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Staphylococcus aureus and Aspergillus Funigatus infections In Making Animal Models of Rhinosinusitis

Renny Swasti Wijayanti[1], Andriana Tjitria Widi Wardani[1], Agung Sulistyanto[1]*

[1] Otolaryngology Department of Faculty of Medicine Sultan Agung Islamic University

* Correspondence: E-mail: rennysw@gmail.com

ABSTRACTS

Rhinosinusitis is an inflammation of the mucosa or mucous membranes of the nose and sinuses, the most common being maxillary sinusitis and ethmoid sinusitis, while frontal sinusitis and sphenoid sinusitis are less common. Rhinosinusitis is caused by any condition that blocks the flow of mucus from the sinuses to the nasal cavity. If rhinosinusitis is not treated or does not heal completely, it can cause several complications for the patient such as infection of the brain, infection / swelling of the tissue around the eyeball, decreased vision function, bone infection around the sinuses, pus coming out of the face, changes in facial shape / protruding / swelling, and sore throat often recur. The main purpose of the medical system in Islam is to maintain health rather than cure disease. Sinusitis that is not immediately treated can also cause permanent loss of the sense of smell. Usually sinusitis is treated with medication. But in certain cases, sinusitis must be treated with surgery. The animal model of rhinosinusitis was made by blocking the right nares of rats by using Merocel tamponade. Then an incision is made in the skin, superior to the maxillary sinus. Intraperitoneal induction and intranasal induction 0.1 ml of a solution of Streptococcus aureus type 1, consisting of 107-109 S. aureus/ml, and Aspergillus Fungigatus 107-109/ml were inoculated into the right maxillary sinus. The same amount of physiological saline was also injected into the left maxillary sinus as a control agent.

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ABSTRAK

Rinosinusitis adalah peradangan pada mukosa atau selaput lendir hidung dan sinus, yang paling umum adalah sinusitis maksilaris dan sinusitis ethmoid, sedangkan sinusitis frontal dan sinusitis sphenoid kurang umum. Rinosinusitis disebabkan oleh kondisi apa pun yang menghalangi aliran lendir dari sinus ke rongga hidung. Jika rinosinusitis tidak ditangani atau tidak sembuh total, maka dapat menyebabkan beberapa komplikasi bagi penderita seperti infeksi otak, infeksi/pembengkakan jaringan di sekitar bola mata, penurunan fungsi penglihatan, infeksi tulang di sekitar sinus, nanah yang keluar dari wajah, perubahan bentuk wajah/menonjol/bengkak, dan sakit tenggorokan sering kambuh. Tujuan utama dari sistem medis dalam Islam adalah untuk menjaga kesehatan daripada menyembuhkan penyakit. Sinusitis yang tidak segera ditangani juga dapat menyebabkan hilangnya indera penciuman secara permanen. Biasanya sinusitis diobati dengan obat-obatan. Tetapi dalam kasus-kasus tertentu, sinusitis harus diobati dengan operasi. Model hewan rinosinusitis dibuat dengan menghalangi nares kanan tikus dengan menggunakan tamponade Merocel. Kemudian sayatan dibuat di kulit, lebih unggul dari sinus maksilaris. Induksi intraperitoneal dan induksi intranasal 0,1 ml larutan Streptococcus aureus tipe 1, yang terdiri dari 107-109 S. aureus / ml, dan Aspergillus Fungigatus 107-109 / ml diinokulasi ke sinus maksilaris kanan. Jumlah garam fisiologis yang sama juga disuntikkan ke sinus maksilaris kiri sebagai agen kontrol.

Keyword:
Rhinosinusitis, Model Hewan

1. INTRODUCTION

Acute rhinosinusitis (rsa) is a common health problem in children and adults. Rsa is defined as a paranasal sinus infection, with accompanying symptoms of more than 10 days and less than 4 weeks. It is difficult to distinguish between bacterial and viral sinusitis, most would agree that viral rhinosinusitis usually resolves within 7 to 10 days, whereas bacterial rhinosinusitis remains persistent, there are no very sensitive and specific signs and symptoms of rhinosinusitis, no specific clinical signs to diagnose it and its management. It is very important to distinguish between the symptoms of allergic or vasomotor rhinitis and complications of acute respiratory tract infection (ispa). (almutairi et al., 2017) (leung and katial, 2008) (jochen w. L. Cals, md, 2010) (sedaghat et al., 2014)

If rhinosinusitis is not treated or does not heal completely, it can cause several complications for the sufferer such as infection of the brain, infection/swelling of the tissue around the eyeball, decreased vision function, infection of the bones around the pus sinuses out of the face, changes in face shape / protruding/swelling, and strep throat often relapse.

