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ความชุกของกลุ่มโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรังในโรงพยาบาลศรีนครินทร์

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The Prevalence of Asthma-COPD Overlap Syndrome (ACOS) in Srinagarind Hospital

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หลักการและวัตถุประสงค์: โรคหืดและโรคปอดอุดกั้นเรื้อรังเป็นโรคทางระบบทางเดินหายใจที่พบบ่อยและมีความสำคัญทางสาธารณสุขของไทย มีลักษณะทางคลินิกบางอย่างที่มีความคาบเกี่ยวกันระหว่างทั้งสองโรค ในปี พ.ศ. 2558 ได้มีการจัดทำแนวทางการดูแลรักษากลุ่มโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรังโดย Global Initiative for Asthma (GINA) และ Global Initiative for Chronic Obstructive Lung Disease (GOLD) ซึ่งใช้ลักษณะกลุ่มอาการต่างๆ เป็นตัวคัดแยกผู้ป่วยออกเป็นโรคหืด โรคปอดอุดกั้นเรื้อรังและโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรัง การศึกษานี้จัดทำเพื่อศึกษาความชุกของกลุ่มโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรังโดยใช้เกณฑ์การวินิจฉัยดังกล่าว

วิธีการศึกษา: เป็นการศึกษาเชิงพรรณนา ณ จุดเวลาใดเวลาหนึ่งแบบตัดขวาง โดยเก็บข้อมูลจากคลินิกโรคหลอดลม ณ โรงพยาบาลศรีนครินทร์ ตั้งแต่เดือน ตุลาคม 2558 ถึง พฤศจิกายน 2559 ข้อมูลอาการทางคลินิกเก็บรวบรวมโดยใช้แบบสอบถามร่วมกับเก็บข้อมูลผลการตรวจสมรรถภาพปอดและข้อมูลจากภาพถ่ายรังสีทรวงอก

Background and Objective: Asthma and chronic obstructive pulmonary disease (COPD) are common respiratory diseases in Thai and cause substantial public health issues. There are some clinical characteristics that overlapped between these two conditions. In 2015, Global Initiative for Asthma (GINA) along with Global Initiative for Chronic Obstructive Lung Disease (GOLD) established an asthma-COPD overlap syndrome (ACOS) guideline, which had a syndromic approach that classify patients into asthma, COPD and ACOS. This study aimed to identify the prevalence of ACOS based on these guidelines.

Methods: This descriptive cross-sectional study was performed in airway clinic at Srinagarind hospital between October 2015 and November 2016. Clinical data were gathered by using questionnaires. Spirometry information and chest radiographic results were also collected.

Results: One hundred and sixty-nine patients were included in this study. The prevalence of asthma, COPD and ACOS were 42.60%, 41.15% and 11.24%, respectively. Among 19 patients who were diagnosed with ACOS, 7 patients (36.84%) were previously recognized as COPD

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ผลการศึกษา: ผู้ป่วยทั้งหมด 169 ราย เข้าร่วมในการศึกษานี้ พบความชุกของโรคหืด, โรคปอดอุดกั้นเรื้อรัง และโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรัง ร้อยละ 42.60, 41.15 และ 11.24 ตามลำดับ โดยในผู้ป่วย 19 รายที่เข้าได้กับกลุ่มโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรัง 7 ราย (ร้อยละ 36.84) เคยได้รับการวินิจฉัยว่าเป็นโรคปอดอุดกั้นเรื้อรังมาก่อน และ 12 ราย (ร้อยละ 63.16) เคยได้รับการวินิจฉัยโรคหืดมาก่อน อายุเฉลี่ย (± ค่าเบี่ยงเบนมาตรฐาน) ของผู้ป่วยโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรังคือ 62 (± 9.78) ปี พบมีผู้ป่วย 8 ราย (ร้อยละ 42.11) ในกลุ่มนี้เคยสูบบุหรี่มาก่อน และ 16 ราย (ร้อยละ 84.21) มีอาการภูมิแพ้ร่วมด้วย ค่าเฉลี่ย (± ค่าเบี่ยงเบนมาตรฐาน) ของปริมาตรของอากาศที่ถูกขับออกในวินาทีแรกของการหายใจออกอย่างเร็วและแรงเต็มที่หลังจากพ่นยาขยายหลอดลมในการตรวจสมรรถภาพปอดคือ 1.72 (± 0.35) ลิตร หรือคิดเป็นร้อยละ 71 (± 20.58) เมื่อเทียบกับค่าอ้างอิง

