

# Eye Changes and Risk of Ocular Medications During Pregnancy and Their Management

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**Purpose:** To review various eye changes during pregnancy and potential risks of eye medications to the mother and her fetus.

**Methods and Materials:** We performed a literature search through internet using the medical search headings, effect of pregnancy in eyes, ocular changes in pregnancy, eye medication in pregnancy. We also performed a manual search using references from these articles, review articles and standard text books and manufacturers product advice.

**Data extraction:** All relevant articles including the original articles, review papers, case studies, and relevant book chapters were extracted and reviewed.

**Conclusion:** Little has been published to evaluate the eye changes in pregnancy. Eye changes in pregnancy are a well established entity in the field of ophthalmology. The risk of giving ophthalmic medicines to pregnant woman is low. The effects of pregnancy on the eyes and there management are reviewed in this article.

**Key words:** fetus, ocular changes, ophthalmic medications, physiological eye changes, pathological eye changes, pregnancy.

**D**uring pregnancy, various physiological changes take place in body due to the hormonal effects of the placenta. These hormones have effects on most organ systems, including the eyes. This article outlines both normal physiological changes in eye during pregnancy and pathological changes in the eye that can occur from pregnancy. Moreover a brief discussion of ocular medications and their potential effects on the fetus are reviewed. Through this article we review the following:

- The physiological changes in eyes during pregnancy
- Pathological effects of pregnancy in eyes.
- Effect of Ophthalmic medications in pregnancy.

**The physiological changes in eyes include the following:**

**The Intra-ocular Pressure:** The normal intra-ocular pressure (the fluid pressure within the eye) may decrease slightly due to certain hormonal and circulatory change<sup>1,2</sup>. The decrease in intra ocular pressure may persist for several months post-partum. This could be advantageous to patients suffering from Glaucoma, a condition where the raised intra-ocular pressure damages the optic nerve that transmits visual information to the brain.

**Contact Lens intolerance:** The sensitivity of the pregnant mother's cornea also decreases significantly due to the associated fluid retention of ocular tissues (especially during the last trimester of pregnancy) <sup>(1,2)</sup> This may cause problems for contact lens wearers who

may traumatize their corneas more than usual, resulting in red, irritated eye and relative contact lens intolerance.

**Change in refraction:** The tendency of fluid retention affects your refraction. This means that your current spectacles or contact lenses may be temporarily either too weak or too strong, depending upon your specific refractive error. It is usually a temporary change, and you need not get your eyes re-tested during the later stages of pregnancy and for at least the first 6 weeks after child birth. Unless the patient is insisting, it is best to defer prescribing new glasses until several weeks postpartum.

**Dry Eyes:** Some women experience dry eyes during pregnancy. This is usually temporary and goes away after delivery. Lubricating eye drops which are safe to use during pregnancy can lessen the discomfort of dry eyes.

#### **Pathological effects of pregnancy on eyes include the following**

**Diabetic Patients:** Pregnancy can have an adverse outcome on the state of pre-existing diabetic retinopathy. The worsening of the disease depends on the severity of diabetic retinopathy before pregnancy. Early stages of diabetic retinopathy usually stay quite stable, but the more advanced stages (especially the proliferative diabetic retinopathy stages) tend to progress fast during pregnancy.

**Gestational diabetes** poses a very low risk for the development of retinopathy. Usually eye examination is not required for pregnant woman who had developed gestational diabetes<sup>1,2</sup>.

In patients who had nonproliferative diabetic retinopathy, studies demonstrated that as many as 50 % of them may show an increase in their nonproliferative retinopathy, which often improves by the third trimester and postpartum. Approximately 5-20 % of these patients develop proliferative changes, the risk being higher in those patients who had severe nonproliferative retinopathy at beginning of their pregnancy. An ophthalmologic examination at least once every trimester is recommended<sup>1,2</sup>.

