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Current Issue

Vol 8 No 1 (2021): Effect Of Dyspnea On The 1-Year Survival Of Patients With Progressive Disease At Cipto Mangunkusumo Hospital

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Abstract

Background: Dispnea as a subjective sensation is a sign of certain underlying disease which need to be diagnosed and treated to prevent the mortality, especially in patients with progressive disease. Previous study has shown that patients with dyspnea at admission have higher mortality.
Objective: To determine the association between dyspnea with 1 year survival in patients with progressive disease who were admitted to RSCM. Methods: A retrospective cohort study was conducted by tracing the medical records of 155 patients with progressive disease who were hospitalized at RSCM during August 2018 until December 2019. Recruited subjects were adults patients who 18 years above diagnosed with COPD, heart failure, malignancy or CVD. Identity, dispnea, and survival data were collected through medical records. Statistical analysis was conducted by using multivariate and Kaplan Meier analysis using SPSS software. Results: In this study, the survival rate of patients with progressive disease who were admitted to RSCM in August 2018-December 2019 was 34.8% with a mean survival of 163 days and a median survival of 72 days. Among the patients 49% had dyspnea. The survival rate of patients with dispnea was 11% with a mean survival of 115 days and a median survival of 29 days. Dyspnea was significantly associated with survival with p < 0,05 and adjusted HR 1.928 (95% CI: 1.225 - 3.03). In the subgroup analysis of heart failure, malignancy, and CVD, dispnea was associated with survival with p<0,05 and the HR value for every group 16,59 (95% CI: 2,20 – 124,73), 2,18 (95% CI: 1,33 – 3,58), and 2,90 (95% CI: 1,34 – 6,28). Conclusion: Dyspnea has significant association with survival.
Key words: dyspnea, progressive disease, survival.

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Effect Of Dyspnea On The 1-Year Survival Of Patients With Progressive Disease At Cipto Mangunkusumo Hospital

Vol 8 No 1 (2021)

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Abstract

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Key words: dyspnea, progressive disease, survival.

Blood CD4 And CD8 Count as predictors of 30 Days mortality Insevere Pneumonia patients at the dr. Ciptomangunkusumo national general Hospital Jakarta

Vol 8 No 1 (2021)

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Abstract

Background: Severe pneumonia is a major health problem in Indonesia and also in the world. The immune system is known to play important role in the pathogenesis of pneumonia, but few studies have assessed the relationship between blood CD4 and CD8 count and mortality from severe pneumonia in negative HIV population.
Methods: This study was a prospective cohort study conducted at Cipto Mangunkusumo General Hospital from June to August 2020. The outputs were 30-days survival rate and optimal cut-off value for blood CD4 and CD8 count to predict 30-days mortality and mortality risk. Data analysis used Kaplan-Meier survival, ROC curves and multivariate Cox regression.
Results: Of the 126 subjects, there was one subject who was lost to follow up. The 30-days mortality rate was 26.4%. The optimal cut-off value for blood CD4 count was 406 cells/μL (AUC 0,651, P=0,01, 95%CI 0,541-0,760, sensitivity 64%, specificity 61%), blood CD8 count was 263 cells/μL (AUC 0,639, P=0,018, 95% CI 0,534-0,744, sensitivity 62%, specificity 58%). CD4 blood count < 406 cells/μL had a crude HR of 2,696 (P=0,008, 95%CI 1.298-5.603), blood CD8 count < 263 cells/μL had a crude HR of 2,133 (P=0,042, 95%CI 1,035-4,392) and adjusted HR of 2,721 (P=0,005, 95%CI 1,343-5,512). If sepsis and pulmonary tuberculosis were added to the blood CD4 and CD8 count, the AUC value was 0,752 (P=0,000, 95%CI 0,662-0,842).
Conclusion: Blood CD4 and CD8 count had poor accuracy in predicting 30-days mortality in patients with severe pneumonia. Groups with lower blood CD4 and CD8 count had a higher risk of 30-days mortality.
Keywords: severe pneumonia, CD4 count, CD8 count, 30 days mortality

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Tuberculous pericarditis mimicking Bacterial pericarditis in Pericardial effusion

Vol 8 No 1 (2021)

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Abstract

Tuberculosis (TB) is one of the infectious diseases with the highest prevalence which causes high mortality worldwide. Although rarely found, TB pericarditis can be life threatening because it can cause pericardial effusion which, if left untreated, can cause death due to cardiac tamponade. A 44 years old man presented with cardiac tamponade with clinical appearance of Tb, but

pericardial fluid analysis favored bacterial pericarditis. Pericardial fluid analysis showed fluid glucose was 4, fluid protein was 5.320, LDH was 3.781, yellow, cloudy, cell count: 1.716, polymorphonuclear (PMN) 85,2, mononuclear (MN) 14,8. Patient then diagnosed with severe pericardial effusion with sign of tamponade due to bacterial pericarditis with differential diagnosis was tuberculous pericarditis. On the 4th day of treatment, it was found out from the results of GenXpert that there was Mycobacterium tuberculosis in the pericardial fluid with increased Adenosine deaminase (ADA) level, and Chest X-ray showed milliary TB. The patient was then given category 1 anti-tuberculosis drug and methylprednisolone 40 mg. The diagnosis of TB pericarditis is challenging, it requires knowledge about its pathogenesis and thorough analysis in its diagnosis. Not only depending on one tool, but still clinical assessment and confirmation with definite diagnostic tools such as culture or histopathology.

Keywords: bacterial pericarditis, diagnosis, pericardial fluid, PMN, tuberculous pericarditis

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Characteristics Of Outpatients With Tuberculosis And Human Immunodefi¬ciency Virus At Dr. Hasan Sadikin General Hospital Bandung In 2019

Vol 8 No 1 (2021)

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Abstract

Background: The burden of tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infection is still alarming with high number of cases and mortality especially in West Java. This is affected by delayed treatment in these patients due to difficulty in diagnosis of TB in HIV patients. Clinical presentations were commonly atypical.

Objective: This study aims to identify sociodemographic characteristics, clinical manifestations, and additional findings of outpatients with TB and HIV at Dr. Hasan Sadikin General Hospital Bandung in 2019.

Methods: A retrospective descriptive-observational study on medical records of outpatients in Directly Observed Treatment Short-course (DOTS) and HIV units of Dr. Hasan Sadikin General Hospital Bandung was conducted at 1 January-31 December 2019. Results: There were 22 outpatients with the diagnosis of TB with first category of treatment and HIV, mean age of 34,91 ± 7,68 years, 9,87 ± 19,07 months since HIV diagnosis, BMI of 17,9 ± 2,95. Majority were male (86,4%), married (55%), working (70,6%),

in high school (88,2%). Chronic cough (18,6%) was commonly found. There were equal number of patients with positive and negative AFB sputum smear. Most were pulmonary TB (53.3%), Rifampicin sensitive (25%), CD4 cell count of <200 cells/mm3 (77,3%) and stage IV of HIV (72,7%). Most patients had available chest x-ray results (85%), with pulmonary TB (60%) and unilateral infiltrate (40%).

Conclusion: Most of the patients were male in productive age with low BMI, stage IV HIV with low CD4 cell count. Most patients were found with common cough, diagnosed as pulmonary TB, with chest x-ray results showed pulmonary TB with unilateral infiltrate. There were equal number of positive and negative results on AFB sputum smear and most were rifampicin sensitive.

Keywords: tuberculosis, HIV, characteristics

Pengaruh Diabetes Melitus Terhadap Konversi Kultur Sputum Dini Pada Pasien Tuberkulosis Resistan Obat Ganda

Vol 8 No 1 (2021)

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Abstract

Background: Multidrug-resistant tuberculosis (MDR TB) is a form of tuberculosis infection caused by mycobacterium strains that are resistant to at least two of the main first-line drugs, i.e. isoniazid and rifampicin. In general, MDR TB treatment success rate in Indonesia is only 47%. One of the factors that may influence the treatment outcomes is Diabetes Mellitus (DM). Early sputum culture conversion was associated with better treatment outcomes compared to late sputum culture conversion. Late sputum culture conversion is associated with poor outcomes and increased mortality rate (50%-80%).

Objective: This study aimed to assess the effects of DM on early sputum culture conversion among MDR TB patient who received short-term regimen therapy.

Methods: This was a retrospective cohort observational analytical study conducted at Borang MDR TB of Mohammad Hoesin General Hospital Palembang from April 2019 to January 2020.

Results: A total of 91 participants were included in the study with DM prevalence of 27%. Early sputum culture conversion was found in 11 subjects with DM (44%) and in 45 non-DM subjects (68%). Analysis results showed that MDR TB patient with DM has 2,7 times of having late sputum culture conversion (RR 2,7; 95% CI, 1,061 – 7,013, p= 0.037) compared to non-DM counterpart.

Conclusion: Diabetes Mellitus affects sputum culture conversion among MDR TB patients receiving short-term regimen therapy at Mohammad Hoesin General Hospital Palembang.

Keywords: multidrug-resistant tuberculosis, diabetes mellitus, sputum culture conversion.

Manifestasi Ekstra Paru Coronavirus Disease 2019

Vol 8 No 1 (2021)

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Abstract

Nowadays, pandemic of COVID-19 impacts worldwide. Coronavirus Disease 2019 affect respiratory system dominantly. However, this virus can also affect other organ systems besides lungs, such as skin, eyes, and heart. This review article was aimed to describe the manifestation of Coronavirus Disease in another organ besides lungs.

Key words: manifestation, extra pulmonary, Coronavirus Disease 2019

MODALITAS PEMERIKSAAN PENUNJANG PADA PENEGAKAN DIAGNOSTIK PNEUMOCYTIS PNEUMONIA (PCP) PADA HIV/AIDS

Vol 8 No 1 (2021)

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Abstract
Pneumocystis jirovecii pneumonia (PCP) is an opportunistic fungal infection in respiratory system caused by fungal organisms that cause pneumonia. The incidence of PCP is relatively low. Appropriate investigations are needed to establish diagnostics for suspected PCP infection in HIV / AIDS patients. Detection of PCP cases should be done as early as possible, so that prophylaxis and PCP treatment are not delayed and can reduce mortality.
Keywords: Investigation diagnostics, pneumocystis pneumonia, HIV/AIDS

EFEK PEMBERIAN TERAPI VITAMIN D TERHADAP PERBURUKAN PASIEN RAWAT INAP COVID-19

Vol 8 No 1 (2021)

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Abstract

Background: Corona virus disease 2019 (COVID-19) is a new disease caused by the SARS-CoV2 virus and announced to be a global pandemic. Symptoms can vary in different people and are divided into asymptomatic, mild, moderate, and severe. Vitamin D is said to have an effect on lowering the risk of microbial infection and death. Therefore, vitamin D is given to COVID-19 patients with the hope of reducing clinical deterioration and mortality.
Objective: To assess the effect of vitamin D on clinical deterioration and mortality in COVID-19 patients based on studies that have been conducted.
Methods: Searching randomized controlled trials and cohorts in three databases, namely PubMed, Scopus, and Cochrane. Articles will be selected and then subjected to a critical review using guidelines from the University of Oxford's Center for Evidence-based Medicine (CEBM).
Results: A total of three studies were selected with one randomized controlled trial and two cohort studies. All studies claim that offering vitamin D therapy decreased the incidence of admission of patients to the ICU (invasive mechanical ventilation) and mortality. Study drawbacks may bias and influence the significance of the association between vitamin D administration and

clinical deterioration.