สรุป: พบความชุกของโรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรังประมาณร้อยละ 11 ควรจำแนกผู้ป่วยกลุ่มนี้ออกจากโรคหืดและโรคปอดอุดกั้นเรื้อรัง เนื่องจากการรักษาจำเพาะของแต่ละโรคนั้นมีความแตกต่างกัน

คำสำคัญ: โรคที่มีความคาบเกี่ยวกันระหว่างโรคหืดและโรคปอดอุดกั้นเรื้อรัง, โรคหืด, โรคปอดอุดกั้นเรื้อรัง, ความชุก

and 12 patients (63.16%) were previously recognized as asthma. The mean (±SD) of age in ACOS group was 62 (±9.78) years. Eight patients (42.11%) were previous smokers. Sixteen patients (84.21%) had allergic symptoms. The mean (±SD) post-bronchodilator forced expiratory volume in one second (FEV1) and percentage of post-bronchodilator FEV1 were 1.72 (±0.35) liters and 71(±20.58)%, respectively.

Conclusion: The prevalence of ACOS among asthma and COPD patients is approximately 11%. Sorting out ACOS patients from asthma and COPD is necessary due to their individual and specific pharmacotherapy.

Keywords: Asthma-COPD Overlap Syndrome, Asthma, COPD, Prevalence

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Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are common important pulmonary diseases in Thai. Distinguishing asthma from COPD is relatively difficult, especially in smokers and elderly patients. Some patients have clinical features of both asthma and COPD. The terminology “asthma-COPD overlap syndrome (ACOS)” was used in this condition[1]. ACOS was heterogeneous disease including; asthma with fixed airway obstruction, smoking asthma, asthma with emphysema and COPD with significant bronchodilator response. In the past, many criteria were used for diagnosing ACOS resulting in a variety of the prevalence[2,3].

Until 2015, Global Initiative for Asthma (GINA) along with Global Initiative for Chronic Obstructive Lung Disease (GOLD) established the asthma-COPD overlap syndrome (ACOS) guideline which characterized ACOS based on persistent airflow limitation with combination of asthma and COPD features[1].

It is vital to classify ACOS from asthma or COPD due to their individual and specific pharmacotherapy. Furthermore, ACOS patients are more likely to have exacerbation, hospital admission and use more the costs of treatment[4-6,11,12]. Because of the standard criteria had recently been published, the increasing prevalence of ACOS had been proposed. However, there were limited data about the prevalence of ACOS in Thailand. The aims of this study was to identify the prevalence of ACOS in airway clinic, Srinagarind hospital, Thailand based on 2015 GINA and GOLD criteria for ACOS[1].

Methods

This cross-sectional descriptive study was performed in the airway clinic at Srinagarind hospital

between October 2015 and November 2016. The inclusion criteria were patients who were diagnosed asthma or COPD and also had spirometry and chest radiographic results. We excluded patients with concomitant diseases such as bronchiectasis, interstitial lung disease, lung cancer, pleural disease, pulmonary embolism, neuromuscular disease and congestive heart failure. Informed consents were obtained from all participants. This study was approved by Khon Kaen University ethics committee.(HE-581378)

