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PERIODONTAL DISEASE ASSOCIATED WITH CORTICOSTEROID IN ASTHMA PATIENTS-A SYSTEMATIC REVIEW

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ABSTRACT

To observe the changed in periodontal disease in asthma patients using corticosteroid drugs. Electronic searches on Wiley, Pubmed, and Cochrane were conducted to identify articles published in dental journals from January 2004 to December 2017 focusing on the effects of corticosteroid use in asthma patients. Manual searches of published full-text articles and related articles were performed afterwards. Of the 73 studies that explain this, only 3 studies were compatible with the inclusion criteria. The initial database search produced 195 articles. All articles were selected for full-text review. There were 3 studies selected for inclusion, with 97.837 patients as subjects. Most studies were using inhaled corticosteroids in addition to the use of systemic corticosteroid drugs, and antihistamines. One studies mention that there no evidence of association been asthma and periodontal disease from the adolescent population. Corticosteroids are used in the treatment of asthma diseases, but the use of corticosteroid drugs, especially with inhaled methods, increases the risk of periodontal disease compared to patients who do not use corticosteroid drugs.

Keywords: Asthma, Corticosteroid, Drugs, Periodontal disease

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INTRODUCTION

Asthma is a respiratory disease with characteristics of inflammation and bronchoconstriction, which can occur in any age group, such as children, adolescents, adults, and elderly [1]. Infection in the respiratory tract, allergies, exposure to allergens, and weather changes are the trigger factors in asthma with different symptoms and limited respiratory tract. This condition can limit the activity and the acute condition can cause the main problem in health care and in some cases, the condition can become fatal and cause death [2]. The prevalence of asthma is about 300 million people in the world and this number is assured to increase by 100 million people in 2025 [3]. Therefore, the pharmacological choices to treat asthma disease are by reducing the disease symptom, controlling the disease, and providing additional therapy [2].

In adults, the prevalence of asthma disease is higher in women than men. Recently, the more effective and available treatment for asthma is by using inflammatory medication (e. g. inhaled glucocorticosteroid) and also can by adding bronchodilator agent (e. g. agonist β2) if necessary [4]. Patients who are using an inhaler must be given a clear instruction of use: 4 times daily. A long-term of the drug's usage can cause a health problem in the oral cavity [3]. McDerra *et al.* [5]. Found that 4–10 y old children with asthma disease usually have more plaque and calculus than healthy children without asthma. They also have a higher prevalence of gingivitis. In 1992, Von Wowern *et al.* [6]. Also reported that the reduced composition bone mineral of the mandible may be caused by the used of systemic corticosteroid.

MATERIALS AND METHODS

This systematic review was written based on the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) for reporting the events evaluated by interventions and health care behaviors [7]. PICO questions (population, intervention, control, and outcome) [8] used in this systematic review were:

P (population): children, adults, and elderly patients who are suffering from asthma

I (intervention): the use of anti-asthmatic drugs corticosteroid and antihistamines

C (comparison/control): healthy patients without asthma

O (outcome): the relation between periodontal disease and asthma patients who were using anti-asthmatic drugs such as corticosteroid

Search strategy

The electronic searches were conducted on Wiley Online Library, PubMed, and Cochrane Online Library databases focusing on English literature, which supports this study. The searches were done to identify published articles in the dental journal from January 2004 to December 2017, focusing on the use of the anti-asthmatic drug's effects on periodontal disease in asthma patients. The MesH keywords used in this search were "asthma" and "corticosteroid". The searches were limited to English articles, publication date, and type of articles. The manual searches of the full-text articles were done afterward. There were 73 studies compatible with this, but only 3 studies were compatible with the inclusion criteria. The drugs used in this study were anti-asthmatic drugs (e. g. corticosteroid) and antihistamines.

The specific keywords were used in this search and the results were evaluated based on PICO questions characteristics.

Eligibility criteria

The inclusion criteria in this systematic review are based on parameters which are the articles that published in English from January 2004 to December 2017 about periodontal disease associated with corticosteroid in asthma patients and at least 24-30 mo after using follow up evaluation. The age of patients was about 7-86 y old.

While the exclusion criteria used in this systematic review are the article that published in not in English, articles in any systematic review and meta-analyses, the articles only explaining other respiratory diseases.

