
GLAUCOMA MEDICATION DURING PREGNANCY AND NURSING

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ABSTRACT

Risks that glaucoma medications pose to the fetus and neonate must be balanced against the risk of vision loss in the mother. There is no high level evidence for harmful effects on the fetus and neonate of medications used to treat glaucoma. All topical and systemic glaucoma medication should be avoided during the first trimester of pregnancy. Systemic carbonic anhydrase inhibitors, topical prostaglandin analogues and antimetabolites during surgery should be avoided absolutely.

Some topical medications are deemed compatible with lactation by the American Academy of Pediatrics, however, caution should still be practiced.

KEYWORDS

Glaucoma - Pregnancy - Nursing

INTRODUCTION

The treatment of a pregnant or nursing women with glaucoma is controversial and challenging (1,2). No clinical studies exist on the fetal effects of commonly used glaucoma medications, and it is unlikely that trials will be performed. A trial to establish "safety and efficacy" of ophthalmic solutions is difficult to perform because of medicolegal constraint and limited sample size. Moreover, drug companies have low financial incentives to evaluate their products in this small population (3). Therefore, we must rely on the information gathered from case reports and animal studies.

WHICH GLAUCOMA TREATMENT IS SAFE FOR THE PREGNANT WOMAN?

A. CONSERVATIVE

If the patient has early glaucoma or is only a suspect, stopping medications for a number of months should not pose any great risk to vision. Intraocular pressure (IOP) tends to decrease during pregnancy in healthy patients, especially during the second and third trimesters (4). However, in one retrospective review, almost 30% of pregnant glaucoma patients experienced an *increase* in IOP during pregnancy (5).

B. LASER TRABECULOPLASTY

If pregnancy is established and treatment is necessary, laser trabeculoplasty (LTP) is probably the best initial therapy and a good alternative to medication. However, the efficacy of LTP is often low in these young patients.

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C. MEDICATION

Table I summarizes the U.S. FDA's categories of safety for medications during pregnancy. There are no glaucoma medications that fall into category A. The medical therapy of glaucoma contains five groups of drugs: beta-blockers (betaxolol, carteolol, levobunolol, metipranolol, and timolol), carbonic anhydrase inhibitors (CAIs) (brinzolamide, dorzolamide and acetazolamide), alpha2-agonists (brimonidine), parasymphomimetics (pilocarpine) and prostaglandin analogues (bimatoprost, latanoprost, and travoprost). Brimonidine is a category B drug, but it has been shown to cross the placenta. It could potentially cause apnea in neonates if used through parturition, like described in children younger than two years old who were treated with this medication (6). Beta blockers, CAIs, prostaglandin analogues, and parasymphomimetics are classified as category C. There have been reports of fetal complications from topical beta blockers, concerning fetal bradycardia and cardiac arrhythmia (7). However, none have been seen with low dose timolol in gel formulation. Fetal complications have also been reported with systemic acetazolamide. Forelimb deformity in fetuses induced by acetazolamide given to pregnant mice has been described, concluding that this medication is teratogenic (8,9,10). In humans, there is a case report describing the association between a sacrococcygeal teratoma in a neonate and the maternal use of acetazolamide (11). There is one case report of complications with topical CAIs (12) in a neonate who also had low birth weight and impaired kidney function. Prostaglandins are known to stimulate uterine contraction and may cross the blood-placental barrier; prostaglandin analogues should be avoided during pregnancy to minimize risk of premature labor (13).

As the greatest risk of medication to the developing fetus is in the first trimester, when organ systems develop, discontinuation of medications should occur prior to conception and through the first trimester. If medications cannot be stopped then the use of beta blockers, topical CAIs, alpha agonists and parasymphomimetics can be continued. Prostaglandin analogues in mono- or combinationtherapy should be withdrawn. However, beta blockers and al-

Table 1: Medication safety during pregnancy according to the U.S. FDA

Category A	Safety established using human studies
Category B	Presumed safety based on animal studies
Category C	Uncertain safety; No human studies; Animal studies show adverse effect
Category D	Unsafe; Evidence of risk that in certain clinical circumstances may be justifiable

pha agonists should be discontinued after the 8th month of pregnancy, to avoid complications in the neonate. Timolol 0.1% gel once daily is probably a safe option, due to the low dosage and low systemic absorption. If necessary it can be combined with dorzolamide or brinzolamide twice daily. Systemic CAIs are potentially teratogenic but topical CAIs appear to be safe.

A significant reduction in the systemic absorption has been observed when performing punctal occlusion and simple eye lid closure after drop administration (14).

D. SURGERY

If a woman has advanced glaucoma and elevated pressures or if she is taking multiple medications, serious consideration should be given to surgery before conception. During pregnancy, filtering surgery can be considered if glaucoma is progressive and an adequate IOP cannot be obtained with LTP or with the medications mentioned above.