The demographic data were demonstrated with percentage and mean with standard deviation. Baseline characteristics between groups were compared by using Pearson chi-square and Fisher's exact tests for categorical variables. We used one-way ANOVA for parametric and Kruskal-Wallis test for non-parametric in case of numerical variables. Significant differences were defined as $p< 0.05$. The normal distribution was tested by Shapiro-Wilk W test and Skewness/Kurtosis test. All statistical analysis was performed with Stata/MP software version 11.0 (Stata Corp, College Station, TX). Eligible patients were consented and performed the questionnaire that contained required data in syndromic approach according to the ACOS guideline. The first complete spirometry data of each patient was used. Data were collected include the ratio of forced expiratory volume in one second and forced vital capacity (FEV1/FVC), forced expiratory volume in one second (FEV1), forced vital capacity (FVC), forced expiratory flow at 25-75% of the pulmonary volume (FEF25-75%), peak expiratory flow (PEF) pre and post-bronchodilator with percentage change. The first chest radiography performed at the time of diagnosis was interpreted for hyperaeration condition. Ashtma, COPD and ACOS were defined according to asthma-COPD overlap syndrome (ACOS) guideline 2015. In asthma group, selected criteria were age of onset before 20 years old, variation of symptoms over minutes or hours, worsening symptoms occurred overnight or in the early morning, symptoms triggered by dust or allergen, variable airflow limitations, previous diagnosis as asthma, symptoms varied seasonally, family history of asthma, immediate response to bronchodilator and normal chest x-ray. In COPD group, selected criteria were age of onset after 40 years old, persistence of symptoms despite treatment, symptoms only good and bad days not return to normal and exertional dyspnea, chronic cough, persistence of airflow limitation (FEV1/FVC<0.7), history of exposure to smoke or biomass fuels, symptoms slowly worsening over time, rapid acting bronchodilator treatment provided only limited relief, previous diagnosis of COPD and hyperaeration detected in chest x-ray. Each item was scored as one point. If the patients had characteristics such mentioned above in asthma criteria equal to COPD criteria, they will be classified into ACOS group. However, if the patients met greater characteristics in asthma criteria than in COPD criteria, they were classified into asthma group. Similarly, if the patients matched greater COPD characteristics than in asthma criteria, they were classified into COPD group.

Results

A total of 169 patients were included in this study. The mean (±SD) age was 62.72 (±11.81) years; mean (±SD) weight and height were 61.18 (±11.64) kilograms and 161.12 (±7.18) centimeters, respectively. Overall patients had mean (±SD) age of onset of symptoms was 46.88 (±15.22) years old. Majority of the patients had a history of exposure to tobacco smoke or biomass fuel (97%). Forty-one percent of the patients had family history of asthma. One-fifth of the patients (20.14%) had hyperaeration detected from chest radiography. Regarding spirometry-related data, forty-seven percent of the patients had post-bronchodilator FEV1/FVC ratio less than 70. Mean (±SD) percentage of post bronchodilator FEV1 was 73.43% (±17.24%). Before we used the 2015 guideline to identify ACOS patients, 91 out of 169 patients (53.85%) were clinically diagnosed asthma, while 78 (46.15%) patients were diagnosed COPD. After analyzing by using syndromic approach scoring as mentioned above, the results showed that the prevalence of the ACOS among asthma and COPD patients was 11.24% (19 out of 169 patients) and the diagnosis of asthma and COPD patients were 42.60% and 46.15%, respectively. In the ACOS group, 63.16% of the patients were previously diagnosed with asthma

while 36.84% of the patients were previously diagnosed with COPD. (as shown in Table 1).

The baseline characteristics of the patients in each group were demonstrated in Table 2. In ACOS group, the mean (±SD) age was 62.05 (±9.78) years old. Eight patients (42.11%) were previous smoker. None of them were currently smoked. The mean (±SD) age of onset was 41.16 (±18.24) years old. However, we found that 9 of 19 patients (47.37%) were in the age of onset over 40 years old. Three factors that were most frequently found in ACOS group were symptoms triggered by dust or allergen (89.47%), allergic history (84.21%) and dyspnea on exertion (78.95%), respectively.