Selection of study

The specific keywords were used by participating authors to find the articles by reviewing and selecting the abstract and full-text articles. The authors then selected the articles that were compatible with the inclusion criteria independently. After that, all the abstract and full-text articles were downloaded and evaluated individually. The eligibility criteria was used to identify the articles which will be used in this systematic review.

Data extraction

The data were extracted by the authors with the following parameter: publication year, studies on the animal, and other accompanying diseases. All the full-text articles that were

compatible with the inclusion criteria were reviewed independently by reviewers and evaluated to conclude this systematic review.

RESULTS

The search on the database resulting in 195 initial articles (190 articles from Wiley Online Library, 4 articles from PubMed database, and 1 article from Cochrane Online Library). Because of the irrelevant titles, 73 articles were excluded. After the discussion between the authors, another 70 articles were excluded because of several reasons. The title and the abstract of the articles were reviewed again and as the results, only 3 studies were qualified to be analyzed. The diagram flow of the articles selection was shown in fig. 1 with a total of 3 articles chosen from 195 initial articles. After 195 articles were reviewed, 3 articles were selected to be included in this systematic review, while another 192 articles were excluded because of several reasons.

All the studies were done in the last 15 y in the United States (1), India (1) and Taiwan (1). There were 97 837 patients in these studies, with 19 549 subjects were suffering from asthma and 78 288 patients were healthy individuals. Most of the patients were from the study conducted in Taiwan, which is 96 030. All the studies were using agonist corticosteroid β2 to treat asthma.

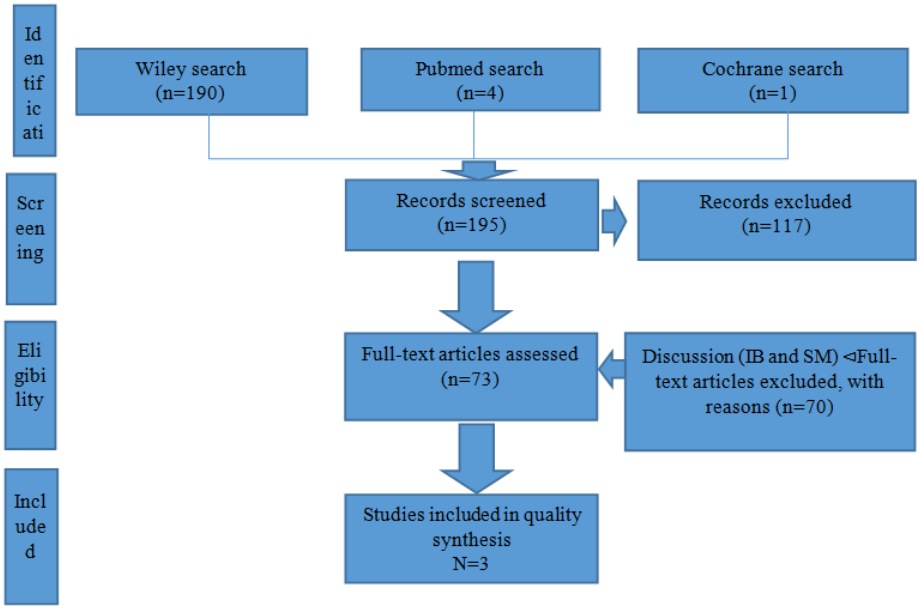

Fig. 1: The diagram flow of the articles selection

Table 1: Data description from the 3 included studies that were reported on anti-asthmatic drugs

Authors (y)	Subject and age	Location	Study design analyzed parameters	Medication	Outcome
Shulman *et al.* (2003)[9]	1.596 adolescent participation (238 asthma dan 1358 non-asthma) Age 13-17 y. o	USA	Case-control GB,CAL,PD,CI	• Anti-asthmatic inhaler for 24 mo • Anti-histamine for 30 mo • Corticosteroid not reported	None of the periodontal measures are associated with severe asthma or with the use anti-asthmatic drugs but some covariance has statistically significant OR (P<0.5)
Sashikiran *et al.* (2007)[10]	211 children, (105 asthma patients, 106 healthy control) Age 6-14 y	India	Case-control PIS	• Agonist Beclomethasone inhaler • Salbutamol inhaler • Salbutamol tablet • each one-year usage	There was a significant value of P<0.05
Shen *et al.* (2017)[2]	Adult participants (96,030) with 19, 206 asthma and 76, 824 non-asthma with an average age of 41.5	Taiwan	Cohort retrospective PIS and GI	• Systemic corticosteroids ICS+long-acting • Theophylline • Montelukast • Omalizumab • Each one-year usage	All periodontal parameters were assessed and the results were significant (P<0.001) in the asthma group

