·Review·

Management of glaucoma in pregnancy: risks or choices, a dilemma?

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Abstract

• The treatment of glaucoma in and around pregnancy offers the unique challenge of balancing the risk of vision loss to the mother as against the potential harm to the fetus or newborn. Most anti-glaucoma drugs (*i.e.* beta-blockers, prostaglandin analogues, carbonic anhydrase inhibitors topical and systemic, cholinergics, anticholinesterases, and apraclonidine) are considered category C agents and ophthalmologists are usually limited to treating patients with the category B drugs of brimonidine and dipivefrin. Brimonidine is generally the preferred first-line drug in the first, second and early third trimester. Late in the third trimester, brimonidine should be discontinued because it can induce central nervous system depression in newborns wherein topical carbonic anhydrase inhibitors may be the optimal choice. Glaucoma surgery can be performed with caution in second and third trimester if the patients have a strong indication for the procedure. However, anesthetics, sedative agents, and antimetabolites still have potential risk for the fetus. Argon laser trabeculoplasty (ALT) or selective laser trabeculoplasty (SLT) is an alternative treatment that can be performed in all trimesters. Carbonic anhydrase inhibitors and β-blockers are certified by the American Academy of Pediatrics for use during nursing. However, low doses of these medications should be considered when used in the breast feeding period. Optimum treatment for glaucoma in pregnancy must not be withheld so as to prevent any further deterioration in progressive vision loss and quality of life.

• **KEYWORDS:** glaucoma; pregnancy; brimonidine; argon laser trabeculoplasty-selective laser trabeculoplasty

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INTRODUCTION

Traditionally, glaucoma specialists have commonly confronted issues that can derange the treatment of glaucoma in pregnant patients, because most of the women treated are generally beyond childbearing age. This situation is undergoing a change since advances in reproductive technology empower women to conceive at increasingly older ages. Glaucoma occurs generally in adults over the age of 40, but may occasionally be seen in females of childbearing age. Often, patients may have preexisting glaucoma which originally commenced in childhood (*i.e.* anterior segment dysgenesis or congenital glaucoma) or glaucoma secondary to uveitis, diabetes, *etc.* Glaucoma is not only being detected but glaucoma suspects in younger ages are also being identified due to the availability of new diagnostic avenues and an increased clinical awareness of the disease.

Women who are 35 years or older are generally aware that their age might possibly increase their baby's risk of birth defects, and they thus may be more driven than younger patient in order to decrease the risk associated with any medications. In some cases, patients are so hesitant to comply with medications during pregnancy that the rate of nonadherence shoots up, with some patients discontinuing drug use. In reality, most known teratogenic drugs increase the risk of major birth defects by only 1% to 3%[1].

In general, treatment is indicated for patients with glaucoma or glaucoma suspects who are at risk for developing functional impairment or decreasing in vision-related quality of life from the disease. The rate of disease progression is of fundamental importance in considerations of treatment for glaucoma patients. Treatment is generally indicated when the risks of progressive disease outweigh the risks and potential side effects of treatment *i.e.* for patients with definitive glaucomatous visual field loss, particularly in circumstances when such loss has been determined to be progressive at a measurable rate. Changes of the optic nerve and/or retinal nerve fiber layer (RNFL) characteristic of glaucoma predict functional vision loss in glaucoma and thus patients with such documented structural evidence of progressive damage should generally be treated with intraocular pressure (IOP) lowering therapy.

No published data nor any 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 in pregnancy is difficult to pilot because of medicolegal constraints and limited sample size.

The treatment of glaucoma in and around pregnancy offers the unique challenge of balancing the risk of vision loss to the mother as against the potential harm to the fetus or newborn. This article describes these difficulties inherent in treating pregnant glaucoma patients and enlightens how to minimize the risk to the fetus while preserving the mother's vision.

Epidemiology Glaucoma has been reported to occur in roughly 2%-3% of pregnant adults over the age of 40, though the prevalence increases appreciably with age for all races and ethnicities. Few data exist regarding the prevalence of glaucoma prior to the age of 40, particularly in women of childbearing age. In one Japanese study, the prevalence of open angle glaucoma, defined by a visual field defect along with corroborating optic nerve head changes was 0.48%, 0.42%, and 0.73% among women aged 15-24, 25-34 and 35-44, respectively [2]. Additionally, women of childbearing age may have acquired glaucoma early in childhood (congenital glaucoma, anterior segment dysgenesis, or glaucoma after cataract formation), or glaucoma resulting from coexisting conditions presenting early in life, *i.e.* uveitis or diabetes.