Conclusion: Administration of vitamin D in hospitalized COVID-19 patients to reduce clinical worsening of patients.

Keywords: Adult, COVID-19, Vitamin D, cholecalciferol, calcifediol

Diagnosis Banding Ground Glass Opacities Pada CT-Scan Toraks Di Era Covid 19

Vol 8 No 1 (2021)

ABSTRAK

Ground glass opacities (GGO) merupakan suatu gambaran radiologis non spesifik pada CT-scan toraks dengan berbagai macam etiologi, mulai dari inflamasi, infeksi, edema paru, perdarahan, penyakit interstisial paru hingga keganasan. Saat ini diketahui bahwa GGO juga dapat terdeteksi pada CT-*scan* toraks pasien-pasien dengan COVID 19. Temuan CT-*scan* toraks tipikal infeksi pneumonia COVID-19 berupa GGO yang dominan bilateral, lobus bawah dan perifer. Seringkali kemunculan gambaran GGO pada CT-*scan* toraks dikorelasikan dengan adanya infeksi COVID-19, padahal GGO bisa disebabkan oleh berbagai macam penyakit. Selain itu, probabilitas bahwa gambaran CT-*scan* toraks menunjukkan COVID-19, sangat tergantung pada probabilitas pra-tes infeksi, yang akhirnya ditentukan oleh prevalensi infeksi komunitas. Oleh, karena beragamnya diagnosis banding GGO, perlu pemahaman mengenai etiopatogenesis, penilaian morfologi dan, distribusi GGO. Meskipun diagnosis pasti tidak bisa dibuat hanya berdasarkan pencitraan saja (CT-*scan* toraks), kombinasi klinis dan pencitraan secara substansial meningkatkan akurasi diagnosis.

Kata kunci: *Ground glass opacities*, CT-*scan* toraks, COVID-19

ABSTRACT

Ground glass opacities (GGO) are non-specific radiological features in the lung parenchyma on chest CT with various etiologies, ranging from inflammation, infection, pulmonary edema, pulmonary hemorrhage, interstitial lung diseases to malignancy. It is currently known that GGO can also be detected on chest CT of patients with COVID 19. Imaging finding in COVID-19 pneumonia are predominantly bilateral, basal and peripheral GGO. Ground glass opacities on chest CT are correlated with the presence of COVID-19 infection, even though GGO can be caused by various diseases. In addition, the probability that the chest CT shows COVID-19, highly depends on the pre-test probability of infection, which is ultimately determined by the prevalence of community infection. Because GGO have wide and varied differential diagnoses, it is necessary to understand the etiopathogenesis, morphological criteria, and distribution of GGO. Although a definite diagnosis cannot be determined by imaging alone (chest CT), the combination of clinical and imaging substantially increases the accurate diagnosis.

Key words: Ground glass opacities, chest CT, COVID-19

Hospital-Acquired Coronavirus Disease 2019 (Covid-19) In The Beginning Of Epidemic In Indonesia

Vol 7 No 2 (2020)

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a novel acute respiratory disease that has been declared as a pandemic by World Health Organization (WHO) since March 11th 2020. General clinical manifestations of COVID-19 are fever, dry cough, and fatigue. Nonetheless, the majority of COVID-19 cases are asymptomatic. In Indonesia, COVID-19 was reported for the first time on March 2nd 2020. However, in the mid of March 2020 our hospital discovered 2 patients with COVID-19 sign and symptoms that were presented after being cared for several days, even though at that time our hospital hadn't had any cases yet. Those patients were checked and all of them were positive for COVID-19. The objective of this case report is to raise the awareness of hospital-acquired COVID-19 infection possibility especially in the region with minimal cases so that healthcare staffs always be vigilant and don't let their guard down towards COVID-19 dissemination threat which is still going on.

Keywords: respiratory medicine, internal medicine

ABSTRAK

Coronavirus disease 2019 (COVID-19) merupakan sebuah penyakit pernapasan akut baru yang dinyatakan sebagai sebuah pandemi oleh World Health Organization (WHO) pada tanggal 11 Maret 2020. COVID-19 memiliki manifestasi klinis umum berupa demam, batuk kering, dan lemas, namun sebagian besar kasus COVID-19 bersifat asimptomatik. COVID-19 pertama kali dilaporkan di Indonesia pada tanggal 2 Maret 2020. Akan tetapi, pada pertengahan bulan Maret 2020 di rumah sakit kami terdapat 2 pasien dengan tanda dan gejala COVID-19 yang muncul setelah beberapa hari dirawat di rumah sakit, meskipun pada saat itu rumah sakit kami belum memiliki kasus. Kedua pasien akhirnya diperiksa dan keduanya didapatkan positif COVID-19. Tujuan laporan kasus ini adalah untuk meningkatkan kewaspadaan terhadap kemungkinan terjadinya infeksi nosokomial terutama pada daerah dengan jumlah kasus yang masih minimal agar tenaga medis tidak lengah dalam menghadapi ancaman penyebaran COVID-19 yang masih akan terus berlanjut.

Kata kunci: respiratory medicine, ilmu penyakit dalam.

DRESS (Drug rash with eosinophilia and systemic symptoms) syndrome In Patient with Anti Tuberculosis Drugs

Vol 7 No 2 (2020)

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ABSTRACT

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a type of life-threatening drug reaction. Clinical manifestations are morbilli form skin lesions, accompanied by fever, eosifnophilia and systemic involvement which can cause multi-organ failure. The incidence of DRESS syndrome is among 1: 1000 to 1: 10,000 patients, with 10% of mortality rate. Current literature shows that DRESS syndrome can be caused by anti-tuberculosis drugs, including ethambutol (53.5%), rifampicin (26.7%), pyrazinamide (20%), streptomycin (13.3%), and isoniazid (6.7%).

Case Report

A 42-year- old man has been known to suffer from pulmonary TB and undergo anti-tuberculosis drug therapy category I for 3 weeks. The patient has been known to have a history of allergy to ceftriaxone and ibuprofen drugs in previous treatments. The patient underwent a second treatment in the hospital with generalized erythema and scaly itchy skin. The physical examination showed that the patient had 39.1OC of body temperature with icteric sclera. The laboratory examination showed that the eosinophil was increased from 13% to 27%, accompanied by leukocyte 14,400 / UL, haemoglobin10 g / dL, and platelets 86,000 / UL. The examination on kidney and liver function resulted 57.0 mg / dl ureum and creatinine 2.39 mg / dl, and AST 458 IU / l, ALT 155 IU / l, total bilirubin 2,281 mg.dl, γ-glutamyltransferase 134 IU / l, ALP 357 IU / l, INR 1.79. At the beginning of the treatment, the scaly skin of the patient resembled the appearance of xerosis cutis. The development of the treatment showed that the patient fulfilled the DRESS syndrome diagnosis criteria based on RegiSCAR. The patient was treated in an intensive isolation room, and the anti-tuberculosis drugs discontinued.

Conclusion

DRESS syndrome is a drug reaction that can cause death. Diverse skin lesions and hypersensitivity reaction at slow onset make diagnosis difficult to establish. Therefore, diagnosing with RegiSCAR in the beginning and stopping the drug are important in the management of DRESS syndrome.

Keywords: drug eruption, DRESS syndrome, anti-tuberculosis drugs, RegiSCAR, pulmonary TB

Bilateral Chylothoraks, Chyloperitoneum, Lympedema Lower Extremity In Follicular Lymphoma, Asthma Attack

Vol 7 No 2 (2020)

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ABSTRACT

Introduction

Chylothoraksand chyloperitoneum are rare condition characterized by milky appearing fluid with elevated trigliseride. Lymphoma is found in 70%as etiology.

Case Ilustration

A women came to emergency room with chief complain shortness of breath since 4 days before admission. In physical examination found tachypnoe, tachycardia, decreased of vesicular in left side hemithorax, with wheezing in the hemithoraxdextra, dull in abdominal percussion and swelling in bilateral lower extremity. Chest radiology found a pleural effusion in bilateral thorax cavity. From CT abdominal and abdominal ultrasonography we found enlargement of paaraortalympnode, intraabdminalextraluminal mass.

Discussion

Chylothorax and chyloperitoneum diagnosed based onpleural trigliserid levels1100 mg/dL, 1290 mg/dL and 1030 in the peritoneal fluid.From sitology and immunohistochemistry showed a follicular lymphoma.We have done chest tube, pleurodesis with bleomycin, inhalation therapy and chemotherapy. Now she have finished the sixth series of chemetherapy and she have partial response.

Conclusion

We thought chylothorax in this patient caused by follicular lymphoma. Chemotherapy was given as underlying treatment.

Keywords: chylothorax, chyloperitoneum, follicular lymphoma

ABSTRACT

Introduksi

Chylothoraks dan chyloperitoneum merupakan kondisi yang jarang ditemukan yang ditandai dengan adanya cairan putih seperti susu dengan peningkatan kadar trigliserida. Lymphoma ditemkan sebagai etiologi sekitar 70%.

IlustrasiKasus

Seroang perempuan datang keruang emergensi RS Muhammad Hoesin Palembang dengan keluhan utama sesak sejak 4 hari sebelum masuk rumah sakit. Dari pemeriksaan fisikditemukan takipnoe, takikardia, penurunan vesikuler pada hemithoraks kiri disertai wheezing, redup pada saat perkusi abdomen dan edema pada bilateral ektremitas inferior. Dari foto thoraks didapatkan efusi pleura kiri. Dari pemeriksaan CT Scan dan USG abdomen didapatkan adanya pembesaran kelerjar getah bening paraaorta dan massa intraabdomen extraluminal.

Diskusi

Chylothorax dan chyloperitoneumdidiagnosis berdasarkankan dengan trigliserida pada cairan pleura kiri 1100 mg/dL, cairan pleura kanan 1290 mg/dL dan cairan ascites 1030 mg/dL. Dari pemeriksaan sitology serta imunohistokimia dengan kesan limfoma folikuler. Kami lakukan pemsangan chest tube, pleurodesis dengan bleomisin, terapi inhalasi dan kemoterapi. Pasien sudah menyelesaikan 6 seri kemoterapi dan memiliki respon remisi parsial untuk penyakitnya ini.

Kesimpulan

Kami berpikir penyebab chylothoraks pada pasien ini adalah follicular lymphoma. Kemoterapi diberikan sebagai terapi definitive.

