Management of Rhinosinusitis During Pregnancy: Systematic Review and Expert Panel Recommendations

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Introduction

Background: Sinusitis is reported to be prevalent in 13-16% of adult females in the United States. Given its high prevalence in women of childbearing age, management of rhinosinusitis (RS) during pregnancy requires special and thoughtful considerations.

Objectives: 1. Conduct a systematic literature review for acute and chronic rhinosinusitis (CRS) management during pregnancy 2. Make evidence-based recommendations.

Methods: Medline and Embase databases were searched using "rhinitis" OR "sinusitis" OR "rhinosinusitis" AND "pregnant" OR "women" OR "gender". Additional terms included "skull base", "CSF" AND "pregnancy", AND "corticosteroid", AND "aspirin". Title, abstract and full manuscript review was independently conducted by two authors (DL, AJ). Referenced articles were further reviewed. Each manuscript was then reviewed and graded on level of evidence. An international, multidisciplinary expert panel was then created. Experts from the fields of Rhinology (PHH, JAS), Allergy-Immunology (LB, MAR), and Obstetrics-Gynecology (LAC) were invited. They were selected based on their expertise in a) systematic reviews and evidence-based management of rhinosinusitis (DL, LB, PHH, VJL) and in its complications and associated medico-legal aspects (JAS), b) expertise in medication/therapeutics of CRS, Allergy & Asthma (LB, MAR), as well as in c) Obstetrics & Perinatal issues (LC). Each expert was provided with the full results of our systematic review, and was asked to provide their input based on this review and their expertise. These expert opinions were then reviewed and synthesized into an expert panel recommendation by the first (DL) and senior authors (VJL). Next, these recommendations was shared with all experts and, collectively and iteratively reviewed, and a final expert panel opinion formalized.

Results: Our search yielded 3052 abstracts. After initial screening, 88 full manuscripts were reviewed. No studies related to CRS management during pregnancy that were levels 1, 2, or 3 were found. A two-author, single expert opinion on management of rhinologic disease during pregnancy was found. Given the lack of any studies on CRS management during pregnancy we decided to synthesize expert panel opinions. The expert panel opinions are presented here.

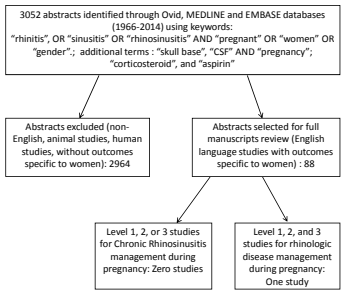

Figure 1: Flow diagram illustrating results and search methodology of the systematic review

Oral Corticosteroids for CRS exacerbations in Pregnancy?

Evidence Level: Zero; no studies found.

Expert Panel Recommendations: Corticosteroids (CCS) in short bursts, may be safe after the first trimester. Use is better justified in severe CRS especially if causing exacerbation of asthma. Consult with patient's obstetrician.

Remarks: While CCS are used in asthma the risk of CRS is less so than asthma and thus risks of CCS outweigh risk of undertreated CRS especially in the first trimester when oral steroids may be teratogenic. Steroids may cause hyperglycemia/worsen diabetes and thus patients should undergo diabetes testing prior to starting steroids, especially if a longer course of CCS is being considered.

Topical corticosteroids for CRS Maintenance during pregnancy?

Evidence Level: Zero; no studies found

Expert Panel Recommendations: All modern nasal CCS should be safe to use for CRS maintenance during pregnancy at recommended doses including budesonide, fluticasone and mometasone. The off-label use of budesonide irrigations or CCS nasal drops is not recommended.

Remarks:
The minimal/negligible systemic absorption of intranasal corticosteroids underlies the recommendation of the expert panel.

Oral Antibiotics for acute rhinosinusitis, CRS maintenance, or exacerbations?

Evidence Level: Zero; no studies on antibiotics for acute rhinosinusitis (ARS), acute exacerbations of CRS, and CRS maintenance.

Expert Panel Recommendations: Oral antibiotics that do not harm the fetus may be used for ARS or acute exacerbations of CRS. Long-term macrolide or doxycycline use for CRS is not recommended. Penicillin and cephalosporin are the safest classes, and can be given when endoscopic evidence of purulence is present. Antibiotics that put the fetus at risk such as tetracyclines, aminoglycosides, trimethoprim-sulfamethaxazole and fluoroquinolones should not be used during pregnancy.

