Table 1. Karakteristik Demografis Subyek

Karakteristik	FK (n=113)		FTPP (n=72)	
	N	(%)	N	(%)
Jenis Kelamin				
Laki – Laki	34	30,1	46	63,9
Perempuan	79	69,9	26	36,1
Usia				
17-19 tahun	30	26,5	14	19,4
20-23 tahun	80	70,8	58	80,6
24-25 tahun	3	2,7	-	-
Tempat Tinggal				
Bersama Orang Tua	42	37,2	21	29,2
Bersama Keluarga Lain	7	6,2	6	8,3
Kos	64	56,6	45	62,5
Uang saku per hari				
Tidak menerima uang saku	10	8,8	12	16,7
< 20 ribu	44	38,9	27	37,5
20 ribu – 50 ribu	48	42,5	26	36,1
50 ribu – 100 ribu	8	7,1	6	8,3
> 100 ribu	3	2,7	1	1,4

Perilaku Merokok

Responden yang pernah mencoba merokok satu atau dua hisap paling banyak pada mahasiswa FTPP (50%) sedangkan pada mahasiswa FK 23,9%. Mahasiswa FK yang merokok sebanyak 7,1%, sedangkan di FTPP 27,8% (Tabel 2). Responden yang mempunyai perilaku merokok seluruhnya laki-laki. Responden FK yang merokok adalah 23,5% sedangkan responden FTPP 43,5%.

Tabel 2. Karakteristik Responden Berdasarkan Perilaku Merokok

Karakteristik	FK	FTPP
Pernah merokok satu atau dua isap		
Pernah	27 (23,9%)	36 (50%)
Tidak Pernah	86 (76,1%)	36 (50%)
Merokok 1 batang/hari pada 30 hari terakhir		
Ya	8 (7,1%)	20 (27,8%)
Tidak	105 (92,9%)	52 (72,2%)
Usia mulai merokok		
10-12 tahun	-	1/20
13-15 tahun	1/8	5/20
16-18 tahun	5/8	9/20
≥18 tahun	2/8	5/20
Konsumsi rokok dalam sehari		
1-5 batang/hari	7/8	9/20
5-10 batang/hari	1/8	8/20
>10 batang/hari	-	3/20
Uang membeli rokok pada 30 hari terakhir		
≤ 50 ribu	3/8	5/20
60 ribu – 200 ribu	5/8	5/20
200 ribu – 300 ribu	-	8/20
300 ribu – 500 ribu	-	1/20
> 500 ribu	-	1/20
Tempat biasa Merokok		
Rumah	3/8	3/20
Kampus	-	11/20
Tempat main/nongkrong	5/8	6/20

Distribusi kelompok usia responden pertama kali merokok tertinggi pada usia 16-18 tahun yaitu 9 dari 20 responden FTPP dan 5 dari 8 responden FK. Konsumsi rokok per hari terbanyak 1-5 batang/hari pada 9 dari 20 responden FTPP dan 7 dari 8 responden FK. Responden FTPP sebagian besar merokok di kampus sedangkan responden dari FK sebagian besar merokok di tempat main dan tidak ada yang merokok di kampus.

Faktor yang Memengaruhi Perilaku Merokok

Tabel 3 menunjukkan teman sekampus yang pernah memberikan rokok pada responden dari FTPP lebih tinggi (44,4%) dibandingkan responden FK (15,9%) sedangkan orang tua perokok pada responden FTPP 50% dan pada FK 34,5%. Peraturan merokok di kampus menunjukkan bahwa responden FK (94,7%) menyatakan di kampus tidak diperbolehkan merokok sedangkan responden FTPP menyatakan bahwa di kampus tidak ada peraturan untuk melarang merokok.

Tabel 3. Faktor yang Memengaruhi Perilaku Merokok

Faktor	FK		FTPP	
	N	%	N	%
Teman kampus pernah memberikan rokok				
Ya	18	15,9	32	44,4
Tidak	95	84,1	40	55,6
Teman kampus perokok				
Ya	101	89,4	72	100
Tidak	12	10,6	-	-
Orang tua perokok				
Ya	39	34,5	36	50
Tidak	74	65,5	36	50
Keluarga/teman serumah perokok				
Ya	41	36,3	43	59,7
Tidak	72	63,7	29	40,3
Peraturan merokok di kampus				
Tidak ada peraturan	5	4,4	48	66,7
Tidak diperbolehkan	107	94,7	10	13,9
Tidak diperbolehkan, tetapi ada pengecualian	1	0,9	14	19,4

Kebiasaan Berisiko terhadap Kesehatan

Pada penelitian ini dinilai juga kebiasaan yang berpotensi mengganggu kesehatan seperti konsumsi alkohol, mengunyah sirih/pinang dan mengisap rokok elektrik/vaping. Jumlah responden FK yang mengkonsumsi alkohol, mengunyah sirih, konsumsi pinang dan mengkonsumsi rokok elektrik/vaping masing-masing adalah 2 responden (1,77%), 18 responden (15,9%), 24 responden (21,24%), dan 4 responden (3,54%). Redangkan responden FTPP yang mengkonsumsi alkohol, mengunyah sirih, dan konsumsi pinang lebih tinggi daripada mahasiswa FK, yaitu yaitu 13 responden (18,05%), 15 responden (20,83%), 22 responden (30,56%).

