



Review article

Coexistence of asthma and polycystic ovary syndrome: A concise review



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ABSTRACT

Asthma may be associated with polycystic ovary syndrome (PCOS), and possibly patients with PCOS have a more severe type of asthma. The purpose of this systematic literature review is to summarize evidence of a coexistence of PCOS and asthma using the available literature. The search was completed on 01.01.2016. English language articles were retrieved using the search terms 'Asthma' AND 'PCOS', 'Asthma' AND 'systemic inflammation', 'Asthma' AND 'metabolic syndrome', 'asthma' AND 'gynaecology', 'PCOS' AND 'systemic inflammation', 'PCOS' AND 'metabolic syndrome', 'PCOS' AND 'allergy'. Five papers meeting prespecified search criteria were found of which two were registry studies of relevance. The current literature supports a coexistence of PCOS and asthma and gives us an indication of the causes for the possible link between PCOS and asthma. Further research in the area must be conducted to determine the exact nature and magnitude of the association.

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1. Introduction

Polycystic ovary syndrome (PCOS) is the most common

endocrine disorder among women of fertile age affecting approximately 6–7% [1]. PCOS is a multifactorial heterogeneous condition characterized by anovulation, infertility, hyperandrogenism, hirsutism, insulin resistance, bleeding disorders (absence of menstruations >3 months), polycystic ovaries (seen by ultrasound) [2], heart and lung diseases and overweight [3]. A strong overlap is seen between PCOS and the metabolic syndrome with insulin resistance, hypertension, dyslipidaemia and overweight being central aspects of the conditions. Therefore, PCOS is perceived as a metabolic

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syndrome [4,5].

It is estimated that as many as 50% of all patients with PCOS are overweight but how weight affects the pathogenesis is still unknown [6]. A weight loss of 5% improves the endocrinological profile and thereby the chance of ovulation and pregnancy [7]. Weight loss can be achieved primarily by lifestyle changes through diet and exercise. If overweight patients with PCOS reduce their diet to 1200–1500 kcal/day combined with moderate exercise (30 min a day) 5 days a week they will improve their metabolic-, endocrine- and fertility-profile [8,9].

PCOS is associated with low-grade systemic inflammation. This inflammation causes an elevation of certain biomarkers such as CRP, interleukin-18 (IL-18), monocyte chemo attractant protein-1 and leucocytes. Furthermore, endothelial dysfunction and increased oxidative stress are seen [10,11].

Asthma is a complex and chronic inflammatory disorder of the airways characterized by local and systemic inflammation, reversible airway obstruction, airway hyperresponsiveness and increased mucus production. Immunologically asthma is characterized by a T-helper cell 2 (Th2)-immune response with a resulting increased IgE formation and eosinophilia. A number of cytokines (IL-4, -5, -13, -17 -22, and TNF) are activated during the Th2 immune response. These cytokines induce the inflammatory histological changes seen in the epithelium of the respiratory tract [12]. In addition to the local inflammation of the respiratory tract, asthma is also associated with elevated systemic inflammation seen by for example elevated CRP levels, which is deteriorated by obesity [13]. A majority of adult patients with asthma are women and many are obese [14]. Both men and women experience an improvement in their respiratory symptoms after weight loss [15]. As with obesity a higher prevalence of the metabolic syndrome is seen among patients with asthma [16,17].

PCOS and asthma share many common features regarding metabolic control, systemic inflammation, allergy, menstrual cycle and female sex hormones. Both conditions are aggravated by obesity and improved by weight loss. Therefore we hypothesize that a coexistence of PCOS and asthma is present.

By clarifying a possible link between PCOS and asthma, we will be able to target the treatment of both conditions and stress the importance of a multidisciplinary approach. Herein we review the evidence for a coexistence of PCOS and asthma.

2. Evidence of a co existence of PCOS and asthma

A systematic literature search was performed using the PubMed database, Google Scholar, Embase, Web of Science, SCOPUS, and Cochrane library retrieving papers from 1938 to 2015. Search terms were: Asthma AND PCOS, Asthma AND systemic inflammation, Asthma AND metabolic syndrome, asthma AND gynaecology, PCOS AND systemic inflammation, PCOS AND metabolic syndrome, PCOS AND allergy. Cross-references were scrutinized to identify additional studies. We were interested in original studies, case reports, cohort studies, controlled trials, and review articles. Five articles were found. Among those two registry studies were of relevance.