When compared ACOS with asthma and COPD, it was found that patients in ACOS group were older than the asthma group, but younger than the COPD group. Smoking history were highly found in the COPD group (57.69%), followed by the ACOS group (42.11%), and asthma (37.50%). Family history of asthma was frequently found in the asthma group, followed by the ACOS and COPD group. The patients with symptoms improved immediately after bronchodilator treatment were found most in the asthma group (66.67%), followed by the ACOS group (36.84%) and the COPD group (24.36%). There is a statistically significant difference of percentage of post-bronchodilator FEV1 in each groups; the worst lung function was those patients in the COPD group, followed by the ACOS and asthma group, respectively as shown in Table 3.

Interestingly, according to the ACOS guideline, the definite diagnosis of COPD defined as patient did not have the features of asthma. Likewise, the definite diagnosis of asthma, patient should not have the features of COPD. If scoring was exactly followed this ACOS guideline, only 4 out of a total 169 patients would have been confidently diagnosed with asthma whereas none of the patients would have been confidently diagnosed with COPD, as shown in Table 4. The different scores of the asthma features and those of COPD features were presented in Table 5.

Table 1 Prevalence of ACOS, asthma and COPD by scoring according to ACOS guideline 2015[1]

Disease diagnosed by scoring	Number of patients (%)	Number of patients previously diagnosed asthma (%)	Number of patients previously diagnosed COPD (%)
ACOS	19 (11.24)	12 (63.16)	7 (36.84)
Asthma	72 (42.60)	60 (83.33)	12 (16.67)
COPD	78 (46.15)	19 (24.36)	59 (75.64)

Table 2 Baseline characteristics of patients with ACOS, asthma and COPD

Factors	ACOS (N=19)	Asthma (N=72)	COPD (N=78)	p-value
Age (year)	62.05 (±9.78)	57.79 (±12.77)	67.44 (±9.27)	<0.001
Age of onset (year)	41.16 (±18.24)	39.67 (±12.95)	54.94 (±12.28)	<0.001
Weight (kg)	60.86 (±8.88)	64.11 (±11.72)	58.55 (±11.65)	0.016
Height (cm)	161.11 (±6.16)	160.79 (±7.07)	161.43 (±7.57)	0.827
Smoking history, no. (%) (pack-year in median(IQR))	8 (42.11)	27 (37.50)	45 (57.69)	0.042
Exposure to tobacco smoke or biomass fuels, no. (%)	3 (15.79)	18 (25.00)	17 (21.79)	0.725
Allergic condition, no. (%)	16 (84.21)	54 (75.00)	37 (47.44)	<0.001
Family history of asthma, no.(%)	9 (47.37)	39 (54.17)	22 (28.21)	0.005
Symptoms triggered by dust or allergen, no. (%)	17 (89.47)	62 (86.11)	50 (64.10)	0.003
Dyspnea on exertion, no. (%)	15 (78.95)	56 (77.78)	56 (71.79)	0.696
Chronic bronchitis, no. (%)	2 (10.53)	5 (6.94)	5 (6.41)	0.760
Variation in symptoms over minutes, hours, days, no. (%)	2 (10.53)	30 (41.67)	12 (15.38)	<0.001
Variation in symptoms over season, no. (%)	13 (68.42)	48 (66.67)	46 (58.97)	0.571
Immediate response to bronchodilator, no. (%)	7 (36.84)	48 (66.67)	19 (24.36)	<0.001
Symptoms slowly worsening over time, no. (%)	6 (31.58)	7 (9.72)	35 (44.87)	<0.001

Values are expressed as mean ± SD

Table 3 Comparison of percentage of post bronchodilator FEV1 among ACOS, Asthma and COPD.