Diskusi

Sebagian besar responden FK adalah perempuan (69,9%) sedangkan pada responden FTPP sebagian besar laki-laki (63,9%). Responden laki-laki atau perempuan mempunyai kesempatan sama untuk mendapatkan informasi mengenai kesehatan sehingga dapat meningkatkan pengetahuannya tentang kesehatan.[10] Hasil Riskesdas Provinsi Papua Barat 2013 menyatakan perokok laki-laki 39,7% sedangkan perokok perempuan 2,3%.[12]

Sebanyak 70,8% responden FK dan 80,6% responden FTPP mayoritas berusia 20-24 tahun dan Riskesdas Papua Barat 2013 menyatakan perokok usia 20-24 tahun adalah 19,1%.[12] Dewasa muda dan remaja merupakan sasaran utama produsen rokok, karena semakin dini mereka merokok, potensi menjadi perokok hingga usia tua semakin tinggi. Akibatnya potensi masalah kesehatan dimasa mendatang juga sangat besar.[6,7]

Hasil penelitian ini menunjukkan responden FK yang merokok lebih rendah yaitu 7,1% sedangkan pada FTPP 27,8%. Responden FK yang

menyatakan pernah mencoba merokok adalah 23,9% dan pada FTPP 50% responden pernah mencoba merokok. Kadar et al[9] menyatakan bahwa faktor yang memengaruhi perilaku merokok pada mahasiswa adalah pernah mencoba merokok.

Penelitian ini juga menunjukkan usia mulai merokok paling banyak adalah 16-18 tahun yaitu 62,5% pada FK dan 45% pada FTPP. Hasil penelitian ini sesuai dengan GATS 2011 yang menyatakan bahwa 75% perokok mulai merokok pertama kali pada usia <20 tahun, usia mulai merokok 17-19 tahun sebanyak 39,9% dan 15-16 tahun sebanyak 23,0%.[13] Pada penelitian ini responden merokok 1-5 batang/hari sebanyak 87,5% pada FK dan 45 % pada FTPP. Hasil penelitian ini lebih tinggi dari penelitian GATS 2011 yang menyatakan bahwa responden yang merokok <5 batang/hari adalah 5,1%.[13]

Harga rokok masih cukup mahal di daerah timur Indonesia sehingga konsumsi rokok juga sedikit pada kelompok yang belum berpenghasilan misalnya mahasiswa.[14] Selain itu, kebiasaan konsumsi rokok <5 batang sehari juga menunjukan kelompok ini masih dalam tahap mencoba dan bukan masuk golongan adiksi berat.[15,16]

Responden FK yang merokok sebagian besar mengatakan bahwa tempat yang biasa digunakan untuk merokok adalah tempat main/nongkrong (62,5%). Baharuddin[17] melaporkan bahwa 25% responden merokok di tempat main seperti toko, warnet, restoran, dan lain-lain karena remaja lebih banyak menghabiskan waktu bersama teman sebaya. Responden FTPP yang merokok sebagian besar mengatakan bahwa tempat yang biasa digunakan untuk merokok adalah kampus (55%). Kadar et al[9] menyatakan bahwa masih terdapat mahasiswa yang merokok di sekitar kampus. Perbedaan tempat merokok kemungkinan berhubungan dengan aspek sosiologis dan lingkungan. Merokok identik dengan kebiasaan tidak sehat dan menimbulkan citra buruk jika dilakukan oleh petugas/ mahasiswa kesehatan. Di sisi lain, lingkungan fakultas kesehatan sangat intensif mensosialisasikan kawasan bebas asap rokok seperti di kampus dan fasilitas kesehatan,[9] sehingga mahasiswa kesehatan tidak nyaman merokok di kampus.

Mahasiswa non-kesehatan relatif lebih bebas dalam merokok dan lingkungan non-kesehatan kurang mensosialisasikan kawasan bebas asap rokok.[15] Hasil penelitian ini menunjukkan perbedaan persepsi responden terhadap peraturan merokok di kampus. Sebanyak 94,7% responden FK menyatakan bahwa di kampus tidak diperbolehkan merokok dan ada peraturan mengenai kawasan dilarang merokok. Sebaliknya, pada 66,7% responden FTPP menyatakan bahwa di lingkungan kampus tidak ada peraturan dilarang merokok/zona bebas asap rokok. Berdasarkan hal tersebut, perlu dilakukan penelitian lanjutan mengenai pengaruh sosial budaya, lingkungan serta penegakan peraturan mengenai kebiasaan merokok pada remaja secara umum.

Hasil penelitian ini menunjukkan 15,9% responden FK dan 44,4% responden FTPP mengatakan bahwa teman kampus pernah memberikan rokok. Baharuddin[14] menyatakan bahwa perilaku merokok paling dipengaruhi oleh teman sebaya. Dari 32 responden yang merokok, terdapat 29 responden yang mempunyai teman perokok. Oleh karena itu, semakin banyak mahasiswa merokok, semakin besar kemungkinan temannya menjadi perokok juga.[18]

