



Allergy Medications During Pregnancy



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ABSTRACT

Allergic diseases are common in women of childbearing age. Both asthma and atopic conditions may worsen, improve or remain the same during pregnancy. Primary care physicians commonly encounter women receiving multiple medications for pre-existing atopic conditions, who then become pregnant and require medication changes to avoid potential fetal injury or congenital malformations. Each medication should be evaluated; intranasal and inhaled steroids are relatively safe to continue during pregnancy (budesonide is the drug of choice), second-generation antihistamines of choice are cetirizine and loratadine, leukotriene receptor antagonists are safe, sparing use of oral decongestants during the first trimester and omalizumab may be used for both uncontrolled asthma and for antihistamine-resistant urticaria. Medications to avoid during pregnancy include intranasal antihistamines, first-generation antihistamines, mycophenolate mofetil, methotrexate, cyclosporine, azathioprine and zilueton. Common allergic diseases may develop *de novo* during pregnancy, such as anaphylaxis.

Key Indexing Terms: Pregnancy; Allergic diseases; Treatment safety. [[Am J Med Sci 2016;352\(3\):326–331.](#)]

INTRODUCTION

In the United States, more than 40% of women of childbearing age suffer from rhinitis and up to one-third of them experience worsening symptoms during pregnancy.¹ Asthma affects up to 8% of pregnant women in the United States.² The prevalence of anaphylaxis is approximately 2%,³ whereas chronic urticaria affects 0.5-1% of the general population.⁴ Hence, it is not at all uncommon for a woman with a pre-existing allergic condition to become pregnant. The most common concern is to identify effective medications that are safe for pregnant patients. This article reviews the most common medications used to treat, and to avoid, for pre-existing allergic conditions that continue during pregnancy. Additionally, allergic conditions that develop during pregnancy will be discussed.

ALLERGY MEDICATIONS FOR THE PREGNANT PATIENT

Pre-existing atopic conditions may worsen, remain the same or improve with pregnancy.⁵⁻⁷ As with non-pregnant patients, the initial management of allergic conditions during pregnancy is taking allergen avoidance measures. Pharmacotherapy is initiated when avoidance measures have failed to control symptoms. Selection of medications for allergic conditions during pregnancy should be based on Food and Drug Administration risk categories (Table 1). Category A and category B drugs are safe to use during pregnancy, whereas category D and category X drugs should be avoided. This leaves category C drugs (animal reproduction studies have shown the adverse effect on the fetus and there are no adequate and well-controlled

studies in humans) that should be considered on a case by case scenario. The most critical time that a potentially teratogenic drug could induce congenital malformations is during the first trimester. There are currently no category A medications used to treat allergic conditions during pregnancy; most medications belong to category B or category C. Table 2 summarizes allergy medications that should be completely avoided during pregnancy along with suitable alternatives presently believed to be safe. Ideally, these medications should be started before conception (to assure tolerance and efficacy) and women should be made aware of this advantage when planning to become pregnant.

Intranasal Steroids

Intranasal steroids (INS) (e.g., fluticasone, mometasone, budesonide, flunisolide and triamcinolone) are the drugs of choice for allergic rhinitis. It is not uncommon to see patients with established allergic conditions using these medications at the time of conception. These medications, virtually all category C drugs, are considered safe during pregnancy by current guidelines; if they were and remain effective, it is reasonable to continue them.⁸ However, most allergists would switch patients to budesonide, the only category B INS with extensive safety evidence for pregnant patients.⁸ Notably, rhinitis of pregnancy (discussed later) does not respond to INS.⁹ Furthermore, patients should be encouraged to continue avoidance measures of known allergens. Some effective measures include closing windows, using air conditioning, limiting exposure to the outdoors when pollen counts are high, wearing sunglasses, showering before bedtime, avoiding exposure to animal dander

TABLE 1. FDA pregnancy risk categories.

