Analysis of Factors Affecting Healing of Acute Pharyngitis Viral Patients in Puskesmas I, Klungkung-Bali

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Abstract

Antibiotic resistance is closely related to the inappropriate use of antibiotics, namely the indication, dose, frequency, and duration of use. Permenkes No. 5 of 2014 states that acute pharyngitis is given antibiotic therapy if it meets the diagnostic criteria using the center criteria, but this criterion is difficult to apply because doctors take longer to diagnose. Previous research at the Klungkung I Primary Health Center used diagnosis utilizing a swab test. It was found that 100% of bacterial pharyngitis patients were negative. The strategy of delaying antibiotics for 3 days can prevent antibiotic resistance, but in therapy, without antibiotics, it is important to increase the effectiveness of therapy, it is deemed necessary by the researchers to conduct a study to analyze the factors that affect the recovery of patients with acute pharyngitis, which are mainly caused by viruses. Analyzing the factors that affect the recovery of viral pharyngitis patients. The design of the cross-sectional study was through observation of the medical record data of patients who came to the Klungkung Primary Health Center I for 3 months and got diagnostic facilities using the swab test. Patients who got a negative swab test were analyzed for the factors that influenced their recovery. Anti-inflammatory variables, rest, and paracetamol significantly affected the recovery of acute pharyngitis patients (p <0.05), and the importance index in CART analysis found that paracetamol was the most influential, followed by rest, administration of vitamins, and anti-inflammatory. Antibiotics, anti-allergies, and cough medicines do not affect the recovery of patients with acute pharyngitis viral. Paracetamol has the most effect on patient recovery, followed by rest and administration of vitamins, anti-inflammatory has very little effect on the recovery in patients of acute pharyngitis viral.

Keywords: acute pharyngitis, cure, CART.

INTRODUCTION

Pharyngitis is inflammation of the pharyngeal wall which can be caused by viruses (40-60%), bacteria (5-40%), allergies, trauma, toxins, and others. Viruses and bacteria invade the pharynx and cause a local inflammatory reaction. Group A hemolytic streptococcal bacterial infection can cause severe tissue damage because these bacteria release extracellular toxins that can cause rheumatism, heart valve damage, acute glomerulonephritis due to impaired glomerular function due to the formation of antigen-antibody complexes (1).

Viral pharyngitis gives symptoms of cough, runny nose, conjunctivitis, fatigue, body feeling unwell, and moderate-grade fever, whereas bacterial infection is not accompanied by cough, runny nose, and conjunctivitis. It is not recommended that antibiotics be given as therapy for viral pharyngitis, but in fact, pharyngitis accompanied by cough (a characteristic feature of viral pharyngitis) is treated with antibiotics, that empirical diagnosis is no longer visible to use considering that history by looking at signs and symptoms is very difficult to use for distinguishing viral pharyngitis and bacteria (Sutema, 2018). For medical management, in addition to self-management by patients who can help reduce or treat pharyngitis symptoms, therapy is also needed to eradicate the main cause, one of which is the administration of antibiotics. Antibiotics are only given in cases of proven pharyngitis due to bacterial infection, for example in Group A Streptococcus f-haemolyticus (GAS) infection. Giving antibiotics aims to kill bacteria to prevent com-
Antibiotics of choice are amoxicillin, penicillin V, and benzathine penicillin. In patients with a history of penicillin allergy, the choice of antibiotics is cephalaxin, cefadroxil, clindamycin, clarithromycin, and azithromycin. Administration of paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) can be considered for the management of cases of pharyngitis. 

Treatment of viral pharyngitis does not require antibiotics, but the fact is that in Klungkung I Primary Health Center, in particular, almost all diseases diagnosed as acute pharyngitis are treated with antibiotics. In addition, empirical diagnosis is no longer visible to use, considering that the history of signs and symptoms is difficult to distinguish between viral and bacterial pharyngitis. A large amount of use of antibiotics and their misuse is thought to be the main cause of the high number of pathogens and resistant commensal bacteria worldwide. Reducing the number of inappropriate antibiotic use is the best way to control the occurrence of bacterial resistance.