Hasil penelitian ini menunjukkan bahwa kebiasaan lain responden FK dan FTPP adalah mengisap vape dan konsumsi alkohol yang lebih tinggi pada responden merokok daripada yang tidak merokok. Rosiana[19] menyatakan konsumsi minuman beralkohol lebih tinggi pada perokok daripada bukan perokok. Seorang perokok cenderung menjadi peminum atau menggunakan narkoba karena dengan merokok mereka ingin mencoba hal lain yang lebih menantang dan juga aspek adiksi nikotin yang memengaruhi struktur otak yang memudahkan adiksi zat lain seperti alkohol atau putau.[15] Selain itu efek kesenangan lebih terasa pada saat orang merokok disertai minum alkohol daripada hanya merokok saja atau minum alkohol saja.[18] Berbeda halnya dengan kebiasaan mengunyah pinang dan mengunyah sirih yang menunjukkan hasil lebih tinggi pada responden tidak merokok daripada yang merokok. Diperlukan penelitian lebih lanjut yang dapat menjelaskan mengapa kebiasaan mengunyah pinang/sirih cukup tinggi pada bukan perokok dibandingkan perokok yang dikaitkan dengan aspek adiksi, psikologis, finansial, manfaat/risiko kesehatannya maupun aspek sosial budaya. Kamosorei et al[19] menyatakan bahwa menurut kepercayaan masyarakat papua, kebiasaan mengunyah pinang dan sirih dapat membawa dampak positif bagi kesehatan terutama untuk menghilangkan rasa sakit gigi, membuat gigi menjadi kuat, menghilangkan bau mulut dan menghilangkan stres. Kebiasaan tersebut diwariskan oleh para leluhur dan bahaya menyirih pinang belum disadari masyakat Papua. Diperlukan penelitian lebih lanjut mengenai kebiasaan

menyirih pinang dan dampaknya bagi kesehatan pada masyarakat Papua.

Kesimpulan

Mahasiswa fakultas teknik memiliki tingkat kebiasaan merokok lebih tinggi dari mahasiswa fakultas kedokteran dan ditemukan perilaku berisiko tinggi seperti konsumsi alkohol, vape serta menyirih. Diperlukan dukungan lingkungan dan institusi untuk meningkatkan larangan merokok di kampus dan membuat larangan merokok di fakultas yang belum terdapat peraturan larangan merokok di Universitas Papua.

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Evidence Based Case Report

Association Between Active or Passive Smoking and Allergic Rhinitis: an Evidence-Based Case Report

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Abstract

This evidence-based case report (EBCR) aims to investigate the association between active or passive smoking with allergic rhinitis by summarizing existing studies on the topic. A literature search was done on major databases with keywords related to this study's research question. The literature was appraised using CEBM University of Oxford for etiology study and systematic review sheets. The search obtained two articles for critical appraisal, includes a meta-analysis and a cohort study. The studies were appraised as valid, important, and applicable to the writer's setting. Saulyte et al' s[2] article described RR active smoking with allergic rhinitis of 1.02 (95%CI 0.92-1.15), with no significant association. They resolved the heterogeneity by making subgroups. The cross-sectional subgroup with RR 1.09 (95%CI 1.06-1.12) is statistically significant. There was a significant association in passive smoking and obtained RR 1.10 (95%CI 1.06-1.15). In the study by Mlinaric et al[4] the RR of active and passive smoking compared to non-smoker are 1.82 and 2.00; both show statistical significance. Both active and passive smoking is associated with a high risk of allergic rhinitis in adults and children.

Keywords *active smoking, passive smoking, allergic rhinitis.*

Hubungan Perokok Aktif dan Pasif dengan Rhinitis Alergi: Laporan Kasus Berbasis Bukti

Abstrak

Pada laporan kasus berbasis bukti ini bertujuan untuk menginvestigasi hubungan antara perokok aktif dan perokok pasif pada pasien dengan rinitis alergi. Dilakukan pencarian literatur menggunakan kata kunci yang berhubungan dengan kasus pada beberapa search engine, kemudian dilakukan penilaian kelayakan dengan lembar appraisal dari CEBM University of Oxford for etiology study and systematic review sheet. Dari pencarian didapatkan dua artikel yang mepresentasikan kasus tersebut, yaitu studi meta analisis dan studi cohort. Studi meta analisis oleh Saulyte et al[2] menyatakan RR pada perokok aktif dengan rinitis alergi adalah 1,02 (95%CI 0,92-1,15). Pada subgrup potong lintang didapatkan perbedaan bermakna dengan RR 1,09 (95%CI 1,06-1,12). Pada studi cohort oleh Minaric et al didapatkan RR pada perokok aktif 1,82 dan pada perokok pasif 2,00, keduanya menunjukan angka yang signifikan. Pada perokok aktif dan pasif berhubungan dengan risiko tinggi pada rinitis alergi di pasien dewasa dan anak-anak.

Kata kunci: *perokok aktif, perokok pasif, rhinitis alergi.*

Introduction

Allergic rhinitis is an immunologically mediated symptomatic disease that affects 10-20% of the global population. Worldwide prevalence of allergic rhinitis increases in the last decade. The possible explanation is due to changing exposure to tobacco smoke. Several studies have investigated the relationship between tobacco smoke exposure to allergic disease, and whether smoking causes allergic rhinitis remains inconclusive.[1,2]

Despite increasing campaigns about the danger of smoking, active or passive smoking rates still increases worldwide. It is estimated more than a third of the global population is passive daily passive smokers; most of them were children who were exposed to tobacco smoke at home.[3] The aim of this evidence-based case report (EBCR) is to analyze the association between active or passive smoking with the incidence of allergic rhinitis and compare the risk of allergic rhinitis in active or passive smokers in children and adults.

Case Illustration

Thirty-nine years old male patient came with his six years old son. They both experienced sneezing, runny and itchy nose, breathing through the mouth, and did not complain of any pain. These symptoms had occurred throughout the year, especially in the morning. The father already underwent a skin prick test and was diagnosed with allergic rhinitis, and symptoms had disappeared after two years of treatment. At the moment, they both experienced these symptoms two days a week. The father had no sleep disturbance and impairment of daily activities. However, the child experienced sleep disturbance. The father was an active tobacco smoker for more than ten years. The father intensely rubbed his nose, and his nasal mucosa looked pale. His son showed persistent mouth breathing, allergic shiners, nasal mucosa was livid with serous secretion, and postnasal drip. The father was diagnosed with mild intermittent allergic rhinitis and his son of moderate-severe intermittent allergic rhinitis. Based on the case illustration, the clinical question formulation: **i**s there any association between active or passive smoking and allergic rhinitis in adults and children?

