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MANAGEMENT OF GLAUCOMA DURING & POST PREGNANCY

Ophthalmology

Dr. Amola Gandhi* Ex Senior Resident At Sant Paramanand Hospital, New Delhi .*Corresponding Author

Dr. Rahul Gandhi Ex Senior Resident At Arun Asafali Hospital, New Delhi.

ABSTRACT

The treatment of Glaucoma in and around pregnancy offers the unique challenge of balancing the risk of vision loss to mother and as against the potential harm to fetus and new born. Ophthalmologists are usually limited to treating pregnant glaucoma patients with category-B drugs but most of anti-glaucoma drugs (I.e. B-Blocker, Prostaglandins Analogues are category-C drugs but α-Agonist are choice of drug in 1st and 2nd trimester of pregnancy but avoided in 3rd trimester & new born as it causes CNS depression in children so for that time B-Blocker & carbonic anhydrase inhibitor are drug of choice. ALT (argon laser trabeculoplasty) SLT (selective laser trabeculoplasty) is an alternative for glaucoma treatment during pregnancy & can be done in all trimesters. Glaucoma surgery (trabeculectomy with mitomycin-c OR valve surgery) can be performed with caution & risk & benefit counting in pregnancy. Surgery should be avoided in 1st trimester due to risk of exposure of anesthetic agents & anti metabolites. Lactating mother should be given β-Blocker or pg analogues but avoid α-Agonist as it secret in brest milk & leads to CNS depression in new born. So optimum treatment of glaucoma should not be withheld during pregnancy otherwise it may be lead to further deterioration in visual field & quality of life.

KEYWORDS

Glaucoma, Pregnancy, -Agonist, Glaucoma surgery.

INTRODUCTION:

Traditionally, majority of women treated with glaucoma are beyond the child bearing age but in advance world and advance reproductive technology empower women to conceive at older ages. Glaucoma usually occur in adult over the age of 40 but sometimes women with child bearing age of 30 also have pre-existing childhood glaucomas or secondary glaucomas (due to uveitis or steroids or diabetes mellitus) and due to awareness in today's world pregnant female hesitate to use Anti glaucoma drug or stop using it during pregnancy. But known teratogenic drugs increase risk of major birth defect by only 1 to 3% [(1)]. Treatment is generally indicated when risk of progressive diseases out weight the risk of potential side effect of treatment.(i.e. patient with progressive disc changes, or visual field loss, or Retinal nerve fiber layer loss (RNFL) loss on optical coherence tomography (OCT) this cases should be treated with IOP lowering therapy.) No published data nor any clinical trials exist on fetal effect of commonly use anti glaucoma drugs and unlikely the trials will be performed so this article only described treatment of glaucoma during and post pregnancy and its Unique challenge to balance risk of vision loss to mother against potential harm to fetus & new born.

(2) Epidemiology: Roughly 2-3 % pregnant adult over the Age of 40 have been reported for glaucoma but prevalence is increasing with age for all race & ethnicity [(2)]. Prevalence of glaucoma prior to age of 40 in child bearing Age in Japanese Study is 0.48 % (15 - 24 Years), 0.42 % (25 - 34 Years), 0.73 (33 - 45 Years) [(3)].

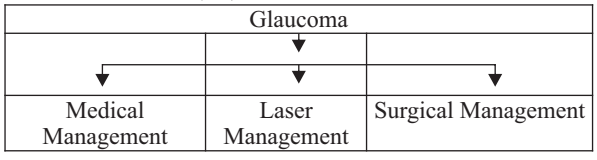
(3) Effect of pregnancy on IOP: It is estimated that during pregnancy intraocular pressure reduced by 10% with reduction being marked in 3rd trimester but also reduced in several months post partum and this is due to fluctuation of 2 hormones.
(1)β-hcg
(2) Progesterone

One study of pregnant women, the mean iop of 1st trimester patients was average 2mm of hg higher than 3rd trimester patients [(4)]. Glaucoma remains steady during pregnancy so patient can be there for off-treatment during pregnancy. Increase level of progesterone & relaxin may decrease iop and increase co-efficient of facility of aqueous outflow during pregnancy[(5)] and also due to hormonal changes aqueous out flow increase & episcleral venous pressure decrease also reduce iop[(5)] so majority of women have steady glaucoma during pregnancy only small percentage (around 10%) pregnant Glaucoma patient may show progression of diseases[(6)].

(4) Current available treatment regimes: The "target iop" is best guessed iop range for each patients in which further rate of progression for diseases is minimal or unlikely to affect patient's quality of life in ophthalmologist"s opinion[(7)]. "Target iop" decided by many factors & they are.

