Review Article

Allergic Rhinitis during Pregnancy -an Update of Management

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Abstract

The concurrence of allergic rhinitis and pregnancy is common. The diagnosis of allergic rhinitis is easily and reliably made, by eliciting the characteristic symptoms on history. This diagnosis is easily confirmed by using the radioallergosorbent test (RAST) or enzyme-linked immunosorbent assay(ELISA) tests. Nasal symptoms, particularly obstruction, are often aggravated in pregnancy, through several possible mechanisms. The disease is often pre-existing and sometimes coincidental during pregnancy, and can worsen, improve, or stay the same during pregnancy. Besides ameliorating the detrimental effects of AR on the patient's quality of life, correct treatment is important for controlling concomitant asthma. If possible, it is important to highlight the risks of not taking such medications at a pre-conception visit. Although most medications for AR readily cross the placenta, there are several choices of treatment for controlling the symptoms during pregnancy. The choices may be varied depending on the disease course and symptoms, and inhaled corticosteroids are considered to be the first-line medical treatment. In addition, either a first-generation antihistamine, such as chlorpheniramine, or a second-generation antihistamine, such as cetirizine or loratadine, can be prescribed as the second-line medical treatment. As an alternative, intranasal cromolyn can be prescribed safely. Some of the leukotriene receptor antagonists and nasal decongestant sprays can only be prescribed when other methods are no longer valid and strict benefits can be expected. It is considered safe to continue immunotherapy during pregnancy.

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Introduction

Many patients are reluctant to treat sinonasal disease during pregnancy and the otolaryngologist must be knowledgeable of all medical evidence and guidelines that are available. A review of gestational rhinitis, sinusitis, and epistaxis will be discussed, including the diagnostic and therapeutic limitations and physiological changes specific to pregnancy. Physiological changes during pregnancy account for a distinct condition known as "rhinitis of pregnancy," as well as an increased incidence of epistaxis and worsened underlying sinonasal disease[1]. During the first and second trimester, there is increased circulating blood volume that is mostly contained within plasma volume and shifts to the extravascular space by the third trimester. Estrogen also has a direct cholinergic effect on nasal mucosa, causing vascular engorgement and increased mucosal gland activity, thereby causing or amplifying a preexisting sinonasal condition that usually resolves within 5 days postpartum[2,3]. Approximately 20-40% of women in their childbearing years report symptoms of rhinitis and sinonasal disease and 10-30% of these patients experience worsened symptoms during pregnancy[2]. The most common causes of sinonasal disease requiring medical attention during pregnancy include allergic rhinitis, bacterial sinusitis, and "rhinitis of pregnancy"[4]. There is also an increased incidence of rhinitis medicamentosa during pregnancy because mothers are inclined to abuse topical nasal decongestants that they believe entail a lower risk to the fetus than oral medications[5]. The purpose of this review is the effective management of allergic rhinitis in pregnancy is thus important and can be undertaken in complete safety, and the pregnant patient should not be made to suffer the symptoms.

Definition

Rhinitis is defined clinically by a combination of two or more nasal symptoms: running, blocking, itching, and sneezing. Allergic rhinitis occurs when this inflammation is IgE-mediated, following exposure to allergen[6].

Prevalence

While wide variations in reported prevalence exist, allergic rhinitis is acknowledged to be the most common allergic condition, affecting 10-25% of the population[7], is a global phenomenon, and appears to be increasing in

prevalence[8,9]. Given the common nature of the condition of pregnancy, clearly these conditions co-exist frequently!

Pregnancy and Nasal Problem

Clearly all nasal diseases can occur with the same frequency in pregnancy as they do in the non-pregnant population. While allergic rhinitis is a very common condition, the clinician must remember the other nasal conditions which can cause these nasal symptoms. Table I lists the differential diagnosis. Table II lists the predisposing causes of the subgroup of 'non-allergic non-infectious rhinitis'.

Table- I: Differential diagnosis of allergic rhinitis

Infectious rhinosinusitis (nonspecific)
Specific rhinosinusitis
- tuberculosis (TB)
- sarcoid
- syphilis
- leprosy, etc.
Non-allergic non-infectious rhinitis (see Table II)
Mechanical nasal obstruction:
- deviated septum
- hypertrophic turbinates
Tumours:
- nose/nasopharynx
- benign (e.g. polyps)/malignant
Cerebrospinal fluid (CSF) rhinorrhoea

Table- II: Non-allergic non-infectious inflammation of the nose and sinuses

Occupational
Non-allergic rhinitis with eosinophilia syndrome ('NARES') (like allergic rhinitis, but IgE levels and skin tests are normal)
Hormonal: Puberty, pregnancy, menstrual, postmenopausal
Drug-induced: systemic: aspirin, NSAIDs, antihypertensives, etc.
Local: Sympathomimetic overuse (rhinitis medicamentosa); cocaine
Irritants: Pollution; air-conditioning; cold air
Food intolerance (Note: This is not true IgE-mediated allergy)
Emotional, probably autonomic mediated (stress, sexual ('honeymoon rhinitis'))
Atrophic rhinitis: Primary or secondary
Gastro-oesophageal reflux
'Idiopathic rhinitis' or 'vasomotor rhinitis'.
NSAIDs - nonsteroidal anti-inflammatory drugs.

