehabilitation, 2008, 12 (23) : 4422-4426. The DOI: 10.3321 / j.i SSN: 1673-8225.2008.23.008.

[9] Wu Wei, Li Zhenqing, Yang Jianzhong, Chen Guang, Kang Lixing, Sun Jianting, Zhang Hua, Liu Miao. Experimental study on the treatment of chronic osteomyelitis with degradable antibiotic sustained-release carrier [J]. Practical orthopedic journal, 2013, 12 (3) : 229-231, 1. DOI: 10.3969 / j.i SSN. 1008-5572. 2013.03.012.

[10] RissingJP,BuxtonTB,WeinsteinRS,etal.Modelofexperimentalchronicosteomyelitisinrats.[J].Infection&Immunity,1985,47(3):581-6.

[11] Chen Lianyuan, LI Xiaoquan. Effect of jiudu Huayu Decoction on chronic osteomyelitis in rats [J]. Chinese Journal of Orthopedics and Traumatology,2000.

[12] Gao C F, Li X Q. Effect of 5% sodium cod liver oleate on modeling of chronic osteomyelitis [J]. Chinese medicine bonesetting,2002,14(9):2.

[13] Lin JIE. Effect of Li Kangping on X-ray examination and bone pathological histology of diseased limbs in rats with chronic osteomyelitis [C]/ The 7th Academic Conference of Chinese Medicine Constitution of China Association of Traditional Chinese Medicine.

[14] Wu Hong, Wang LAN, SHAO Haibo. Treatment of chronic osteomyelitis in rats with qingmei Prescription [J]. Guizhou Medicine,2014,000(012):1122-1123.

ISSN: 2414-1895 DOI: 10.6919/ICJE.202206_8(6).0018

[15] Zhou Chenggang, ZHOU Qinglai. Effect of qfushengji powder on the treatment of chronic osteomyelitis [J]. Chinese journal of orthopaedics,2008,16(3):4.

[16] Shen Lin, DU Jingyuan, Yang Jiayu, et al. Modeling method of chronic suppurative osteomyelitis and determination of related indexes [J]. Chinese Journal of Orthopedics and Traumatology,1989(5):3-6. (in Chinese).

[17] HarrasserN,GorkotteJ,ObermeierA,etal.Anewmodelofimplant-relatedosteomyelitisinthemetaphysisofrattibiae[J].BMCMusculoskeletalDisorders,2016,17(1).

[18] Hao Jian-hua, Mei Xing-ming, Xie Bao-gang, Wang Xiao-dong, Li Wei, Zha-Ga-hu, Mai Xia, Chen Xiao-yi. Preparation of bone defect model of tibial osteomyelitis in rats by adsorption of Staphylococcus aureus with gelatin sponge [J]. Biological bone materials and clinical research, 2016, 13 (1) : 1-3, inserted after 1. DOI: 10.3969 / j.i SSN. 1672-5972.2016.01.001.

[19] Feng Jianbo, Li Chencheng, Liu Jinyue, Wang Xiaomin, PENG Jiachen. Establishment of traumatic osteomyelitis model by Kirschner wire implantation of Staphylococcus aureus biofilm [J]. Chinese Journal of Tissue Engineering Research,202,26(5):700-705.

[20] Sodnom-IshB, EoMY OhJH, SeoMH, YangHJ, LeeJH, KimSM. Decompression effects on bone healing in rat mandible osteomyelitis.SciRep.2021Jun3; 11 (1): 11673. doi: 10.1038 / s41598 - 021 - 91104 - 7. - pmid: 34083570; PMCID: PMC817558.8