(1) Iop of presentation.
(2) Age of patient.
(3) Amount of pre-existing glaucoma damage.
(4) Rate of progression.
(5) Life expectancy of patient.
(6) Status of fellow eye.
(7) F/h/o glaucoma

"Target iop" should be re-evaluated & re adjusted continuously on short time intervals. Treatment goal should be to maintain quality of life of mother and not to harm fetal or neonatal life and we have to do balance of both of this. (5-7)



(A) Medical Management (Topical Anti glaucoma drugs)

(1) β-Blocker: Topical & systemic β-Blockers are category-c drugs in pregnency. This drug decrease intra ocular pressure by decreasing aqueous humor production [(8)]. Some β-blocker have local anesthetic property, intrinsic sympathomimetic activity. Selective β-blockers are betaxolol. Non Selective β-Blockers are timolol, metoprolol, cartelol, levobunolal. Non selective β-blockers have systemic cvs & respiratory side effect. Selective β-blocker due to lack of intrinsic sympathomimetic activity ↑se blood flow to optic nerve head i.e. betaxolol so called neuro-protective. Topical drug is safe in 2nd, 3rd trimester of pregnancy & lactating mother & they can also given to a child under 12yr of age [(9)].

(2) α-Agonist: Topical *α*-agonist are category-b drugs in pregnancy. This drug decrease iop by two mechanism [(10)]. (1) Decrease aqueous humor production. (2) Increase uveoscleral outflow of aqueous humor. Non selective *α*-agonist are adrenaline & nor adrenaline. Selective *α*-agonist is brimonidine. Alpha-agonist's iop reduction capacity is lower than *b*-blocker so they used in glaucoma as 2nd line drug with β-blocker & pg analogues. This drugs have high local side effect i.e. conjunctival hyperemia, blephroconjunctivitis. This drugs are contraindicated in newborn & Child <12 yr of age as it causes cns depression & Apnea in Children (11). This drug can cross hemato encephalic blood brain barrier & hemato placental blood brain barrier so possible to secret in brest milk so c/i in lactating mother as in cause Apnea in newborn (11). So despite of its status as category-b drug for pregnancy they only use in 1st & 2nd trimester of pregnancy & discontinued in 3rd trimester and postpartum for safety of newborn (12).

(3) Prostaglandin Analogues: Topical drugs are classified as cat-c

drugs. They decrease iop by increasing uveoscleral outflow of aqueous humor [13]. They are 1st line & most potent drugs currently use for glaucoma management [14]. Local side effects are high i.e. conjunctival hyperemia, increasing length of eyelash, increase iris pigmentation. Systemic side effects are less but it can cause miscarriage in animal study[15] & this drug are oxytocic so it can increase uterine muscle tone contraction & cause premature labour [16]. This drug causing premature labour or miscarriage in pregnant lady & moebius syndrom or transverse limb detect in newborn suggesting data is uncertain [17]. So use with caution in 1st trimester & 3rd trimester but 2nd trimester & postpartum period is safe to use & Also safe for newborn & child <12yr of age [18].

(4) Parasympathomimetics(miotic drugs): Topical drugs are cat-c drugs. They decrease iop by 2 mechanism (1) Increase outflow of aqueous humor via trabecular pathway. (2) Decrease pupillary block (19). So useful for both open angle and angle closure glaucoma. Animal study shows reproductive toxicity but no adequate trials done on humans (20). Its Excretion in human milk is also not known (21). Use with caution during & post pregnancy.

(5) Carbonic anhydrase Inhibitor: This are the only anti glaucoma drugs clinically use in both oral & topical form. They are cat-c drugs for pregnancy. They Reduce Intra ocular pressure by inhibiting carbonic anhydrase Enzyme II present on ciliary body & decrease Aqueous humor production i.e. dorzolamide, brinzolamide (topical) acetazolamide (oral). Side Effect of systemic drug is paraesthesia, malaise, gastrointestinal disturbance, metabolic acidosis. Systemic drug is c/i in sulpha allergy patients, metabolic acidosis patients, ↓se Na+ or high K+ level Patients. Side effect of topical drug is ocular burning sensation, bitter taste in mouth, headache. In animal study topical dorzolamide & brinzolamide cause vertebral body malformation in rabbit but no report exist on human study [22]. Also their secretion in brest milk is uncertain so this drug should be use with caution during & post pregnancy. Systemic acetazolamide in high dose may result in potential metabolic complication in new born [23]. One case report of neonatal Sacrococcygeal teratoma report in pregnant lady with maternal acetazolamide use [24]. Another case report of neonatal renal tubular acidosis of maternal glaucoma c oral acetazolamide use[25]. Other case report of no fatal side effect to new born in which 12 mother use oral acetazolamide during pregnancy[26]. So by this data american academy of pediatrics approve use of oral acetazolamide during nursing [27]. So oral acetazolamide use with very caution in late pregnancy & avoid over dose of drug & moniter neonatal electrolyte to avoid serious side effect.

(6) Osmotic Agents: They are cat-c drugs[28]. No Sufficient animal or human trials available for study.

(7) Rho - Kinase Inhibitor: Newer anti glaucoma drug i.e. ripasudil & netarsudil. Not been classified get because lack of study on this drugs[29]. Decrease iop by ↑se trabecular outflow of aqueous humor & decrease episclearl venous pressure. There is no human study available so its safety in pregnancy & lactation is yet unknown.

