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REVIEW ARTICLE

Review: Side Effects of Some Commonly Used Allergy Medications (Decongestants, Anti-Leukotriene Agents, Antihistamines, Steroids, and Zinc) and Their Safety in Pregnancy

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Abstract

Objective: The aim of this study was to evaluate the safety and side-effects of common allergy medications.

Methodology: A literature search was undertaken. We searched the databases of Pubmed, MEDLINE, EMBASE databases, and Cochrane Library from 1990 to October 2016, using key words: Allergy, Medications, Antihistamines, Decongestants, Montelukast, Side effects, Adverse Events, Adverse, Effects, Zinc, Steroids, Pregnancy, Reviews, RCT, and Case Report.

Results: Antihistamines can cause undesired anti-cholinergic effects including mydraisais, sedation, dry eyes, dry mouth, constipation and urinary retention. Significant overdose of antihistamines can cause serious toxicity and even death. Cetirizine or loratadine are preferred based on their good safety profile and recommendation in multiple guidelines during pregnancy. Side effects are more common with oral decongestants than with topical sprays. Decongestant side-effects include nausea, vomiting, insomnia, dizziness, elevated blood pressure, restlessness, anxiety, hallucinations, seizure, psychosis, headache, urinary dysfunction, stroke, intracranial bleed, arrhythmias, and myocardial infarction. Anti-leukotriene agents, topical steroids, and intranasal steroids are generally well tolerated. Intranasal zinc has been reported to cause zinc-induced anosmia syndrome which is characterized by nasal burning followed by anosmia and can be distinguished from post-viral anosmia based on history.

Conclusion: Although serious side-effects can occur, the majority of the common allergy medications reviewed in this article was well-tolerated and had only rare serious side effects.

Keywords

Allergies, Allergy treatment, Side effects, Adverse events, Adverse effects, Allergy medication, Steroids, Antihistamines, Decongestants, Anti-leukotriene agents

Introduction

Allergic conditions are common, although most individuals with allergies do not seek medical care [1]. In the United States allergy medications are readily available over the counter. While most people will report relief of their symptoms with readily available allergy treatments, approximately 7% of patients who take these medications will experience adverse effects (AEs), which can be severe [2]. This article will review side effects reported in the literature for some of the most common prescription and over-the-counter allergy medications.

Literature Review Results

Decongestants

Decongestants can be useful medications allergic rhinitis with congestion. Particularly in the spring and winter months many people use or misuse excessive doses of decongestant agents to relieve allergic congestive symptoms without a physicians' prescription. Nasal decongestants include the oral decongestants phenylephrine and pseudoephedrine, as well as topical sprays (Phenylephrine, Oxymetazoline) and an inhaler Propylhexedrine. The majority of the agents used as decongestants stimulates α-adrenergic receptors and reduce edematous mucosal tissue volume and mucus secretions by causing vasoconstriction of the upper respiratory tract, paranasal sinuses, and nasal mucosa [3]. Decongestants are safe for many patients, but a significant number of side-effects have been reported. Adverse effects of deconges-

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tants result from a direct effect on adrenergic receptors and stimulation of the CNS.

Both oral and nasal decongestants are contraindicated for patients with heart disease, hypertension, thyroid disease, diabetes, and men with benign prostatic hypertrophy. Nasal decongestants, however, appear to have significantly less risk [4,5]. Decongestants should not be taken with Monoamine oxidase inhibitors as they can lead to a life-threatening rise in blood pressure. Side effects are more common with oral decongestants than with topical sprays and include nausea, vomiting, insomnia, dizziness, elevated blood pressure, restlessness, anxiety, hallucinations, seizure, psychosis, headache, urinary dysfunction, stroke, intracranial bleed, arrhythmias, and myocardial infarction [3,6,7]. Although decongestants may lead to hyper excitability and an increased risk of seizure, a recent animal study showed a paradoxical effect in which phenylephrine potentiates the anticonvulsant effect and neutralizes the sedative effect of diazepam in rats [8]. Rare serious side effects that have been reported in the literature include a case report of an otherwise healthy 37-year-old woman who presented with acute-onset spinal artery vasospasm resulting in quadriplegia after decongestant (ephedrine) use [9].