Aspirin desensitization for aspirin exacerbated respiratory disease (AERD)?

Evidence Level: Zero; no studies on AERD in pregnancy

Expert Panel Recommendations: Aspirin desensitization for AERD should be discontinued during pregnancy.

Remarks: Aspirin is considered category D. Aspirin and all other NSAIDs should be avoided as they pose unacceptable fetal risks, particularly premature closure of the ductus.

Anti-leukotriene medications for CRS?

Evidence Level: Zero; no studies on CRS.

Expert Panel Recommendations: Avoid these for CRS maintenance. However, montelukast can be continued/ initiated for recalcitrant asthma during pregnancy, especially in those with prior response.

Remarks: Given the lack of data regarding the efficacy of these drugs in CRS and lack of data regarding teratogenicity, the consensus of this panel was to avoid these drugs in treating CRS. Montelukast is not teratogenic in animals and the ACOG recommend that it could be considered in recalcitrant asthma in patients who have shown a favorable response prior to pregnancy.

Systemic and Topical Decongestants, antihistamines, and immunotherapy for CRS?

Evidence Level: Zero; no studies on CRS.

Expert Panel Recommendations: Oral decongestants should not be used. First generation antihistamines should be avoided given their sedative and anticholinergic properties. Allergen immunotherapy is likely safe to continue during pregnancy. However, initiation or build of therapy should be not be done during pregnancy for risk of anaphylaxis.

Remarks: No studies assessed these drugs in CRS. Oral decongestants may increase the risk of fetal gastroschisis, and also contribute to hypertension. Decongestants are also not effective in treating CRS

Routine maintenance therapy for CRS during pregnancy?

Evidence Level: Zero; no studies on CRS "maintenance" therapy in pregnancy.

Expert Panel Recommendations: Saline nasal rinses and a topical CCS nasal spray are likely suitable maintenance therapy for CRS during pregnancy.

Remarks: Studies in allergic rhinitis during pregnancy find saline nasal lavage and nasal CCS sprays safe and effective.

Performance of sinus surgery with recurrent CRS with polyps prior to planned pregnancy?

Evidence Level: Zero; no relevant studies.

Expert Panel Recommendations: Surgery may be considered prior to the pregnancy. In general, surgery that is not for a life threatening process should be avoided during pregnancy. However, office procedures under local anesthesia (polypectomy and/or turbinate reduction) may be some alternatives in severely symptomatic CRS pregnant patients.

Category	Description
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women. Or, Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
C	Animal studies have shown an adverse effect, or no animal studies have been conducted, and there are no adequate and well-controlled studies in pregnant women.
D	Adequate, well-controlled, or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
X	Adequate, well-controlled, or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.

Table 1: Categories of Pharmaceutical Agents Assessing Risk for Use in Pregnancy

Vaginal births versus planned Caesarian section for those with large skull base erosions secondary to CRS, or skull base resection, or patients with history of CSF rhinorrhea?

Evidence Level: Zero; no relevant studies.

Expert Panel Recommendations: Skull base erosions such are not contraindications for a normal delivery. Generally speaking, cesarean section should be reserved for the standard obstetrical indications. However, a highly individualized approach must be undertaken. Ultimately the patient & obstetrician should determine means of delivery. The risks of intrapartum CSF leak may be much higher in large skull base resections for malignancies, rather than limited defects from CRS or standard transsphenoidal pituitary tumor resections.

Conclusions

This comprehensive, systematic review yielded no level 1, 2, or 3 studies pertaining to the management of rhinosinusitis during pregnancy.

Given the lack of interventional studies on the management of rhinosinusitis during pregnancy we found it necessary to generate expert panel recommendations (level 5). These recommendations were given very careful consideration. Nevertheless, given the lack of high-quality objective evidence, these are grade D recommendations. These must be utilized and modified as determined after a thoughtful and individualized review of the pregnant patient, and in consultation with their obstetrician.

Acknowledgements and Affiliations

I would like to thank Kathleen Carlson and Lisa A. Marks for their assistance in designing the search. I would also like to thank my mentor Dr. Devyani Lal for her invaluable guidance and support

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