Commentary: Pregnancy hormone to control intraocular pressure?

Pregnancy and the body

Pregnancy is a time of profound physiological changes in a woman's body. In addition to the circulatory system changes and rearrangements in the abdomen, there are massive fluctuations in the hormonal levels, potentially leading to changes in each and every organ in her body.

Pregnancy and the eye

Studies in pregnant women have shown that there is increased retention of water in the corneal stroma probably due to hormonal changes. Central Corneal Thickness (CCT), Anterior Chamber Depth (ACD), and Anterior Chamber Angle (ACA) are higher in the third trimester of pregnancy than postpartum.[1] There is increased plasticity of the anterior chamber before delivery, which presumably helps to counteract the excess intraocular pressure (IOP) rise during the second stage of labor.

Pregnancy, IOP, and glaucoma

During pregnancy, IOP is reduced in healthy women. Mechanisms proposed to include progesterone and relaxin induced increased aqueous outflow facility, decreased episcleral venous pressure, and gestational metabolic acidosis. For glaucoma patients in pregnancy, though a majority still shows the reduction in IOP, it can increase or remain stable too. This variable course of IOP may be due to the interplay of various hormones in pregnancy. Visual fields have also shown a variable outcome in pregnancy with a study showing progression in IOP or visual fields in 35% of the subjects.[2]

Glaucoma Medications in Pregnancy

Though topical medications are one of the easiest ways to control IOP, their risks in pregnancy have not been well established. There are currently no glaucoma medications in the United States Food and Drug Administration (FDA) Category A, which implies safety demonstrated in human trials. Brimonidine is classified under Category B, which presumes safety based on animal studies. Beta Blockers, Carbonic Anhydrase inhibitors, parasympathomimetics, and prostaglandin analogs are classified under Category C with uncertain safety.[3] Selective LASER Trabeculoplasty (SLT) or Minimally Invasive Glaucoma Surgery (MIGS) may be options for pregnant glaucoma patients to reduce or stop unsafe glaucoma medications for the duration of the pregnancy. Since side effects during organogenesis are more dangerous, it is important to plan surgical or laser intervention before conception especially in uncontrolled glaucoma patients. Management of glaucoma during pregnancy is a delicate balance and may need collaboration between ophthalmologist, obstetrician, and neonatologist in high-risk pregnancies.[4,5]

Relaxin and glaucoma

Relaxin is a protein hormone presumed to be behind much of the IOP lowering effect in pregnancy. It is available commercially[6] and there is even a patent for its use, which expires in 2021.[7] As mentioned in the accompanying study,[8] relaxin has found experimental use in diseases such as cerebral cavernoma, osteosarcoma, and heart failure.[6] In this study, the authors looked for the Relaxin receptor Relaxin/Insulin-Like Family Peptide Receptor 1 (RXFP1) in sections of the anterior segment of the eye and found it in inner uveal, corneoscleral and cribriform meshwork and Schlemm's canal endothelium.[8]

Another recently studied Relaxin gene knockout ($Rln^{-/-}$) mice showed that they had higher IOP, thicker corneas, larger endothelial cells, and lower endothelial cell density.[9] They also found RXFP1 mRNA expression in the retina, cornea, sclera, and choroid, while RXFP2 was only in the cornea.

Even though Relaxin seems to have a potential to lower IOP, another study that used relaxin 2 in mice as eyedrops, intravitreally and intravenously found no lowering of IOP or change in arterial or venous diameter after 1 or 3 hours afterward.[10]

Hope that newer targets for glaucoma medications would help us to medically treat uncontrolled glaucoma especially if a surgical option is not feasible.

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