Purposeful abuse: Nasal decongestants have significant potential for abuse. Long-term use of decongestant nasal spray (and occasionally with oral decongestants) can cause rebound nasal congestion known as rhinitis medicamentosa (RM). A review of 33 cases of rhinitis medicamentosa showed only seven cases had duration of use less than one year and about half had duration of use more than two years [10]. In the review, approximately 2/3 of the cases of RM resulted from inappropriate treatment of allergic rhinitis. The long duration of use prior to the onset of RM is also consistent with a recent Cochrane review noting that short-term use of nasal decongestants do not seem to increase the risk of adverse events in adults. The effectiveness and safety of nasal decongestants in children is yet to be determined [11].

Fortunately, rhinitis medicamentosa with nasal congestion appears readily reversible with suitable treatment [10]. Treatment of RM is immediate withdrawal, although adjuvant use of steroid nasal or oral corticosteroids during the withdrawal may be useful [12,13].

The oral decongestant pseudoephedrine has become the preferred starter chemical for thousands of methamphetamine (Meth) labs in the Unites States [14]. Fearing that customers will shy away pseudoephedrine products and because of the meth lab association, some drug companies are replacing over-the-counter pseudoephedrine with phenylephrine, which cannot be made into methamphetamine.

Antileukotriene agents

Leukotriene inhibitors were initially designed as add-on therapy for asthma; however, they also have proven efficacy and FDA approval for use in allergic rhinitis. The Antileukotriene agents in the United States include montelukast and zafirulast which act by antagonizing the leukotriene receptor, and zileuton which inhibits leukotriene synthesis. In general, antileukotriene agents appear to be well tolerated. Drug metabolism occurs via the Cytochrome P450 system in liver, creating the potential for interactions with other medications using the P450 system; however, no such drug interactions have been reported to the FDA [15] Rare, but serious side effects of Montelukast have been reported. In 2009 the FDA mandated a label change for Montelukast after reports of neuropsychiatric side effects [16]. Merck listed reports of agitation, aggression, depression and suicidality [17]. Despite the label change, multiple studies failed to find a definitive link between montelukast and suicidality, which is why there was no black box warning. A 2011 review article failed to find evidence of change in both the use of Montelukast and neuropsychiatric events after the label change [16].

In a Japanese study on the use of montelukast for treatment of perennial allergic rhinitis, there were no serious adverse effects and one discontinuation due to adverse effects. The most common adverse effects in any of the treatment groups were nasopharyngitis, pharyngitis, and acute sinusitis [18]. Montelukast-induced metamorphopsia, a type of visual distortion in which straight lines appear wavy or disappear, has also been reported in the literature [19].

Intranasal steroids

Intranasal steroids are considered first line therapy to reduce inflammation, nasal congestion, and post-nasal drip in allergic rhinitis and are many are now available over-the-counter [20]. Intranasal steroids have low bioavailability, alleviated most of the harmful side effects of systemic steroids. The second-generation intranasal corticosteroid (INC) agents currently in use (mometasone, fluticasone, ciclesonide) further minimize systemic bioavailability (< 1%) compared with older INCs and compared with oral agents and reduces the risk for systemic adverse events [21]. While concern exists among prescribers and patients that these agents may reach the systemic circulation in sufficient concentration to produce significant adverse effects, the available evidence does not support these concerns. The safety and efficacy of intranasal corticosteroids (INCs) are well established for the management of allergic rhinitis and nasal polyps over three decades of use [21,22]. A review of the safety and efficacy of memetasone furoate nasal spray concluded it has a favorable benefit-risk ratio [23].

The side effect profiles of INCs consist primarily of a low incidence of mostly mild and often transient local adverse events, with nasal dryness and irritation, mild

epistaxis, headache, and pharyngitis being the most common adverse effects [21,23]. Proper technique, directing the spray laterally and away from the septum, minimizes these effects. If the symptoms persist despite proper technique, they tend to resolve with cessation of therapy. There is no clinical evidence that intranasal steroid sprays suppresses the function of the hypothalamus-pituitary-adrenal axis, reduces bone density, or inhibits growth in children, unlike with oral or inhaled steroids, when nasal steroids are administered at clinically relevant doses [23,24].