Patient recovery factors can be classified into 2, namely, dependent factors such as education, work, income, medication (drug consumption), and food consumption (nutrition), etc. as well as independent factors such as age, gender, rest status, etc. In Nurmaida (2014), it was found that a significant factor in influencing the recovery of ARI patients who were diagnosed empirically (the cause was not yet certain for viruses or bacteria) was the administration of antibiotics (p = 0.041), while other factors were gender (p = 0.184), age (p = 0.700), education (p = 0.384), occupation (p = 0.178), marital status (p = 0.700), income (p = 1,000), number of hours of sleep/day (p = 0.634), habits consuming vitamins (p = 0.625), and food consumption patterns (p = 0.584) were not significant in healing ARI. In acute pharyngitis patients who are included in ARI, especially those caused by viruses, antibiotics in theory cannot be given so they are not included in the factors that affect the patient's recovery, so further research is needed to find out what factors affect the recovery of patients suffering from pharyngitis. An acute virus without giving antibiotics, and can be a reference for pharyngitis therapy in health centers, most of which are caused by viruses using the binary logistic regression method. The hypothesis in this study was the factors studied as independent variables (vitamins, anti-inflammatory, and rest) affected the recovery of viral pharyngitis patients at Klungkung I Primary Health Center.

METHODS

The study design used an observational method with a cross-sectional study approach. The data used in this study is secondary data in the form of medical records taken in October 2016 - January 2017 where the medical records describe the diagnosis of acute pharyngitis diagnosed using laboratory tests through a swab test using RADT (Rapid Antigen Diagnostic Test). The sampling technique used in this study was carried out through non-probability sampling with the type of consecutive sampling, in which patients aged 12-45 years with a diagnosis of acute pharyngitis caused by viruses and recorded in the medical record will be selected as samples. Then the sample was divided into two large groups, namely patients with acute pharyngitis caused by a virus where treatment was cured and failed. The two groups collected patient data which contains the independent variables studied.

The population of this study was all patients in the age group 12-45 years who came to the Klungkung I Primary Health Center with symptoms of acute pharyngitis. In this study, there were 5 independent variables (giving antibiotics, giving paracetamol, giving anti-inflammatory, vitamins, and rest), and one variable was equal to 10 patients, so the overall sample size was 60 patients. 

Statistical analysis to see the influencing factors with the CART method which can describe the relationship between the response variable (dependent variable) and one or more predictor varia-
The demographics of the study subjects were determined by age and gender in Table 1.

Table 1. Distribution of Patients by Gender and Age

| Characteristics     | ∑ | %     |
|---------------------|---|-------|
| **Age**             |   |       |
| Adolescent (12-18 years) | 14 | 23.33 |
| Adult (19-45 years)  | 46 | 76.67 |
| **Gender**          |   |       |
| Male                | 40 | 66.66 |
| Female              | 20 | 34.34 |

Patients in this study can be seen from the characteristics of their age and gender. As many as 23.3 percent of patients in this study were patients from the adolescent group while 76.67 were patients from the adult group. Based on gender, information was obtained that 66.66 percent were male patients, while the remaining 34.34 percent were female patients.

In line with the research Rasmala Dewi, obtained research results that based on age, adults or the elderly will be more quickly exposed to bacteria and viruses that cause respiratory tract infections (4). Therefore, elderly people are more susceptible or susceptible to various kinds of infectious diseases. This vulnerability occurs because of reduced production of immunoglobulins that act as antibodies and decreased response of the body's protective system, co-morbidities that arise after a decline in the structure and function of the body's organs, functional disorders of the body, errors in nutrition and poor environmental conditions (4).

Then based on gender. According to the results of the study, from 85 patients, the male sex was more dominant, namely 49 people 57.64%, while the female sex was 36 patients 42.36%. This is in line with Ladipa's research (2018) that men have a higher risk of respiratory tract infections than women because there are environmental and behavioral differences between men and women, for example, such as self-awareness in terms of maintaining daily health (4).

The male sex is more susceptible to respiratory tract infections because the majority of men are smokers and often drive vehicles and are exposed to air pollution from the outside. In addition, men are more active in activities so they are exposed to more air than more dominant women. Staying at home, as a result, is easy to get tired and tend to have a weakened immune system, compared to women (4).

The factors that influence the patient's recovery can be identified from the bivariate analysis. The method used for bivariate analysis is the chi-square method. Each factor is identified based on a preliminary theory, which is then examined for the significance of its effect on recovery. The results of the effect independent variable on the dependent variable, namely the cure for viral pharyngitis patients can be seen in Table 2.