Studies on patients with proliferative diabetic retinopathy have shown that a progression of disease may occur in as many as 45 % of them. However, in those patients who had laser treatment before pregnancy, the risk of progression was reduced by 50 %. Hence; initiation of laser photocoagulation is

recommended prior to pregnancy. In patients with proliferative diabetic retinopathy, monthly ophthalmic examinations are warranted. Proliferative diabetic retinopathy may regress at the end of the third trimester or postpartum. Pan retinal laser photocoagulation is effective during pregnancy in inducing regression of proliferative retinopathy. Almost all retinal specialists would aggressively treat patients with high-risk characteristics of proliferative retinopathy as defined by the Diabetic Retinopathy study. In patients with proliferative diabetic retinopathy that does not meet the high risk criteria, some would treat one or both eyes, given the fact that some patients have progressed rapidly during pregnancy. Patients with proliferative diabetic retinopathy cesarean section should be considered to prevent vitreous hemorrhage due to Valsalva maneuver used during labor. Proliferative diabetic retinopathy are definitely not an indication to terminate the pregnancy.

Diabetic macular edema may develop or worsen during pregnancy. It may be reasonable to observe such patients until they reach postpartum, especially given that studies have shown that most cases have resolved spontaneously after delivery<sup>1,2</sup>.

It is therefore important for woman with advanced diabetic eye disease to seriously take their visual future into consideration when planning their pregnancy and these decisions should only be made after consultation with their ophthalmologist. The proliferative or advanced diabetic eye changes should be treated and stabilized before planned pregnancy.

**Pregnancy Induced Hypertension (Pre-eclampsia):** The onset of hypertension in an otherwise normotensive pregnant woman, with generalized edema and/or proteinuria is termed pregnancy induced hypertension (PIH) or pre-eclampsia. If these changes are associated with seizures, then the disorder is classified as eclampsia. The incidence of PIH in otherwise healthy women is approximately 5% and is more common in primigravidas. The onset of this disorder usually is after 20<sup>th</sup> week of gestation. PIH has various maternal and fetal consequences, including ocular sequelae in up to one third of cases. The most common ocular complaint is visual blurring; however other symptoms have been reported, including photopsias, scotomas, and diplopia. The protean ocular manifestations include retinopathy, optic neuropathy, serous retinal detachment and occipital cortical changes. The changes that occur in PIH induced retinopathy are similar to changes from hypertensive

retinopathy. The most common finding is focal arteriole narrowing, which also may be diffuse. Other changes may include retinal hemorrhages, retinal edema, cotton wool spots, nerve fiber layer infarcts and vitreous hemorrhage and papilledema. A positive correlation exists between the severity of PIH and degree of retinopathy, however most changes are reversible once PIH resolves.

**Cortical blindness** has also been seen in association with severe preeclampsia/eclampsia around the time of delivery.

In the past, changes in retinal vessels were considered a risk factor for placental insufficiency and fetal mortality and induction for delivery<sup>3</sup>. Both an old and a recent study of patients with pre-eclampsia and eclampsia, found that those patients with retinal hemorrhages and cotton wool spots had a higher rate of fetal mortality<sup>4</sup>.

**Central serous retinopathy (CSR):** although not typical, CSR has been reported to occur during pregnancy<sup>5</sup>. Although more common in third trimester, it has been reported to occur in the first and second trimesters. The diagnosis is clinical one. Observation is the treatment of choice as the condition resolves spontaneously in first few months postpartum and has been known to occur in future pregnancies. A weak plus lens (hyperopic correction) may provide temporary visual assistance.

#### **Intracerebral and other tumors:**

**Pituitary adenomas:** With pregnancy, previously asymptomatic pituitary adenomas or micro adenomas may enlarge and result in various ophthalmic symptoms, such as headache, visual field change, and / or visual acuity loss. It is recommended that pregnant patients with pituitary adenomas and micro adenomas have monthly ophthalmic follow up with visual field assessment to rule out enlargement. Symptomatic pituitary adenomas may require the combined efforts of an ophthalmologist, obstetrician, neurosurgeon, and endocrinologist to decide upon medical, surgical, or radiation treatment. One potentially visual threatening complication of pituitary adenomas is the sudden increase in pituitary size from infarction or hemorrhage referred to as pituitary apoplexy. This condition may present as a sudden onset of headache, visual loss, and / or ophthalmoplegia. Pregnancy is one of several potential risk factors for its occurrence. The management of

such patients includes a neurosurgical opinion for potential surgical decompression.