Inhaled chronic steroid use in children has been associated with a greater risk of cataracts and ocular hypertension, in some studies, but it is unknown if this data can be extrapolated to chronic intranasal corticosteroids [25]. Some studies have demonstrated a link between intranasal steroids and cataract formation, but the results have been inconsistent. More recent studies and meta-analyses have failed to demonstrate this link [26]. There have been reports of turbinate atrophy, ulceration and septal perforation, but these are rare [26]. Biopsies taken from patients on nasal steroids have not revealed evidence of these harmful changes [26].

Antihistamines

Histamine plays an important role in allergic reactions and antihistamines have a role in the treatment of allergic rhinitis, allergic conjunctivitis, and urticarial [15,27]. Antihistamines can be further classified as 1st generation, 2nd generation, and nasal.

Terfenadine and astemizole, are antihistamines known slow repolarization resulting clinically as prolongation of the QT interval and torsade de pointes [28]. Because of cardiac arrhythmia risk, terfenadine and astemizole have been removed from the US market, but only scarce clinical data are available on other antihistamines [28]. In a 2015 review of case reports, five antihistamine agents resulted in more concerning arrhythmias (cetirizine, desloratadine, diphenhydramine, fexofenadine, loratadine) and 6 in less concerning arrhythmias (alimemazine, carbinoxamine, cyclizine, cyproeptadine, dexchlorpheniramine and doxylamine) [28]. Hypersensitivity reactions with antihistamines are rare, but can occur [29].

First generation (old) H1 antihistamines: Common first generation antihistamine medications available in US include diphenhydramine, hydroxyzine, and doxepin (also a tricyclic antidepressant). First Generation H1 blockers can cross the blood brain barrier and interfere with neurotransmission in the central nervous system, which can cause sedation [15,27]. Antihistamines are effective in relieving the symptoms of allergic rhinitis, such as nasal stuffiness and watery eyes, due to anti-cholinergic action. This can cause undesired anti-cholinergic effects including mydraisais, sedation, dry eyes, dry mouth, constipation and urinary retention [15,27,30]. Overdose can cause serious toxicity and even death in severe circumstances [15]. Diphenhydramine also has α blocking action, which can cause orthostatic hypotension, especially in the elderly [27]. There is also recent evidence that use of first-generation antihistamines may increase the risk of dementia [31]. There is no specific antidote for antihistamine overdose and treatment is supportive particularly for ingestions of first generation compounds [32].

Second generation (new) H1 antihistamines: The second generation histamine H(1)-receptor antagonists are important therapeutic tools in the treatment of allergic conditions. They are among the most widely prescribed and have an excellent overall safety profile [33]. Common antihistamine medications available in the US include: Cetirizine, Levocetirizine, Loratidine, and Fexofenadine. The second generation antihistamines were developed to try to minimize the undesirable and unpredictable side effects mentioned above. As a result, the second generations are less likely to cause side effects, although it is impossible to completely avoid all side effects. Only small amounts of the newer antihistamines cross the blood-brain barrier and thus do not cause as much sedation. Overdoses are not likely to cause serious toxicity or death. The newer antihistamines are more selective for the H1 receptor, which means that they are less likely to cause the anticholinergic effects mentioned above, but nevertheless, anticholinergic effects have still been reported, especially in the elderly [15].

Intranasal antihistamines: Azelastine intranasal antihistamine is used for allergic rhinitis. Nasal antihistamine sprays are generally well tolerated. Common side effects include bitter taste in the mouth, headache, drowsiness, dry mouth and nose, pyrexia, cough, epistaxis, sneezing, rhinalgia, upper respiratory infection, vomiting, nasal burning and irritation, eye redness, and oropharyngeal pain [34-36].