CHANGES OF INTRAOCULAR PRESSURE IN PREGNANCY

IOP has been proclaimed to fall during pregnancy. It is estimated that during pregnancy, IOP diminishes up to 10%, with this reduction being marked in the third quarter. The reductions not only occur through out the pregnancy but also persist for several months postpartum. This reduction in the IOP is primarily attributed to the fluctuating levels of two important hormones β-human chorionic gonadotropin (B-hcg) and progesterone.

In one study of pregnant women, the mean IOP of first trimester patients was on average 2 mm Hg higher than that of third trimester patients[3]. The probable risk of birth defects combined with patients' apprehensions has been tempting ophthalmologists to put anti-glaucoma medications on hold during pregnancy. In fact, it may suggest that glaucoma be stable during pregnancy and the patients therefore be off-treatment during pregnancy[4-5]. Studies of healthy women as compared to those with ocular hypertension showed that IOP decreased as pregnancy progresses, and research demonstrated a statistically significant drop in pressure from the first to the third trimester [4-5]. Potential mechanisms for this IOP reduction included greater aqueous uveoscleral outflow facility due to hormonal changes, hormone induced blockage of ocular hypertensive effect of endogenous corticosteroids, decreased episcleral venous pressure from reduction of venous pressure in the upper limbs and mild metabolic acidosis resulting from gestation. Specifically, increased levels of progesterone and relaxin may decrease IOP and increase the coefficient of facility of aqueous outflow during pregnancy[3-5].

However, the extent to which these IOP changes should be extrapolated in pregnancy with pre-existing glaucoma is still an enigma [6]. The evolution of glaucoma during pregnancy is variable despite the so called theoretical hormonal protecting factor. Most patients generally remain stable during pregnancy although a small percentage (about 10%) have increased IOP or progression of the disease[7].

The studies showing an association between pregnancy and lower IOPs, however, did not include pregnant women were known glaucomatous patients. In addition, no large studies have analysed IOP in pregnant glaucoma patients. The largest such trial is a retrospective case series from Harvard Medical School that reviewed pregnant women with pre-existing glaucoma and reported that 57% eyes had stable IOPs and visual fields during pregnancy while 18% eyes had increased IOP despite stable visual fields. In fact, 18% of eyes experienced progressive visual field loss with stable or elevated IOPs. Although patients who experienced changes in IOP required additional hypotensive medications, none of them required surgical intervention. The investigators therein concluded that the course of glaucoma during pregnancy was highly variable, and further affirmed that pregnant women should be monitored closely for changes in IOP and visual field loss[7-8].

Treatment Goals The target IOP is the IOP range at which, in the ophthalmologists' opinion, the estimated rate of progression is unlikely to affect the patient's quality of life. Although recommended by most experts, there is insufficient evidence that using target IOP is associated with better clinical outcomes. The determination of a target IOP is based upon consideration of the amount of existing glaucoma damage, the rate of progression, the IOP at which the damage has occurred, the life expectancy of the patient, and other factors including status of the fellow eye and family history of severe glaucoma[3-8].

The use of target IOP in glaucoma requires ongoing continual re-evaluation and adjustments. The benefits and adversities of escalating treatment to reach a target IOP must tend to a equilibrium. Uncertainties regarding the short- and long-term variations of IOP, accuracy of tonometer readings, patient's life expectancy, adherence to therapy and estimated progression rates remain unresolved. Treatment goals include IOP, visual function and structural (optic disc, RNFL) outcomes and quality of life. Risks that topical and systemic medications exposed to the fetus and neonate must be balanced against the risk of vision loss in the mother[3-8].

ANTI-GLAUCOMA MEDICATIONS

Beta-blockers Oral β-blockers are categorized as class C medications in pregnancy. No specific categorization is available for topical β-blockers. Topical β-adrenoceptor blocking drugs such as timolol, betaxolol, carteolol, levobunol, and metipranol decrease the production of aqueous humour and subsequently lower the IOP[9-10].