Evidence Research Strategy

Articles search through PubMed and Cochrane was conducted on June 18th, 2020, to identify all potentially eligible studies using keywords relevant to the clinical question. The search retrieved 1722 papers in both databases. The result was sorted by inclusion and exclusion criteria resulting in 53 eligible studies for abstract screening. All abstracts were screened, a large majority of the articles were excluded because through abstract screening, the articles were not suitable to answer the clinical question (Figure 1). Critical appraisal for relevance and validity yielded two articles; studies by Saulyte et al[2] and Mlinaric et al[4] provided sufficient data and are usable in answering the clinical question.

Results

The study by Saulyte et al[2] entitled “Active or Passive Exposure to Tobacco Smoke and Allergic Rhinitis, Allergic Dermatitis, and Food Allergy in Adults and Children: a systematic review and meta-analysis.” The papers included 196 studies, and 97 of them discussed allergic rhinitis. Another study is “Passive Smoking and Respiratory Allergies in Adolescents” by Mlinaric et al.[4] Saulyte et al[2] presented heterogeneity on active or passive smoking for allergic rhinitis and an asymmetry funnel plot for active smoking and the impact of allergic rhinitis. The considerable amount of heterogeneity is due to a difference in design, case, and exposure definitions and adjustment. The authors analyze the data by making subgroups based on study design and age to address the heterogeneity. For the publication bias of active smoking, Egger’s test yielded a non-significant (p-value = 0.27), and it is confirmed that no there is no missing data

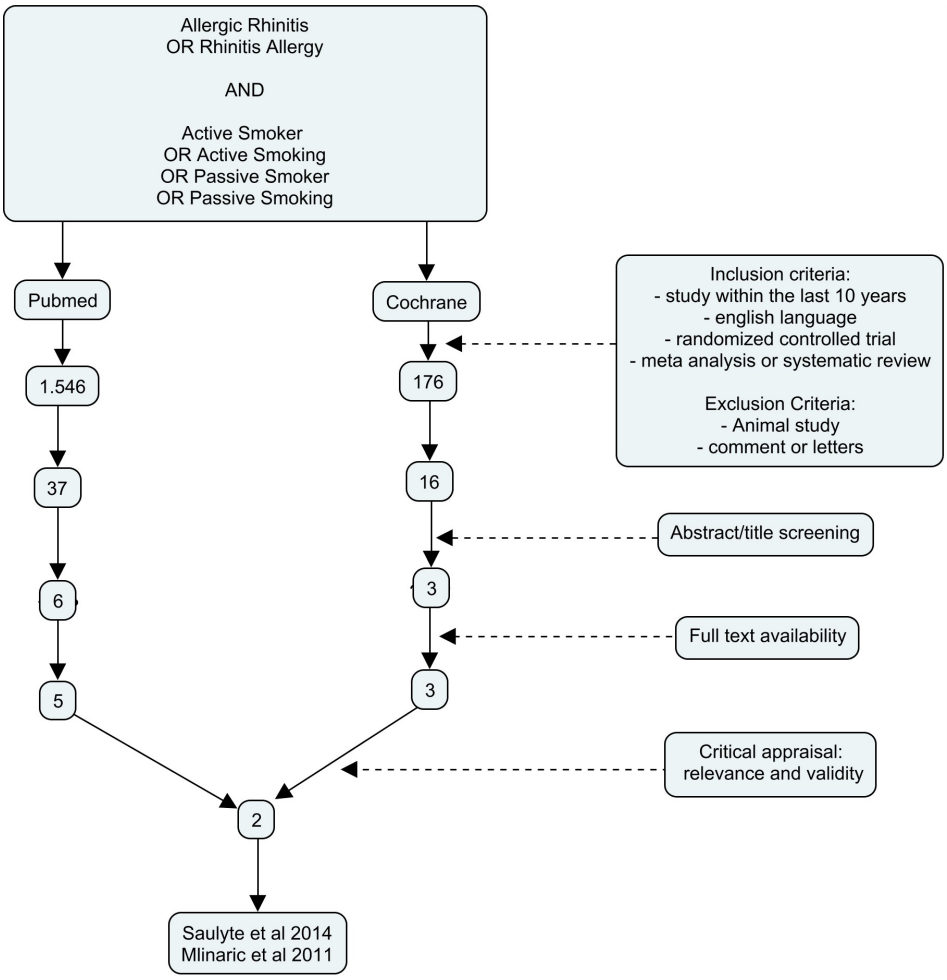

Figure 1. Literature Search Strategy

The study by Mlinaric et al[4] investigates the impact of active or passive exposure to smoke and allergic condition on IgE levels and allergic disease diagnosis. The study consisted of 155 adolescents consisting of non-smokers, active smokers, and passive smokers. The smoking habit was examined through a survey, the physician confirmed the diagnosis of asthma and rhinitis, and the IgE levels were counted using the ELISA method. The result is presented with X2, p-value, and the geometric mean for the IgE level. The results of both studies are presented in Table 1. Critical appraisal results for both studies are described in Table 2 and Table 3.

