

# Treating Glaucoma During Pregnancy

What we know and how to proceed.

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**A**ppropriate management of the pregnant patient requires a balance between the treatment's risk to the fetus and the risk to the mother if treatment is reduced or suspended. A complete lack of prospective human data complicates this dilemma. The typical package insert<sup>1</sup> for a glaucoma drug states that there are "no adequate, controlled studies in humans" and cautions that the drug "should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus." Such advice is of little practical value.

This article briefly reviews the available information regarding the use of glaucoma medication during pregnancy and lactation, and it proposes guidelines for treatment.

## GLAUCOMA MEDICAL THERAPY IN PREGNANCY

### Human Experience

Glaucoma is uncommon in women of childbearing age, and anecdotal data regarding the effects of glaucoma medications in humans are minimal. Many pregnant women, however, use systemic drugs that are similar or identical to glaucoma medications. There is extensive, uncontrolled experience with beta-adrenergic blockers and alpha-adrenergic agonists in patients with hypertension. Parasympathomimetics and carbonic anhydrase inhibitors (CAIs) have also been used systemically. In addition, the side effects noted in newborns treated with glaucoma medications provide help in choosing treatment for patients in the late stages of pregnancy.<sup>2,3</sup>

### Animal Experience

Animal reproductive studies are performed for all new medications, but their relevance to humans is unclear. Known human teratogens may have no noticeable effect in laboratory animals, just as animal teratogens may cause no abnormalities in humans. Moreover, these studies generally employ doses that are much higher than those achieved with clinical use.<sup>2-5</sup>



### Pharmacology

All topical glaucoma medications are systemically absorbed to some degree, and basic pharmacology implies that glaucoma medications will enter the fetal circulation. Transplacental diffusion correlates with low molecular weight, lipid solubility, a lack of protein binding, and non-ionized status.<sup>2</sup> All glaucoma drugs are of low molecular weight and are (to some degree) lipid soluble, unbound, and not ionized; thus, they cross the placenta.<sup>1</sup> The same logic implies that maternal glaucoma medications are present in breast milk.

## RISKS OF MEDICAL THERAPY

### Teratogenicity

Birth defects commonly occur. Approximately 3% of women who use glaucoma medication during pregnancy will bear children with an abnormality by chance alone.<sup>2</sup> Because the major organ systems develop early, the embryo of a woman on chronic therapy will be exposed to medication during critical stages of development before the patient is aware that she is pregnant. No glaucoma medication, ophthalmic anesthetic, or

diagnostic drop is known to be a human teratogen. Nonetheless, none has been proven to be risk-free.<sup>3</sup> Patients should be informed that medical treatment carries some risk, but they may be assured that the available data suggest that such risk is very low.

### Risk to the Pregnancy

The effects of glaucoma medications on the maintenance of an established pregnancy are not known. All ophthalmic prostaglandin analogs can cause contraction of uterine smooth muscle, and the original package insert for travoprost included a caution against its use by women who were or desired to become pregnant (this warning was removed). It is not known if the very low systemic levels achieved with topical use are of realistic risk, but, in the absence of better data, it seems reasonable to avoid prostaglandin analogs in women who are or desire to become pregnant.

### Risk to the Fetus and Newborn

Both beta-adrenergic blockers and brimonidine have been reported to cause serious toxicity, including respiratory and central nervous system depression, in neonates treated for glaucoma. These drugs will be present in the newborn if used by the mother close to delivery. CAIs, including oral acetazolamide, have been used for decades in infants with congenital glaucoma and are well tolerated.

## MANAGING THE CURRENTLY PREGNANT OR LACTATING PATIENT

### Background

Fortunately, glaucoma is generally a slow-moving condition. In the Early Manifest Glaucoma Trial, only approximately two-thirds of individuals with glaucoma who were untreated showed progression over the course of 6 years.<sup>6</sup> Regarding determining how aggressively to treat an individual patient, her degree of damage is usually more important than her IOP, because the more advanced the disease is, the greater the chance is that a small degree of worsening will cause symptomatic damage.

When using topical therapy, always follow three principles. First, prescribe the minimum medication sufficient to achieve the target IOP. Second, employ nasolacrimal occlusion in order to decrease systemic absorption. Third, discuss the patient's treatment with her obstetrician and pediatrician.

### Drug Choice

During months 1 through 8 of pregnancy, beta-blockers, alpha-agonists, and/or CAIs are probably safe. Prosta-

glandin analogues are not recommended. Pilocarpine is probably safe, but it is poorly tolerated by most young patients.

During month 9 of pregnancy, the use of both beta-blockers and alpha-agonists should generally cease to avoid complications in the neonate. If the use of these agents is continued, consult the patient's pediatrician and advise the patient to discontinue using her medication at the onset of labor. The use of topical CAIs may be continued.

During lactation, topical CAIs and prostaglandin analogs are reasonable choices. If the patient uses beta-blockers or alpha-adrenergic agonists, then the infant should be monitored closely by the pediatrician for evidence of systemic toxicity, which may be severe.

If the patient's IOP is approximately the same as prior to her pregnancy, no change in follow-up is indicated. If her IOP is higher than usual, she should undergo more frequent visual field and optic nerve examinations.

## MANAGING THE PATIENT CONSIDERING PREGNANCY

With patients who have childbearing potential, it is best to discuss their reproductive plans prior to pregnancy. Appropriate treatment depends on the degree of the patient's glaucomatous damage, the height of her IOP, her personal preferences, and the number of pregnancies she plans.

Offer laser therapy to patients with glaucoma who are amenable to this treatment. Advise those whose disease requires medical treatment that their medication will reach the baby and that early pregnancy is the period of greatest risk to the fetus. A woman who is attempting to conceive a child should avoid using a prostaglandin analog. One who has advanced disease and marginal pressure control may benefit from surgical intervention prior to conception. Encourage patients to contact you as soon as they become pregnant. □

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