Experimental animal models are widely used to study the pathogenesis of diseases, examine the results of treatment, and the development of early healing. This is for the prevention of surgery in patients who require expensive costs and greater risks.

2. METHODS

This research is an experimental study with a posttest group design. The location of this study was conducted at ibl fk sultan agung islamic university semarang with male white rats (rattus norwegians) with the sprague dawley strain as a try animal. The study sample involved 15 rats. The sample size in this study was 5 rats for each group that had been randomized, namely 3 treatment groups. Data collection was obtained by conducting histopathological analysis of maxillary sinus mucosa samples from all study test subjects. The data obtained are tabulated and analyzed descriptively using spss application version 22.

3. RESULTS AND DISCUSSION

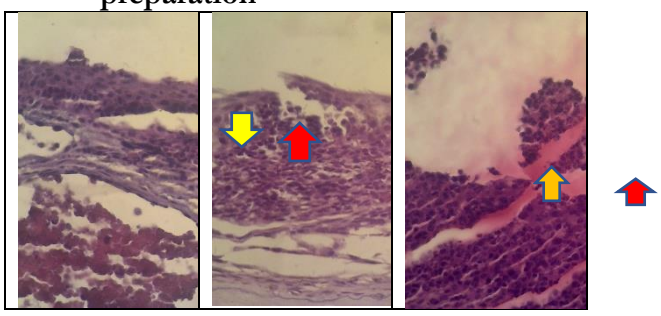
3.1. Results

Based on the results of the study obtained the results of the histopathological picture is as follows:

Table 4.1 Results of histopathological readings of sinus preparations

No	kelp	Signs of acute inflammation			
		Edema	Hyperemia	A Lack of Neutrophils	Necrosis
1	K	Negative	Negative	Negative	Negative
2	K	Negative	Negative	Negative	Negative
3	K	Negative	Negative	Negative	Negative
4	K	Negative	Negative	Negative	Negative
5	K	Negative	Negative	Negative	Negative
6	P14	Positive	Positive	Light	Positive
7	P14	Positive	Positive	Light	Positive
8	P14	Positive	Positive	Moderate	Positive
9	P14	Positive	Positive	Light	Positive
10	P14	Positive	Positive	Light	Positive
11	P21	Positive	Positive	Moderate	Positive
12	P21	Positive	Positive	Hard	Positive
13	P21	Positive	Positive	Hard	Positive
14	P21	Positive	Positive	Hard	Positive
15	P21	Positive	Positive	Hard	Positive

4. **Picture 4.1 Sinus histopathological preparation**



a. Control group overview	b. Picture of the 14-day treatment group, Stroma sub epithelium edema, and hyperchys, accompanied by a pair of leukocytes (yellow arrows) and epithelial necrosis (red arrows)	c. Picture of the 21-day treatment group, Stroma sub epithelium edema, and hyperchys, accompanied by a pair of leukocytes (yellow arrows) and epithelial necrosis (red arrow)

At 14 to 21 days post-infection, rat infected with S. aureus had an increased frequency of sneezing, nose rubbing, and nasal discharge compared to controlling rat. After S. aureus treatment, rats in groups A and B were euthanized on days 14 and 21, respectively. The control rat (group k) were turned off on the 21st day. The maxillary sinuses of the control rat had a healthy mucosa, while rat in the P14 (14-day treatment) and P21 (21-day treatment) had mucosa with swelling and mild to hard edema. In the P14 group, the discharge of the clinking nose lining the mucosal surface can also be observed. Mucosal sinus coloring of the P14 and P21 groups showed dramatic histological changes. Epithelial cells from mouse sinus tissue in the P14 group appeared damaged or destroyed. In addition, the sinus mucosa is swollen with infiltration of characterized inflammatory cells, including neutrophils, lymphocytes, and plasma cells, as well as the presence of necrosis in these areas (Picture b). In the mucosal tissue of mice of the P21 group, we observed mucosal swelling, infiltration of inflammatory cells in the epithelial and subepithelial layers of tissues, as well as slight hypertrophy of epithelial cells (Picture c). In contrast to the experimental group, tissue samples from the control group were observed as normal respiratory mucosa with columnal ciliated epithelium and no significant infiltration of inflammatory cells infiltrated into the subepithelial layer of tissue. In both groups, we observed messy cilia and in the absence of cilia, many large protrusions or pods appeared as spherical body towers.

3.2 Discussion

Rhinosinusitis is an inflammation of the paranasal sinuses caused by infection. Fungi are one type of microorganism that can cause infection of the paranasal sinuses. Fungal infections of the paranasal sinuses include irrational use of drugs such as prolonged use of antibiotics and steroids, impaired sinus ventilation, and a moist environment. The type of fungus that most often causes fungal rhinosinusitis is Aspergillus.