Kata kunci: chylothorax, chyloperitoneum, follicular lymphoma

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Hipoalbuminemia Pada Pasien Sakit Kritis

Vol 7 No 2 (2020)

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ABSTRAK

Hipoalbuminemia pada keadaan sakit kritis merupakan penanda mortalitas yang penting. Patofisiologi terjadinya hipoalbuminemia pada pasien sakit kritis memiliki beberapa penyebab, meliputi penurunan produksi, adanya mediator peradangan, kebocoran vascular, serta malnutrisi. Pemberian albumin manusia intravena perlu dipertimbangkan diberikan untuk hypoalbuminemia pada sakit kritis

Kata kunci: Hipoalbuminemia, sakit kritis

ABSTRACT

Hypoalbuminemia in critical illness is an important marker of mortality. The pathophysiology of hypoalbuminemia in critical illness including decrease of production, inflammation marker, vascular leakage, and malnutrition. Administration of intravenous human albumin is needed to be considered for treatment of hypoalbuminemia in critical illness.

Keywords: hypoalbuminemia, critical illness

Mekanisme Hepatotoksisitas Dan Tatalaksana Tuberkulosis Pada Gangguan Hati

Vol 7 No 2 (2020)

Ivan Banjuradja*, Gurmeet Singh**

Abstrak Abnormalitas fungsi hati merupakan efek samping tersering pemberian regimen obat anti tuberkulosis (OAT) standar dimana menyebabkan 11% penghentian pemberian OAT pada pasien tuberkulosis (TB). Hepatotoksisitas terutama berhubungan dengan pemberian isoniazid (INH), rifampisin (RIF) dan pirazinamid (PZA) pada golongan OAT lini pertama. Manifestasi hepatotoksisitas bervariasi antara hanya berupa abnormalitas fungsi hati sampai kejadian gagal hati akut. Adapun pedoman tatalaksana TB dengan cedera hati akibat OAT sebagian besar masih didasarkan pada opini ahli. Dalam tinjauan pustaka ini akan dibahas mengenai mekanisme kelainan hati akibat OAT, tatalaksana penghentian, mekanisme reintroduksi OAT pada pasien-pasien yang mengalami kelainan fungsi hati, dan tatalaksana pengobatan pada pasien TB dengan riwayat gangguan fungsi hati sebelumnya.

Kata kunci: obat anti tuberkulosis, hepatotoksisitas

Abstract The abnormalities of liver function are the most common antitubercular side effect, which resulted in 11% drug discontinuation. Hepatotoxicity was mainly associated with the isoniazid (INH), rifampicin (RIF), and pyrazinamide (PZA) administration. The manifestation of hepatotoxicity was greatly varies, from asymptomatic abnormal liver function test to disastrous acute liver failure. Most of the recommendation for the management of liver injury related to antitubercular are based on expert opinion. This literature review will discuss the mechanism of antitubercular inducing liver injury, diagnostic work up, reintroduction of antitubercular, and management of tuberculosis in patients with previous liver dysfunction history.

Keywords: antitubercular, hepatotoxicity

Acute Exacerbation Of Asthma And COPD: What To Do As The Frontliners

Vol 7 No 2 (2020)

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Abstract : Exacerbations characterized by an increase in patients' symptoms above baseline, represent an important feature of the clinical manifestation and natural history of asthma and chronic obstructive pulmonary disease (COPD). Acute asthma and COPD exacerbations are the most common respiratory diseases requiring emergent medical evaluation and treatment. Asthma and COPD exacerbations impose an enormous economic burden on health care budget. In daily clinical practice, a distinction between bronchial asthma and exacerbated COPD is difficult because symptoms are similar. Exacerbations represent a change in symptoms and lung function from the patient usual status. The decrease in expiratory airflow can be quantified by lung function measurements such as peak expiratory flow (PEF) or forced expiratory volume in 1 second (FEV1), compared with the patient's previous lung function or predicted values. Medications most commonly used for exacerbations are oxygen supplementation, bronchodilators inhalation, corticosteroids, and antibiotics. For severe asthma attacks the administration of magnesium is a possible additional option. Invasive ventilation remains a last resort to ensure respiratory function and indications for this are given in patients with clinical signs of impending exhaustion of breathing. Keyword : exacerbation, asthma, COPD, lung function, medications

Abstrak :

Eksaserbasi yang ditandai oleh adanya perburukan gejala pasien, merupakan salah satu bagian penting dari manifestasi klinis dan perjalanan penyakit pasien dengan asma dan penyakit paru obstuktif kronis (PPOK). Eksaserbasi asma akut dan PPOK merupakan penyakit respirasi yang paling umum ditemukan yang membutuhkan evaluasi dan pengobatan medis segera. Eksaserbasi asma dan PPOK memiliki dampak ekonomi yang besar pada pembiayaan kesehatan. Dalam praktik klinis sehari-hari, perbedaan antara eksaserbasi asma dan PPOK kadang disulitkan oleh gejalanya yang serupa. Eksaserbasi menunjukkan adanya perubahan pada gejala dan fungsi paru dari status pasien biasanya, Penurunan pada aliran eksiprasi dapat dinilai oleh pengukuran fungsi paru seperti alur puncak ekspirasi (APE) atau volume paksa eksiprasi 1 detik (VEP1), dibandingkan dengan nilai fungsi paru sebelumnya atau nilai prediksi. Medikasi yang biasanya digunakan untuk eksaserbasi adalah suplementasi oksigen, inhalasi bronkodilator, kortikosteroid dan antibiotik. Pada pasien serangan asma berat, pemberian magnesium dapat menjadi opsi tambahan. Ventilasi invasif merupakan pilihan terakhir bantuan fungsi respirasi pada pasien dengan tanda ancaman gagal nafas. Kata kunci : eksaserbasi, asma, PPOK, fungsi paru, medikasi

Sistem Penapisan Pasien Coronavirus Disease 2019 (COVID-19) RSUD Kramat Jati

Vol 7 No 2 (2020)

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ABSTRAK

Coronavirus Disease 2019 (COVID-19) memiliki spektrum manifestasi klinis yang sangat luas meliputi hampir semua bagian disiplin ilmu kedokteran. Keterbatasan dan ketersediaan uji diagnosis yang ada saat ini menyebabkan hambatan deteksi awal pasien dengan kecurigaan COVID-19. Penulisan artikel ini bertujuan untuk mengenalkan sistem penapisan COVID-19 yang digunakan di Rumah Sakit Umum Daerah (RSUD) Kramat Jati, Jakarta Timur

Kata kunci: COVID-19, Rumah Sakit Umum Daerah, Kramat Jati, Penapisan

ABSTRACT

Coronavirus Disease 2019 (COVID-19) has a broad spectrum of clinical manifestations encompassing almost all of medical disciplines. Limitation and availability of current diagnostic tests hinder early detection of suspected COVID-19 patients. This article aims to introduce the COVID-19 screening system used in Kramat Jati Regional Public Hospital, East Jakarta

Keywords: COVID-19, Regional Public Hospital, Kramat Jati, Screening

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ALOX5 Gene Polymorphism And Effects Of Omega-3 Fish Oil On Lung Function In Asthma

Vol 7 No 2 (2020)

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Abstract

Background: Omega-3 as a local source plays a role in the arachidonic pathway in asthma therapy, related to an improvement of lung function. The anti-inflammatory effects of omega-3 are known to be related to genetic factors, one of which is on ALOX5

gene polymorphism

Objective: This study aims to determine the profile of ALOX5 polymorphism and the effects of omega-3 fish oil on lung function in asthma in Surabaya

Methods: The method was pre-experimental design, using a purposive sampling technique for data collection from June 2017 to January 2018 in Surabaya. The intervention provided was fish oil which contains 1000 mg of omega-3 for 1 month. The different test using paired t-test to compare before and after getting the intervention. The research subjects were 27 adult outpatient asthmatics and 23 non-asthma patients (as the comparison on genetic testing.

Results: The results of improvement in lung function showed a significant difference (p=0.00) in PEF0 values (average: 217,96L/sec) and PEF4 (average: 325,00L/sec). Of the 27 study subjects, only 23 people could have genetic testing by a buccal swab. Asthma patients had more mutant II genotypes (39,13%) than wild types (30,43%). In this study, the relationship between ALOX5 gene polymorphism and lung function improvement cannot be tested because the number of samples is relatively limited. There was one subject who had constant PEF value (mutant II) and decreased PEF value (mutant III)

Conclusion: Fish oil is effective in improving lung function, especially in asthma patients with wild genotype type.

Keywords: ALOX5, asthma, PEF, fish oil, omega-3

Abstrak

Pendahuluan: Omega-3 sebagai sumber lokal berperan dalam jalur arakidonik dalam terapi asma, terkait dengan peningkatan fungsi paru. Efek antiinflamasi omega-3 diketahui berkaitan dengan faktor genetik, salah satunya pada polimorfisme gen ALOX5

Tujuan: Penelitian ini bertujuan untuk mengetahui profil polimorfisme ALOX5 dan efek minyak ikan omega-3 terhadap fungsi paru-paru penderita asma di Surabaya.

Metode: Metode yang digunakan adalah studi pre-eksperimental dengan teknik pengambilan sampel purposive sampling untuk pengumpulan data dari bulan Juni 2017 sampai Januari 2018 di Surabaya. Intervensi yang diberikan adalah minyak ikan yang mengandung 1000 mg omega-3 selama 1 bulan. Uji beda menggunakan paired t-test untuk membandingkan sebelum dan sesudah mendapat intervensi. Subjek penelitian adalah 27 pasien penderita asma dewasa rawat jalan dan 23 pasien non asma (sebagai pembanding pada pengujian genetik). Hasil peningkatan fungsi paru menunjukkan perbedaan yang signifikan (p = 0,00) pada nilai PEF0 (rata-rata: 217,96L / detik) dan PEF4 (rata-rata: 325,00L / detik). Dari 27 subjek penelitian, hanya 23 orang yang dapat menjalani pengujian genetik dengan swab bukal. Pasien asma memiliki lebih banyak genotipe mutan II (39,13%) dibandingkan tipe liar (30,43%). Dalam penelitian ini, hubungan antara polimorfisme gen ALOX5 dengan peningkatan fungsi paru tidak dapat diuji karena jumlah sampel yang relatif terbatas. Ada satu subjek yang memiliki nilai PEF konstan (mutan II) dan mengalami penurunan nilai PEF (mutan III).

Kesimpulan: Minyak ikan efektif meningkatkan fungsi paru-paru, terutama pada penderita asma tipe wild genotype.