Zinc

Zinc plays a role in immune function and although not commonly prescribed by physicians, people commonly use zinc for everything from the common cold to allergies. Oral zinc is thought to be safe when used appropriately [15]. Toxic doses of Zinc, thought to be 100-300 mg, have multiple side effects. The most common are nausea, vomiting and epigastric discomfort. Multiple studies have revealed increased LDL:HDL ratios. Due to the interaction of zinc and copper, toxic doses of zinc have also led to low copper levels with anemia and neutropenia [37].

Commercial preparations of intranasal zinc were removed from the US market by the FDA in June 2009 due to reports of permanent anosmia. Intranasal zinc has been reported to cause zinc-induced anosmia syndrome which is characterized by nasal burning followed by anosmia and can be distinguished from post-viral anosmia based on history [38,39].

Topical steroids

Topical steroids are used for multiple types of allergic skin

conditions including eczema, hives, angioedema, and dermatitis. Stinging frequently occurs when a topical steroid is first applied. Local side effects of topical steroids include skin atrophy, acne, striae, senile purpura, telangiectasia, rosacea, and localized hypertrichosis [40-42]. Topical steroids can also cause, aggravate, or mask skin infections [40,41]. Chronic high-potency steroid use can cause steroid rosacea, pustular psoriasis, steroid withdrawal, or periorificial dermatitis [40]. Systemic reactions such as hyperglycemia, glaucoma, and adrenal insufficiency have also been reported following topical application [41].

Allergy medications during pregnancy

Allergic diseases are common in pregnancy and may worsen, improve, or remain stable during pregnancy [43]. Allergen avoidance measures to known allergens are the best first-line approach to allergy treatment during pregnancy. In general, intranasal and inhaled steroids are relatively safe to continue during pregnancy (budesonide is the drug of choice), second-generation antihistamines are preferred to first-generation antihistamines and the anti-histamine drugs of choice in pregnancy are cetirizine and loratadine. Leukotriene receptor antagonists appear safe. Use of oral decongestants during the first trimester should be counseled against. Due to low benefit and higher risk, intranasal antihistamines are best avoided during pregnancy.

Intranasal steroids in pregnancy: Intranasal steroids (INS) 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. Rhinitis of pregnancy can mimic allergic rhinitis symptoms, but does not respond to INS [43].

Intranasal steroids are considered safe during pregnancy and it is reasonable to continue them in pregnancy, if needed. Budesonide should be considered the ideal INS due to its extensive safety evidence for pregnant patients [43-45].

Intranasal antihistamines in pregnancy: Azelastine should be avoided during pregnancy [46]. It has been associated with minor adverse effects on fetal animals and no safety data are available in humans. This medication is also costly and is associated with sedation [43,46].

Oral antihistamines in pregnancy: Due to less side effects, second generation antihistamines are preferred to first generation antihistamines for pregnant patients. Diphenhydramine has been associated with fetal development of cleft palate administered during the first trimester [44]. Cetirizine or loratadine are preferred based on their good safety profile and recommendation in multiple guidelines during pregnancy [47-50]. Cetirizine may also relieve nausea and vomiting during pregnancy [51]. Both fexofenadine and desloratadine have been associated with low-birth-weight offspring in animal models, so should be avoided in pregnancy [43,48].

Antileukotriene agents in pregnancy: Leukotriene receptor antagonists are considered safe to use for both asthma and allergic rhinitis during pregnancy [43,52].

Oral decongestants in pregnancy: Decongestant use in pregnancy is generally avoided due to the possibility of vasoconstriction of the uterine arteries, which reduces fetal blood supply. Most oral decongestants (except pseudoephedrine) are teratogenic in animals [53]. However, pseudoephedrine use in the first trimester has been associated with the development of fetal gastroschisis [54,55]. Using decongestants while breast-feeding may cause irritability, insomnia, and infant tachycardia [56]. Also, pseudoephedrine has been shown to reduce mean milk volume in breastfeeding mothers by 24% [57].

Nasal decongestants in pregnancy: There is little safety data available for intra-nasal decongestants in pregnancy [43,53].

Topical steroids in pregnancy: The treatment of atopic dermatitis during pregnancy starts with avoidance measures and use of emollients, but if needed, low-potency topical glucocorticoids have been shown to be safe during pregnancy [58]. However, these should be limited to low-level and mid-level potency steroids, as higher potency agents have been implicated in fetal growth restriction [59].

