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Literature Review

MANAGEMENT PATIENT OF SWINE INFLUENZA

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ABSTRACT

Influenza is an acute respiratory diseases caused by various influenza virus which infect the upper and lower respiratory tract and often accompanied by systemic symptoms such as fever, headache and muscle pain. Influenza spreads through the air. Swine influenza comes from swine and can cause an outbreaks in pig flocks. Even this is a kind of a rare case but the swine influenza could be transmitted to human by direct contact with infected swine or through environment that already being contaminated by swine influenza virus. There are 3 types of swine influenza virus namely H1N1, H3N2 and H1N2. Type H1N1 swine-virus had been known since 1918. Avian influenza virus infection is transmitted from one person to another through secret containing virus. Virus is binded into the mucous cells of respiratory tract before it is finally infecting the cells itself. Management patients with H1N1 influenza is based on the complications and the risk. Besides, it is also need to consider the clinical criteria of the patient. Therapy medicamentosa is applied to the patients by giving an antiviral, antibiotics and symptomatic therapy. Prevention can be done by avoid contact with infected animal or environment, having antiviral prophylaxis and vaccination.

Key words: *influenza, swine, infection, H1N1, management patient*

ABSTRAK

Influenza atau flu merupakan penyakit pernafasan akut yang disebabkan oleh bermacam virus influenza yang menginfeksi saluran pernafasan bagian atas maupun saluran pernafasan bagian bawah serta seringkali disertai gejala sistemik seperti demam, sakit kepala dan nyeri otot. Flu dapat menular melalui udara. Flu babi adalah jenis flu yang berasal dari babi dan dapat mewabah pada kawanan ternak babi. Flu babi dapat menular ke manusia melalui kontak langsung dengan hewan babi atau lingkungan yang telah terinfeksi virus flu babi, meskipun hal ini terbilang jarang terjadi. Terdapat 3 jenis virus flu babi yaitu H1N1,H2N3 dan H1N2. Virus flu babi tipe H1N1 telah diketahui sejak tahun 1918. Infeksi virus avian influenza ditransmisikan dari satu orang ke orang lain melalui pembawa virus tertentu. Virus melekat pada sel mukosa pada saluran respirasi sebelum akhirnya menginfeksi sel tersebut. Penatalaksanaan pasien dengan H1N1 didasarkan pada komplikasi dan risiko yang mungkin terjadi. Selain itu, perlu juga ada pertimbangan mengeneai criteria klinis yang dimiliki pasien. Terapi medikamentosa diterapkan kepada pasien dengan memberikan antivirus, antibiotik dan terapi sistomatis. Tindakan pencegahan dilakukan dengan cara menghindari kontak langsung dengan hewan maupun lingkungan yang terinfeksi virus, serta melakukan profilaksis antivirus dan vaksinasi.

Kata kunci: *flu, babi, infeksi, H1N1, penatalaksanaan pasien*

INTRODUCTION

Influenza is an acute respiratory diseases caused by various influenza virus that infect the upper and lower respiratory tract and often accompanied by systemic symptoms such as fever, headache and muscle pain. Influenza spreads through the air. Several epidemical evidence of influenza cases showed high morbidity rate especially for patient with higher risk caused by pulmonary complication.[1,2]

Swine influenza comes from pig and could cause an outbreaks in pig flocks. Clinical signs of this disease are fever, appetite loss, weight loss, sluggishness, cough, sneezes, cold and asphyxiate. Pig incubation usually given

in 1 to 3 days. It has low mortality rate (1% to 3%) and the infected animals are usually getting better in 5 until 7 days. Some pigs are showed a severe pneumonia symptoms as a major cause of death. Secondary bacteria infection could occurs. The process of viral internalization could be happened within 24 hours after infection and become disease after 7 to 10 days.[3,4,5]

Animal to human swine influenza virus transmission is rarely happen. But it can be transmitted through a direct contact between infected pig and human, also by living in environment that already being contaminated with swine influenza virus under special circumstances. Once human are infected, they could transmitted the virus to one and another with the same way of influenza virus works through cough or sneeze.[3]