Topical β-blockers are effective IOP-lowering agents. All non-selective β-blockers have comparable IOP-lowering efficacy. However, topical and systemic β-blockers are poorly additive with respect to lowering IOP. Although some β-blockers have intrinsic sympathomimetic activity (ISA) or α-blocking properties, their clinical properties are similar to those of other non-selective β-antagonists. However, ISA may reduce respiratory and cardiovascular side-effects related to β-blockade. Timolol, and possibly all other β-blockers, have minimal IOP-lowering efficacy during sleep. Non-selective topical β-blockers are contraindicated in patients with asthma, chronic obstructive pulmonary disease (emphysema and bronchitis), some cases of congestive heart failure, bradycardia, and heart block[9-10].

Betaxolol is relatively safer than a non-selective β-blocker in patients with known reactive airway disease. However, the IOP-lowering efficacy of betaxolol, despite being a relatively selective β-1-blocker, is less than that of non-selective β-blockers.

Although ophthalmologists may be reluctant to prescribe this class of drugs to pregnant glaucoma patients, most obstetricians are pretty comfortable with this type of therapy, because they do not hesitate to prescribe oral β-blockers to control hypertension during pregnancy. Systemic use of β-adrenoceptor blocking drugs near term may result in fetal and neonatal bradycardia, arrhythmia, hypotension and hypoglycaemia[11-12]. Respiratory distress and apnoea have also been reported following in utero exposure. The data on the safety of discontinuing treatment 24-48h before delivery are conflicting [9-12]. When reported, neonatal symptoms due to β-blockade are usually mild and resolve within 48h. However, none of the side-effects has been reported with low dose timolol (*i.e.* 0.1%) in gel formulation.

Alpha Agonists Adrenergic agonists reduce IOP by decreasing aqueous formation and increasing outflow. They also may affect episcleral venous pressure. Adrenergic agonists are contraindicated in infants and children because of increased propensity for systemic side effects. IOP-lowering efficacy of adrenergic agonists is less than that of timolol. This class is often additive to prostaglandin analogues but not to non-selective β-blockers. Local side effects include hyperemia and blepharoconjunctivitis. Systemic circulatory effects include dry mouth, drowsiness and tachyarrhythmias[13].

Brimonidine is classified as a category B medication by the FDA. However, no well-controlled human studies have been done to rule out potential teratogenic effects. Additionally, brimonidine poses substantial risk to the newborn, having been reported to cause central nervous system depression and apnea. The drug penetrates the hematoencephallic blood-brain barrier, and can cross the hemato-placental barrier and possibly excrete into breast milk, posing a real risk of apnea or hypotension in neonates and infants. Thus, despite its status being as a category B drug, even if brimonidine is used during pregnancy, it should be discontinued before labor and during breastfeeding to prevent potential fetal apnea [14-15].

Bunazosin, despite being a selective α1A antagonist, increases uveoscleral outflow. Although it is well-tolerated, the ocular hypotensive efficacy of topical bunazosin is weaker than that of topical timolol.

Prostaglandin Analogues Prostaglandin analogues (PGAs) are the most effective IOP-lowering agents of all topical glaucoma medications, and generally are first line therapy. Prostaglandin analogues such as latanoprost, bimatoprost, travoprost and tafluprost reduce IOP by increasing the uveoscleral outflow of aqueous humour. Common side effects of prostaglandin analogue drops include conjunctival hyperemia, reversible increase of eyelash length-thickness-pigmentation, irreversible increase of iris pigmentation and increase of eyelid skin pigmentation[16].

Prostaglandin analogues are classified as category C drugs and are associated with a notable incidence of miscarriage in animal studies. Prostaglandins, being oxytocic and luteolytic, can increase uterine tone and stimulate uterine contractions producing premature labor. Since they may act as abortifacients, there are concerns regarding their use in pregnancy. In fact, travoprost is a prodrug that will hydrolyse in the cornea to become fluprostenol a type of prostaglandin that is highly selective for F2α receptors, which is used to induce abortion in animals by causing uterine smooth muscle contractions[16-19].

Latanoprost exposure in pregnancy has not been associated with an increased risk of congenital malformations or spontaneous abortion in exposed infants. Low birth weight was found to be more common in latanoprost-exposed babies than in the non-exposed controls, however no other differences were observed between groups [18]. There are no published data regarding the use of bimatoprost or travoprost in pregnancy.