Table 2. Results of the effect of independent variables on Pharyngitis.

| No | Recovery Factor | Giving | Recovery | Pearson Chi-Square |
|----|----------------|--------|----------|-------------------|
| 1  | Antibiotic     | Yes    | 22       | 7                  | 0.261 |
|    |                | No     | 27       | 4                  |       |
| 2  | Anti-inflation | Yes    | 2        | 2                  | 0.090 |
|    |                | No     | 47       | 9                  |       |
| 3  | Vitamin        | Yes    | 37       | 6                  | 0.163 |
|    |                | No     | 12       | 5                  |       |
| 4  | Rest           | Yes    | 14       | 14                 | 0.043 |
|    |                | No     | 46       | 35                 |       |
| 5  | Paracetamol    | Yes    | 43       | 5                  | 0.002 |
|    |                | No     | 6        | 6                  |       |
| 6  | Cough Drug     | Yes    | 37       | 9                  | 0.655 |
|    |                | No     | 12       | 2                  |       |
| 7  | Anti-histamine | Yes    | 24       | 6                  | 0.739 |
|    |                | No     | 25       | 5                  |       |
Based on the results of the analysis, it was found that the anti-inflammatory variables, rest, and paracetamol significantly affected the recovery of acute pharyngitis patients. This can be seen from the significant value of each of these variables which is less than 0.05. Based on the results of the analysis, it is also known that the use of antibiotics, vitamins, anti-inflammatory, allergy, and cough medicines in acute pharyngitis has no significant effect on the cure of acute pharyngitis.

**Analysis results using the CART (Classification And Regression Trees) method.**

Simultaneously, the influence of each factor can be identified using CART analysis. This analysis is used to see the effect of each variable along with the level of importance (most influential) on recovery. The results of the CART analysis can be seen in Table 3 and Figure 1.

**Table 3. Results of CART Analysis.**

| No | Variable            | Score | Importance |
|----|---------------------|-------|------------|
| 1  | PARACETAMOL         | 100.00| |||||||||
| 2  | REST                | 52.32 | ||||| |
| 3  | VITAMIN             | 43.52 | ||||| |
| 4  | ANTI-INFLAMMATION   | 27.38 | |||| |
| 5  | ANTI-HISTAMINE      | 2.56  | |||
| 6  | ANTIBIOTIC          | 0.00  |          |
| 7  | COUGH DRUG          | 0.00  |          |

Based on the analysis results obtained in table 3, regarding the importance index of each variable. Paracetamol as one of the drugs given to patients gives the best results in providing healing. The next variable that had the greatest effect on recovery was the rest factor, followed by vitamins and anti-inflammatory, respectively.

Comparatively, the administration of antibiotics in bivariate analysis and the use of CART did not affect the cure of pharyngitis. The visual picture of CART analysis can be seen in the following figure:

**Figure 1. CART**

Visualization of CART in this study is an optimal tree analysis, where the algorithmically insignificant variables have been trimmed. Based on these results, it is clear that paracetamol is the most important differentiating factor in this study. This means that paracetamol gives a very significant impact and is likely to provide healing for pharyngitis patients. The second node as a differentiator is indicated by the rest variable, then the third node is indicated by the variable of vitamin administration $(5)$. In giving paracetamol it is known that out of 60 patients, 81.7% recovered and 18.3% did not recover, and in patients who did rest, 89.6% recovered and 10.4% did not recover, but on the contrary, in patients without rest obtained results 10.4% did not recover and 89.6% recovered. As well as giving vitamins, the results were 85.7% cured, and 14.3% did not recover.

**DISCUSSION**

**Factors Affecting the Healing of Viral Pharyngitis Patients**

The symptoms that arise in acute pharyngitis depend on the accompanying
microorganism. Acute pharyngitis is caused by bacteria severe headache, fever or, malaise, painful swallowing, vomiting, and possibly coughing but rarely occurs. Pharyngitis due to bacterial infection group A streptococci can be estimated by using the Center criteria, namely fever, anterior cervical lymphadenopathy, tonsilar exudate, and no cough. Pharyngitis caused by viruses usually has symptoms of a sore throat severe and may be accompanied by coughing, hoarseness, and substernal pain. Fever, chills, malaise, myalgia, and headache may also occur. Then, symptoms of fungal pharyngitis are sore throat and swallowing pain. On examination, white plaque appears hyperemic oropharynx and another pharyngeal mucosa.