There are 3 type of swine influenza virus namely H1N1, H3N2 and H1N2. Swine virus type H1N1 has been known since 1918, causing pandemic and death of 40-50 million people. This virus was dissapear until in year 1957 Influenza A (H2N2) pandemic was infected 250.000 people in Hongkong within 3 weeks before it abated. In 1968, another influenza pandemic caused by Influenza A (H3N2) was named Hongkong Influenza. In 1977, epidemic swine influenza (H1N1) was re-emerge in Fort Dix, New Jersey and infected more than 200 people, some of them were severe and one was dead.[6,7]

In March 2009, Influenza A (H1N1) first emerged in Mexico, then it was reported in United States and spread in some parts of other countries, including Indonesia. On April 2009, WHO was announced the occurrence of the pandemic phase 5. Until October 2009, 195 countries were reported their Influenza A (H1N1) cases.[5,8]

INFLUENZA A VIRUS

Influenza virus A is the RNA virus which is the member of the Orthomyxoviridae family. There are 3 type of influenza virus which are Influenza virus A, B and C. RNA nucleus consist eight segments of genee and surrounded by 10 layers of protein (influenza A) or 11 layers of protein (influenza B).[2]

Influenza virus A is divided into subtype based on two protein on the surface, Hemaglutinin (H) and Neuraminidase (N). There are 16 kind hemagglutinin subtype and 9 neuraminidase subtype.Virus type is based on these proteins, for example Influenza A subtype H3N2 which express Hemaglutinin 3 and Neuraminidase 2. Influenza A has 16 kind of H subtype and 9 kind of N subtype. Geneome Influenza A and Influenza B have eight segments single stranded RNA which coding the structural and non structural protein.[3]

Influenza A is more pathogeneic than Influenza B. Influenza A is zoonosis infection and usually infect the most of birds, pigs, horse, dogs and humans. Reasort genees segment can occur when influenza virus infects a cell simultaneously.[2]

H1N1 virus called as swine influenza because the laboratory test showed that several genees in this virus was equal to influenza virus that infect the swine in North America but further studies show that these two viruses are different. HINI virus has 2 genees of the common influenza virus which usually possessed by European swine called gene NA segment, gene HA segment, gene NP segment and gene NS segment from the classical swine and triple reasortment swine. PB2 and PA derived by triple reasortment swine which come from avian species and PB1 derived by swine triple reasortment from human.[9]

PATHOPHYSIOLOGY

Avian influenza virus infection is transmitted from one person to another through secret containing virus. Virus is binded into the mucous cells of respiratory tract before it is finally infecting the cells itself. Influenza infection is occured after secret transfer in the exhalation from one to another. If it is not neutralized by antibodies, virus would strike the respiratory tract and the cells. In host cell, after cellular dysfunction and degeneeration happens, along with replication of the virus and release of viral replication. Almost all cells in the respiratory could support replication of the virus. After the virus has led to respiratory tract infections, the virus infects many cell replication and damage epithelial cilia through direct cytopatic effect or apoptosis. The amount of virus in the respiratory tract is correlated with the severity of the disease and the degree of inflammatory cytokine pro-kemokin. Increased levels of cytokines pro inflammatory such as interferon α, interleukin 6, tumor necrosis factor occur in the blood and respiratory secretions. And may contribute to systemic symptoms and fever. Duration of viral replication depend on the age and the invulnerabILIty status. Shelding usually lasting during three to five days in the adult, often reaches the second week in children, and could survive for weeks on a host immunocompromised.[1]

CLINICAL SYMPTOMS

After the incubation period is complete 1- 5 days, the onset of disease is tend to increase rapidly were actually causing symptoms. Clinical symptoms divided into specific symptoms and non specific, based on CDC (2009) stricken with symptoms reported is: cough (98 %), febris (96%), weak (89 per cent), headache (82 %), cold (80 %), muscle pain (80 %), nausea (55 %), abdominal pain (50 %), diarrhea (48 %), shortness of (48 %), joint pains (46 %). The symptoms above are known as ILI-fever (Influenza Like Illnes) which has temperature more than 39,8^{o}C accompanied by one or more symptoms of cough ingest, pain on swallowing, without any causes other the influenza.[10]