Kata kunci: ALOX5, asma, PEF, minyak ikan, omega-3

Frekuensi Mutasi Gen KatG S315T M.Tuberculosis Pada Pasien MDR TB Di Sumatera Selatan

Vol 7 No 2 (2020)

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Pendahuluan

Indonesia menempati peringkat kelima kasus MDR TB tertinggi di dunia. MDR TB terjadi karena resistensi terhadap obat Rifampisin dan INH yang disebabkan oleh mutasi pada gen M.Tb. Resistensi terhadap obat INH dapat disebabkan oleh beberapa gen tetapi paling sering terjadi karena mutasi gen katG S315TM.Tb. Angka kejadian mutasi gen katG ini bervariasi ditiap daerah. Mutasi gen katG S315TM.Tb dapat menimbulkan resistensi tingkat tinggi terhadap INH.

Tujuan

Mengetahui frekuensi mutasi gen katG S315TM.Tb diantara semua pasien MDR TB di Sumatera Selatan.

Metode

Sebanyak 118 pasien MDR TB yang menjalani pengobatan di RSMH Palembang dari februari 2019 hingga mei 2020 dilakukan pemeriksaan PCR-RFLP laboratorium mikrobiologi FK UNSRI untuk melihat alel kodon 315 gen katG M.Tb.

Hasil

Frekuensi mutasi gen katG S315T M.Tb diantara pasien MDR TB di Sumatera Selatan adalah 48,33%. Pada kelompok mutasi gen katG S315T M.Tb didapatkan indeks massa tubuh yang lebih rendah, jumlah M.Tb yang lebih tinggi dan lesi radiologis yang lebih luas pada saat diagnosis.

Simpulan

Resistensi obat isoniazid pada pasien MDR TB mayoritas disebabkan oleh mutasi gen katG S315T M.Tb. Mutasi ini akan menyebabkan resistensi INH tingkat tinggi. Tingginya angka resistensi INH akan mempengaruhi pengobatan MDR TB.

Kata kunci : MDR TB, mutasi gen katG S315T M.Tb, INH, PCR-RFLP

Pola Bakteri Pasien Rawat Inap Pneumonia Komunitas Dewasa RS Hasan Sadikin Bandung Tahun 2018

Vol 7 No 2 (2020)

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Abstrak

Latar Belakang: Pneumonia komunitas merupakan masalah kesehatan serius karena penyakit ini termasuk dari sepuluh penyakit yang paling banyak ditemukan di rumah sakit dengan angka kematian tertinggi ketiga di dunia. Kegagalan terapi yang diakibatkan karena resistansi kuman terhadap regimen yang diberikan dapat menyebabkan bertambahnya beban klinis untuk rumah sakit. Tujuan: Penelitian ini bertujuan untuk mengetahui pola bakteriologi dan data resistansi yang berguna sebagai salah satu pertimbangan untuk terapi empiris pneumonia. Metode: Penelitian ini dilakukan menggunakan desain deskriptif kuantitatif. Data diambil secara retrospektif dari semua hasil uji kepekaan kuman pasien rawat inap di Bangsal Ilmu Penyakit Dalam RSUP Dr. Hasan Sadikin periode 1 Januari – 31 Desember 2018 yang memenuhi kriteria inklusi dan eksklusi. Data yang dicari adalah bakteri penyebab pneumonia dan hasil uji kepekaan yang dihitung berdasarkan resistansi. Hasil: Sebanyak 189 dari 307 data pasien peumonia merupakan infeksi bakteri tunggal dengan 116 diantaranya disebabkan oleh bakteri gram negatif sementara 76 sisanya merupakan infeksi bakteri gram positif. Bakteri gram positif yang paling banyak ditemukan adalah Staphylococcus aureus pada 11 pasien. Bakteri gram negatif yang paling banyak ditemukan adalah Klebsiella pneumoniae pada 26 pasien. Resistansi paling tinggi pada bakteri gram negatif ditemukan pada 17 dari 25 pasien infeksi Pseudomonas aeruginosa terhadap tigecycline. Resistansi terendah pada bakteri gram negatif ditemukan pada 1 dari 26 pasien Klebsiella pneumoniae untuk tigecycline. Resistansi paling tinggi untuk bakteri gram positif paling banyak ditemukan berbagai antibiotik yang diujikan kepada Staphylococcus haemolyticus sementara tidak ditemukan resistansi bakteri gram positif terhadap linezolid. Kesimpulan: Bakteri yang paling banyak ditemukan adalah bakteri gram negatif Klebsiella pneumoniae. Angka resistansi bakteri gram negatif paling banyak ditemukan pada Pseudomonas aeruginosa terhadap tigecycline sementara angka resistansi bakteri gram negatif ditemukan paling tinggi pada Staphylococcus haemolyticus terhadap berbagai antibiotik. Kata Kunci: pneumonia komunitas, pola bakteri, resistansi.

Abstract

Background: Community-Acquired Pneumonia (CAP) is a serious health problem due to its high hospital incidence and mortality rate. Failure to properly treat the infection, mainly caused by the antimicrobial resistance, may increase clinical burden. Objective: This study aims to observe bacterial pattern and resistance in hospitalized pneumonia patients which may be included in future treatment consideration.

Method: This research was conducted using descriptive quantitative design. Retrospective data of Department of Internal Medicine inpatients with susceptibility test results available from January 1st – December 31st 2018 which fulfilled the inclusion and exclusion criteria was collected through total sampling method. Patients' data were analyzed and reported by etiological agent and susceptibility test results. Result: Approximately 189 out of 307 available pneoumonia cases were single infections with 116 caused by gram-negative bacteria while 76 were caused by gram-positive bacteria. Staphylococcus dan Klebsiella were the most common gram-positive and negative bacteria found with 11 cases and 26 cases. Highest antibiotic resistance on gram-negative and gram positive bacteria was observed in 17 out of 25 Pseudomonas aeruginosa patients to tigecycline and Staphylococcus haemolyticus on various antibiotics respectively, while the lowest was observed on Amikacin on 4 cases and no resistance found on any patients for linezolid.

Conclusion: The most encountered single CAP etiological agents in Hasan Sadikin Hospital Bandung came from gram-negative bacteria group, which are Klebsiella pneumoniae and Pseudomonas aeruginosa. Tigecycline was the most resisted antibiotic by gram-negative bacteria, while tetracycline was resisted the most by gram-positive bacteria.

Keywords: bacterial pattern, community-acquired pneumonia, resistance.

Six Minute Walk Test: Maximum Capacity Prediction Instrument For Mongoloid Adults With COPD

Vol 7 No 2 (2020)

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Abstract:

This study compared prediction of O2 max from total distance of six minute walk test (6MWT) based on Mongoloid's formula to Caucasian's formula in Indonesia (Mongoloid) adults with chronic obstructive pulmonary disease (COPD). It involved 44 COPD subjects (38 males) and used total distance from 6MWT to predict O2max with Nury's formula (Indonesia-Mongoloid) [(0,053 total distancemeter)+ (0,22 ageyears)+ (0,032 heightcentimeter) – (0,164 weightkilogram)– (2,228 gendermale=0, female=1) - 2,287] and Cahalin formula (American-Caucasian) [(0,006 x total distancefeet) + 3,38].The Prediction of O2max with Nury's formula was 9,35 (1.98-15.89) ml/ kg/min and Cahalin formula is 3.73 (2.21-4.57) ml/kg/min. We found significant different statistically (p<0,05) in the O2max. We concluded that O2max prediction with Cahalin formula showed that the functional capacity was underestimated. This study showed maximum capacity(O2 max) prediction in Mongoloid adults with COPD could not be predicted by Caucasian's formula.

Keywords : six minute walk test, COPD, Nury's formula, Mongoloid

Abstrak

Penelitian ini membandingkan nilai prediksi O2 maksimum dari jarak tempuh yang diperoleh pada uji jalan enam menit (6MWT) pada subjek PPOK dewasa Indonesia (Mongoloid) yang dihitung dengan rumus prediksi O2 max berbasis Mongoloid terhadap rumus berbasis Kaukasoid. Penelitian ini melibatkan 44 subjek penelitian (38 laki-laki). Menggunakan jarak tempuh yang diperoleh dari 6MWT, dihitung prediksi O2 max dengan rumus Nury (Indonesia- Mongoloid) = (0,053 jarak totalmeter)+ (0,22 umurtahun)+ (0,032 tinggi badancentimeter) – (0,164 berat badankilogram) – (2,228 Jenis kelaminlaki-laki=0, perempuan =1) - 2,287 dan Rumus Cahalin (Amerika-Kausasoid) = (0,006 x Jarak totalkaki) + 3,38.Prediksi O2 maksimum dengan rumus Nury sebesar 9.35 (1.98-15.89) ml/kg/min, sedangkan dengan rumus cahalin 3.73 (2.21-4.57) ml/kg/min). Terdapat perbedaan bermakna (p<0.05).

Disimpulkan: menggunakan O2 max prediksi dengan rumus Cahalin menampilkan kapasitas fungsional dibawah nilai sesungguhnya (underestimate), dengan demikian prediksi kapasitas maksimum pada PPOK mongoloid tidak bias diprediksi

menggunakan rumus Kaukasoid.

Kata kunci: uji jalan enam menit, PPOK, rumus Nury, Mongoloid

DENGUE FEVER IN THE ERA OF COVID-19 PANDEMIC

Vol 7 No 1 (2020)

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ABSTRACT

COVID-19 is an ongoing pandemic with similar clinical manifestations to other infectious diseases. Until this day there is no exact guideline for the diagnosis and treatment of COVID-19. This case report describes a dengue fever case in a patient with high risk of COVID-19 infection. Rapid detection of this disease helps patients to receive early treatment and also contain the spread of the disease. Due to similar initial symptoms and lab results, a nasopharyngeal swab is recommended on the fifth day of fever, due to high viral load on said days. Clear anamnesis and accurate interpretation of lab and radiologic modalities helps avoidance of unnecessary early medications for COVID-19

Keywords: COVID-19, dengue fever, viral infections

WELLENS' SYNDROME, A PRESENTING SIGN OF LAD OCCLUSION : A CASE REPORT

Vol 7 No 1 (2020)

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ABSTRAK

Latar belakang: Di era pentingnya tindakan reperfusi, ada beberapa pola EKG atipikal yang dapat mengancam jiwa sindrom koroner akut risiko tinggi yang perlu diperhatikan. Salah satunya adalah sindrom Wellens dengan karakteristik adanya abnormalitas gelombang T (gelombang T biphasic atau T dalam terbalik) pada hasil elektrokardiogram (EKG) pasien dalam episode tanpa nyeri dada. Hal ini menunjukkan stenosis pada arteri koroner proksimal anterior descending kiri (LAD) derajat tinggi yang dapat mengakibatkan infark akut pada dinding anterior miokard (AMI) jika tidak dilakukan pengobatan maupun reperfusi.

Tujuan: Untuk menyajikan kasus Wellens sindrom yang mengancam jiwa, sindrom koroner akut risiko tinggi.