Pharyngitis in this study has been confirmed through a swab test, namely RADT (Rapid Antigen Detection Test) that the cause is a virus, almost all patients get negative results for bacteria, so it can be said to be positive due to viruses. In diseases caused by viruses, it is not rational to be treated with antibiotics, where the virus that causes acute pharyngitis can heal by itself (self-limiting disease) for approximately one week.

Classification and Regression Trees (CART) is a method or algorithm of the decision tree technique. CART is a nonparametric statistical method that can describe the relationship between the response variable (dependent variable) and one or more predictor variables (independent variables). According to Breiman et al (1993), when the response variable has continuously shaped the method used is a regression tree (regression trees), whereas if the response variable has a categorical scale the method used is the classification tree method (classification trees).

The response variable in this study has a categorical scale, so the method to be used is the tree classification method. Binary Trees provide an interesting and often enlightening way to view data in a classification or regression problem. They should not be used to override other methods. Through the CART method applied in this study, it obtained data that the things that had a significant effect on the recovery of viral pharyngitis patients were giving paracetamol, rest, and vitamins. Paracetamol, which is a symptomatic drug, is very likely to give CART, it does not represent the opportunity for rest to improve recovery, but in theory and research, rest can increase the immune system through stimulation of pro-inflammatory hormones wherein this condition the adaptive immune response is stimulated and increases so that the inflammatory response as a marker increases. So the researchers can conclude that the process of viral eradication is increased, and more foreign bodies are attacked and paralyzed in the first immunity (initial) which correlates with an increase in the inflammatory response in the beginning. The provision of vitamins provides a great opportunity for recovery where the specific vitamins that are given here are vitamins C and B complex, which can act as a modulating agent for cellular immunity, especially those related to CD8 cells and NK cells.

Anti-inflammatory administration provides a chance of cure but is very small, and is not illustrated in the CART tree, where in theory anti-inflammatory can function to treat pain and swelling (swelling and redness) and relieve fever. Anti-inflammatory is a series of immunoregulatory molecules that control the pro-inflammatory response of the immune process. This stimulation causes the release of inflammatory mediators such as histamine, serotonin, bradykinin, and prostaglandins which cause an inflammatory reaction such as heat, pain, redness, and swelling, and are accompanied by impaired function. The patient's recovery is strongly associated with the disappearance of signs and symptoms, from the doctor's history, the observed symptoms of inflammation can be reduced by administering anti-inflammatory, but it is not certain that the causative factor, namely the virus has been cleared maximally, because anti-inflammatory has something to do with controlling the pro-inflammatory response. This resulted in a relatively low correlation between anti-inflammatory administration and the recovery of viral pharyngitis pa-
patients on the CART method test results and was statistically insignificant using Chi-square.

a) Effect of Paracetamol on the recovery of patients with Acute Pharyngitis

In this study, the results showed that paracetamol has the largest contribution and contributor to the opportunity to cure viral pharyngitis patients. Symptoms accompanying viral pharyngitis patients in this study ranged from fever 80%, dizziness 36.67%, cough 60%, runny nose 50%, and sore throat 36.67%. Giving paracetamol as symptomatic therapy, namely relieving symptoms of fever, because paracetamol acts as an antipyretic. Paracetamol is the first choice in treating symptoms of fever, one of the most popular analgesics and most commonly used antipyretic drugs worldwide, available without a prescription, both in mono and multi-component preparations, and the drug of choice in patients who cannot be treated with anti-nonnestoidal inflammatory drugs (NSAIDs), such as people with bronchial asthma, peptic ulcer disease, hemophilia, people who are sensitive to salicylates, children under 12 years, pregnant or breastfeeding women. It is recommended as a first-line treatment of pain associated with osteoarthritis. The mechanism of action includes peripheral effects (inhibition of COX), and central neuronal pathways (COX, serotonergic descent, L-arginine on the cannabinoid system pathway. Paracetamol is a drug with good tolerance and side effects occur in the gastrointestinal tract. In connection with this, the administration of paracetamol, in this case, is as a fever therapy (antipyretic), where inflammation is a natural response, as a marker of the body's defense process which manifestations of symptoms in the form of tumor, rubor, heat, and dolor. The patient is declared cured, which is the loss of signs and symptoms, due to heat (heat) being the main symptom that can be felt and measured fever (heat) is a manifestation of the body's defense response that mediates inflammation. So this can lead to antipyretic administration in this case paracetamol contributes to the greatest opportunity for patient recovery.