The classification of fungal rhinosinusitis is divided into invasive and non-invasive. Ball fungus and allergic fungal sinusitis belong to the rhinosinusitis of noninvasive fungi. Invasive sinusitis includes chronic invasive fungal rhinosinusitis and invasive fulminant disease that occurs in immunosuppression patients. Chronic invasive fungal sinusitis is divided into granulomatous and non granulomatous.

The ostiomeatal complex (KOM) is a drainage site for the anterior sinus groups (frontalis, anterior ethmoid, and maxillary) and plays an important role in the transport of mucus and debris and maintaining sufficient oxygen pressure to prevent bacterial growth. Obstruction of ostium sinus in KOM as a predisposing factor that plays a role in the occurrence of chronic rhinosinusitis. However, the other two factors also play a role in the occurrence of chronic rhinosinusitis. Interruptions in one or more of the above factors will affect other factors and then trigger a cascade that develops into chronic rhinosinusitis with pathological changes in the sinus mucosa as well as the nasal mucosa.

Stagnation of the mucosa in the sinuses forms a rich medium for the growth of various pathogens. The early stages of rhinosinusitis are often viral infections that generally last up to 10 days and it is completely cured in 99% of cases. However, a small number of patients can develop secondary acute bacterial infections commonly caused by aerobic bacteria (i.e. Streptococcus pneumonia, Haemophilus influenza, Moraxella catarrhalis). Initially, the resulting acute rhinosinusitis involved only one type of aerobic bacteria. In the presence of persistent infection, the mixed flora of organisms and sometimes fungi contribute to the pathogenesis of chronic rhinosinusitis.

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Fungi contain intrinsic proteases that can induce cytokines via the activation of PAR receptors on various cell types, possibly through a type 2 T helper (Th) response. Mushroom extracts can inhibit JAK-STAT1 signals in the epithelium, an effect that can inhibit Th1 and improve the response of Th2. Mushrooms also likely play a key role in classic allergic fungal rhinosinusitis. Lastly, the cell wall of the fungus contains chitin, which has been shown to induce the Th2 response in some human and animal models, but the role of chronic rhinosinusitis remains unclear. Today, most researchers suspect that fungi may play an important role in the etiology of rhinosinusitis.

To develop the most appropriate model of rhinosinusitis several factors need to be addressed. First, it is important to choose practical animals as well as suitable bacteria for this model. Secondly, it is necessary to determine the dosage and duration of infection. Lastly, it is important to correctly identify qualitative and quantitative analyses to investigate the existence of biofilm. To identify suitable animals, we consider availability, low cost, and ease of use. Sheep are problematic due to their high cost and difficulty in use. Alternatively, mice are advantageous for use in medical research due to their small size, low cost, availability, rapid reproduction rate, and easy to use.

Rat share high genetic homology with humans and can be genetically manipulated. Although rats had the same advantages as a rat, their small sinus cavities presented a challenge for rhinosinusitis studies. According to the literature, the biofilm S. aureus has been closely associated with unfavorable outcomes in CRS patients. S. aureus biofilm is also known to negatively impact the outcome of endoscopic sinus surgery by causing mucosal inflammation and causing postoperative infection. After careful analysis, we chose S. aureus and A. Fumgigatus for this model because of their ability to easily form biofilms and their role in influencing the outcome of sinus-related infections. To investigate the success of our proposal the model was necessary to first find sinus maxillary in rat. We observed that the antrostomist is located about 3 mm beside the center line and 4 mm below the eye is the location of the maxillary sinus. In a previous study using sheep model rhinosinusitis, 1 ml of bacterial and fungal cultures in a suspension of 0.5 McFarland was injected into the frontal sinuses. Another study evaluating the rabbit model of rhinosinusitis showed that sinus damage formed within 5 days post-infection and can last for several weeks. According to previous studies using rat rhinosinusitis models, we injected 0.1 ml of 0.5 ml of McFarland S. aureus and A. Fumgigatus suspension into the maxillary sinus. We observed the presence of sinus damage on day 21. In this study, we did not conduct quantitative analysis because the sample size was small. However, this technique has reportedly allowed the quantification of biofilms in the sinonasal mucosa. Quantitative assessments can provide information on the level of bacterial involvement in rhinosinusitis and potentially facilitate the development of more effective treatments.

5. CONCLUSION

Intraperitoneal injection of S. aureus bacteria and Aspergillus fungigatus fungus, as well as administration of the sinus cavity with anthratomy surgery, can induce acute rhinosinusitis characterized by the presence of pro-inflammatory cytokines and immune cells, followed by damage to the sinuses of the epithelia and stroma. In the 21-day treatment group, symptoms were found that were close to acute rhinosinusitis.

6. ACKNOWLEDGEMENTS

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