It is however recognized that certain specific associations exist between pregnancy and nasal conditions. Congestion and inflammation of the nose (and sinuses) are recognised as occurring in pregnancy10-12 as a result of hormonal factors (see Table II). A persistent rhinosinusitis may accompany the last trimester of pregnancy, when the severity increases as the blood oestrogen level increases. Symptoms normally resolve shortly after delivery. Severe allergic rhinitis has been associated with significant impairments in quality of life, sleep and work performance[13].

Diagnosis

The lay public too often labels all nasal symptomatology indiscriminately as 'sinus' or 'hay fever'. A definite diagnosis should always be made for nasal symptoms. Fortunately, the diagnosis of allergic rhinitis is extremely easily and reliably made. The basis of diagnosing allergic rhinitis is the history, and the symptoms are remarkably accurate (Table III).

Table- III: Symptoms specific to allergic rhinitis

Itch: Nasal/conjunctival/palatal
Sneezing many times in a row
Watery discharge: Rhinorrhoea/lacrimation
Reaction to specific allergens/situations: House dust; making beds; pollen; cats; dogs; feathers
Seasonal nature (although perennial nature does not exclude diagnosis)
Asthma/eczema
Family history of hay fever/asthma/eczema.

Examination is far less reliable, and identification of the classic 'pale blue' swollen, wet, inferior turbinates requires good lighting, a degree of experience and arguably a nasal speculum to achieve - and even then it is far less reliable than the history. Specialty consultation with otorhinolaryngologists or allergologists may assist if the diagnosis is uncertain. Confirmation of the diagnosis is done by either blood (radioallergosorbent test (RAST) or enzyme-linked immunosorbent assay (ELISA)) tests or the far cheaper and equally reliable skin-prick tests; both options are probably safe in pregnancy, but because of the small risk of hypersensitivity reaction, blood tests are advised in the pregnant state. Computed tomography (CT) scanning of the nose and sinuses is almost never necessary for allergic rhinitis. It is useful in excluding other nasal problems, particularly sinusitis. However, while the dose of radiation from current spiral CT scans is far less than it used to be, and the fetus can theoretically be shielded, radiologists are extremely reluctant to undertake CT scanning in pregnancy unless absolutely necessary, because of the issue of radiation scatter.

Management

As a general rule, medications should be avoided or used at the lowest dose that controls symptoms during pregnancy. However management of allergic rhinitis during pregnancy includes allergen avoidance, pharmacotherapy, education and possibly immunotherapy. Surgery (cautery, injection or reduction of hypertrophied turbinates) is rarely needed.

Allergen Avoidance and Environmental Control

The identification of allergens and instigation of allergen avoidance makes complete sense, and clearly puts the fetus at no risk. Symptoms of allergic rhinitis can be significantly mitigated by avoiding the allergen when this is possible.

No Treatment and Simple Non-specific Measures

There are times when, despite the diagnosis of allergic rhinitis, the symptoms are mild and no treatment is required. Nonspecific treatment measures may include the use of external nasal dilators, avoidance of irritants, and humidification. Nasal saline drops or sprays are a useful and safe option to help clear the nose, particularly before eating or sleeping[14].

Pharmacotherapy

Clearly it is a concern in pregnancy that the administration of systemic and even local pharmacotherapy might have a deleterious effect on the fetus. Caution is always advised when administering a drug to a pregnant woman, as most medications cross the placenta. The risk of fetal malformation represents a major fear and is highest during the first trimester, the time of most organogenesis. Fear of the possible teratogenicity of medication used for allergic rhinitis is largely based upon animal experiments and isolated associations in case reports. However medication is often avoided in pregnancy even when necessary, because of alarming information on drug labels or encountered in patient education. These cautions should be balanced against the fact that upper airway disease, if uncontrolled, has a significant, negative effect on quality of life, and several studies have shown that it can exacerbate coexisting asthma, which might in turn adversely affect the outcome of a pregnancy[15]. Furthermore, nasal obstruction may affect the pregnant mother's eating, sleeping and emotional well-being, which indirectly could adversely affect pregnancy[16]. For example, rhinitis during pregnancy may cause significant upper airway obstruction during sleep, which has been associated with pregnancy-induced hypertension and intrauterine growth retardation[17]. Medication is therefore indicated based on an exact clinical diagnosis, when the benefit of the drug outweighs risk, and when the drugs are carefully chosen and appropriately administered. Under these circumstances, risk should be negligible. In 1979 the US Food and Drug Administration (FDA) published a drug classification system[18] to assist in understanding the risk of any specific drug. It has five pregnancy precaution categories: A, B, C, D and X (Table IV).