A recent population-based retrospective cohort study using data linkage in a Australian statewide hospital morbidity database including 2566 patients with PCOS (ICD-10: E28.2; polycystic ovary syndrome or ICD-9: 256.4; polycystic ovaries) and a control group of 25,660 women without the PCOS diagnosis determined the prevalence of all hospitalizations from 15 years of age until a median age of 35.8 years. The study showed that 10.6% of patients with PCOS were admitted to hospital because of asthma compared to only 4.5% among the control group. Furthermore, a higher prevalence of respiratory diseases in general (22.8 vs. 14.2%) was seen among the patients with PCOS [18]. This indicates an association

between PCOS and respiratory diseases in general, but especially asthma, which possibly is more severe among PCOS patients.

These observations were confirmed in a Danish national registry-based study including 19,199 patients with PCOS, and 57,483 age-matched controls. The PCOS patients were divided into two groups according to the diagnostic criteria of inclusion [19]. In all 1217 women with PCOS who fulfilled the Rotterdam criteria “ (2 out of 3): 1. oligo- and/or anovulation, 2. clinical and/or biochemical signs of hyperandrogenism, and 3. polycystic ovaries and exclusion of other etiologies (congenital adrenal hyperplasias, androgen-secreting tumours, Cushing's syndrome)” [20] or had clinical and/or biochemical hyperandrogenism were included (group A). The rest of the women with PCOS included had the ICD:10 diagnosis of PCOS or hirsutism (L680, E28.2) (group B). This registry-based study showed a higher prevalence of asthma and a greater usage of asthma and allergy medications among patients with PCOS. In total 3.2% (group A)/3.0% (group B) of patients with PCOS had asthma in contrast to 2.2% of a population-based matched control group. Moreover, 19.5% (group A)/19.2% (group B) of the patients with PCOS had used asthma medication at some point in their lives compared to 14.1% in the control group; within the last year these rates were 6.4% (group A)/6.5% (group B) and 4.7% for the control group, respectively. The same tendency was seen in regards to use of corticosteroids and allergy-related medicine (ATC codes R06A, H02AB); 28.1% (group A)/30.6% (group B) of the PCOS patients had used these medications at some point, which was only seen in 23.2% of the control group. Within the last year 8.9% (group A)/9.1% (group B) of the PCOS patients versus 6.3% of the control subjects had used these medications.

The two studies above uses different diagnostic criteria to select the PCOS populations. This leads to the possibility of a slightly different group of women with PCOS in the two studies.

By using the ICD:9 diagnosis patients with polycystic ovaries are included - and they may not have polycystic ovary syndrome and therefore it can interfere with the observations made. The ICD:10 diagnosis on the other hand insures patients with polycystic ovary syndrome. Finally, by using the international accepted Rotterdam criteria to select the PCOS patients the selection bias is minimize.

In spite of the use of different diagnostic criteria, these studies underline the possibility of a link or a coexistence of PCOS and asthma seen through the rate of admission and the usage of asthma and allergy medication.

3. Supporting evidence of a coexistence of PCOS and asthma

3.1. Other aspects of female reproduction

Asthma and the female reproduction interact in several aspects (Table 1). Asthma has been associated with irregular menstruation and sex hormones, as seen in patients with PCOS. The association between asthma and female sex hormones has been known since 1938 [21] when a study associated worsening of asthma symptoms with the female menstruation cycle. These cyclic deteriorations of asthma symptoms during the luteal phase and/or during the first days of menstruation are termed premenstrual asthma (PMA). PMA is defined as a decrease of ≥ 20 –40% in the peak expiratory flow (PEF) and is experienced by 30–40% of all female asthma patients [22]. PMA is associated with a more severe type of asthma characterized by an increase in asthma symptoms and a greater usage of rescue medicine [23]. Among women admitted because of asthma attacks as many as 46% were in their premenstrual phase of their cycle [24]. Additionally, the concentration of female sex hormones in sputum changes through the menstrual cycle, showing a raised level of testosterone in the luteal phase [25].

Irregular menstruations have also been associated with asthma.

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