

Eye and Pregnancy

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ABSTRACT

Hormonal, metabolic, hemodynamic, vascular and immunological changes that occur during pregnancy can affect the function of the eye. These changes are commonly transient, but in some cases they may be permanent and have consequences even after childbirth. The ocular effects of pregnancy may be physiological or pathological and can be associated with the development of new ocular pathology or may be modifications of pre-existing conditions. The most common physiological changes are alterations of corneal sensitivity and thickness, decreased tolerance to contact lenses, decreased intraocular pressure, hemeralopia and refractive errors. Possible posterior segment changes include worsening of diabetic retinopathy, central serous chorioretinopathy, increased risk of peripheral vitreochorioretinal dystrophies and retinal detachment. Thus, it should be kept in mind that the presence of any ocular symptoms in a pregnant woman requires ophthalmologic examination and further management.

Key words: eye, pregnancy, refractive error, hormones

Introduction

During pregnancy various changes in hormonal, immunological, metabolic, hematologic and cardiovascular status can be observed. These modifications in turn cause a number of alterations in the whole body including the eye. Ocular changes in pregnancy are related to adnexa of the eye, anterior and posterior segment and can cause decreased intraocular pressure. The mentioned ocular changes may be temporary, transitory, completely transient or in some cases even permanent. Likewise they may also be physiological or pathological. Further these changes may be associated with the development of new diseases or alternatively can cause alterations in pre-existing conditions¹⁻⁴. Additionally pathology of pregnancy itself can further complicate present ocular conditions^{5,6}.

Nowadays a large number of young people including women of childbearing age have shown great interest in refractive surgery thus it should be emphasized that pregnancy causes changes in the eye making the results of any refractive surgery unpredictable. It is therefore recommended that refractive procedures in pregnant women be postponed till after delivery⁷.

Physiologic Ocular Changes Occurring in Pregnancy

Sensitivity of the cornea is known to be decreased in pregnancy, occurring mostly in the third trimester and subsiding in the postpartum period. However some investigations failed to relate this decrease in corneal sensitivity to the duration of gestation^{8,9}. Increase in corneal thickness observed in pregnant women may be the consequence of corneal oedema resulting from increased water retention during pregnancy^{1,4,9}. Conversely some investigations found no difference in corneal thickness of pregnant and non-pregnant women¹⁰. Changes in corneal curvature and steeping may also occur during pregnancy particularly during the second and third trimesters. These changes are usually reversible and resolved in the postpartum period or after cessation of breastfeeding¹¹.

Pregnant women appear to suffer more from lacrimal dysfunction than non pregnant women; in both groups the prevalence of tear dysfunction is more elevated in women with higher parity¹². As a result of altered tear film, corneal oedema and changed corneal curvature contact lens intolerance may occur even though they had been successful contact lens wearers prior to pregnancy¹¹. In such cases it is recommended to wait several weeks after delivery before prescribing a new refraction⁷.

Although glaucoma is generally a disease of the elderly it may affect women of childbearing age¹³. Nowadays there is a trend for later childbirth and thus the frequency of glaucoma during pregnancy may increase. A decrease in intraocular pressure (IOP) has been observed during pregnancy and often persists for several months after delivery. The decrease in IOP can lead to changes in women with pre-existing glaucoma which can improve during this period. Various underlying mechanisms propose to explain the cause of decrease in IOP during pregnancy, namely; an increase in outflow as a result of hormone levels modification, a decrease in systemic vascular resistance, decrease in episcleral venous pressure, increased tissue elasticity and generalised acidemia during pregnancy¹⁴. It is also possible that IOP is not in fact reduced during pregnancy but rather could be the result of measurement error. The physiological changes in late pregnancy may reduce corneal rigidity, making the results of applanation tonometry falsely low. Likewise an increase in corneal thickness could also affect the measured values of IOP¹⁵. However it should be emphasized that despite the apparent reduced IOP level in pregnant women many glaucoma patients still need to continue treatment since glaucoma damage may advance during pregnancy and progressive visual field loss can occur¹⁴.