Additionally, a systematic review documented that oral or vaginal use of misoprostol in pregnancy is associated with an increased risk of Moebius syndrome and terminal transverse limb defects[20], though it is unclear whether the very low drug concentrations used in ophthalmic prostaglandin formulations are sufficient enough to elicit this side effect. While some

pharmacologists uphold that latanoprost and travoprost have insufficient active ingredients to cause adverse effects on the foetus, others believe that the use of prostaglandins is generally contra-indicated in pregnant women[17,19]. Therefore, these medications should be used with caution.

Carbonic Anhydrase Inhibitors Carbonic anhydrase inhibitors (CAIs) are effective IOP-lowering agents. CAIs reduce IOP by suppressing aqueous humor production through inhibition of the isoenzyme carbonic anhydrase II in the ciliary body. CAIs are the only category of drugs available commercially in both topical and systemic formulations to lower IOP. For systemic CAIs, major side effects include paresthesia, malaise, gastrointestinal disturbances, renal disorder, blood dyscrasia, and metabolic acidosis. For topical CAIs, side effects include ocular burning, stinging, bitter taste, superficial punctuate keratopathy, blurred vision, tearing, headache, and transient myopia. CAIs may increase ocular blood velocity; however, there is insufficient evidence for any clinical benefit of this effect for glaucoma patients. Systemic CAIs are contraindicated with sulfonamide allergy, with depressed sodium and/or potassium blood levels, and in metabolic acidosis. Topical CAIs and systemic CAIs are poorly additive with respect to lowering IOP[21-23].

Brinzolamide is classified as a category C medication in pregnancy. In animal studies, there was a statistically lower fetal body weight with the oral medication (375 times the human ophthalmic dose). However, no organ malformations were seen even at this high dose [24]. Dorzolamide is also classified as category C medication. There were malformations of the vertebral bodies in rabbits exposed to dorzolamide during pregnancy, suggesting that brinzolamide may be a better alternative. No controlled reports of brinzolamide or dorzolamide exist in human pregnancy. As such, it may be used during pregnancy with caution when the possible benefit to the mother outweighs the theoretical risk to the fetus. It is uncertain if these medications are excreted in human milk, and thus their safety in breastfeeding is unknown[24-26].

Acetazolamide is classified as a category C medication. Acetazolamide may result in potential metabolic complications to the newborn or breast-feeding child. Systemic high dose carbonic anhydrase inhibitors in rats can result in forelimb anomalies which may suggest that this medication is teratogenic [27-29]. One case report of neonatal sacrococcygeal teratoma was reported in a pregnant woman with maternal oral acetazolamide use [30]. In 1989, a newborn infant developed metabolic acidosis, hypocalcaemia, and hypomagnesaemia because the mother had been treated with acetazolamide, pilocarpine, and timolol for glaucoma throughout her pregnancy [31]. The blood concentration of acetazolamide is related to the serum carbon dioxide level and chloride ion concentration, which are indicators of metabolic acidosis especially if patients have renal dysfunction [32-33]. In 2000, there was another reported case of the transplacental passage of acetazolamide that led to transient neonatal renal tubular acidosis and low birth weight during the treatment of maternal glaucoma with oral acetazolamide [24]. On the other hand, there were no fetal adverse effects in 12 pregnant women who used oral acetazolamide for idiopathic intracranial hypertension management [34]. Also another case report demonstrated that acetazolamide plasma levels were low in infants exposed to the medication through breast milk [25]. Therefore, acetazolamide is approved by the American Academy of Pediatrics for use during nursing [8]. Thus there are limited data on which to base an assessment of the safety of acetazolamide in human pregnancy. Preclinical studies have demonstrated teratogenic risk, however available data from human pregnancies do not suggest a significantly increased risk of congenital malformations or spontaneous abortion following exposure. As yet it is difficult to draw conclusions from the available data as they are currently too limited to exclude any increase in risk. Use of acetazolamide in late pregnancy has been statistically associated with neonatal electrolyte imbalance and metabolic acidosis. Hence following exposure, monitoring of the neonatal electrolytes along with therapeutic dose monitoring of acetazolamide concentration in the blood is recommended as a means of preventing overdose and serious side-effects[24,31,35].