Drug delivery formation: A
ll topical drug have systemic side effect which are reduced by decrease its systemic absorption by simple nasolacrimal duct occlusion for 5 minutes after putting eye drops. This option should discuss with all women who continue their pregnancy with topical anti glaucoma drug use.

(B) Laser Surgery: Argon laser trabeculoplasty & selective laser trabeculoplasty are considered in pregnancy to reduce number of topical anti glaucoma medication. ALT& SLT are safe in all trimester & post partum period of pregnancy [30]. Long term iop control by ALT & SLT is questionable so they use for short term iop control in glaucoma [31].

(C) Glaucoma Surgery: If woman have advanced glaucoma and iop is uncontrolled after using maximum medical therapy (MMT) serious consideration should be given to glaucoma surgery before conception i.e. (filtration surgery). After conception, surgery is only last option where advance glaucoma C uncontrolled iop C maximum medical therapy (MMT) & laser surgery[32]. Pregnant female has risk of side effect of anesthetic agents & Anti metabolites and postoperative drug usage[33]. So surgery should only be perform in 2nd & 3rd trimester and avoid in 1st trimester because 1st trimester is most important for organogenesis of fetus. Cryosurgery & diode laser surgery is safe & performed under local anaesthesia during pregnancy if iop is uncontrolled & can be use as an alternate to filtration surgery(34-36).

(5) Treatment According to Stage of Pregnancy:

Time of pregnancy	Treatment of choice	Other treatment options	Role of surgery	C/I or Use C⁻ Caution
1st Trimester	• -agonist	• B-blocker • Pg analogue • Carbonic anhydrase Inhibitor	• Laser surgery Can be done. • Anti glaucoma surgery best to avoid.	• Surgery always done with caution or better to avoided. • Use drugs other than alpha-agonist with caution.
2nd Trimester	• B-blocker • Pg analogue • agonist	• Carbonic anhydrase Inhibitor	• Laser surgery & anti glaucoma surgery both can be performed.	• with caution.
3rd Trimester	• B-blocker	• Carbonic anhydrase Inhibitor	• Laser surgery& anti glaucoma surgery both Can be performed	• -agonist use to be avoided near labour. • Pg analogue can cause pre mature labour so better to avoid.s
Post Partum (lactating)	• Pg analogue	• Carbonic anhydrase inhibitor • B-blocker	• Laser surgery & anti glaucoma surgery both can be performed.	• agonist are not to be used as it cause cns depression in new borns. • are better to use with caution and check electrolytes of newborn if systemic drugs are used.B-blocker also should be used with caution as it may secret in to brest milk.
Child (<12 yr)	• B-blocker • Pg analogue	• Carbonic anhydrase Inhibitor	• Laser surgery & anti glaucoma surgery both can be performed.	• Carbonic anhydrase inhibitor use ↓ caution. • Avoid use of alpha-agonist as it cause cns depression in child. • B-blocker are most effective. • Pg analogues are 2nd choice after b-blocker for this age group.

1st trimester is most important time for organogenesis so α-agonist as a cat - B drug is most safe during this period use b-blocker, pg analogue & anti glaucoma surgery with very caution. 2nd trimester we can continue α-agonist or replace it with β-blocker (monitor fetal heart sound) or pg Analogue (check for abortion) but laser & anti glaucoma surgery both can perform safely. 3rd trimester β-blocker & carbonic anhydrase inhibitor can be use with caution but avoid α-agonist (fetal side effect) & pg analogue (pre mature labour). Post partum period & lactating mother should be given β-blocker(can be secret in brestmilk) or pg analogue but avoid α-agonist as it causes fetal cns depression &

apnea but carbonic anhydrase inhibitor can be used with caution & check for electrolyte Imbalance(if systemic acetazolamide is given).

(6) FDA according drugs for their safety in pregnancy:-

Cat A-Deemed safe.
B - Possible safe.(alpha agonists)
C - Adverse drug Reaction in Animal Study.(b-blockers,carbonic anhdyase inhibitor,pg analogues,miotics)
D -Definite risk but possible benefit.
X-Drugs with known risk to fetus cannot be outweighed by possible benefit.(systemic acetazolamide)

Prefered mode of delivery method in pregnant glaucoma female is lscs over vaginal delivery as vaginal delivery may increase episcleral venous pressure during labour due to stress in delivery or decrease optic nerve head blood flow.

(7) CONCLUSION:- To choose to start families later in life is now common place for women so frequency of glaucoma around pregnancy is increasing. Risk - benefit assessment for glaucoma treatment in pregnancy is difficult because lack of availability of data but optimum treatment to pregnant glaucoma female is must that any further deterioration in vision and quality of life. As a general rule, 1st trimester is very cautious time for fetus because it is the most important time for fetal organogenesis & chances of fetal malformation are highest at this time. Nevertheless, the fear of uncertain drug teratogenicity should not discouraged doctor from prescribing treatment when their benefit to mother are thought to out weight the risk to fetus.

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