GB: Gingival Bleeding

CAL: Clinical Attachment Level

PD: Probing Depth

CI: Calculus Indeks

PIS: Periodontal Indeks

GI: Gingival Indeks

Table 1 showed two case-control studies and one cohort retrospective study. The studies were conducted in 2003, 2007, and 2017. The patients' age mean was 41.5 y old. In the 13–17 y old group, the participant numbers were 1.596 people, while in the 6–14 y old group, the participant numbers were 211 people. Sashikiran *et al.* [10] observed their asthma patients who were using inhaled corticosteroid β2, salbutamol inhaler, and salbutamol tablet in treating asthma. In the USA, Shulman *et al.* [9] and in Taiwan, Shen *et al.* [2] also observed the same condition where their asthma patients also used anti-asthmatic drugs in their treatment.

DISCUSSION

In this study, there was a significant difference in the inflammation of the gingiva between asthma patients and healthy individuals, especially the one who were using inhaled corticosteroid. The corticosteroid immunosuppressive effect may influence the response of the periodontal tissue. These agents inhibit the host response, thus resulting in the clinical expression of gingivitis [11]. The two included studies also reported about a positive association between medications for asthma and periodontal diseases. However, one study showed a negative relation between asthma and periodontal diseases. None of the periodontal measures are associated with severe asthma or with the use of anti-asthmatic drugs. The last study observed that subjects were taking medications and were less subject show gingival changes. The first reason is that the subjects were using a low dose for less time comparing to the others study. The second one is the subject were not paying attention in the clinical procedure or not using the drugs as directed. The last reason is maybe the effect of the anti-asthmatic drugs were different between adult's patients and children patients because the hormonal changes effect in adults is associated with puberty.

Periodontal diseases are body reaction caused by plaque bacteria on the tooth crown which then extends into the gingival sulcus and impair the adjacent gingiva such as chronic inflammation, gingival bleeding, pocket depth increased, and loss of alveolar bone. Most common bacteria found in people suffering from periodontal disease are porphyromonas gingivalis, Treponema denticola, tannerella forsythia and A. actinomycetemcomitans. The bacterial antigen will trigger the host immune response, and resulting in the effect of the disease. In the diseases like asthma, the immune response is a mechanism which involved in the pathogenesis and the disease progression. Even though most of the patients of this disease are adults, there was a significant portion shown in the children and adolescence group [9, 12].

Hyppa *et al.* [13] reported that gingivitis in children who were suffering from asthma was explainable. Some immune response changes and they usually breathe from the mouth (mouth breathing), especially while the episodes of acute asthma attacks and dehydration of the alveolar mucosa. Karl *et al.* [14] reported that the prevalence of periodontal disease and saliva flow were lower in asthma patients than non-asthma patients. The higher prevalence of calculus in children with asthma is caused by the increasing calcium and phosphorus level in saliva excreted by the submaxillary and parotid gland. Wotman *et al.* [15] reported that children with asthma have more calculus than healthy children. Lenander *et al.* [16] reported that even the flow of saliva was reduced, myeloperoxidase concentration was increased in asthma patients. IgE concentration in gingival tissue was increased in asthma patients which cause periodontal destruction.

Even though the published studies had reviewed about asthma patients with different ethnic and social-economic population with different severity of the disease and the types and doses of the drugs, the study in asthma patients who were using inhaled corticosteroid must providing information and proper guidance, because if it is not well controlled, this will cause inflammation of the gingiva and caries because of the reduced flow of saliva [17]. Especially in children patients who were using their drugs at night, before sleep, and without cleaning or rinsing their mouth after usage [11].

CONCLUSION

Anti-asthmatic drugs such as corticosteroid and anti-histamine were usually used in asthma disease treatment, but the use of corticosteroid drugs especially with inhaled methods increased the risk of periodontal diseases like gingivitis and severe periodontitis than the one who does not use corticosteroid drugs. All the asthma patients who were using anti-asthmatic drugs should check their oral health periodically. Further study is required to produce more specific information with more samples and better methodology.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICT OF INTERESTS

There are no conflict of interest in this study

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