Ilustrasi kasus: Seorang pria berusia 48 tahun, perokok berat, datang ke ruang gawat darurat rumah sakit National Cardiac Center Harapan Kita (NCCHK) dengan nyeri dada berulang dalam waktu 18 jam sebelum datang ke rumah sakit. Pemeriksaan EKG menunjukkan irama sinus dengan T negatif yang dalam di V2-V4, tanpa gelombang Q patologis. Pasien diduga sebagai Wellens Sindrom, sindrom koroner akut dengan risiko tinggi. Pasien kemudian dilakukan intervensi koroner perkutan dini (PCI). Ditemukan 90% sumbatan pada LAD proksimal dan berhasil di lakukan pemasangan satu stent.

Kesimpulan: Semua pasien dengan/ tanpa riwayat angina dengan EKG yang dicurigai sebagai sindrom Wellens harus menjalani terapi invasive reperfusi sesegera mungkin. Setiap pasien dengan temuan EKG khas Sindrom Wellens tidak boleh menjalani segala bentuk tes jantung lainnya untuk menegakan diagnostik lebih lanjut karena risiko terjadinya kematian jantung mendadak.

Kata kunci: Sindrom koroner akut risiko tinggi, sindrom Wellens, obstruksi arteri *descending* kiri

anterior; revaskularisasi, perubahan Elektrokardiografi

HRCT FINDINGS IN DELAYED DIAGNOSIS OF TUBERCULOSIS WITH CYSTIC BRONCHIECTASIS AND BRONCHIOLE ECTASIS

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ABSTRACT

Bronchiectasis is an abnormal, chronic enlargement of the bronchi and associated with a clinical syndrome of cough, sputum production and respiratory infections. Bronchiectasis may appear in association with pulmonary tuberculosis. A 69 years old woman who had recurrent cough since 3 years ago and treated with the diagnosis of allergic bronchitis. Since 5 months ago she had complained cough and shortness of breath. She was admitted to Intensive Care Unit with reduced consciousness and used ventilator for almost a month, had chronic hypercapnea and no response with antibiotic therapy and inhalation. After two weeks, she had improved by tuberculosis treatment and macrolid antibiotics even though pCO2 levels were difficult to decreased.

Keywords: Bronchiectasis, HRCT, Hypercapnea, Tuberculosis,

DELAMANID: PROFIL KEAMANAN TERHADAP JANTUNG PADA PENGOBATAN TUBERKULOSIS RESISTEN OBAT

Vol 7 No 1 (2020)

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ABSTRAK

Delamanid adalah antituberkulosis baru yang dikembangkan untuk mengobati (Tuberkulosis resisten obat)TB-RO. Dalam proses pengembangan delamanid, selain aspek efikasi, aspek keamanan menjadi perhatian khusus terkait potensi efeknya terhadap jantung berupa pemanjangan interval QT. Namun, data pendukung yang diperoleh masih dalam skala kecil dan belum lengkap. Data keamanan lainnya dibutuhkan dalam rangka pengobatan TB-RO. Sehingga, *monitoring* aktif dibutuhkan untuk meningkatkan pelayanan dan keamanan pasien.

Kata Kunci: Delamanid, *monitoring* keamanan, jantung, interval QT, *patient safety*

CENTRAL VENOUS CATHETERIZATION

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ABSTRACT

Central venous catheters (CVCs) are essential for the management of some critically ill patients and those with limited vascular access to provide interventions and monitoring. The procedure is catheher was inserted into a venous great vessel that traditionally located in the subclavian vein, internal jugular vein, or femoral vein. Central venous access has several clinical indications, contraindications and complications that must be considered. Most central lines are placed today via the Seldinger technique, in which the chosen vein is cannulated with a needle, a guide wire is inserted to maintain a tract through the skin into the vein, and the catheter is then inserted over the wire into the vein before the wire is removed. This procedure is generally performed with ultrasound guidance to improve the safety of this procedure. Full sterile technique must be used to decrease catheter-related infections.

Keywords: central venous catheter, criticall ill patients, vascular access, venous great vessel

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ORIGINAL ARTICLE

ALOX5 GENE POLYMORPHISM AND EFFECTS OF OMEGA-3 FISH OIL ON LUNG FUNCTION IN ASTHMA

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ABSTRACT

Background: Omega-3 as a local source plays a role in the arachidonic pathway in asthma therapy, related to an improvement of lung function. The anti-inflammatory effects of omega-3 are known to be related to genetic factors, one of which is on ALOX5 gene polymorphism

Objective: This study aims to determine the profile of ALOX5 polymorphism and the effects of omega-3 fish oil on lung function in asthma in Surabaya

Methods: The method was pre-experimental design, using a purposive sampling technique for data collection from June 2017 to January 2018 in Surabaya. The intervention provided was fish oil which contains 1000 mg of omega-3 for 1 month. The different test using paired t-test to compare before and after getting the intervention. The research subjects were 27 adult outpatient asthmatics and 23 non-asthma patients (as the comparison on genetic testing.

Results: The results of improvement in lung function showed a significant difference (p=0.00) in PEF0 values (average: 217,96L/sec) and PEF4 (average: 325,00L/sec). Of the 27 study subjects, only 23 people could have genetic testing by a buccal swab. Asthma patients had more mutant II genotypes (39,13%) than wild types (30,43%). In this study, the relationship between ALOX5 gene polymorphism and lung function improvement cannot be tested because the number of samples is relatively limited. There was one subject who had constant PEF value (mutant II) and decreased PEF value (mutant III)

Conclusion: Fish oil is effective in improving lung function, especially in asthma patients with wild genotype type.

Keywords: ALOX5, asthma, PEF, fish oil, omega-3

Abstrak

Pendahuluan: Omega-3 sebagai sumber lokal berperan dalam jalur arakidonik dalam terapi asma, terkait dengan peningkatan fungsi paru. Efek antiinflamasi omega-3 diketahui berkaitan dengan faktor genetik, salah satunya pada polimorfisme gen ALOX5

Tujuan: Penelitian ini bertujuan untuk mengetahui profil polimorfisme ALOX5 dan efek minyak ikan omega-3 terhadap fungsi paru-paru penderita asma di Surabaya.

Metode: Metode yang digunakan adalah studi pre-eksperimental dengan teknik pengambilan sampel purposive sampling untuk pengumpulan data dari bulan Juni 2017 sampai Januari 2018 di Surabaya. Intervensi yang diberikan adalah minyak ikan yang mengandung 1000 mg omega-3 selama 1 bulan. Uji beda menggunakan paired t-test untuk membandingkan sebelum dan sesudah mendapat intervensi. Subjek penelitian adalah 27 pasien penderita asma dewasa rawat jalan dan 23 pasien non asma (sebagai pembanding pada pengujian genetik). Hasil peningkatan fungsi paru menunjukkan perbedaan yang signifikan (p = 0,00) pada nilai PEF0 (rata-rata: 217,96L / detik) dan PEF4 (rata-rata: 325,00L / detik). Dari 27 subjek penelitian, hanya 23 orang yang dapat menjalani pengujian genetik dengan swab bukal. Pasien asma memiliki lebih banyak genotipe mutan II (39,13%) dibandingkan tipe liar (30,43%). Dalam penelitian ini, hubungan antara polimorfisme gen ALOX5 dengan peningkatan fungsi paru tidak dapat diuji karena jumlah sampel yang relatif terbatas. Ada satu subjek yang memiliki nilai PEF konstan (mutan II) dan mengalami penurunan nilai PEF (mutan III).

Kesimpulan: Minyak ikan efektif meningkatkan fungsi paru-paru, terutama pada penderita asma tipe wild genotype.

Kata kunci: ALOX5, asma, PEF, minyak ikan, omega-3

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ALOX5 GENE POLYMORPHISM AND EFFECTS OF OMEGA-3 FISH OIL ON LUNG FUNCTION IN ASTHMA

INTRODUCTION

Asthma is a heterogeneous disease that contains episodic wheezing, coughing, and chest tightness. Asthma can reduce work productivity or days lost from school, increase health costs, and the risk of hospitalization, reduce the quality of life, and even cause death.[1] Asthma prevalence reaches 4,5% and is among the 10 largest non-communicable diseases in Indonesia. In East Java, the prevalence of asthma is estimated to have reached 5,1%.[2] Asthma can be influenced by the interaction of genetic and environmental factors, which not only affect the inflammatory process but also affect complex and interactive phenotypes.[3-6] During this time asthma treatment focuses on long-term synthetic drug therapy, which can cause adverse event problems such as methylxanthine's narrow therapeutic range of drugs,[7-10] worsen asthma exacerbations due to long-acting beta-2 single agonist[11], or oropharyngeal candidiasis due to inhaled corticosteroid.[1]

Indonesia is a maritime country, has great potential in fish production which can be processed into fish oil, such as salmon, cod, etc. Fish consumption can prevent asthma in adult patients. A high omega-3 fish oil intake of fish oil has a protective effect on asthma. In Indonesia, research on fish oil has been much done, including containing omega-3.[12-14] The amount of omega-3 polyunsaturated fatty acids (n-3 PUFA) in fish oil, consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Omega-3 has an anti-inflammatory effect and been proven effective for chronic inflammatory diseases, such as in asthma.[15] Eicosapentaenoic acid is a competitive substrate with arachidonic thereby reducing inflammation of the respiratory tract and bronchoconstriction. It can inhibit the activity of ALOX5 which can increase leukotrienes which are inflammatory factors in asthma.[16]

Monitoring is needed in the treatment of asthma to ensure the therapy is safe and effective.[1] Omega-3 fish oil has been proven clinically effective in lung function in the treatment of asthma.[17] Peak flow rate assessments are commonly used as monitoring effectiveness of asthma treatment.[18] This study aimed to determine the profile of ALOX5 polymorphism and the effects of omega-3 fish oil on lung function in asthma in Surabaya.

METHOD

Research design

The research method was pre-experimental design. Data collection was carried out from June 2017 to January 2018 in Surabaya through filling out questionnaires. The ethics committee of the University of Surabaya approved the study protocols (No. 011/KE/I/2017).

Research variable

The independent variable of this study was fish oil and ALOX5 polymorphism. While the dependent variable of this research was lung function. Omega-3 contains a total of 1000 mg of these oils, with 180mg of EPA, 120mg of DHA. ALOX5 polymorphism gene was distinguished by the size of the fragment into 4 genotype categories, namely: Wild type with a size of 267 bp (base pairs), mutant 1 with a size of 255 bp, mutant II with a size of 261 bp, and mutant III with a size of 273 bp.[19]

The peak expiratory flow (PEF) value is a pulmonary function test, as measured with peak flow meter (*Medical Center Trading Corporation Pioneer St. Cor. Shaw Blvd., Pasig City*). PEF is the maximum ability to expel air in the lungs from the maximum inspiratory state through the mouth in liters per minute units. The pulmonary function test was measured 2 times. The first was done before the intervention (PEF_0) and at week 4^{th} (PEF_4), was after receiving omega-3 fish oil therapy for 4 weeks (therapy for one month).