Discussion

Allergic rhinitis is a common disease but still always an exciting topic to discuss from the epidemiology, etiology, diagnosis, and treatment points. Sea Allergy Forum Effective Management of Allergic Rhinitis 2020 stated that allergic rhinitis's primary etiology is from the air. It can be polluted air, pollen, and exposure to environmental tobacco smoke. So the number could be determined by the prevalence of active or passive smoking in the population. Worldwide, 14% of adolescents aged 13-15 are active smokers, with countries reaching a prevalence of 40% and more than one-third of children live with at least one adult smoker.[2]

Tobacco smoke contains many toxic substances and pro-inflammatory effects. It may precipitate allergic sensitization in two different ways, direct and indirect. The first way, tobacco smoke directly affecting IgE production on the cellular level.[6-8] Kim et al[7] study showed that the increase of total IgE level was correlated with a cumulative smoking exposure and the elevated total IgE level associated with the increased risk of sensitization to common allergy.[7] The second way is the indirect pathway by increasing the permeability of respiratory epithelium and reducing its protective barrier; therefore, the pathogenesis of allergic rhinitis from tobacco smoking remains inconclusive.

Table 1. The Result of All Studies

Author	Exposure	Results RR (95% CI)	Summary
Saulyte et al[2] Systematic review, 97 studies for AR, 139 studies in total	The study explained both active and passive exposure to tobacco smoking, but the duration and amount of exposure were still unclear. This study also discussed the impact on dermatitis allergy and food allergy, but not discussed in this study.	**Active smoking** - All studies (fixed effect): 1.02 (0.92-1.15) - All studies (random effect): 1.06 (1.03-1.08) - Cross-sectional subgroup: 1.09 (1.06-1.12) - ISAAC criteria subgroup: 1.39 (1.34-1.44) - Children subgroup: 1.35 (1.30-1.39) - Adult subgroup: 0.84 (0.81-0.87) **Passive smoking** - All studies (fixed effect): 1.08 (1.07-1.10) - All studies (random effect): 1.10 (1.06-1.15) - Cross sectional subgroup: 1.08(1.07-1.10) - ISAAC subgroup: 1.10 (1.09-1.12) - Children subgroup:1.08(1.07-1.09) - Adult subgroup:1.17(1.10-1.24)	The study's risk result is higher due to the increased number of patients, differences in designs, case, and exposure definition and adjustment.
Mlinaric et al[4] A retrospective cohort study, 155 samples	The study consisted of 155 adolescents, including 31 active smokers, 60 passive smokers, and 64 non- smokers. The subjects undergo total and specific IgE antibody examination. Physician previously confirmed allergy diagnosis (asthma and AR)	**Active smoking** - RR 1,82, x^2 4.45, p 0.034 - Total IgE level: 53,67 IU/ml - Mean smoking exposure 1.69±1.79 years **Passive smoking** - RR 2.007, x^2 9.29, p 0.002 - Total IgE level: 76,69 IU/ml - Mean smoking exposure 16.18±2.20 years	Clinical manifestation of allergic disease is more frequent in an active and passive smoker than in a non-smoker. Total IgE level is significantly higher in a passive smoker than the active smoker

*RR; **Relative Risk

Table 2. Critical Appraisal of Systematic Review from Saulyte et al[2] in 2014

Validity					
PICO	**Appropriate searching**	**Relevant study included**	**Quality assessment of trials**	**Heterogeneity**	**Level of evidence**
+	+	+	+	+	1A

+, yes (mentioned explicitly in the article)

These two articles include one meta-analysis and one cross-sectional study. There were two different study designs, so the total number of samples and data processing were also different. Saulyte et al,[2] reported a systematic review and meta-analysis study, 196 studies, published in 139 articles and carried out in 51 countries. They found 97 studies on allergic rhinitis, 91 on allergic dermatitis, and eight on food allergy. Of the 97 studies, 34 studies on active smoking and 63 studies on passive smoking. Mlinaric et al[4] did a cross-sectional study about the impact of active or

passive exposure to smoke and allergic condition on IgE levels and diagnosis of allergic disease. The study consisted of 155 adolescents: 64 non-smokers, 31 active smokers, and 60 passive smokers. The smoking habit was examined through an interview with questions about the duration of smoking and the number of cigarettes consumed per day. The diagnosis of asthma and rhinitis was confirmed previously and the IgE levels were counted from the venous blood sample using the ELISA method. The result is presented with X2, p-value, and the geometric mean for the IgE level.

Overall, Saulyte et al[2] reported no significant difference in active smoking with allergic rhinitis (RR 1.02; 95%CI 0.92-1.15). The relative risk for allergic rhinitis in the active smoking group is 1.02 times higher than in the non-smoking group. This result is deemed non-significant by looking at the confidence interval, which ranges between 0.92-1.15. This result can be affected by the data heterogeneity. To eliminate heterogeneity, Saulyte et al[2] analyze the data in subgroups defined by study design and age of participants. Cross-sectional subgroups with RR 1.09 (95%CI 1.06-1.12) are statistically significant in study design subgroups.[2] In subgroups analysis based on participants age, children and adolescent showed the RR is 1.4 (95%CI 1.24-1.59) for active smoking and 1.09 (95%CI 1.04-1.14).[2]

Mlinaric et al[4] presented the data of allergic diseases with X2, so we converted the data to RR for this study. The RR of active smokers compared to non-smokers was 1,82 and is statistically significant. On the other hand, passive smokers' RR compared to non-smoker is 2.007 and shows statistical significance.[6] We also count the number needed to harm, wherein the active smoker group, the number needed to harm is four, and in the passive smoker group, the number needed to harm is 5. Both groups experience significantly higher allergic conditions compared to non-smoker. Smoke can precipitate allergic conditions by directly influencing the release of IgE or increasing permeability of respiratory epithelium that causes other allergens' entry.