During pregnancy certain changes in the visual field such as bitemporal loss, concentric constriction, and enlarged blind spots can be observed. These changes are generally asymptomatic and shown to be completely reversible, usually 10 days after delivery¹⁴. Several reasons can explain this visual field loss. Magnetic resonance imaging studies show that the size of the pituitary gland increases during a normal pregnancy¹⁶ and thus could press and damage the optic chiasm causing bitemporal visual field changes. Likewise, another cause of visual field damage could be glaucoma or brain tumours¹⁴. However, symptomatic patients inevitably require further investigation and follow up.

Pre-Existing Ocular Conditions and Pregnancy

Progression of diabetic retinopathy (DR) occurs at least temporarily during pregnancy. Although the cause of this progression is not entirely understood the consensus is that this mechanism is multi-factorial with important contributory factors including hyperglycaemia, duration of diabetes before conception, baseline status of retinopathy, rapid control of blood glucose during pregnancy, coexisting hypertension, preeclampsia and changes in retinal blood flow^{17,18}. More recently there is growing evidence suggesting that in the progression of retinopathy activation and adaptation of the immune system during gestation could also have certain role. It is established that during pregnancy, certain components of the immune system that are knowingly implicated in the pathogenesis of DR are activated^{19,20}. It is commonly believed that the severity of DR may regress at least to some degree in the postpartum period although the rate

and timing of this regression is still relatively unknown. Whilst the rate of regression of DR at the end of pregnancy or the postpartum period is substantial careful monitoring of these patients is necessary to optimize the vision and pregnancy outcomes²¹. Studies describe that about 10% of women with diabetes without any signs of retinopathy prior to pregnancy tend to develop some background retinopathy during pregnancy. Furthermore less than 0.2% of pregnant women with diabetes progressed to proliferative stages of the disease. It was reported that as many as 50% with non-proliferative retinopathy may develop an increase in retinopathy, often improving by the third trimester and during breastfeeding. Between 5 and 20% can develop proliferative changes, where women are at higher risk if they had non-proliferative retinopathy at the beginning of pregnancy. Patients with proliferative diabetic retinopathy (PDR) showed a progression of the disease in as many as 45% of cases. Laser treatment before pregnancy appears to substantially minimise this risk, whilst no recurrence of the disease was reported if regression of proliferation was observed prior to pregnancy^{22–24}. Sight-threatening DR in pregnancy is a rare disease yet it can have devastating consequences for mother and child. Established sight-threatening retinopathy should therefore be treated at an earlier stage in pregnant women compared to non-pregnant diabetics with a similar disease. Laser photocoagulation should be considered for pregnant women with severe pre-proliferative diabetic retinopathy²⁵. It should be emphasized that DR should be carefully monitored before conception and during pregnancy. All known risk factors must be taken into account when planning pregnancy in diabetic women and during the follow-up of their retinopathy. Counselling addressing the risks of retinopathy progression prior to planning pregnancy is highly recommended. Careful eye examination before and during the first trimester should be performed in these patients in order to detect severe non-proliferative DR or high-risk DR with prompt laser treatment if necessary. Follow-up visits should be adapted according to the severity of this complication. Macular oedema may also develop or worsen during pregnancy and is generally linked to women who have diabetes accompanied by proteinuria and hypertension. It can spontaneously regress postpartum and therefore should not be treated too rapidly²⁶. Given the fact that diabetes takes longer than five years to develop morphological changes corresponding to DR, women with gestational diabetes would not develop this complication during pregnancy and therefore fundus examination in these women is not obligatory despite their glucose blood level²⁷.

Major hormonal changes emerge during pregnancy. The pituitary gland is one of the most affected organs with altered anatomy and physiology followed by consequential enlargement. Pituitary adenomas may cause problems by their hormone secretion that affects the mother and fetus as well as causing an increased risk of tumour growth²⁸. Pituitary adenomas can change size and consequently cause changes in visual field, however

are more often than not, asymptomatic. Clinically significant tumour growth may occur in 2.7% of patients with microadenomas, in 22.9% of patients with macroadenomas without prior ablative treatment and 4.8% of those with macroadenomas and previous ablative treatment. Women with macroadenomas should have visual fields assessed periodically during gestation. Thus, should symptomatic tumour growth occur, reinstatement of the dopamine agonist is usually successful in shrinking the tumour. If the pregnancy is sufficiently advanced, induced delivery is also an option whilst transsphenoidal de-bulking is rarely necessary²⁹. Some of the brain tumours observed in pregnant women such as glioblastomas, meningiomas and melanomas can also influence vision and cause visual field disturbances with symptoms depending on the tumour location. However, it should be noted that most do not show significant changes in behaviour during gestation³⁰.