Omega-3 fish oil therapy was given for 4 weeks, because some previous studies proved a decrease in inflammatory breath flow from omega-3 therapy for 4 weeks.[15,20] In a previous study by Mickleborough dan Rundell,[20] that high intake of omega-3 for 4 weeks caused a positive change in the

methacholine dose needed to evoke bronchoprovocation in >40% of adult asthmatics. It is even known that only in 3-week omega-3 fatty acids-enriched fat blend (0.7 g/day) given to people with allergic asthma can reduce airway inflammation by lowering exhaled respiratory nitric oxide levels and serum eosinophils.[21]

Population and Sample Research

The population was adult outpatient asthmatics in Rungkut sub-district, Surabaya. The criteria of this research subject were: >18 years old, no other respiratory diseases, did not smoke or drink alcohol, had asthma treatment level in step 1 based on the Global Initiative for Asthma (2019) guideline,[1] which did not use controller therapy.

Method of collecting data in Statistics

Research subjects were obtained by purposive sampling method. The intervention provided was fish oil which contains 1000 mg of omega-3, 180 mg of EPA, 120 mg of DHA. The fish oil was given to patients at once-daily doses, then followed up every week for 4 weeks. The normality test used Shapiro Wilk, and continued with a different test using paired t-test (parametric) or Friedman Test (non-parametric) to compare before and after getting the omega-3 fish oil for 4 weeks. In this study, there were 2 groups, namely: test group was asthma patients and received omega-3 fish oil intervention for 4 weeks. While control group was a non-asthma subject as a comparison of genetic testing.

Genetic Test Method

ALOX5 polymorphism gene was tested at the Purification and Molecular Biology Laboratory, Faculty of Biotechnology, Universitas Surabaya. Buccal swabs (by cotton swab) were performed on each patient for the purpose of DNA extraction tests. The samples were stored at -20^{o}C, and was extracted no more than four weeks before the DNA was extracted. The determination of the type of polymorphism of each subject was done by the PCR method.

RESULT

Subjects in this study were grouped according to gender, age, and treatment history (table 1). The number of subjects based on subject characteristics included age and gender. Most respondents had was late adolescence (17-25 years old) which was 26 of 27. And there were more female respondents (20 of 27) than male (7 of 27).

Table 1. Frequency Distribution of Respondent Characteristics

Characteristics		Frequency (n: 27)	Percentage (%)
Gender	Male	7	25,92
	Female	20	74,07
Age (years)	Late Teenagers (17-25)	26	96,29
	Early Adult (26-35)	1	3,70
	Late Adults (36-45)	0	0

In 27 study subjects who were given omega-3 fish oil, changes in lung function values were found have significant differences PEF values between before and after the intervention. The average value of PEF_0 was 217.96 L/sec and PEF_4 was 325.00 L/sec. From 27 samples, there were 21 people experienced increasing PEF value (77,78%), 1 constant (3,70%), and 5 people had to decrease PEF value (18,52%). The normality test using Shapiro Wilk showed p value PEF_0 (0,002) and PEF_4 (0,089), so the difference test used Friedman Test and if p value<0,000 means that the significant difference between PEF_0 and PEF_4 (Figure 1).

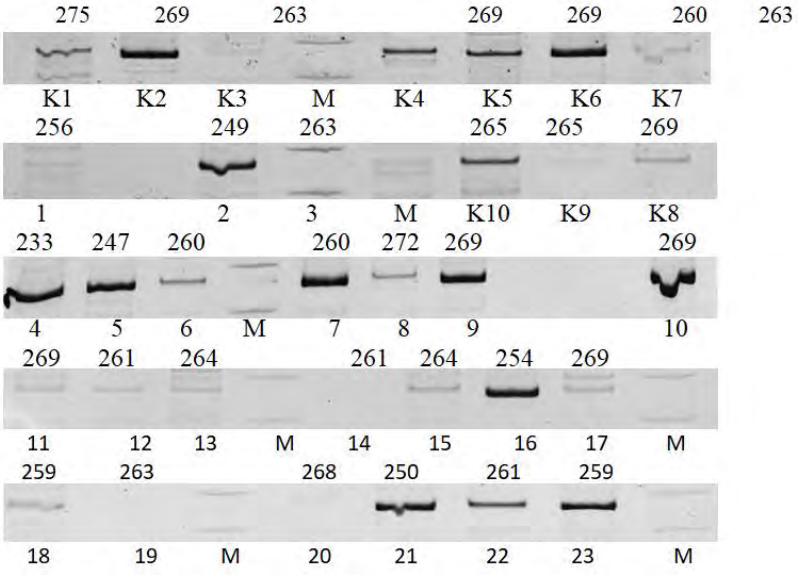

Figure 1. The Gel of ALOX5 Polymorphism Gene Test.

M: Marker (200-300 basepairs); K: Control group; 1-23: Test group

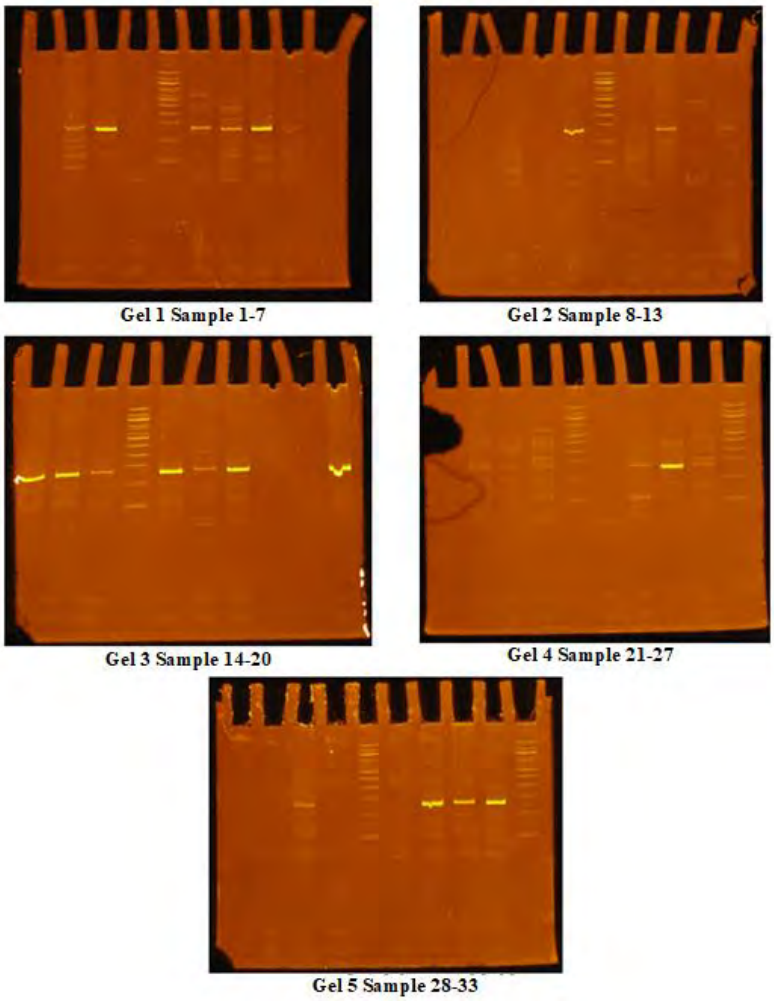

Figure 2. ALOX5 Gene Test Result

Statistical tests can be carried out if there is no frequency of reality or also called an actual count of 0 and the frequency of expectations <5. The control group in this study used non-asthma subjects (10 people). The control group showed that 60% of wild type, 30% of mutant II, and 10% of mutant III category. However, none was included in the mutant I category. In the test group, 39,1% of mutant II category, 30,4% included in the wild type category, 26,08% included in the mutant I category. While in the mutant III category there was only 4,3%.

Of the 27 study subjects, only 23 people could have genetic testing, cause there were genetic samples data (taking buccal swab) of 3 subjects that cannot be read after the PCR process. The results of ALOX5 polymorphism genes test showed the differences in genetic patterns between asthma and non-asthma patients. Most asthma groups have wild type genotype categories, whereas those in the non-asthma group have mutant II genotype categories (Table 2).

Table 2. Frequency Distribution of ALOX5 Polymorphism Genes Test

GENOTYPE	**Frequency**		**TOTAL**
	Control Group	**Test Group**	

	(non-asthma)	(asthma)	
WILD TYPE	6	7	13
MUTANT I	0	6	6
MUTANT II	3	9	12
MUTANT III	1	1	1
TOTAL	10	23	33

Table 3. Cross Tabulation of ALOX5 Polymorphism and PEF Value of Omega-3 Fish Oil for 4 Weeks

GENOTYPE	Frequency of Change in Lung Function			TOTAL
	Increased	Constant	Decreased	
WILD TYPE	7	0	0	7
MUTANT I	6	0	0	6
MUTANT II	8	1	0	9
MUTANT III	0	0	1	1
TOTAL	21	1	1	23

This study also compared the effect of genotype on lung function measured in the test group which can be seen in table 3. This study cannot be tested statistically. Statistical tests can be done if there is no reality frequency or also called Actual Count of 0 and the expected frequency was <5. The results of the study in table 3 explain that the sample of this study consisted of test and control groups. In the control group showed the wild type (6 of 10), mutant II (3 of 10) and mutant III (1 of 10). But no one is included in the category of mutant I. In the test group, it showed mutant II (9 of 23), the wild type (7 of 23), and mutant I (6 of 23). While in mutant III there were only 1 of 23. The highest number was obtained in the mutant II genotype with the increased PEF value as many as 8 of 23 people and there was only one person who had the mutant III genotype had decreased asthma symptoms.

DISCUSSION

Omega-3 has been proven effective for chronic inflammatory diseases, including the respiratory tract such as asthma.[15,22] Through the ALOX5 pathway, fish oil reduces arachidonic acid involved in bronchoconstriction and inflammation in the respiratory tract, a substrate for substrate synthesis for eicosanoid synthesis that produces inflammatory mediators, especially LTC4 (Leukotriene C4). Leukotriene C4 production is inhibited so that EPA competes with arachidonic acid which used as an ALOX5 substrate.[16,22]

The 5-Lipoxygenase is encoded by ALOX5, which is located on chromosome 10q. The wild type (5 repeat allele or 5/5) is the major allele among various populations, including both African Americans and whites, and is thus referred to as the major repeat variant. Compared to the wildtype, another variants (non-5 repeats) have been associated with variable response to leukotriene inhibitors and leukotriene receptor antagonists, supporting the notion that the wildtype is associated with increased production of leukotrienes, reduced lung function, and potentially worse asthma control.[23] Another study by Kalayci et al.,[24] also supports that patients with wildtype (5/5) more expressing ALOX5 mRNA and produce LTC4, so it must have a lower bronchodilator response.