Methazolamide is also classified as a category C medication. Skeletal malformations have been reported in rats, but with dose 40 times higher than the human dose. No controlled investigations exist in human pregnant women. Details regarding whether the drug is excreted into human milk are unknown.

Drug Delivery All eye drops have potential systemic side effects which could possibly be avoided, or at least minimized, by reducing systemic absorption of the medication. Simple nasolacrimal occlusion and eyelids closure are handy techniques that can reduce these systemic adverse effects [36]. Additionally, both nasolacrimal occlusion and eyelids closure can increase eye-drug contact time resulting in higher intraocular drug concentrations, and less systemic absorption. Punctal plugging can reduce tear drainage and improve mean tear meniscus levels such that systemic absorption of drug is lowered [36-37]. However, there are no direct studies on systemic absorption of glaucoma medications with punctal plugging. Nonetheless, these options should be discussed with women who choose to continue topical IOP-lowering therapy in and around pregnancy.

ROLES OF SURGERIES

Role of Argon Laser Trabeculoplasty and Selective Laser Trabeculoplasty Argon laser trabeculoplasty (ALT) or selective laser trabeculoplasty (SLT) may be considered in pregnant women to eliminate or reduce the number of necessary safe medications. It enables maintaining IOP within target limits with a lower number of hypotensor drugs.

Laser trabeculoplasty could be a good treatment option if allowed by the morphology of the angle. This is infrequent in the types of glaucoma exhibited by women in reproductive age. It is not very effective in cases due to angular alterations which are inherent to the disease or to the presence of angular synechiae. Inflammatory or congenital glaucoma or those developed during infancy due to anterior chamber deformations such as the Peters-Rieger syndrome or Axenfeld syndrome or aniridia frequently compromise the angle and therefore the results of ALT or SLT are more limited.

Also unfortunately, ALT appears to be less effective in maintaining IOP control in young patients [28]. A retrospective study of Argon laser trabeculoplasty reported that 60% of lasered patients had uncontrolled IOP and required glaucoma surgery within two years following ALT [38]. However, given the short time-frame of pregnancy, trabeculoplasty may still be considered in these patients.

Role of Glaucoma Surgery If a woman has advanced glaucoma and elevated pressures despite taking multiple medications, serious consideration should be given to surgery before conception. After conception, glaucoma surgery could be considered during pregnancy if the glaucoma is progressive and an adequate IOP cannot be obtained despite laser trabeculoplasty and the use of maximum safe medications. However, there are specific risks of glaucoma surgery in pregnant patients, including the risks of local and general anesthesia, and the need for post-operative medications. Additionally, glaucoma filtration surgery in pregnant patients may be at relatively higher risk of failure because of young patient age and contraindicated antimetabolite usage [39-40]. 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 the minimum to these potentially teratogenic anesthetic agents.

Role of Cryosurgery Cryosurgery can be carried out with local anesthesia and could be repeated if IOP is not sufficiently controlled. Anatomic differences in the morphology and position of the ciliary body must be taken into account in congenital and childhood glaucoma, as well as possible complications in patients with thin sclera or inflammatory glaucoma. In these cases, surgical difficulty is greater because frequently patients are found who were intervened several times and have angular compromise which limits the type of surgery. In fact diode laser cyclodestruction when carried out under local anaesthesia can be a safe and valuable alternative to filtering surgery in pregnancy .

PREFERENCE ACCORDING TO STAGE OF PREGNANCY

Because most glaucoma drugs (*i.e.* β-blockers, prostaglandin analogues, CAIs topical and systemic, cholinergics, anticholinesterases, and apraclonidine) are considered category C agents by the FDA, ophthalmologists are usually limited to treating patients with the category B drugs of brimonidine and dipivefrin.

Ophthalmologists avoid treating pregnant patients with category C drugs unless the potential benefit for the patient justifies the risk to the fetus. A soft exception to this rule is the use of β-blockers.

Pre−conception Ideally, a discussion of the treatment plan of a woman's glaucoma should be initiated before pregnancy begins. In this way, the adverse effects of medications can be prevented during the first trimester, when most organogenesis is occurring. Additionally, alternate effective methods to lower IOP (including surgery if necessary) can be explored or achieved prior to pregnancy beginning. Known patients of glaucoma of childbearing age should inform their doctor immediately whether they suspect they are pregnant, or whether they are planning to start or add to their family.