Peribulbar or sub-tenon lidocaine appears to be safe for the fetus. It is desirable to defer surgery until the second trimester of pregnancy to reduce the fetus' exposure to potentially teratogenic anesthetic agents. The patient should be positioned with the uterus displaced laterally so as to avoid aortic and vena caval compression by the gravid uterus (15). Postoperatively, topical erythromycin and steroids in ointment or in drops using punctal occlusion are safe. Antimetabolites, such as 5-fluorouracil (5-FU) or mitomycin C (MMC), should not be used on a pregnant woman for medicolegal reasons. Pregnant surgeons may also want to avoid handling these agents as occupational medicine does not allow the pregnant surgeons to handle MMC or 5-FU.

E. DIODE LASER CYCLODESTRUCTION

Diode laser cyclodestruction can be a valuable alternative to filtering surgery (16).

WHICH GLAUCOMA TREATMENT IS SAFE FOR THE NURSING WOMAN?

Again, the risks and benefits of glaucoma treatment to the infant versus vision loss in the nursing mother must be discussed.

A. LASER TRABECULOPLASTY (LTP)

If a woman decides to give breast feeding and the eye pressure is insufficient under control, LTP is probably the best initial therapy before medication is started. This in spite of the lower efficacy of LTP in these younger population.

B. MEDICATION

Beta blockers are concentrated in the breast milk and should be avoided while nursing, despite the American Academy of Pediatrics statement that beta blockers are compatible with lactation (17, 18). It is unknown whether *alpha agonists* are excreted in the human breast milk, but given the potential severity of their side effects in an infant, they should be avoided during nursing. *Systemic CAIs* (acetazolamide, methazolamide) are considered compatible with lactation by the American Academy of Pediatrics, but given the unknown concentration found in the breast milk, they should be used with caution or avoided in order to prevent hepatic and renal effects in the infant. *Topical CAIs* are generally considered safe and are approved by the American Academy of Pediatrics for use during lactation. It is unknown whether *prostaglandin analogues* are excreted in human breast milk. A risk to the suckling child cannot be excluded, so that this drugs should not be used during lactation. The toxicity of *miotics* during lactation is unknown. However, miotics can often be intolerable to a woman of childbearing age due to local side effects (myopia, brow ache).

C. SURGERY

If surgery is offered to a nursing mother, the mother should be instructed to store her breast

milk ahead of the surgery and the operation should be timed immediately after nursing to avoid significant anesthetic concentrations in breast milk. Care should always be coordinated with the pediatrician, and the mother should be instructed on the symptoms of medication side effects on her nursing child.

D. DIODE LASER CYCLODESTRUCTION

Assumed that the cyclodestruction is performed with local anesthesia, this laser treatment is a safe alternative to filtering surgery. Again storing breast milk ahead of the anesthesia is necessary to avoid concentrations in breast milk.

DISCUSSION

Childbearing plans should be addressed with all women of reproductive age who have glaucoma. The risks that glaucoma treatment pose to the fetus versus the risk of vision loss in the mother must be discussed. Also, it is probably a good practice to remind would-be mothers that a certain percentage of pregnancies will be anomalous by chance despite glaucoma treatment.

Questions about the safety of vaginal delivery in a woman with glaucoma occasionally arise. There is no literature which addresses these questions. The theoretical risks of vision loss from elevated eye pressure and decreased blood flow to the optic nerve during the pushing phase of labor should be discussed with the mother and may depend on the stage of the glaucoma. These concerns may also need to be addressed with the obstetrician.

TAKE HOME MESSAGES

- There is no high level evidence for the fetal effects of medications used to treat glaucoma. Evidence is largely derived from case reports and animal studies.
- Address glaucoma management prior to conception in women of childbearing age.
- Risks that topical and systemic medications pose to the fetus and neonate must be balanced against the risk of vision loss in the mother.

- All glaucoma medications should be avoided during the first trimester of pregnancy to minimize possible teratogenic effects.
- Avoid prostaglandin analogues all nine months to minimize risk of premature labor.
- In the second and third trimesters, beta blockers, alpha agonists, topical carbonic anhydrase inhibitors and miotics have been safely used but consider stopping the first two listed prior to childbirth to avoid complications in the newborn infant.
- If surgery is necessary during pregnancy, postpone it until the second trimester and avoid antimetabolite use.
- Some topical medications are deemed compatible with lactation by the American Academy of Pediatrics, however, caution should still be practiced.
- Beta blockers, alpha agonists and systemic CAIs should be avoided during nursing.
- Topical CAIs, prostaglandins, and miotics are reasonable choices during lactation.

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