There are mild criteria (outpatient with surveillance) such as without a symptom or symptoms at least, without fever tightness, no pneumonia, no comorbid and young age. Middle criteria (isolation room) such as comorbid factor, asfixia, pneumonia, old age, pregnancy, diarrhea and vomiting. Severe criteria (ICU) such as pneumonia broad, breath failure, sepsis, shock, declining consciousness, Artery Respiratory Distress Syndrome (ARDS) and Multiple Organ Dysfunction Syndrome (MODS).[8]

CASE IDENTIFICATION

Definitin of cases

A. Cases of alleged (suspect): someone with symptoms ILI accompanied by history:
   - Contact with the confirmation influenza virus H1N1 2009, 7 days before sick.
   - Visit where areas there is one or more cases of influenza virus with new confirmation H1N1 2009, 7 days before ILI
   - Reside in areas where there is one or more cases confirmation.

B. Probable case: someone with symptoms alleged (suspect positive laboratory result of influenza but cannot detect the subtype, with the ILI in accordance with clinical symptoms who died because of failed cause of breath which could not be explained and related with epidemology with a case or confirm probable.

C. Must case (confirmation examination): someone from the laboratory is infected by a new influenza virus H1N1 2009 through one or more examination such as Real-Time (RT) PCR, virus culture and increasing 4 times in antibiotic specific influenza a H1N1 viruses with new tests in the neutralization.[8]

CLINICAL FINDINGS

Patients with must case (confirmed) H1N1 virus 2009 with symptoms of the ILI to pneumonia based on the degrees:

1. People with mild state (confirmed): must be the case of the symptoms of ILI fever > 38^0c (cough without pain ingest) with ILI symptom.
2. Heavy state: someone with a must case be obtained (confirmed) clinical syndrome which is ILI accompanied by respiratory infection is a low breath and pneumonia, failed a breath, dehydration and until death. Occurring severe condition previously to be a chronic disease.

Weight degree criteria : fever > 38^o C, Rr> - 24 x/ minutes, hipoxia (SO2 < 90 %), disfungsi organ hipotensi (<90/60), declining conscious, tachicardia, hiperglikemia, photo thoraxabnormal.[11]

Complication ILI :

1. Severe primary viral infection by fail of breath: happens when lung infection viruses infect with clinical symptoms, is not good in the thorax to infiltrate intersisial, and there's a sign ards with severe hypoxia.
2. Pneumonia bacteria, patients often complained of a fever and respiratory symptoms arise who had already died down.Bacterial pathogenes to infect *Staphylocuccus aureus* and are often *Steptococcus pneumonia* and *Hemofilus influenza*.
3. A bacterial virus pneumonia and pneumonia, often occurs in patients who had the disease; a chronic previous (PPOK asthma, DM, GGK, heart failure etc)

Patients with ILI having a high risk occurring complication such as children under 5 years, age above 65 years, child or adult who gets therapy aspirin long term, pregnant woman, patients with comorbid factors and immunodeficiency.[4]

LABORATORY EXAMINATION

Virology Examination

A lot of tests available to detect influenza virus. This test has different sensitivity and specificity. Including several examinations which can be seen in Table I.

Specimens can be obtained through: nasopharyngeal swab, aspirate (wash or nasal swab) swab the endotracheal lavage, bronchoalveolar lavage (BLA), combination of nasopharyngeal or oropharyngeal swab. Oropharyngeal. Tests should be done on the first week until healing (2 - 3 weeks after the onset of disease). Examination of virology should be done in patients with an indication of in-patient medium and heavy.[10,12]

Hematology Examination

DL examination (Hb, Platelets, leucocyte, count of leucocyte, a lymphocyte total). Other examination depends on identification, such as chemicals analysis of the blood. To remove the diagnosis of appeals examined IgG and IgM opposed to culture week and gall *Salmonela thyposa*.

Radiology Examination

Examination of the lateral thoracic pa and their routines; if necessary you can be intensified CT scans in accordance with the indications.

Microbiology Examination

If in thought occurring co-infection by bacteria can detect by sputurn (smear and culture), culture blood and urine based on identification.[10,12]

Table 1. Comparison of sensitivity and specificity of influenza and diagnostic test the CDC, 2009.