**Meningioma of Pregnancy:** Meningiomas are benign, slow growing tumors. Meningiomas may have a very aggressive growth pattern during pregnancy that is difficult to manage. They may regress postpartum but may regrow during subsequent pregnancy. Often ophthalmic symptoms of decreased vision or visual field loss are the first manifestations. Since most of these tumors regress in size postpartum, those patients who are asymptomatic or with mild symptoms can be observed and left untreated. For those patients who require it, treatment usually is surgical. Indications for timing and type of intervention require individual analysis.

**Occlusive vascular disorders:** It is well appreciated that pregnancy represents a hypercoagulable state in which both clotting factors and clotting activity are increased, through various changes that occur with platelets, clotting factors, and arterio-venous flow dynamics. Such changes may be related to the development of central retinal artery and vein occlusion in eye. Both branch and central retinal artery occlusions have been reported to occur in pregnancy. Retinal vein occlusions are less common than arterial occlusions.

**Toxoplasmic Retinochoroiditis:** Pregnant patients with old toxoplasmic retinochoroiditis are usually concerned about the possibility of transmitting toxoplasmosis to the fetus, but in general they need not to be concerned. Congenital toxoplasmosis in the fetus generally results only from active infection of the mother that develops during that pregnancy. The presence of toxoplasmic retinochoroiditis or chorioretinal scars in the mother is regarded as evidence of congenital infection of the mother herself, and does not indicate a new active infection of the mother. In recurrent disease, there are usually pre-existing maternal antibodies that are believed to protect the fetus. Therefore, the fetus should not be at risk for contracting congenital toxoplasmosis and its related birth defects from a mother with toxoplasmic retinochoroiditis or chorio-retinal scars. These patients usually are treated in a similar fashion to patients who are not pregnant. However spiramycin has been recommended as a safer effective alternative.

#### **Miscellaneous disorders:**

**Ptoisis** (drooping of upper eyelid) has been reported to occur during and after normal pregnancy and is usually unilateral. The mechanism is thought to be

due to defects that develop in levator aponeurosis from fluid, hormonal, and other changes from the stress of labour and delivery.

**Uveitis:** The immunosuppressive effects and high steroid levels present in pregnant women may cause improvement in uveitis during pregnancy, with exacerbation after delivery. This has been noted in patients with sarcoidosis<sup>6</sup> and Vogt koyanagi-harada syndrome<sup>7</sup>.

**Conjunctival Blood Vessels:** Changes in conjunctival blood vessels have been described toward the end of pregnancy. These changes include a granularity of conjunctival venules, mild spasm of conjunctival arterioles, and decreased visualization of conjunctival capillaries. Excessive vomiting during pregnancy can cause conjunctival petechiae.

### Ophthalmic medications in pregnancy

**“Doctor, I am pregnant.** Can I still use this eye drops?” This is probably one of the most common questions asked by pregnant women when they visit not only to their ophthalmologist, but also their obstetrician or even family physician. Perhaps it is also one of the few questions that even ophthalmologist and other doctors of various specialties might have difficulty in answering, especially when they have to present evidence to convince their patients. Limited data have been published regarding the potential risk of eye medications to the mother and fetus. When one wishes to administer ophthalmic pharmacologic agents during pregnancy, there should be a clear indication for them. Although most ophthalmic medications, in the doses used and the topical mode of administration, have not been implicated in an adverse fetal outcome, thought should go into using drugs only as necessary. However recommendations are summarized as per the FDA guide lines below for commonly used eye medication.

#### Anti-Glaucoma medications:

**Topical Beta blockers:** (e.g., timolol eye drops) FDA risk category C in first trimester while D in 2<sup>nd</sup> and 3<sup>rd</sup> trimester. B blockers can cause intrauterine growth retardation if used in 2<sup>nd</sup> and 3<sup>rd</sup> trimester and persistent neonatal blockade if used near term. Should be avoided during pregnancy<sup>8,9</sup>.

**Topical and systemic carbonic anhydrase inhibitors** (eg, acetazolamide, dorzolamide) are contraindicated during pregnancy because of potential teratogenic effects<sup>10</sup>.