Determination of diagnosis is essential. Studies that used the standardized ISAAC criteria showed a statistically significant number, RR 1.5 (95%CI 1.35-1.66), two but not on those studies that used their protocols. Mlinaric et al[4] did not mention the diagnostic tools used to diagnose allergic rhinitis since physicians previously made the diagnosis, but to examine further the effect of smoke on the allergic disease, they used IgE measurements.

IgE synthesis is regulated by IL-2, IL-4, and gamma interferon. Active or passive smoking increases IgE levels through a similar mechanism and the stimulation of IL-4.[5,9] IgE levels are the highest in passive smoking groups compared to active smokers and non-smoker, which may be due to the exposure duration. In the study, the mean smoking duration for active smokers was 1.69 (1.79 years, and the mean period of passive smokers' exposure was 16.18±2.20 years. Smoking duration has a cumulative effect on IgE level and allergic sensitization.[6] These results suggest that exposures to active or passive tobacco smoking are associated with a modest increase in allergic rhinitis risk. However, so many factors influence the result. Saulyte et al[2] showed no significant result, especially for the children and adolescent subgroup. This result related to the "atopic march" concept suggests that the sequences tend to remission later in life.[2,9]

Table 3. Appraisal of Etiologic Study from Mlinaric et al[4] in 2011

Validity										Importance (RR)		Applicability			
					Diagnostic										
Study design	Number of patients	Similarity	Measurement of outcome	Follow up	Exposure	Dose-response gradient	Dechallenge-rechallenge	Consistency	biological sense	Active smoking	Passive smoking	Patient similarity	NNH	Expectations	Alternative
CS	155	+	+	-	N/A	N/A	N/A	+	+	1.82	2.00	+	4-5	+	+

+, yes (mentioned explicitly in the article); -, no (mentioned explicitly in the article); N/A, not mentioned in the article. Abbreviations: CS; cross-sectional, NNH; number needed to harm

The study by Mlinaric et al[4] is a cross-sectional design that cannot show the disease progression and the effect of smoking duration on the disease and the relationship between smoking quantity and duration to IgE level. Saulyte et al[2] reported various types of studies, sample variants, and exposure, thus producing heterogeneity, making it difficult to determine the amount of exposure that affects allergic rhinitis. The exposure of groupings, such as duration and number, is also necessary to see the impact of allergic rhinitis.

Conclusion

With a high risk of allergic rhinitis in adults and children. Passive smokers have higher IgE and a higher risk of allergic rhinitis due to longer exposure duration and more common in children. The role of physicians is essential in increasing awareness of health risks associated with smoking. Children are vital, as both active or passive exposure to tobacco smoke has been implicated in the development of "atopic march." Future studies should reduce the bias possibilities and heterogeneity.

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Case Report

Central Serous Chorioretinopathy Associated with Calciu Channel Blocker Consumption: A Case Report

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Abstract

Central serous chorioretinopathy (CSC) is one of the leading causes of blindness in middle-aged population. This case report describes case of CSC associated with amlodipine consumption. A 62-years old woman came with blurry vision on the right eye (RE) for 25 days, prior to admission. Patient was hypertensive and on routine calcium channel blocker (CCB, amlodipine) for the last two months. Initial best corrected visual acuity (BCVA) was 0.3 for her RE and 0.8 on her left eye (0.8). Anterior segment examinations of both eyes were within normal limits. Funduscopy revealed serous retinal detachment on the macula of RE. Optical coherence tomography (OCT) of RE showed subretinal and below choroid fluid accumulation and central macular thickness of 352 µm. Patient was treated with non-steroidal anti-inflammatory drug (NSAID) and vitamins but the complaint worsened. Amlodipine was ceased on the third month of treatment. CSC resolved and final BCVA was 1.0. There might be an association between CCB consumption to incidence of CSC. Our study was the first to describe such occurrence. Further study is required to confirm this association
Keywords*: Central serous chorioretinopathy, calcium channel blocker, amlodipine, calcium ion, pathogenesis.*

Korioretinopati Serosa Sentral Terkait Penggunaan Penghambat Kanal Kalsium: Sebuah Laporan Kasus

Abstrak

Central serous chorioretinopathy (CSC) merupakan salah satu penyebab utama kebutaan pada populasi usia paruh baya. Laporan kasus ini mendeskripsikan sebuah kasus CSC yang berkaitan dengan konsumsi Amlodipine. Seorang wanita berusia 62 tahun datang dengan keluhan pandangan buram pada mata kanan sejak 25 hari sebelum datang ke Rumah Sakit. Pasien didiagnosis dengan hipertensi dan rutin mengkonsumsi calcium channel blocker (CCB, amlodipine) dalam 2 bulan terakhir. Pemeriksaan tajam visual terbaik / best corrected visual acuity (BCVA) di awal menunjukkan hasil 0.3 pada mata kanan dan 0.8 pada mata kiri. Pemeriksaan anterior segmen pada kedua mata dalam batas normal. Pemeriksaan funduskopi menunjukan ablasio retina serosa pada makula mata kanan. Pemeriksaan optical coherence tomography (OCT) pada mata kanan menunjukkan hasil akumulasi cairan pada subretina dan dibawah koroid, serta ketebalan makula sentral yaitu 352µm. Pasien diberikan tatalaksana berupa non-steroidal anti-inflammatory drug (NSAID) dan vitamin, namun keluhan dirasa memburuk. Konsumsi amlodipine dihentikan pada bulan ke 3. CSC dinyatakan sembuh dengan BCVA akhir 1.0. Terdapat kemungkinan hubungan antara konsumsi CCB dengan insidensi CSC. Studi kami merupakan studi pertama yang mendeskripsikan kejadian tersebut. Dibutuhkan studi lebih lanjut untuk mengkonfirmasi hubungan tersebut.
Kata kunci*: Korioretinopati serosa sentral, penghambat kanal kalsium, amlodipine, ion kalsium, patogenesis.*