Influenza Diagnostic Tests	Method	AvailabILIty	Typical Processing Time[2]	Sensitivity[3] for 2009 H1N1 influenza	Distingushes 2009 H1N1 influenza from other influenza a viruses ?
Rapid influenza diagnostic test (RIDT)[4]	Antigene detection	Wide	0.5 hour	10 – 70 %	No
Direct & indirect immunofluorescence assays (DFA and IFA)[5]	Antigene detection	Wide	2 – 4 hours	47 – 93 %	No
Viral isolation in tissue cell culture	Virus isolation	Limited	2 – 10 days	-	Yes[6]
Nucleic acid amplification test (including rRt – PCR)[7]	RNA detection	Limited[8]	48 – 96 hours (6 – 8 hours to perform test)	66 – 100%	Yes

Table 2. The organisation antiviral drug use, organisation, 2009

Population	Pandemic (H1N1) influenza virus 2009	Multiple co-circulating influenza A sub-types or viruses with different antiviral susceptibILIties	Sporadic zoonotic influenza A viruses including H5N1
Mild to moderate uncomplicated clinical presentation			
At-risk[a] population	Oseltamivir or zanamivir (04)	Zanamivir or oseltamivir plus M2 inhibitor[b] (10)	Oseltamivir or zanamivir
Otherwise healthy[c]	Need not treat (03)	Need not treat (09)	Oseltamivir
a. Infants and children aged less than 5, the elderly (>65years), nursing home residents, pregnant women, patients with chronic co-morbid conditions such as cardiovascular, respiratory or liver disease, diabetes, and those with immunosuppression related to malignancy, HIV infection or other disease.			
b. Amantadine should not be used in pregnant women (recommendation 12)			
c. All those not covered by the at-risk definition above.			
Severe or progressive clinical presentation[d]			
At-risk[a] population	Oseltamivir (01) (zanamivir should be used where virus is known to be resistant to oseltamivir, or if oseltamivir unavailable) (02)	Oseltamivir plus M2 inhibitor[b], or zanamivir (05,06,07)	Oseltamivir plus M2 inhibitor
Otherwise healthy			
d. See section 2 Case Description. Would include all patients requiring hospitalization			

MANAGEMENT

Management new patients with influenza a H1N1 2009 was based on some new consideration of the degree of the sick the risk of complications and the results of laboratorium with the criteria consideration adjusted therapy the patient whether policlinic, in-patient, the icu. Almost of influenza cases caused by a new influenza virus H1N1. There is no complications, short duration and the provision of anti virus tend to be needed for the majority of patients.[13]

Management in general

1. Mild case : supportive therapy such as providing an antipyretic rehidration
2. Sufficient case : symptomatic therapy, rehydration, antiviral, antibiotic, if secondary infection was proven, fluids and nutrition therapy
3. Severe case (care ICU) : correction hypoxia with oxygene provision and ventilator assemblies for management strategy of ARDS, monitor hemodynamics for septic shock management, antiviral and antibiotic, parenteral and enteral nutrition

Table 3. Recommendations antiviral a dose of influenza a new H1N.

Oseltamivir	
Oseltamivir is indicated for treatment of patients one year of age and older. For adolescents (13 to 17 years of age) and adults the recommended oral dose is 75 mg oseltamivir twice daily for 5 days. For infants older than 1 year of age and for children 2 to 12 years of age recommended doses are as follows :	
15 kg or less	30 mg orally twice a day for 5 days
15 – 23 kg	45 mg orally twice a day for 5 days
24 – 40 kg	60 mg orally twice a day for 5 days
40 kg	75 mg orally twice a day for 5 days
Zanamivir	
Zanamivir is indicated for treatment of influenza in adults and children (>5 years). The recommended dose for treatment of adults and children from the age of 5 years is two inhalations (2 5mg) twice daily for 5 days	