Allergen immunotherapy in pregnancy: Initiation of allergen immunotherapy is contraindicated during pregnancy, because of the risk of anaphylaxis. However, if a patient who becomes pregnant who is already receiving allergen immunotherapy, it can be continued [60].

Conflict of Interests

The authors declare no conflict of interest.

References

1. (2014) Asthma and Immunology Allergies. American College of Allergy.
2. Flynn CA, Griffin G, Tudiver F (2002) Decongestants and antihistamines for acute otitis media in children.
3. Zeynettin Kaya, Abdullah Tuncez (2013) Adverse Cardiac Effects of Decongestant Agents. Eur J Gen Med 10: 32-35.
4. Rosenfeld RM, Andes D, Bhattacharyya N, Cheung D, Eisenberg S, et al. (2007) Clinical practice guideline: adult sinusitis. Otolaryngol Head Neck Surg 137: S1-S31.
5. (1995) Practice parameters for the diagnosis and treatment of asthma. Joint Task Force on Practice Parameters, representing the American Academy of Allergy Asthma and Immunology and the Joint Council of Allergy, Asthma and Immunology. J Allergy Clin Immunol 96: 707-870.
6. Bektas F, Eken C, Oktay C (2010) Pseudoephedrine-induced paroxysmal supraventricular tachycardia: a case report. J Emerg Med 38: e53-e57.
7. Shao IH, Wu CC, Tseng HJ, Lee TJ, Lin YH, et al. (2016) Voiding dysfunction in patients with nasal congestion treated with pseudoephedrine: a prospective study. Drug Des Devel Ther 10: 2333-2339.
8. Serdyuk SE, Gmiro VE (2014) Phenylephrine potentiates

the anticonvulsant effect and neutralizes the sedative effect of diazepam in rats upon combined intragastric administration. Bull Exp Biol Med 158: 234-247.

9. Snipelisky DF, Kurklinsky AK, Chirila R (2015) Transient Cardiomyopathy and Quadriplegia Induced by Ephedrine Decongestant. Tex Heart Inst J 42: 575-578.

10. Yuta A, Ogawa Y (2013) Clinical review of 33 cases of rhinitis medicamentosa by decongestant nasal spray. Arerugi 62: 1623-1630.

11. Deckx L, De Sutter AI, Guo L, Mir NA, van Driel ML (2016) Nasal decongestants in monotherapy for the common cold. Cochrane Database Syst Rev 10.

12. Elwany S, Abdel-Salaam S (2001) Treatment of rhinitis medicamentosa with fluticasone propionate--an experimental study. Eur Arch Otorhinolaryngol 258: 116-119.

13. Ferguson BJ, Paramaesvaran S, Rubinstein E (2001) A study of the effect of nasal steroid sprays in perennial allergic rhinitis patients with rhinitis medicamentosa. Otolaryngol Head Neck Surg 125: 253-260.

14. Cunningham S, Finlay K, Stoecker C (2015) Is Mississippi's prescription-only precursor control law a prescription to decrease the production and raise the price of methamphetamine? Int J Drug Policy 26: 1144-1149.

15. Estelle F, Simons R, Akdis CA (2014) Middleton's Allergy and Practice. (8th edn), Saunders an imprint of Elsevier Inc, Philadelphia, USA, 1503-1533.

16. Lu CY, Zhang F, Lakoma MD, Butler MG, Fung V, et al. (2015) Asthma Treatments and Mental Health Visits After a Food and Drug Administration Label Change for Leukotriene Inhibitors. Clin Ther 37: 1280-1291.

17. Merk package insert, Montelukast Patient Information.

18. Okubo K, Inoue Y, Numaguchi H, Tanaka K, Saito I, et al. (2016) Montelukast in the treatment of perennial allergic rhinitis in paediatric Japanese patients; an open-label clinical trial. J Drug Assess 5: 6-14.

19. Carnovale C, Gentili M, Antoniazzi S, Radice S, Clementi E (2016) Montelukast-induced metamorphopsia in a pediatric patient: A case report and a pharmacovigilance database analysis. Ann Allergy Asthma Immunol 116: 370-371.