Among many women with non-infectious uveitis an increase in disease activity within the first four months of pregnancy occurs. The disease appears to be relatively inactive in later pregnancy with a rebound within six months of delivery³¹. Inflammatory eye diseases such as uveitis can affect females during their reproductive period. The first trimester and postpartum period may be associated with an exacerbation of uveitis and therefore it is important to have available medications that can control the disease and do not cause miscarriage or fetal abnormalities³². Many autoimmune diseases in females are known to improve during pregnancy but worsen in the postpartum period, since pregnancy induces immune deviation promoting anti-inflammatory cytokines that prevent immunological rejection of the allogenic fetus^{33,34}. It is confirmed that pregnancy is associated with improvement of some autoimmune diseases including rheumatoid arthritis and multiple sclerosis and with exacerbation of other autoimmune conditions such as systemic lupus erythematosus. Female patients with uveitis may require close control and if necessary treatment during pregnancy as well as in the early postpartum period^{35,36}. Pregnant state may provoke the recurrence of ocular toxoplasmosis. Acute toxoplasmic retinochoroiditis in pregnancy could be a risk of transplacental transmission due to potential parasitemia with detrimental effects on the developing fetus³⁷. Pregnancy causes a number of physiological alterations in thyroid hormone metabolism. Graves' disease often shows a characteristic course in pregnancy with amelioration of thyrotoxicosis in the second half of pregnancy and exacerbation after delivery. In addition, transplacental passage of maternal TSH receptor antibodies may lead to thyrotoxicosis in the fetus or newborn. The symptoms of thyrotoxicosis are important as they represent a serious condition to both mother and the fetus³⁸. Multiple sclerosis, on the contrary has been known to stabilise during pregnancy especially in the final trimester, and then relapse usually in the first three months postpartum. Some studies link this pattern with estrogen levels³⁹.

Pregnancy is known to cause refractive changes as a result of various hormonal changes which occur during pregnancy. These changes may persist for a few weeks post-partum and during lactation⁷. There has been concern that patients with high myopia are at a risk for developing retinal tears as they go through spontaneous delivery. High myopia is not itself an indication for caesarean section; however the patient should definitely be examined after delivery. Furthermore the literature shows that there is little evidence to support the belief that previous retinal surgery increases the risk of re-detachment of the retina during spontaneous vaginal delivery⁴⁰. Pizzarello researched the existence of worsening myopia in pregnant women. In his study all women with complaints of visual disturbances were found to have experienced a myopic shift from pre-pregnancy levels with a return to near pre-pregnancy levels post partum⁴¹.

Ophthalmic Medications in Pregnancy

Insufficient data is available regarding the effect and potential risk of ophthalmic medications on pregnancy, the fetus and breast milk contamination^{42,43}. Glaucoma medications (beta blockers) are to be avoided or at least used in the lowest possible dose especially in the first trimester when the risk of teratogenesis is highest and should be discontinued several days prior to delivery to avoid beta-blockade in the infant. Carbonic anhydrase inhibitors are known to have teratogenic effects and should be avoided during pregnancy. Their application is contraindicated in mothers who are breastfeeding because of the potential hepatic and renal effects to the infant. However, acetazolamide has been reported to be compatible with lactation according to the American Academy of Paediatrics. Miotics (eg, pilocarpine, echothiophate, carbachol) appear to be safe during pregnancy whilst their toxicity during lactation is unknown. One exception is demecarium, which is toxic and is contraindicated in pregnancy and mothers who are breastfeeding⁴⁴. The widespread use of prostaglandin to induce labour, terminate pregnancy and regulate menstruation has raised concerns of its use in pregnant women⁴⁵. However, according to some reports locally applied prostaglandine analogues have insufficient active ingredients to cause adverse effects on the fetus whilst other reports consider that the use of prostaglandin is generally contraindicated in pregnant women. This suggests that they should be used cautiously during pregnancy and should be discontinued several days before birth⁴⁶. Occasional use of mydriatic drops for the purposes of ocular examination is considered to be safe; however repeated use should be avoided due to potential teratogenic effects of both parasympatholytics (eg, atropine) and sympathomimetics (eg, epinephrine). Use of mydriatics is contraindicated in mothers who are breastfeeding because of anticholinergic or hypertensive effects on the fetus. Corticosteroids are considered to be contraindicated even though there are no known teratogenic effects of topical steroids. They should however be avoided during breast-