Table- IV: Food and Drug Administration format for labeling human prescription drugs

Category	Description of Risk
A	Well-controlled human studies have failed to demonstrate risk to the fetus.
B	Either animal studies show no fetal risk and no human data are available, or animal studies show a risk but human studies do not show fetal risk.
C	Either animal studies indicate a fetal risk and there are no controlled studies in humans, or there are no available studies in humans or animals.
D	Studies show fetal risk in humans, but potential benefits may outweigh the potential risk in certain situations.
X	Studies in animals or humans, or based on human experience show definite fetal risk

Glucocorticosteroids

Systemic glucocorticosteroids are teratogenic in animals. The principal malformations are cleft lip and palate, and cardiovascular malformation[19]. Systemic steroids are generally used by otorhinolaryngologists as short courses to unblock the nose quickly at the start of treatment or as somewhat more prolonged courses for very severe symptoms during the hay fever season. The hormonal side-effects of prolonged administration even in the nonpregnant patient are widely accepted as precluding such use. Prolonged systemic corticosteroids in pregnant women have been implicated in growth retardation[20] and pre-eclampsia. Although the evidence for their teratogenic effects in pregnancy in humans is poor, concerns exist about possible increased risk of cleft lip or palate in the first trimester[21]. It would seem sensible to avoid even these short courses of systemic corticosteroids in pregnancy, whenever possible - certainly in the first trimester. The small concentrations of corticosteroids passed by the lactating mother to the infant present no substantial threat. Inhaled glucocorticosteroids, by contrast, have been extensively used by pregnant women who have asthma, and have not been incriminated in teratogenicity in humans[22]. Various studies have shown that high drug concentrations can be achieved at receptor sites in the nasal mucosa, with minimal risk of systemic adverse effects as the amount of systemic absorption of nasal steroid sprays is negligible[23]. Inhaled corticosteroids are extremely effective particularly for nasal obstruction in allergic rhinitis[24]. Large retrospective studies have suggested that topical corticosteroids may play a role in reducing the risk of asthma exacerbation[25,26]. A review of the use of budesonide in pregnancy showed no risk to the fetus in 6 600 pregnancies[27]. In a randomised, double-blind, placebo-controlled study that looked at the efficacy of fluticasone propionate nasal spray in pregnancy, no effects on the outcomes of the pregnancies were found[28]. Based on their efficacy, their limited systemic absorption, and the existing studies, nasal steroid sprays would seem to be a useful, effective and safe first-line option for use in pregnancy, particularly for nasal obstruction, and particularly after the first trimester. The FDA has assigned intranasal budesonide to category B; all other inhaled and intranasal corticosteroids are rated category C, although they are probably as safe. It is important for the clinician to emphasise and demonstrate the correct use of nasal steroid sprays, both consistent and compliant use, and administration by the correct technique, to ensure optimal benefit (Table V) which demonstrate incorrect technique.

Table-V: Instructions to patients for correct administration of nasal sprays

1. Hold your head in the normal upright position.
2. Place the tip of the nozzle in one nostril.
3. Hold the bottle at 45º to the horizontal.
4. Aim slightly away from the midline of the nose, i.e. towards the outer wall of your nasal passage.
5. Give a spray into the nostril, breathing in slightly through the nose. DO NOT SNIFF DEEPLY.
6. Give a second spray as in 5.
7. Now repeat steps 2-6 for the other nostril.
8. DO NOT BLOW YOUR NOSE FOR 15 MINUTES.
NOTE: Step 4 can be achieved by either of the following instructions:
* 'With the nozzle in your nostril aim for the outer corner of the eye'
OR
* 'Use your right hand for the left nostril, and your left hand for the right nostril'.