First Trimester An indepth discussion of the risks of medication and the best strategy for IOP-lowering should occur as soon as pregnancy is noted as organogenesis has often begun when pregnancy is first identified and medications taken during organogenesis can result in birth defects. Pregnancy discussions should include a discussion of medication concentration/dosage, methods to minimize systemic drug absorption and if medication can be withheld for parts of the pregnancy.

Brimonidine, a category B drug, may be the safest option for the first trimester. Other anti-glaucoma medications such as β-blocker, prostaglandins and carbonic anhydrase inhibitors should be avoided when possible in first trimester to reduce potential teratogenic effects or premature abortion. Discussions with the patient may include observation off-treatment in this critical period.

For glaucoma surgery, anesthetics, sedative agents and antimetabolites are all possible teratogenic agents. Therefore, avoiding surgery in first trimester may decrease the risk of teratogenicity and spontaneous abortion.

Second Trimester In second trimester, brimonidine can be applied and β-blockers can be used with regular fetal heart rate and fetal growth monitoring. If prostaglandin analogues are used, premature labor symptoms and signs should be described to the patient and the medication should be stopped if such symptoms are noted. When topical or oral carbonic anhydrase inhibitors are used as adjuvant therapy, fetal growth retardation monitoring may be considered.

Third Trimester Brimonidine, β-blocker, or topical carbonic anhydrase inhibitors, can be used with caution. Avoidance of prostaglandins may decrease the risk of premature labor, which is particularly important early in the third trimester. Late in the third trimester, brimonidine should be discontinued because it can induce central nervous system depression in newborns. Topical carbonic anhydrase inhibitors may be the optimal choice in this period.

Glaucoma surgery can be performed with caution in second and third trimester if the patients have a strong indication for the procedure. However, anesthetics, sedative agents, and antimetabolites still have potential risk for the fetus.

ALT or SLT is an alternative glaucoma treatment that can be performed in all trimesters. ALT or SLT may be less effective for long term IOP control, but may result in short-term IOP control until the end of pregnancy.

Post-partum Carbonic anhydrase inhibitors and β-blockers are certified by the American Academy of Pediatrics for use during nursing. However, low doses of these medications should be considered when used in the breast feeding period. Brimonidine is contraindicated for use in lactating mothers due to the risk of central nervous system depression in the newborn.

UNMET NEEDS

By far, hardly much data has been published to evaluate the true risk in the use of eye medications during pregnancy. Several reasons may account for this shortcoming. Firstly, few pregnant patients attribute significant adverse effects on the foetus to the topical administration of ophthalmic medications. Secondly, large-scale population surveillance is needed to detect drug teratogenicity. Finally, researchers may not be willing to invest time, money and energy in research that will most likely give a negative association between the two variables studied. Nevertheless, doctors should always be particularly careful when prescribing drugs to pregnant women. The overall level of evidence for the risk of prescribing ophthalmic drugs to pregnant women is low. There is a lack of Meta-analyses and randomised controlled trials in this aspect. Most of the available evidence is based on only individual case reports and animal studies.

CONCLUSION

Untreated or under-treated glaucoma could potentially lead to loss of vision; and although risk assessment for a pregnant patient with glaucoma is difficult because of the lack of safety data, the potential benefits gained from the treatment are likely to outweigh any increase in risk to both the mother and the foetus. Optimum treatment for glaucoma in pregnancy must not be withheld so as to prevent any further deterioration in progressive vision loss and quality of life.

As a general rule, all drugs should be avoided if possible in the first trimester, because the risk of drug-induced foetal teratogenicity is highest during this period than during any other time. Nevertheless, the fear of uncertain drug teratogenicity should not discourage doctors from prescribing treatments when their expected benefits to the mother are thought to outweigh the risk to the foetus.

Method of Literature Search We systematically reviewed the literature to determine all the modalities of treatment for glaucoma in pregnancy through lactation. We conducted a PubMed.gov search using the terms "glaucoma", "pregnancy", "IOP in pregnancy", "anti-glaucoma drugs in pregnancy", "ALT and SLT in pregnancy", "trabeculectomy in pregnancy" and "choice of anti-glaucoma medication in pregnancy". All available relevant articles pertaining to this topic were then reviewed.

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