A	Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.
B	Animal studies have not demonstrated a risk to the fetus, but there are no adequate studies in pregnant women. Or Animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy and there is no evidence of risk in later trimesters.
C	Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in human beings/the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks. Or There are no animal reproduction studies and no adequate studies in human beings.
D	There is an evidence of human fetal risks, but the potential benefits from the use of the drug in pregnant women may be acceptable despite potential risks.
X	Studies in animals or human beings demonstrate fetal abnormalities, or adverse reaction reports indicate evidence of fetal risk. The risk of use in pregnant woman clearly outweighs any possible benefit.

and using zippered casings for bedding (to minimize exposure to dust mites).⁸ Other approaches before starting INS include nasal saline irrigation methods via bulb syringe or various squeeze bottles (i.e., “sinus rinse”). Nonallergic rhinitis (e.g., vasomotor rhinitis) is diagnosed when patients with symptoms of sneezing, rhinorrhea, nasal congestion or postnasal drainage (in any combination or all symptoms together) are present in the absence of a specific etiology. INS are also the drugs of choice for this condition during pregnancy.⁸

Intranasal Antihistamines

Azelastrine is a phthalazinone derivate with histamine-1 receptor binding approximately 10-fold greater than chlorpheniramine,¹⁰ which is available in 2 forms— intranasal azelastrine hydrochloride and azelastrine with sorbitol nasal spray.¹¹ This common intranasal antihistamine used for allergic rhinitis and nonallergic rhinitis should be avoided during pregnancy. It has been associated with minor adverse effects on fetal animals and no safety data are available in humans. This medication is also costly¹² and is associated with sedation.¹³

Oral Antihistamines

Antihistamines are commonly used to treat pruritus and rhinorrhea in the general population. First-generation antihistamines (e.g., brompheniramine and hydroxyzine) are not prescribed by allergists to pregnant patients. Diphenhydramine has been associated with fetal development of cleft palate¹⁴ if administered during the first trimester. There is recent evidence demonstrating the association of first-generation antihistamines use and increased risk of dementia.¹⁵

Second-generation antihistamines are preferred over first-generation agents in both pregnant and non-pregnant individuals. Patients should be started on cetirizine^{16,17} or on loratadine,^{18,19} based on their excellent safety data and recommendation in multiple guidelines for other allergic conditions (e.g., asthma²⁰ and chronic urticaria²¹) during pregnancy. As an added benefit, cetirizine may also relieve nausea and vomiting during pregnancy.²² Both fexofenadine and desloratadine have been associated with low–birth-weight offspring in animal models and are currently classified as category C drugs. The use of high-dose antihistamines

TABLE 2. Drugs to avoid during pregnancy and alternatives.

Condition	Avoid	Alternative
Allergic rhinitis	Oral/intranasal decongestants, intranasal antihistamines	Intranasal steroids, budesonide is preferred ⁸
	First-generation systemic antihistamines	Cetirizine, ^{16,17} loratadine ^{18,19}
	Most second-generation systemic antihistamines	Cetirizine, ^{16,17} loratadine ^{18,19}
Rhinitis of pregnancy	Intranasal antihistamines	Avoidance measures, intranasal steroid trial, ipratropium bromide, limited use of phenylpropanolamine ²⁶
Asthma	Systemic corticosteroids	Inhaled corticosteroids, budesonide is preferred, ²⁸ omalizumab ⁴¹
	Most inhaled long-acting beta agonists	Salmeterol, ²⁸ omalizumab ⁴¹
	Zileuton	Montelukast or zafirlukast ^{23,24}
Atopic dermatitis	Ultraviolet therapy, topical calcineurin inhibitors and high-potency steroids	Low-to-mid potency topical steroids ³⁶
Anaphylaxis	Skin testing, challenges	Serum-specific IgE testing, epinephrine
Chronic urticaria/angioedema	Mycophenolate mofetil, methotrexate, cyclosporine, azathioprine	Cetirizine, loratadine, omalizumab ^{16-19,41}
Drug allergy	Skin testing, challenges	Serum-specific IgE testing

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