Table 4. Recommendation for giving antibiotics to influenza patients

For influenza not complicated by pneumonia a. Previously well adults with acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics. b. Antibiotics should be considered in those previously well adults who develop worsening symptoms (recrudescent fever or increasing dyspnoen). c. Patients at high risk of complications or secondary infection should be considered for antibiotics in the presence of lower respiratory features. d. Most patients can be adequately treated with oral antibiotics. e. The preffered choice includes co-amoxiclav or a tetracycline f. A macrolide such as clarithromycin (or erythromycin) or a fluoroquinolone active against *Streptococcus pneumoniae* and *Streptococcus aureus* is an alternative choice in certain circumstances.
Non-severe influenza-related pneumonia a. Most patients can be adequately treated with oral antibiotics b. Oral therapy with co-amoxiclav or a tetracycline is preffered c. When oral therapy is contraindicated, recommended parenteral choices include iv co-amoxiclav, or a second- or third-geneeration cephalosporin (cefuroxime or cefotaxime). A macrolide (erythromycin or clarithromycin) or a fluoroquinolone active against *S. pneumonia* and *S. aureus* is an alternative regimen where required, e.g. for those intolerant of penicillins. Currently, levofloxacin and moxifloxacin are the only recommended fluoroquinolones licensed in the UK.
For severe influenza-related pneumonia a. Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics. b. An iv combination od a broad-spectrum β-lactamase stable antibiotics such as co-amoxiclav or a second-geneeration (e.g. cefuroxime) or third-geneeration (e.g. cefotaxime) cephalosporin together with a macrolide (e.g. clarithromycin or erythromycin) is preffered. c. An alternative regimen includes a fluoroquinolone with enhanced activity against pneumococci together with a broad-spectrum β-lactamase stable antibiotic or a macrolide. Currently, levofloxacin is the only fluoroqionolone with an iv formulation licensed in the UK.

The management of patients are not separated from the medikamentosa therapy provision:

Antivirus

Influenza virus A H1N1 sensitive to neuraminidase inhibitor (Nals) namely oseltamivir and zanamivir, but resistant to amantadine or rimantadin. The antiviral could reduce the disease alleviate symptoms, for illness, progresivity at preventing disease and death and decrease hospitalization. Based on the research the antiviral beneficial is given the maximum 48 hours after the onset of the disease, 5 days in therapy for patient hospitalization, patients with severe infections or in ICU patients could be given more therapy.[8,13]

Recommendations given of the antiviral that is hospitalized patients with the confirmation, probable or suspect, patient has a high risk, if there are complications and patients with chronic disease.

Antibiotics

Antibiotics can be given if the result of examination positive and secondary infection symptoms is caused by bacteria. Recommendation for giving antibiotic to patients with influenza depend on British Thoracic Society (BTS) can be seen in table 2

If based on clinical and radiological, influenza - the assessment of the weight of pneumonia associated pneumonia can stamp use standard score as PSI, CRUB

Table 5. Regimen antibiotics for infection by bacteria in patients after the flu.[14]