Antihistamines

Antihistamines are effective for the irritating symptoms of watery rhinorrhoea, itch and sneezing, but have until recently been considered to have little or no effect on nasal congestion[29]. The latest agents claim to be more effective for congestion[30]. Antihistamines for nasal symptoms need to be taken systemically, so clearly, safety of the fetus must be considered. While some first-generation antihistamines were shown to be teratogenic in animals[31-33], a large meta-analysis of 200 000 first trimester exposures to first-generation antihistamines[34] failed to show increased teratogenic risk in humans, and they are rated FDA category B. The newer second-generation antihistamines which have less central sedation than their predecessors have been less well studied. Isolated reports of teratogenicity in animal models and the possibility of hypospadias in human offspring raised concerns[35], but follow-up studies[36] dispelled these concerns and a cohort of 2147 women exposed to loratidine did not show risk of major congenital malformations[37]. Data from the Swedish Medical Birth Registry showed no increased incidence of congenital malformations in 917 exposures to cetirizine in pregnancy[35].

Decongestants

Sympathomimetic vasoconstrictor agents are not specific for allergic rhinitis, but at times are used in nasal congestion for short-term relief. Their prolonged use, particularly topically, may lead to tachyphylaxis, rebound congestion and 'rhinitis medicamentosa'. Oral decongestants are sometimes used alone, and at times in combination with antihistamines. Most oral decongestants are teratogenic in animals. Pseudoephedrine use in the first trimester has been implicated in an increased incidence of gastroschisis[38]. It carries an FDA category C rating. It can be considered after the first trimester when the danger of gastroschisis has passed. There are no specific data available concerning the use of decongestants during lactation. Pseudoephedrine does pass into the breast milk. It is recommended that only short-acting forms (e.g. phenylephrine) be used, and taken just after breastfeeding to minimise the concentration in breast milk. Topical nasal decongestants (nasal or ophthalmic). While it would seem logical that these are safer than oral agents, there are no adequate studies on the safety of administration. These drugs therefore carry an FDA category C rating. The limited data available suggest that their use should be limited to severe nasal congestion interfering with sleep, only when really required, preferably after the first trimester and not during labour.

Mast-cell Stabilisers

Mast-cell stabilisers, e.g. sodium cromoglycate, are virtually not absorbed by mucosal surfaces, and considered entirely safe, but, as stated previously, are far less effective than nasal steroids. No eratogenic effect has been found in animals and no adverse effect shown in humans[39]. They carry an FDA category B rating.

Allergen-specific Immunotherapy

Allergen-specific immunotherapy ('SIT', 'hyposensitisation' or'desensitisation') is based upon the repeated exposure of the allergic individual to an extract of the allergen in order to induce a state of immunological tolerance. It is generally used in patients who fail to respond adequately to avoidance, nasal steroids and antihistamines. It is less effective in patients with a wide spectrum of allergens, which is a common situation, and this limits its usefulness. It may be administered by intradermal or sublingual routes ('SLIT'). Systemic reactions may occur in up to 10% of patients, although these are usually mild[40]. There have been a number of case reports of women who have used immunotherapy during pregnancy for the treatment of allergic rhinitis and asthma without any adverse outcomes reported[37]. Metzger et al.[41] showed the safety of SIT in a study of 115 pregnant women with allergic rhinitis. It would seem unwise to initiate immunotherapy in a pregnant patient, but pregnancy is not considered to be a contraindication to the continuation of immunotherapy[42,43].

Discussion

Numerous pregnant women suffer from allergic rhinitis, and particular attention is required when prescribing drugs to these patients. In addition, physiologic changes associated with pregnancy could affect the upper airways.

Evidence-based guidelines on the management of allergic rhinitis have been published. Medication can be prescribed during pregnancy when the apparent benefit of the drug is greater than the apparent risk. Usually, there is at least one "safe" drug from each major class used to control symptoms. All glucocorticosteroids are teratogenic in animals but, when the indication is clear (for diseases possibly associated, such as severe asthma exacerbation), the benefit of the drug is far greater than the risk[42]. Inhaled glucocorticosteroids (eg, beclomethasone or budesonide) have not been incriminated as teratogens in humans and are used by pregnant women who have asthma. A few H1-antihistamines can safely be used as well. Most oral decongestants (except pseudoephedrine) are teratogenic in animals. There are no such data available for intranasal decongestants. Finally, pregnancy is not considered to be a contraindication for the continuation of immunotherapy. The only way to improve the mother's comfort and avoid complications for both mother and child is to perfectly control the disease. Indeed, it would be regrettable to be too prudent and deprive symptomatic patients of active treatments. Patients should be clearly informed of the benefits and risks of drug therapy.[44]

In conclusion, this article attempts to review the current evidence based literature on allergic rhinitis and pregnancy, in the hope of assisting clinicians in treating patients who require treatment in confidence and safety.

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In conclusion, this article attempts to review the current evidence based literature on allergic rhinitis and pregnancy, in the hope of assisting clinicians in treating patients who require treatment in confidence and safety.

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