Disease diagnosed using scoring	Post bronchodilator FEV1 mean (±SD) (liters)	Post bronchodilator FEV1 mean (±SD) (%)	p-value
ACOS	1.72 (±0.35)	71.00 (±20.58)	
Asthma	1.95 (±0.56)	78.31 (±13.24)	0.006
COPD	1.70 (±0.58)	69.53 (±18.67)	

FEV1 = forced expiration volume in 1 second

Table 4 Demonstrated amount of the patients classified into each group based on syndromic scoring from ACOS guideline 2015[1]

Diagnosis	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
Confidence in diagnosis	Definite asthma	Possible asthma	Could be ACOS	Possible COPD	Definite COPD
Scoring	Only A	A > C	A = C	C > A	Only C
N (%)	4	68	19	78	0

A = Summarized score of asthma features, C= Summarized score of COPD

Table 5 Demonstrated difference between asthma feature scores and COPD feature scores

Dx	Asthma													COPD	
ΔScore	6	5	4	3	2	1	0	1	2	3	4	5	6	7	8
N	7	8	8	10	20	19	19	18	19	12	15	3	9	1	1
%	4.14	4.73	4.73	5.92	11.83	11.24	11.24	10.65	11.24	7.19	8.88	1.78	5.33	0.59	0.59

Discussion

In this study, the prevalence of asthma-COPD overlap syndrome (ACOS) was 11.24%. This prevalence was studied in asthma and COPD patients, not in general population. Compared with previous study; Kiljander, et al[7]. study from Finland studied in asthma patients and found the prevalence of ACOS 27.4% in asthma. Their study demonstrated that age over 60 years and a smoking history of more than 20 pack-years in asthma patient were the most influential predictors of ACOS. Studies of De Marco, et al[5]. and Soriano, et al[9]. also demonstrated that the prevalence of ACOS was found more in elderly group. A study of Zeki, et al. that conducted in USA[3] found the prevalence of ACOS in asthma and COPD patients was 15.8% which was quite consistent with our study. However, the criteria used to diagnose the ACOS patients in their study were different. Their criteria were (1) allergic disease consistent with asthma, that is, variable airflow obstruction or airway hyper-responsiveness that is incompletely reversible (with or without emphysema or reduced carbon monoxide diffusion capacity) or (2) COPD with emphysema accompanied by reversible or partially reversible airflow obstruction (with or without an allergic syndrome or reduced DLCO). Comparing with our study that used syndromic approach, the COPD group still had significant bronchodilator responsiveness. Using spirometry criteria alone might not sufficient to diagnose the ACOS.

Unfortunately, the data concerning exacerbation rate of the patients were not periodically recorded in this study. Nevertheless, data concerning the history of exacerbation within the past one year were collected, and exhibited no statistically significant difference among these three groups (p = 0.640). In addition, the previous study of Menezes, et al[4]. revealed that the ACOS patients had more frequent exacerbation

than asthma and COPD patients. Like the study of Bai, et al[10]. exacerbation rate in the ACOS group was higher than in the COPD group. Besides, study of De Marco, et al[5]. showed that ACOS patients had greater hospital admission rate than asthma and COPD patients. All these implications should be further studied in the future studies.

Limitations of our study were the followings. Firstly, we only used syndromic approach, spirometry data and chest radiography. Computer tomography to define emphysema and DLCO test might need for more accurate diagnosis. The other limitation was the classification method. We classified the patients into ACOS group using scoring that asthma features score equal to COPD features score, so we might have lost the patients that perhaps had one score different as demonstrated in Table 5. Further study should be established to identify how much difference should be sufficient to classify the patients. However, strength of our study was this is the first study that demonstrated the prevalence of ACOS according to GINA along with GOLD 2015 guideline in Thailand which may be the prototype research for future studies to identify the prevalence of ACOS patients.

Conclusion

The prevalence of ACOS among asthma and COPD patients in Thailand is approximately 11%. The age group of the ACOS patients is in between asthma and COPD patients. Sorting out ACOS patients from asthma and COPD is necessary due to their individual and specific pharmaco therapy. From our study two-third of ACOS patient were previously diagnosed as asthma. Using syndromic approach from ACOS guideline might help us classify the ACOS patient from asthma and COPD patients but how much difference between asthma and COPD features score being used is still need to be further investigated.

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