feeding since little is known about the risk of their application during lactation. Antibiotics that are considered safe during pregnancy include erythromycin, ophthalmic tobramycin, ophthalmic gentamicin, polymyxin B and the quinolones with the latter two showing to be safe even during breastfeeding. The list of antibiotics that should be avoided during pregnancy include: chloramphenicol, systemic gentamycin, neomycin, rifampin. Acyclovir is generally well tolerated in pregnant women. Treatment using clinically recommended doses has low toxic potential and no adverse effects have been reported regarding its application during pregnancy⁴⁴. There are no known side effects of flourescein and topical anaesthetics drops if used during pregnancy. Drugs against allergies are used to treat inflammatory and allergic conjunctivitis. Although data on ophthalmic antihistamine use during pregnancy and their potential teratogenic risk is very low the use of this group of ophthalmic drugs during pregnancy is considered to be safe^{44,47}.

Patients who are pregnant may require the use of medication to supplement their treatment. However, to ensure a decreased incidence of systemic absorption and toxicity simple measures should be applied. Firstly, prescribing the patient the lowest recommended dose and secondly instructing the patient to correctly administer medication to avoid adsorption by nasal mucosa.

Very little data has been published evaluating the risk of using ophthalmic drugs during pregnancy. There is a

lack of meta-analyses and randomised controlled trials in this area of study. Most of the available evidence is based only on individual case reports and animal studies. As a general rule, all drugs should be avoided if possible in the first trimester since the risk of drug-induced foetal teratogenicity is highest during this period. Despite the lack of data on the risks of eye drug application ophthalmologists should nonetheless continue to prescribe appropriate treatments particularly when their expected benefits to the mother outweigh the risk to the fetus.

Conclusion

It has been reported that the number of pregnant women undergoing regular eye examinations is low. The majority of pregnant women referred to ophthalmologist are those with previously diagnosed high myopia. Most ocular changes in pregnancy are physiological and reversible. Nevertheless, it is advised that such changes should be registered and followed-up at least during pregnancy and in the post-partum period. Pre-existing ocular conditions require regular control at least three times during the pregnancy and even more often in women with pre-existing diabetes. In gestational diabetes significant changes of the eye are not expected. High myopia and previous retinal surgery are no longer an indication for compulsory caesarean section; however still require regular control by an obstetrician and ophthalmologist.

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OKO U TRUDNOĆI

S A Ž E T A K

Hormonske, metaboličke, hemodinamske, vaskularne i imunološke promjene koje se događaju tijekom trudnoće između ostalog utječu i na funkciju očiju. Promjene na očima su obično prolazne, ali u nekim slučajevima mogu ostati trajno s posljedicama koje se manifestiraju i nakon poroda. Promjene koje se javljaju na očima mogu biti fiziološke ili patološke odnosno mogu biti povezane s nastankom i razvojem novih patoloških stanja oka ili može doći do promjena ranijih već postojećih bolesti. Najčešće fiziološke promjene su povećanje osjetljivosti rožnice, zadebljanje rožnice, smanjena tolerancija prilikom nošenja kontaktnih leća, sniženje očnog tlaka, hemeralopia te promjene u refrakciji oka. Promjene koje se mogu pojaviti na stražnjem segmentu oka uključuju pojavu i napredovanje dijabetičke retinopatije, nastanak centralne serozne korioretinopatije, povećani rizik pojave perifernih vitreokorioretinalnih distrofija i odvajanje mrežnice. Treba naglasiti da kod svih promjena na oku koje se jave tijekom trudnoće potreban pregled i liječenje oftalmologa.