b) Effect of Rest on the Healing of Viral Acute Pharyngitis Patients

Rest had an effect on the patient's recovery where the results were that patients who did rest were 89.6% healed and 10.4% did not recover, but on the contrary, 10.4% did not recover and 89.6% recovered. Rest in this case sleep supports the initiation of an adaptive immune response. The attack antigen is picked up and processed by antigen-presenting cells (APCs) which present the antigen fragments to helper T (Th) cells, with the two types of cells forming 'immunological synapses'. The release of interleukin (IL) -12 together with APC induces a Th1 response that supports antigen-specific cytotoxic T cell function and initiates antibody production by B cells. This response ultimately results in long-lasting immunological memory for the antigen. Sleep, particularly slow wave sleep (SWS), and the circadian system play a role in producing a pro-inflammatory hormonal environment with increased growth hormone and prolactin release and decreased levels of the anti-inflammatory stress hormone cortisol. Hormonal changes support the initial steps in producing an adaptive immune response in the lymph nodes. It can be analogized that the stimulation of B lymphocytes and T lymphocytes forms a memory, which supports the consolidation stage in the same attack by the same antigen (second infection).

Measurement of the immune response in adult female subjects who were exposed to bed rest for a long time showed that adult female volunteers (25-40 years) (n = 24) were maintained in a quiet sleep position (6 degrees tilt) head-down bed-rest (HDBR) for 60 days: 8 with HDBR only, 8 with HDBR and regular muscle training, and 8 with HDBR and dietary protein supplements. The primary antibody production rates of the HDBR plus exercise group increased more rapidly (P = .01) and to a higher level than the HDBR-only group (P = .03) and the HDBR plus diet group (trend P = .08). The levels of secondary antibody production between the 3 groups were sim-
The role of vitamin C in lymphocytes is less clear, but it has been shown to increase B and T cell differentiation and proliferation, possibly due to its gene-regulatory effects. Vitamin C deficiency leads to compromised immunity and a higher susceptibility to infections. In turn, infection significantly impacts vitamin C levels due to increased inflammation and metabolic requirements. Furthermore, supplementation with vitamin C appears to be able to prevent and treat systemic infections. Vitamin C prophylaxis is required to prevent infection which provides insufficient, if unsaturated (ie 100-200 mg/day) plasma levels, which optimizes cell and tissue levels. Conversely, good infection treatment requires a higher vitamin dose (gram) to compensate for the increased inflammatory response and metabolic demand.

Vitamin B6 is very important in the biosynthesis of nucleic acids and proteins, therefore the effect on immune function is logical because antibodies and cytokines are formed from amino acids and require vitamin B6 as a coenzyme in metabolism. Human studies show that vitamin B6 deficiency impairs lymphocyte maturity and growth, antibody production, and T cell activity. The mitogenic response of lymphocytes is impaired by decreased dietary vitamin B6 in elderly subjects and is reversed by the administration of vitamin B6. Deficiency effects were seen in decreased DTH antibody receptors, IL-1-b, IL-2, IL-2 receptors, NK cell activity, and 62-64 lymphocyte proliferation. Marginal vitamin B6 deficiency alters the percentage of T-helper cells and slightly decreases immunoglobulin D65. Marginal vitamin B6 deficiency in the elderly is associated with a decreased
number and circulating T-lymphocyte function which can be corrected by short-term (6 weeks) supplementation with 50 mg of vitamin B6/day 66. Decreased IL-2 production, T lymphocyte count, and T proliferation Lymphocytes were observed in subjects experiencing vitamin B6 depletion, which suggests that vitamin B6 deficiency suppresses Th1 and increases Th2 cytokine-mediated activity. (10).