Introduction

Central serous chorioretinopathy (CSC) is one of the leading causes of blindness affecting middle-aged populations. It can be found in patients aged 20 to 64 years and peaks in 39 to 51 years.[1,2] A population based study in Minnesota found that the annual incidence is 9.9 in 100,000 men and 1.7 in 100,000 women.[3] The disease is characterized by a serous detachment due to fluid leakage through the retinal pigment epithelium (RPE).[4,5] CSC is mostly self limiting, however some can progress to severe form and have high recurrence rates. The underlying mechanisms of CSC is still poorly understood. Several hypothesis supported by fundus angiography (FA) and other modalities suggest a fluid leakage at the level of choroid and RPE.[5] The choroid leakage is hypothesized due to choroid hyperpermeability hence accumulation of subretinal fluid leading to increased hydrostatic pressure on underneath RPE that eventually disunite the RPE.[5-7] The RPE also contribute to the malfunction of the water transport leading to subretinal fluid accumulation.[5]

There are several risk factors of CSC, such as pregnancy, stress, cushing's syndrome, collagen vascular disease, alcohol use, allergic respiratory disease, drug consumption hypertension, and family history. Drugs associated with CSC are systemic steroid, antibiotics, and psychopharmacological medications. [4] We present a rare case of CSC in elderly female with chronic consumption of calcium channel blocker (CCB) for pre-existing hypertension.

Case Ilustration

On June 2017, a 62 years old woman visited an opthamology clinic at AINI Eye Hospital Jakarta with a chief complain of blurred vision of the right eye since 25 days ago. The patient had no previous ocular disturbances and did not wear eye glasses. Patient had history of hypertension and was treated with 5 mg amlodipine per day since the past two months. There was no history of steroid or other drug consumption. Complaint of psychological stress was denied. The blood pressure was 120/80 mmHg. Upon ophthalmological examination, patient's best corrected visual acuity (BCVA) was 0.3 on the right eye (RE) and 0.8 on the left eye (LE), both uncorrected by pin hole. Pupillary reflex, cornea, anterior chamber were within normal limits on both eyes. Both lense appeared cloudy. Patient's funduscopy examination revealed a serous retinal detachment on the macular area of the RE and there was no sign of arteriovenous nicking, no retinal hemorrhage, and no cotton-wool spot. Upon ocular coherence tomography (OCT) examination of RE, initial central macular thickness was 352 µm accompanied with subretinal fluid accumulation and RPE detachment (Figure 1).

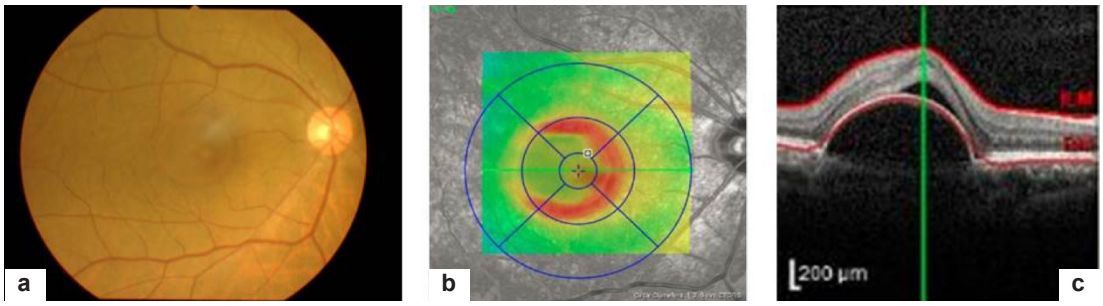

Figure 1. Patient's Initial Condition Prior to Treatment on June 2017 (a) Funduscopy, (b) OCT Examination on August 2017, (c) Subretinal Fluid Accumulation, CMT 352 µm, and RPE Detachment

Upon first visit, patient was treated with topical and oral non-steroidal anti-inflammatory drug (NSAID) and multivitamin consisting of mainly vitamin B and C. However, on August 2017, BCVA of RE worsen to 0.2 and on OCT examination, the serous detachment of the macula did not resolve. The OCT image of CMT also showed CMT increased to 384 µm. (Figure 2). Patient was treated with topical and oral non-steroidal anti-inflammatory drug (NSAID) and multivitamin consisting of mainly vitamin B and C. However, on August 2017, BCVA of RE worsened to 0.2 and upon OCT examination, the serous detachment of the macula did not resolve. The OCT image CMT showed CMT increased to 384 µm (Figure 2).