Antibiotic regimen (doses provided are for adults)	Antibacterial activity	Ecological risk
Outpatients		
Doxycydine 200mg once and then 100mg every 25h	SP, strep, H, MC, MSSA, MRSA, atypicals	Low
Co-amoxiclav 625mg every 8h	SP, strep, MC, MSSA, GNEB	Moderate
Erythromycin 500mg every 6h or clarithromycin 500mg every 12h	SP, strep, MC, MSSA, atypicals	moderate
Levofloxacin 500mg every 24h or moxifloxacin 400mg every 24h	SP, strep, H, MC, MSSA, GNEB, atypicals	High
Non-severe inpatients oral (as for outpatients [see above)]		
Non-severe inpatients, iv (for non-severe inpatients unable to take oral therapy)		
Benzylpenicillin 1.2g every 6h	SP, strep	low
Amoxicillin 500mg to 1g every 8h	SP, strep, H	moderate
Clarithromycin 500mg every 12h	SP, strep, MC, MSSA, atypicals	moderate
Flucloxacillin 1g every 6h plus clarithromycin 500mg every 12h	SP, strep, MC, MSSA, atypicals	moderate
Co-amoxiclav 1.2g every 8h	SP, strep, H, MC, MSSA, GNEB	moderate to high
Amoxicillin 500mg to 1g every 8h plus clarithromycin 500mg every 12h	SP, strep, H, MC, MSSA, atypicals	moderate to high
Cefuroxime 750mg every 8h or cefotaxime 1g every 8h	SP, strep, H, MC, MSSA, GNEB	high
Levofloxacin 500mg every 24h	SP, strep, MC, MSSA, GNEB, atypicals	high
Severe inpatients (patients who require critical care, whether a bed is available or not; all regimens to be given iv initially)		
Co-amoxiclav 1.2g every 8h plus clarothromycin 500mg every 12h	SP, strep, H, MC, MSSA, GNEB, atypicals	moderate to high
Cefuroxime 750mg every 8h or cefotaxime 1g every 8h plus clarithromycin 500mg every 12h	SP, strep, H, MC, MSSA, GNEB, atypicals	high
Levofloxacin 500mg every 24h	SP, strep, H, MC, MSSA, GNEB, atypical	high
Benzylpenicillin 1.8 – 2.4 g every 4h plus clindamycin 600mg every 6h	For proven life-threatening Lancefield group A, C or G streptococcal infection	high
MRSA (in the UK, only for patients with proven MRSA)		
Linezolid 600mg iv / oral every 12h	SP, strep, MSSA, MRSA	low
Other agenets that may be useful in specific circumstances (e.g. if microbiological results are available)		
Trimethoprim 200mg oral every 12h	H, some MSSA/MRSA, some GNEB	low
Co-trimoxazole 960mg oral every 12h (iv; 960mg to 1.44g every 12h)	SP, strep, H, MC, MSSA, some MRSA, GNEB	low to moderate
Piperacillin/tazobactam 4.5mg iv every 8h	SP, strep, H, MC, MSSA, GNEB	moderate
Tigecycline 100mg iv once then 50mg is every 12h	SP, strep, H, MC, MSSA, MRSA, GNEB, atypicals	unclear, probably low to moderate

– 63. Regimen antibiotics for bacterial infection in patients with swine flu can be seen in Table 5

Cortikosteroid

Not give a corticosteroid routine in patients by a new, H1N1 influenza based on reports of Mexico granting a corticosteroid unprofitable.A corticosteroid use higher doses will cause serious side effects due to rising replication of the virus and improve the germ opportunistic infection.[11]

PREVENTION

1. Be careful when contact with persons infected who is someone who can transmit H1N1 virus days before the onset of diseases such as 1 to 7 days, and after the onset of disease (24 hours no fever). An act done is cover nose and mouth or use a mask, wash hand soap and water or alcohol in the normal time 15 until 20 seconds,

Table 6. Antiviral prophylaxis drugs the who recommendations

Agenet	Age Groups (yrs)					
	Duration	1 - 6	7 - 9	10 - 12	13 – 64	≥65
Oseltamivir						
	Begin as soon as exposure identified and continue for 5 -7 days after last known exposure	Weight adjusted doses : - 30 mg/day for ≤15 kg - 45 mg/day for ≤15 kg - 60 mg/day for ≤15 kg - 75 mg/day for ≤15 kg			75 mg/day	75 mg/day
Zanamivir						
	Begin as soon as exposure identified and continue for 5 -7 days after last known exposure	1 – 4 yrs : NA	5 – 6 yrs : 10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily

eat nutritious food, less migration to the epidemic and pandemics.

2. Antiviral prophylaxis can be given to someone with the acts of close contact patients confirmation, case probable, infectious, suspect during the period of high risk patients experienced complications and health officers contact with confirmation, cases of patients probable, suspect infectious table during the period. [14]

Vaccination CDC identify priority to get population main vaccination are pregnant woman, all medical society, age 25 - 64 by the risk of complications and someone who care for infants under 6 months.[13]

SUMMARY

Influenza is respiratory infections caused by influenza virus a subtype H1NI. Virus H1N1 could cause a new transmission between humans. It is because a mutation in the virus.Virus H1N1 influenza totally different with the H1N1 virus seasonal.Known for its clinical symptoms I*nfluenza Like Illness* (ILI) WHO clinically divide light being, weight. Management patients with the H1N1 influenza a new year, in some degree was based on the consideration of the complications and the risk of a laboratory. Consideration also according to this criteria of patients are policlinic, inpatient, icu. Therapy medikamentosa be granted antiviral, antibiotics and therapy symtomatic. Prevention is to avoid contact with an infected, the antiviral prophylaxis, and vaccination.

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