B vitamins are essential nutrients, including thiamine, riboflavin, niacin, vitamin B6, folic acid, vitamin B12, biotin, and tamarind pantothenate. Vitamin B12 is involved in carbon-1 metabolism and there are interactions with folate metabolism. In the vitamin B12-containing state, the irreversible reaction to form 5-methyl tetrahydrofolate (THF) produces an inactive form of folate if it is not declined with methionine synthase. THF 5-methyl can cause folate deficiency secondary to decreased thymidine and purine synthesis and then DNA and RNA synthesis, leading to changes in immunoglobulin secretion. A human study of vitamin B12 deficient patients evaluated changes in immunological indicators after vitamin B12 administration. In these patients, significant decreases were found in the number of lymphocytes and CD8 cells and the number of CD4 cells. In addition, the findings indicated a very high CD4/CD8 ratio and suppressed NK cell activity. Supplementation with vitamin B12 reverses this effect suggesting that it can act as a modulating agent for cellular immunity, especially concerning CD8þ and NK 73 cells. In elderly subjects (aged 70 years) who received more than 4 months in addition to a regular diet, formula Specific nutrients, including nutrients, vitamin E, 8 mg of vitamin B12, and 400 mg of folic acid, showed increased NK cell cytotoxic activity in research subjects (10).

Vitamins support immune function so that they can increase innate immunity in the elderly. A defenseless adult (aged 65 years) with low serum vitamin B12 concentrations has an antibody response to the pneumococcal polysaccharide vaccine. Some of these studies demonstrate the importance of sufficient vitamin B12 status to maintain an adequate immune response, especially in elderly people who have a high percentage (up to 15%) of low serum B12 concentrations.

d) Effect of Anti-inflammatory on the Cure of Viral Acute Pharyngitis Patients.

Infection is the invasion or colonization of pathogenic microorganisms into the body. The disease occurs when an infection causes various changes in the state of health. The presence of several types of microorganisms in a part of the body that is not a proper place for these microorganisms can also be referred to as infection and can cause disease. The period of SBHGA infection occurs in the season cold and early spring in temperate climates, in tropical climates like Indonesia, the highest incidence occurs in the rainy season, so patients with pharyngitis can warm themselves in winter and avoid consuming cold water (ice water).

Inflammation is a condition in response to tissue injury or infection, which can occur in the oral cavity. Inflammation that occurs will go through the body's defense mechanism caused by a response to the influence of local tissue damage, the influence of tissue damage can occur in the presence of bacteria. In particular, I think it is important to properly define the terms 'inflammation' and 'infection'. Just by reading the definition of inflammation on Wikipedia, we learn that 'inflammation is part of the complex biological response of vascular tissue to noxious stimuli, such as pathogens, damaged cells, or irritants (11).

This Result of two randomized control trials has shown that corticosteroid use can reduce the incidence of treatment failure and shorten the time to clinical stability in patients with community-acquired pneumonia. This does not apply to patients with severe influenza virus infection. Our results revealed that steroid treatment prolonged the duration of MV and ICU stay. The effect of steroid use on oxygenation could not be subjected to meta-analysis, owing to the diversity of data. Several studies reported that systemic corticosteroid treatment...
had no discernible influence on the improvement of blood oxygen saturation of patients with severe influenza (11).

CONCLUSION
The factors are can affect the recovery of viral pharyngitis patients are giving paracetamol, rest, giving vitamins, and anti-inflammatories. Paracetamol gives the greatest chance of recovery, after that rest and finally giving vitamins.

SUGGESTION
Based on the research that has been done, some suggestions can be considered for further research, that is:
1) In pharyngitis caused by viruses, antibiotics are not related to the patient's recovery, so it can be said that there is no benefit, therefore antibiotics for viral pharyngitis are not recommended, and for pharyngitis whose cause is unknown, antibiotics can be postponed for at least 3 days considering 90% of causes of acute pharyngitis are preceded by viruses.
2) The time used to assess the patient's recovery can be extended for 5 or 7 days considering that viral infections are self-limiting diseases if they are not accompanied by high fever.
3) Paracetamol is very important and the earliest therapy in the treatment of viral pharyngitis accompanied by fever symptoms. Viral pharyngitis patients are strongly advised to take rest and take vitamins to promote recovery.
4) Avoiding cold weather or areas and consuming cold water (ice water) to prevent bacterial infection that causes acute pharyngitis

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