20. Ferri F (2017) Diseases and Disorders. Allergic Rhinitis. (1st edn), Ferri's Clinical Advisor. Elsevier Health Sciences, Philadelphia, USA, 52-53.

21. Sastre J, Mosges R (2012) Local and systemic safety of intranasal corticosteroids. J Investig Allergol Clin Immunol 22: 1-12.

22. Teper A, Ratner PH (2008) Mometason furoate nasal spray is safe and effective for one-year treatment of children with perennial allergic rhinitis. J Allergy Clin Immunol 121: S52-S53.

23. Zitt M, Kosoglou T, Hubbell J (2007) Mometasone furoate nasal spray: a review of safety and systemic effects. Drug Saf 30: 317-326.

24. Boulet LP, Giguère MC, Milot J, Brown J (1994) Effects of long-term use of high-dose inhaled steroids on bone density and calcium metabolism. J Allergy Clin Immunol 94: 796-803.

25. Behbehani AH, Owayed A, Hijazi ZM, Eslah EA, Al-Jazzaf AM (2005) Cataract and ocular hypertension in children on inhaled corticosteroid therapy. J Pediatr Ophthalmol Strabismus 42: 23-27.

26. Gupta R, Fonacier LS (2016) Adverse Effects of Nonsystemic Steroids (Inhaled, Intranasal, and Cutaneous): a Review of the Literature and Suggested Monitoring Tool. Curr Allergy Asthma Rep 16: 44.

27. Pelletier CE (2003) H1 Blockers. Pharmacology, Smart Charts, Lange Medical Books, New York, 342-344.

28. Poluzzi E, Raschi E, Godman B, Koci A, Moretti U, et al. (2015) Pro-arrhythmic potential of oral antihistamines (H1): combining adverse event reports with drug utilization data across Europe. PLoS One 10: e0119551.

29. Rodríguez del Río P, González-Gutiérrez ML, Sánchez-López J, Nuñez-Acevedo B, Bartolomé Alvarez JM, et al. (2009) Urticaria caused by antihistamines: report of 5 cases. J Investig Allergol Clin Immunol 19: 317-320.

30. Shiga Y, Araki A, Yamamoto T, Kawazoe N, Sato K, et al. (2003) Atresia hymenalis with acute urinary retention under the anti-histamine drug: a case report. Nihon Hinyokika Gakkai Zasshi 94: 448-451.

31. Gray SL, Anderson ML, Dublin S, Hanlon JT, Hubbard R, et al. (2015) Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. JAMA Intern Med 175: 401-407.

32. Ten Eick AP, Blumer JL, Reed MD (2001) Safety of antihistamines in children. Drug Saf 24: 119-147.

33. Walsh GM (2002) Emerging safety issues regarding long-term usage of H(1) receptor antagonists. Expert Opin Drug Saf 1: 225-235.

34. Howland WC, Amar NJ, Wheeler W, Sacks H (2011) Efficacy and safety of azelastine 0.15% nasal spray administered once daily in patients with allergy to Texas mountain cedar pollen. Int Forum Allergy Rhinol 1: 275-279.

35. van Bavel J, Howland WC, Amar NJ, Wheeler W, Sacks H (2009) Efficacy and safety of azelastine 0.15% nasal spray administered once daily in subjects with seasonal allergic rhinitis. Allergy Asthma Proc 30: 512-518.

36. Bernstein JA (2007) Azelastine hydrochloride: a review of pharmacology, pharmacokinetics, clinical efficacy and tolerability. Curr Med Res Opin 23: 2441-2452.

37. Fosmire GJ (1990) Zinc toxicity. Am J Clin Nutr 51: 225-227.

38. Alexander TH, Davidson TM (2006) Intranasal zinc and anosmia: the zinc-induced anosmia syndrome. Laryngoscope 116: 217-220.

39. D Cruze H, Arroll B, Kenealy T (2009) Is intranasal zinc effective and safe for the common cold? A systematic review and meta-analysis. J Prim Health Care 1: 134-139.