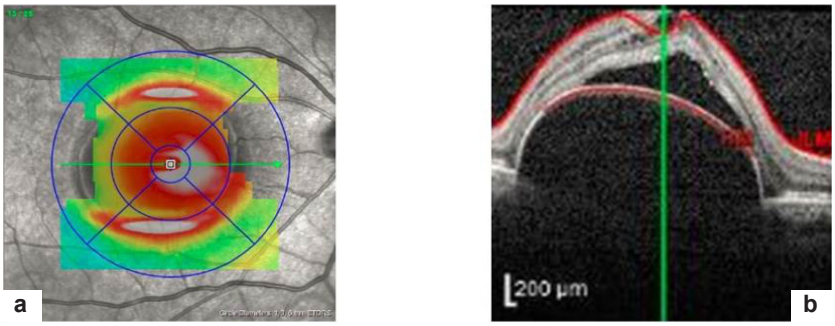

Figure 2. (a) Patient's OCT Examination on August 2017 (b) Subretinal Fluid Accumulation and Increased CMT 384 µm

On September 2017, amlodipine consumption was discontinued and replaced with 50 mg losartan (angiotension II receptor blocker) per day. In November 2017, BCVA was 1.0 on both eyes and notably, there was tremendous resolution on the subretinal fluid of the macula and reduction of CMT to be 168 µm on patient's OCT examination (Figure 3). Patient's blood pressure remained stable throughout the entire outpatient visits.

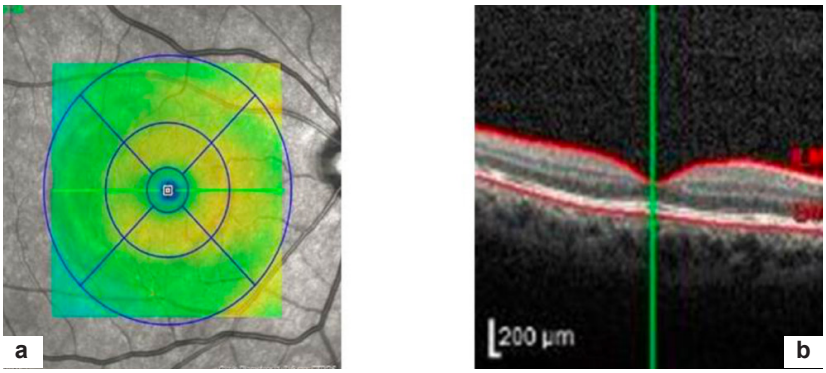

Figure 3. (a) Patient's OCT Result on November 2017 (b) after Cessation of Amlodipin Showing Mark Reduction Of Subretinal Fluid and Central Macular Thickness to be 168 µm

Discussion

CSC is one of the most common vision threatening retinopathies.[8] It affects middle aged population with male predisposition.[1] A study showed that CSC in women usually occur in older age;[9] however, the epidemiology characteristics of CSC in Indonesian population is still unknown. Risk factors associated with CSC are type A personality, cushing's syndrome, pregnancy, systemic steroid use, collagen vascular disease, antibiotic use, allergy respiratory disease, hypertension, psychopharmacological medications, *H. pylori*, and family history.[10]

The condition is described by a serous detachment that separate the sensory-neural part of retina with/without the detachment of RPE.[4,5] Most of CSC is self-limited disease and often resolve within 3-4 months. However, more complicated form of CSC leads to longer recovery time and increased recurrence rate. Our patient exhibited serous retinal detachment with RPE retachment that did not resolve within 3-4 months of therapy. This concordance with Perkins et al[9] finding which desribes older age and the presence of RPE detachment correlates with longer recovery time.

The underlying cause of CSC remains unclear. The detachment occurs due to serous accumulation at subretinal space which increases the hydrostatic pressure of tissue beneath the RPE.[5,11] Source of the fluid leakage is still unclear. Guyer et al[12] found that upon fundus angiography ICG-videography, the leakage originate from choroid vasculature indicating abnormal choroid hyperpermeability. Maumenee[13] suggested that the pathology lied in the RPE dysfunction as seen in the fluorescein angiography (FFA). These findings are consistent

with Gementzi theory whereas the malfunction may arise from choroid, RPE, or contribution of these two.[14] A choroidal hyperpermeability, suggested due to venous congestion and ischemia, leads to reverse of flow to the underneath RPE. When the fluid pressure underneath RPE accumulates, the RPE is pushed forward hence pigment epithelial detachment (PED) and pinpoint areas of leakage ('microdrips' or 'blowouts') occur leading to further damage to RPE.[15.16]

To our knowledge, there has no established literature which discuss the association between CSC and CCB. CCB blocks influx of calcium through ion-specific channels, L-type channel, throughout cell wall. As a result, vascular smooth muscle cells relax, vasodilation occurs, and desirable effect of lowered blood pressure takes place.[17,18] However, CCB also causes intra-capillary hypertension and extravasation of fluids hence producing an undesirable effect of peripheral edema.[19] A study by Zanchetti et al[20] showed this is the most-common dose-dependent side effect of CCB which is also associated with duration of therapy. We thought that this further result in formation of retinal pigment epithelial detachments and deluge the RPE as the blood-brain barrier.[11]

Patient was first treated with topical and oral NSAID which works by decreasing prostaglandin production by inhibit the production of cyclooxygen enzyme (COX), an agent responsible for vasodilatation and increasing blood vessel permeability. A study conducted by Khan et al[21] found that the use of topical NSAID improved CMT and visual acuity up to 30th day after treatment. However, in our case, patient's condition did not improve after NSAID administration. In this case, patient suffered from hypertension and was treated with CCB. The occurrence of CSC may related to consumption of CCB. In addition, patient suffered from hypertension which is associated to endothelial dysfunction as the complication. Patient's BCVA and anatomical condition were observed for five months but there was no improvement. The improvement was evident upon cessation of CCB and replacement to an alternative anti-hypertensive agent leading to the hypothesis of correlation between CSC and chronic CCB use.

Conclusion

In conclusion, there is a possible association between the consumption of CCB (amlodipine) to the development of CSC. Patient also suffered from hypertension which may also contribute to vascular endothelial dysfunction. Further studies are required to confirm the association of CCB consumption as a possible risk factor for CSC.

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