**Prostaglandin analogs (eg, latanoprost) FDA risk category C.** Not well studied, and the reports that do exist are conflicting. The use of latanoprost / travoprost is generally contraindicated in pregnant women<sup>8,9</sup>.

**Mydriatics (Dilating Drops):** Use of occasional dilating drops during pregnancy for the purposes of ocular examination is safe. However, repeated use is contraindicated because of potential teratogenic effects of both parasympatholytics (eg, atropine) and sympathomimetics (eg, epinephrine)<sup>10</sup>.

**Topical Corticosteroids: (Prednisolone) FDA risk category B.** Although systemic corticosteroids are contraindicated in pregnancy, topical steroids have not been reported to have an adverse effect on pregnancy<sup>(10)</sup>, but the safety of their use has not absolutely been established. Therefore, use with care during pregnancy. Avoid their prolonged use in pregnancy.

#### Anti-infection preparations:

**Topical chloramphenicol: FDA risk category is not available.** It is used widely to treat superficial eye infection because of its spectrum and low cost. Many concerns, however, have been documented about this drug's serious side effects—namely aplastic anemia and ‘grey baby syndrome’. A review article in 2002 concluded that the risk of these serious side effects is low and they are unlikely to occur if patients adhere to the prescribed dose and duration of the treatment. Chloramphenicol if given to mother shortly before labor may cause “grey baby syndrome” with cyanosis and hypothermia. Chloramphenicol treatment should be avoided during the last week of pregnancy and breast feeding.

**Gentamicin eye drops: FDA risk Category C.** Should be avoided in pregnancy. Drug should be given only if the potential benefit outweighs the potential risk<sup>8,9</sup>.

**Ciprofloxacin eye drops: FDA risk category C.** Should be used only if the potential benefit outweighs the potential risk<sup>8,9</sup>.

**Tetracycline eye ointment: FDA risk category D.** Positive evidence of human fetal risk exists<sup>8,9</sup>.

**Topical Erythromycin: FDA risk Category B.** Controlled studies done on animals does not indicate risk to fetus. However no adequate and well controlled studies done on pregnant women. Generally considered safe to use in pregnancy<sup>8-10</sup>.

Antibiotics which are safe during pregnancy are amoxicillin, ampicilline, benzylpenicilline,

cabencilline, cloxacilline, Erythromycine and vancomycin.

Antibiotics which should be avoided during pregnancy are, gentamycin, streptomycin, neomycin, and kenamycin, Flourinated quinolones like norfloxacilline and ciprofloxacilline are not considered safe during pregnancy.

**Antiviral eye preparations (Acyclovir eye ointment): FDA risk category B.** Topical acyclovir has not been studied in pregnant woman. However this medicine has not been shown to cause birth defects or other problems in animal studies. So it is considered generally safe for eye application. Systemic acyclovir should only be used during pregnancy if potential benefit justifies the potential risk to fetus<sup>8,9</sup>.

**Fluorescein dye: FDA risk category B.** No known teratogenic effects of fluorescein during pregnancy exist. Most of the retinal specialist avoids fluorescein angiography during pregnancy, especially first trimester.

**Topical anesthetic:** No known contraindications exist to use of topical anesthetic drops in pregnancy<sup>10</sup>.

**Anti-allergic eye drops:** Sodium cromoglycate 2% (FDA risk category B) eye drop is safe to use in pregnancy while antihistaminic eye drops containing naphazoline (FDA category C) are better avoided<sup>8,9</sup>.

## CONCLUSION

Little has been published to evaluate the true risk in the use of eye medication during pregnancy. The overall level of evidence for risk giving ophthalmic drugs to pregnant women is low. Most of the available evidence is based on only individual case reports and animal studies.

The topic of this article provides a practical overview for pregnant women and their treating doctors. Little has been published to evaluate the eye changes in pregnancy; however most of the physiological eye changes are reversible and doesn't warrant urgent ophthalmic help. Fortunately the pathological eye changes during pregnancy discussed above are extremely rare and occasionally seen in daily ophthalmic practice. Opinions from obstetrician,

ophthalmologists, and family physicians are essential to ensure safe pregnancy.

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