40. Mooney E, Rademaker M, Dailey R, Daniel BS, Drummond C, et al. (2015) Adverse effects of topical corticosteroids in paediatric eczema: Australasian consensus statement. Australas J Dermatol 56: 241-251.

41. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ (2006) Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol 54: 1-15.

42. Coondoo A, Phiske M, Verma S, Lahiri K (2014) Side-effects of topical steroids: a long overdue revisit. Indian Dermatol Online J 5: 416-425.

43. Gonzalez-Estrada A, Geraci SA (2016) Allergy Medications During Pregnancy. Am J Med Sci 352: 326-331.

44. Gilbert C, Mazzotta P, Loebstein R, Koren G (2005) Fetal safety of drugs used in the treatment of allergic rhinitis: a critical review. Drug Saf 28: 707-719.

45. Rahimi R, Nifkar S, Abdollahi M (2006) Meta-analysis finds use of inhaled corticosteroids during pregnancy safe: a systematic meta-analysis review. Hum Exp Toxicol 25: 447-452.

46. Ratner PH, Hampel F, Van Bavel J, Amar NJ, Daftary P, et al. (2008) Combination therapy with azelastine hydrochloride nasal spray and fluticasone propionate nasal spray in the treatment of patients with seasonal allergic rhinitis. Ann Allergy Asthma Immunol 100: 74-81.

47. Einarson A, Bailey B, Jung G, Spizzirri D, Baillie M, et al. (1997) Prospective controlled study of hydroxyzine and cetirizine in pregnancy. Ann Allergy Asthma Immunol 78: 183-186.

48. Kallen B (2002) Use of antihistamine drugs in early pregnancy and delivery outcome. J Matern Fetal Neonatal Med 11: 146-152.

49. Moretti ME, Caprara D, Coutinho CJ, Bar-Oz B, Berkovitch M, et al. (2003) Fetal safety of loratadine use in the first trimester of pregnancy: a multicenter study. J Allergy Clin Immunol 111: 479-483.

50. Diav-Citrin O, Shechtman S, Aharonovich A, Moerman L, Arnon J, et al. (2003) Pregnancy outcome after gestational exposure to loratadine or antihistamines: a prospective controlled cohort study. J Allergy Clin Immunol 111: 1239-1243.

51. Einarson A, Levichek Z, Einarson TR, Koren G (2000) The antiemetic effect of cetirizine during pregnancy. Ann Pharmacother 34: 1486-1487.

52. Gideon Koren, Moumita Sarkar, Adrienne Einarson (2010) Safety of using montelukast during pregnancy. Can Fam Physician 56: 881-882.

53. Demoly P, Piette V, Daures JP (2003) Treatment of allergic rhinitis during pregnancy. Drugs 63: 1813-1820.

54. Black RA, Hill DA (2003) Over-the-counter medications in pregnancy. Am Fam Physician 67: 2517-2524.

55. Mitchell JL (1999) Use of cough and cold preparations during breastfeeding. J Hum Lact 15: 347-349.

56. Aljazaf K, Hale TW, Ilett KF, Hartmann PE, Mitoulas LR, et al. (2003) Pseudoephedrine: effects on milk production in women and estimation of infant exposure via breastmilk. Br J Clin Pharmacol 56: 18-24.

57. Cantu C, Arauz A, Murillo-Bonilla LM, López M, Barinagarrementeria F (2003) Stroke associated with sympathomimetics contained in over-the-counter cough and cold drugs. Stroke 34: 1667-1672.

58. Hviid A, Molgaard-Nielsen D (2011) Corticosteroid use during pregnancy and risk of orofacial clefts. CMAJ 183: 796-804.

59. Chi CC, Kirtschig G, Aberer W, Gabbud JP, Lipozenčić J, et al. (2011) Evidence-based (S3) guideline on topical corticosteroids in pregnancy. Br J Dermatol 165: 943-952.

60. Pitsios C, Demoly P, Bilò MB, Gerth van Wijk R, Pfaar O, et al. (2015) Clinical contraindications to allergen immunotherapy: an EAACI position paper. Allergy 70: 897-909.