In contrast with the research, all asthma patients with wild type showed improved lung function, and only a patient with mutant III genotype decreased lung function. In addition, non-asthma patients were more predominantly wild type (6 of 10), whereas in the asthma group are more predominantly mutant II (9 of 23). Further research is needed to determine the role in the ALOX5 gene polymorphism in asthma and non-asthma patients, because the number of samples used is relatively small. Individual factors need further attention in genetic research. Response to individuals that influence many factors, such as genetics, environment, disease, etc. This will affect variations in a person's body in responding to drugs, both with pharmacokinetics and pharmacodynamics in showing the effectiveness and safety of the treatment.[25] Genetic factors are factors that play an important role in the response of individual therapy,[26] and an estimated genetic influence of 20-95% on drug effects.[27] Although there were several factors that cannot be controlled, the effect of the therapy was not influenced by other drugs including asthma treatment, because all respondents were included in asthma therapy step 1 which means not to use asthma therapy routinely.[1] And all patients did not report if during the intervention using other therapies.

In another study that used lung outcome parameters, according to Tse et al.,[26] there was an increase in lung function which was marked by a decrease in the principle of exacerbation, a decrease in the use of beta-2 agonists, and an increase in lung function which increased with peak flow meters in the wild type category. There was no improvement in the function categories of mutants (mutants II and mutants III). But in this study, the effectiveness of therapy was measured by lung function from the PEF value. All study subjects had never seen and used a peak flow meter at PEF_0 before being given therapy), while at the time of measurement before getting therapy (t0) was the first measurement for all research subjects. In addition, other factors that can affect PEF measurements include: gender, height and weight, and socioeconomic status.[28] Poor response on mutant genotypes is also proven by Telleria et al.,[29] in asthma patients receiving leukotriene receptor antagonist therapy after 6 months of treatment with montelukast. The limitations of this study were; respondent's disease history, such as heart and kidney disease, was not carried out the latest examination and was not supported the medical necessity; sampling for the ALOX5 gene test used cotton swabs which for testing were more difficult than blood samples; and researchers could not control race factors that can affect genetic outcomes.

CONCLUSION

In 27 subjects showed significant differences (p value = 0.00) after administration of omega-3 fish oil interventions. Most had increased lung function (77,78%), and there was 1 person who constant (3,70%), and 5 people had to decrease PEF values (18,52%). Most subjects in Surabaya-Indonesia have a wild type genotype (total all subjects), but in asthma patients have more mutant II genotypes (39,13%) than wild types (30,43%). In this study, the relationship between ALOX5 polymorphism and lung function improvement cannot be tested because the number of samples is relatively limited and most subjects have increased lung function (91.30%) and there were significant differences before and after the administration of fish oil therapy (p=0.00). There is one subject that has a constant PEF value (mutant II) and a decrease in PEF value (mutant III).

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ORIGINAL ARTICLE

ALOX5 GENE POLYMORPHISM AND EFFECTS OF OMEGA-3 FISH OIL ON LUNG FUNCTION IN ASTHMA

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ABSTRACT

Background: Omega-3 as a local source plays a role in the arachidonic pathway in asthma therapy related to an improvement of lung function. The anti-inflammatory effects of omega-3 are known to be related to genetic factors, one of which is on ALOX5 gene polymorphism

Objective: This study aims to determine the profile of ALOX5 polymorphism and the effects of omega-3 fish oil on lung function in asthma in Surabaya

Methods: The method was pre-experimental design, using a purposive sampling technique for data collection from June 2017 to January 2018 in Surabaya. The intervention provided was fish oil which contains 1000 mg of omega-3 for 1 month. The different test using paired t-test to compare before and after getting the intervention. The research subjects were 27 adult outpatient asthmatics and 23 non-asthma patients (as the comparison on genetic testing.

Results: The results of improvement in lung function showed a significant difference (p=0.00) in PEF0 values (average: 217,96L/sec) and PEF4 (average: 325,00L/sec). Of the 27 study subjects, only 23 people could have genetic testing by a buccal swab. Asthma patients had more mutant II genotypes (39,13%) than wild types (30,43%). In this study, the relationship between ALOX5 gene polymorphism and lung function improvement cannot be tested because the number of samples is relatively limited. There was one subject who had constant PEF value (mutant II) and decreased PEF value (mutant III)

Conclusion: Fish oil is effective in improving lung function, especially in asthma patients with wild genotype type.

Keywords: ALOX5, asthma, PEF, fish oil, omega-3

Abstrak

Pendahuluan: Omega-3 sebagai sumber lokal berperan dalam jalur arakidonik dalam terapi asma, terkait dengan peningkatan fungsi paru. Efek antiinflamasi omega-3 diketahui berkaitan dengan faktor genetik, salah satunya pada polimorfisme gen ALOX5

Tujuan: Penelitian ini bertujuan untuk mengetahui profil polimorfisme ALOX5 dan efek minyak ikan omega-3 terhadap fungsi paru-paru penderita asma di Surabaya.

Metode: Metode yang digunakan adalah studi pre-eksperimental dengan teknik pengambilan sampel purposive sampling untuk pengumpulan data dari bulan Juni 2017 sampai Januari 2018 di Surabaya. Intervensi yang diberikan adalah minyak ikan yang mengandung 1000 mg omega-3 selama 1 bulan. Uji beda menggunakan paired t-test untuk membandingkan sebelum dan sesudah mendapat intervensi. Subjek penelitian adalah 27 pasien penderita asma dewasa rawat jalan dan 23 pasien non asma (sebagai pembanding pada pengujian genetik). Hasil peningkatan fungsi paru menunjukkan perbedaan yang signifikan (p = 0,00) pada nilai PEF0 (rata-rata: 217,96L / detik) dan PEF4 (rata-rata: 325,00L / detik). Dari 27 subjek penelitian, hanya 23 orang yang dapat menjalani pengujian genetik dengan swab bukal. Pasien asma memiliki lebih banyak genotipe mutan II (39,13%) dibandingkan tipe liar (30,43%). Dalam penelitian ini, hubungan antara polimorfisme gen ALOX5 dengan peningkatan fungsi paru tidak dapat diuji karena jumlah sampel yang relatif terbatas. Ada satu subjek yang memiliki nilai PEF konstan (mutan II) dan mengalami penurunan nilai PEF (mutan III).

Kesimpulan: Minyak ikan efektif meningkatkan fungsi paru-paru, terutama pada penderita asma tipe wild genotype.

Kata kunci: ALOX5, asma, PEF, minyak ikan, omega-3

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ALOX5 GENE POLYMORPHISM AND EFFECTS OF OMEGA-3 FISH OIL ON LUNG FUNCTION IN ASTHMA

INTRODUCTION

Asthma is a heterogeneous disease that contains episodic wheezing, coughing, and chest tightness. Asthma can reduce work productivity or days lost from school, increase health costs, and the risk of hospitalization, reduce the quality of life, and even cause death.[1] Asthma prevalence reaches 4,5% and is among the 10 largest non-communicable diseases in Indonesia. In East Java, the prevalence of asthma is estimated to have reached 5,1%.[2] Asthma can be influenced by the interaction of genetic and environmental factors, which not only affect the inflammatory process but also affect complex and interactive phenotypes.[3-6] During this time asthma treatment focuses on long-term synthetic drug therapy, which can cause adverse event problems such as methylxanthine's narrow therapeutic range of drugs,[7-10] worsen asthma exacerbations due to long-acting beta-2 single agonist[11], or oropharyngeal candidiasis due to inhaled corticosteroid.[1]

Indonesia is a maritime country, has great potential in fish production which can be processed into fish oil, such as salmon, cod, etc. Fish consumption can prevent asthma in adult patients. A high omega-3 fish oil intake of fish oil has a protective effect on asthma. In Indonesia, research on fish oil has been much done, including containing omega-3.[12-14] The amount of omega-3 polyunsaturated fatty acids (n-3 PUFA) in fish oil, consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Omega-3 has an anti-inflammatory effect and been proven effective for chronic inflammatory diseases, such as in asthma.[15] Eicosapentaenoic acid is a competitive substrate with arachidonic thereby reducing inflammation of the respiratory tract and bronchoconstriction. It can inhibit the activity of ALOX5 which can increase leukotrienes which are inflammatory factors in asthma.[16]

Monitoring is needed in the treatment of asthma to ensure the therapy is safe and effective.[1] Omega-3 fish oil has been proven clinically effective in lung function in the treatment of asthma.[17] Peak flow rate assessments are commonly used as monitoring effectiveness of asthma treatment.[18] This study aimed to determine the profile of ALOX5 polymorphism and the effects of omega-3 fish oil on lung function in asthma in Surabaya.

METHOD

Research design

The research method was pre-experimental design. Data collection was carried out from June 2017 to January 2018 in Surabaya through filling out questionnaires. The ethics committee of the University of Surabaya approved the study protocols (No. 011/KE/I/2017).

Research variable

The independent variable of this study was fish oil and ALOX5 polymorphism. While the dependent variable of this research was lung function. Omega-3 contains a total of 1000 mg of these oils, with 180mg of EPA, 120mg of DHA. ALOX5 polymorphism gene was distinguished by the size of the fragment into 4 genotype categories, namely: Wild type with a size of 267 bp (base pairs), mutant 1 with a size of 255 bp, mutant II with a size of 261 bp, and mutant III with a size of 273 bp.[19]

The peak expiratory flow (PEF) value is a pulmonary function test, as measured with peak flow meter (*Medical Center Trading Corporation Pioneer St. Cor. Shaw Blvd., Pasig City*). PEF is the maximum ability to expel air in the lungs from the maximum inspiratory state through the mouth in liters per minute units. The pulmonary function test was measured 2 times. The first was done before the intervention (PEF_0) and at week 4th (PEF_4), was after receiving omega-3 fish oil therapy for 4 weeks (therapy for one month).

Omega-3 fish oil therapy was given for 4 weeks, because some previous studies proved a decrease in inflammatory breath flow from omega-3 therapy for 4 weeks.[15,20] In a previous study by Mickleborough dan Rundell,[20] that high intake of omega-3 for 4 weeks caused a positive change in the

methacholine dose needed to evoke bronchoprovocation in >40% of adult asthmatics. It is even known that only in 3-week omega-3 fatty acids-enriched fat blend (0.7 g/day) given to people with allergic asthma can reduce airway inflammation by lowering exhaled respiratory nitric oxide levels and serum eosinophils.[21]

Population and Sample Research

The population was adult outpatient asthmatics in Rungkut sub-district, Surabaya. The criteria of this research subject were: >18 years old, no other respiratory diseases, did not smoke or drink alcohol, had asthma treatment level in step 1 based on the Global Initiative for Asthma (2019) guideline,[1] which did not use controller therapy.

Method of collecting data in Statistics

Research subjects were obtained by purposive sampling method. The intervention provided was fish oil which contains 1000 mg of omega-3, 180 mg of EPA, 120 mg of DHA. The fish oil was given to patients at once-daily doses, then followed up every week for 4 weeks. The normality test used Shapiro Wilk, and continued with a different test using paired t-test (parametric) or Friedman Test (non-parametric) to compare before and after getting the omega-3 fish oil for 4 weeks. In this study, there were 2 groups, namely: test group was asthma patients and received omega-3 fish oil intervention for 4 weeks. While control group was a non-asthma subject as a comparison of genetic testing.

Genetic Test Method

ALOX5 polymorphism gene was tested at the Purification and Molecular Biology Laboratory, Faculty of Biotechnology, Universitas Surabaya. Buccal swabs (by cotton swab) were performed on each patient for the purpose of DNA extraction tests. The samples were stored at -20^{0}C, and was extracted no more than four weeks before the DNA was extracted. The determination of the type of polymorphism of each subject was done by the PCR method.

RESULT

Subjects in this study were grouped according to gender, age, and treatment history (table 1). The number of subjects based on subject characteristics included age and gender. Most respondents had was late adolescence (17-25 years old) which was 26 of 27. And there were more female respondents (20 of 27) than male (7 of 27).

Table 1. Frequency Distribution of Respondent Characteristics

Characteristics		Frequency (n: 27)	Percentage (%)
Gender	Male	7	25,92
	Female	20	74,07
Age (years)	Late Teenagers (17-25)	26	96,29
	Early Adult (26-35)	1	3,70
	Late Adults (36-45)	0	0

In 27 study subjects who were given omega-3 fish oil, changes in lung function values were found have significant differences PEF values between before and after the intervention. The average value of PEF_0 was 217.96 L/sec and PEF_4 was 325.00 L/sec. From 27 samples, there were 21 people experienced increasing PEF value (77,78%), 1 constant (3,70%), and 5 people had to decrease PEF value (18,52%). The normality test using Shapiro Wilk showed p value PEF_0 (0,002) and PEF_4 (0,089), so the difference test used Friedman Test and if p value<0,000 means that the significant difference between PEF_0 and PEF_4 (Figure 1).

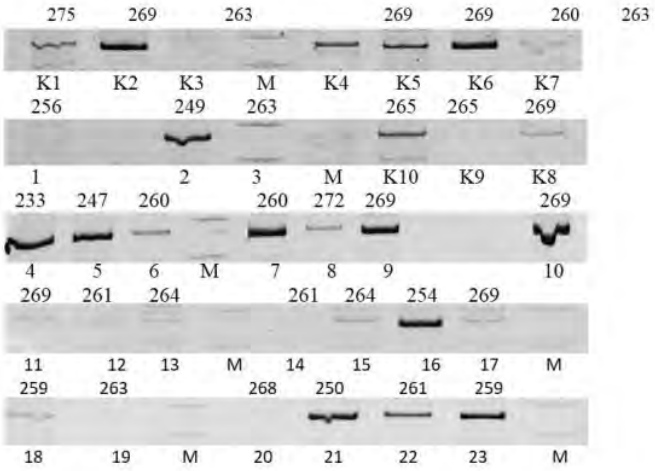

Figure 1. The Gel of ALOX5 Polymorphism Gene Test.

M: Marker (200-300 basepairs); K: Control group; 1-23: Test group

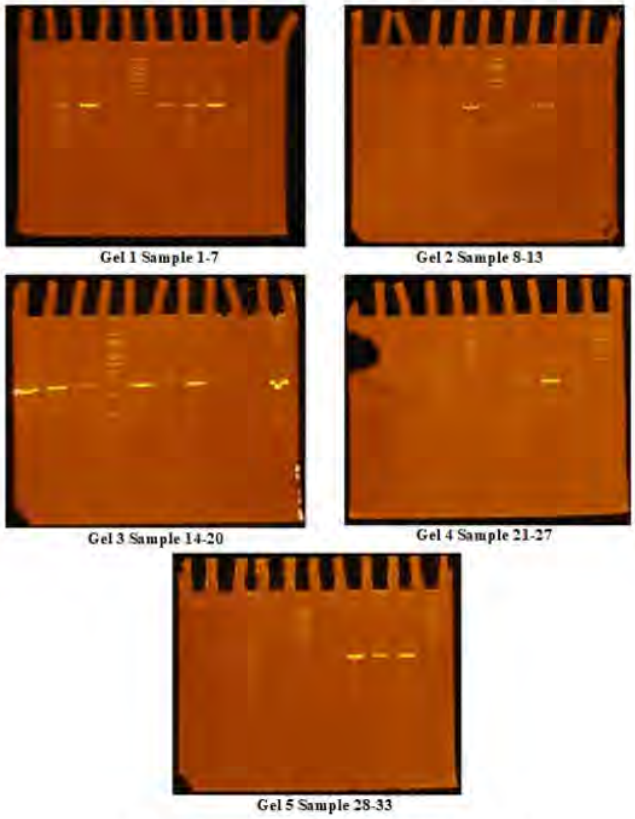

Figure 2. ALOX5 Gene Test Result

Statistical tests can be carried out if there is no frequency of reality or also called an actual count of 0 and the frequency of expectations <5. The control group in this study used non-asthma subjects (10 people). The control group showed that 60% of wild type, 30% of mutant II, and 10% of mutant III category. However, none was included in the mutant I category. In the test group, 39,1% of mutant II category, 30,4% included in the wild type category, 26,08% included in the mutant I category. While in the mutant III category there was only 4,3%.

Of the 27 study subjects, only 23 people could have genetic testing, cause there were genetic samples data (taking buccal swab) of 3 subjects that cannot be read after the PCR process. The results of ALOX5 polymorphism genes test showed the differences in genetic patterns between asthma and non-asthma patients. Most asthma groups have wild type genotype categories, whereas those in the non-asthma group have mutant II genotype categories (Table 2).

Table 2. Frequency Distribution of ALOX5 Polymorphism Genes Test

GENOTYPE	Frequency		TOTAL
	Control Group	Test Group	

	(non-asthma)	(asthma)	
WILD TYPE	6	7	13
MUTANT I	0	6	6
MUTANT II	3	9	12
MUTANT III	1	1	1
TOTAL	10	23	33

Table 3. Cross Tabulation of ALOX5 Polymorphism and PEF Value of Omega-3 Fish Oil for 4 Weeks

GENOTYPE	Frequency of Change in Lung Function			TOTAL
	Increased	Constant	Decreased	
WILD TYPE	7	0	0	7
MUTANT I	6	0	0	6
MUTANT II	8	1	0	9
MUTANT III	0	0	1	1
TOTAL	21	1	1	23

This study also compared the effect of genotype on lung function measured in the test group which can be seen in table 3. This study cannot be tested statistically. Statistical tests can be done if there is no reality frequency or also called Actual Count of 0 and the expected frequency was <5. The results of the study in table 3 explain that the sample of this study consisted of test and control groups. In the control group showed the wild type (6 of 10), mutant II (3 of 10) and mutant III (1 of 10). But no one is included in the category of mutant I. In the test group, it showed mutant II (9 of 23), the wild type (7 of 23), and mutant I (6 of 23). While in mutant III there were only 1 of 23. The highest number was obtained in the mutant II genotype with the increased PEF value as many as 8 of 23 people and there was only one person who had the mutant III genotype had decreased asthma symptoms.

DISCUSSION

Omega-3 has been proven effective for chronic inflammatory diseases, including the respiratory tract such as asthma.[15,22] Through the ALOX5 pathway, fish oil reduces arachidonic acid involved in bronchoconstriction and inflammation in the respiratory tract, a substrate for substrate synthesis for eicosanoid synthesis that produces inflammatory mediators, especially LTC4 (Leukotriene C4). Leukotriene C4 production is inhibited so that EPA competes with arachidonic acid which used as an ALOX5 substrate.[16,22]

The 5-Lipoxygenase is encoded by ALOX5, which is located on chromosom 10q. The wild type (5 repeat allele or 5/5) is the major allele among various populations, including both African Americans and whites, and is thus referred to as the major repeat variant. Compared to the wildtype, another variants (non-5 repeats) have been associated with variable response to leukotriene inhibitors and leukotriene receptor antagonists, supporting the notion that the wildtype is associated with increased production of leukotrienes, reduced lung function, and potentially worse asthma control.[23] Another study by Kalayci et al.,[24] also supports that patients with wildtype (5/5) more expressing ALOX5 mRNA and produce LTC4, so it must have a lower bronchodilator response.

In contrast with the research, all asthma patients with wild type showed improved lung function, and only a patient with mutant III genotype decreased lung function. In addition, non-asthma patients were more predominantly wild type (6 of 10), whereas in the asthma group are more predominantly mutant II (9 of 23). Further research is needed to determine the role in the ALOX5 gene polymorphism in asthma and non-asthma patients, because the number of samples used is relatively small. Individual factors need further attention in genetic research. Response to individuals that influence many factors, such as genetics, environment, disease, etc. This will affect variations in a person's body in responding to drugs, both with pharmacokinetics and pharmacodynamics in showing the effectiveness and safety of the treatment.[25] Genetic factors are factors that play an important role in the response of individual therapy,[26] and an estimated genetic influence of 20-95% on drug effects.[27] Although there were several factors that cannot be controlled, the effect of the therapy was not influenced by other drugs including asthma treatment, because all respondents were included in asthma therapy step 1 which means not to use asthma therapy routinely.[1] And all patients did not report if during the intervention using other therapies.

In another study that used lung outcome parameters, according to Tse et al.,[26] there was an increase in lung function which was marked by a decrease in the principle of exacerbation, a decrease in the use of beta-2 agonists, and an increase in lung function which increased with peak flow meters in the wild type category. There was no improvement in the function categories of mutants (mutants II and mutants III). But in this study, the effectiveness of therapy was measured by lung function from the PEF value. All study subjects had never seen and used a peak flow meter at PEF_0 before being given therapy), while at the time of measurement before getting therapy (t0) was the first measurement for all research subjects. In addition, other factors that can affect PEF measurements include: gender, height and weight, and socioeconomic status.[28] Poor response on mutant genotypes is also proven by Telleria et al.,[29] in asthma patients receiving leukotriene receptor antagonist therapy after 6 months of treatment with montelukast. The limitations of this study were; respondent's disease history, such as heart and kidney disease, was not carried out the latest examination and was not supported the medical necessity; sampling for the ALOX5 gene test used cotton swabs which for testing were more difficult than blood samples; and researchers could not control race factors that can affect genetic outcomes.

CONCLUSION

In 27 subjects showed significant differences (p value = 0.00) after administration of omega-3 fish oil interventions. Most had increased lung function (77,78%), and there was 1 person who constant (3,70%), and 5 people had to decrease PEF values (18,52%). Most subjects in Surabaya-Indonesia have a wild type genotype (total all subjects), but in asthma patients have more mutant II genotypes (39,13%) than wild types (30,43%). In this study, the relationship between ALOX5 polymorphism and lung function improvement cannot be tested because the number of samples is relatively limited and most subjects have increased lung function (91.30%) and there were significant differences before and after the administration of fish oil therapy (p=0.00). There is one subject that has a constant PEF value (mutant II) and a decrease in PEF value (mutant III).

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