

Topical intraocular pressure therapy effects on pregnancy

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Purpose: To assess the course of intraocular pressure (IOP), visual field progression, and adverse effects of antiglaucoma medication used during pregnancy.

Methods: Thirteen eyes of eight patients with glaucoma were examined. Their clinical records were reviewed to compare IOP, number of medications, and visual field indices (VFI) before, during, and after pregnancy using a two-tailed paired *t*-test.

Results: In seven (87.5%) of the eight patients, no disease progression was observed. IOP (mmHg) remained stable (baseline 17.3 ± 3.6 ; first trimester 17.4 ± 5.2 , $P = 0.930$; second trimester 18.1 ± 4.7 , $P = 0.519$; third trimester 20.2 ± 8.7 , $P = 0.344$; and postpartum 21.5 ± 7.6 , $P = 0.136$). The mean number of glaucoma treatments fell from 1.7 ± 0.52 before pregnancy to 0.83 ± 0.75 ($P = 0.04$) in the second and third trimesters. In one patient, IOP increased during pregnancy and there was further visual field loss. In the only patient kept on fixed combination timolol–dorzolamide therapy throughout pregnancy, labor was induced because of delayed intrauterine growth.

Conclusions: No changes in IOP and VFI were detected in most patients despite a reduction in the number of hypotensive agents required. Delayed intrauterine growth in one patient under fixed combination timolol–dorzolamide treatment was observed whereas no other adverse effects were detected.

Keywords: intraocular pressure, antiglaucoma medication, glaucoma, pregnancy, breast-feeding, adverse effects

Introduction

Glaucoma progression during pregnancy varies among individuals¹ and many ophthalmologists are uncertain about the safest medical treatment during pregnancy.²

Material and methods

Eight women with glaucoma were followed at the glaucoma department of our hospital during their pregnancy. All pregnancies took place in the years between 2002 and 2010. By reviewing the clinical records, baseline, pregnancy, and postpartum intraocular pressure (IOP), glaucoma medication, and visual field indices (VFI), mean defect (MD), and loss variance (LV), (tendency-oriented perimetry; G1-TOP strategy, Octopus 1-2-3 perimeter Haag-Streit AG, Bern, Switzerland) were recorded and compared using a two-tailed paired *t*-test. Visual field loss progression was defined as an MD increase of at least 5 dB or the appearance of a new glaucomatous scotoma.

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Results

Thirteen eyes of eight women with the following types of glaucoma: congenital glaucoma (3), developmental glaucoma (2), postkeratoplasty glaucoma (1), pigmentary glaucoma (1), and bilateral ocular hypertension (1) were included in the study. Table 1 provides data on glaucoma type, age at the time of pregnancy, and surgical procedures before pregnancy.

All patients had glaucoma in both eyes with the exception of patients 2 and 4, who only had glaucoma in the right eye, and patient 7, who had suffered a left-eye evisceration as a child due to perforating trauma. Thus, IOP measurements were made in 13 eyes of the eight patients. Moreover, visual field testing was not possible in patients 5, 6, and 7 because of low visual acuity (VA) (counting fingers or less) in one eye. Accordingly, the visual field data correspond only to 10 of the 13 eyes examined. Table 2 provides the data recorded for VA, IOP, the medications used during pregnancy, and visual field loss progression.

Before pregnancy, the mean IOP was 17.3 ± 3.6 mmHg and rose to 17.4 ± 5.2 ($P = 0.930$), 18.1 ± 4.7 ($P = 0.519$), 20.2 ± 8.7 ($P = 0.344$) and 21.5 ± 7.6 ($P = 0.136$) mmHg during the first, second, and third trimester, and postpartum, respectively.

No differences were detected in the MD ($P = 0.249$) or LV ($P = 0.463$) before and after pregnancy.

The mean number of IOP-lowering medications fell from 1.7 ± 0.52 before pregnancy to 0.83 ± 0.75 ($P = 0.04$) in the second and third trimesters and was 1.17 ± 1.7 postpartum.

In patient 2, IOP increased during pregnancy (44 mmHg in the third trimester) and there was progression of visual field loss in the right eye. This primigravida woman was carrying twins, and had been prescribed total bed rest due to a risk of premature birth. She could not visit our center during the third trimester and went into spontaneous labor in week 32. After Caesarean section (C-section) due to twin babies, she underwent a trabeculectomy, which achieved

good control of pressure (IOP was 14 mmHg with timolol maleate 3 months after surgery).

Latanoprost was used, alone or in combination, for 3 months in two women (patients 4 and 8) who did not notify their state until second trimester. After that period, latanoprost was discontinued, since there is still insufficient evidence to consider this drug safe.³

Pregnancies were full-term in seven of the eight women. Deliveries were vaginal in five of the eight women; in one of them forceps were used. In patient 6, labor was induced in gestation week 36 and baby was delivered by C-section because of delayed intrauterine growth. This was the only patient kept on fixed combination timolol–dorzolamide therapy throughout pregnancy.

Patients 2 and 4 underwent C-sections due to twin pregnancies.

Six patients required postpartum ocular hypotensive treatment. Of these, five (Patients 3, 4, 6, 7, and 8) decided to continue breastfeeding and were instructed to occlude the nasolacrimal duct with a fingertip for 5 minutes after eye drop instillation to minimize systemic absorption.⁴

Discussion

The present study is the first to document both the course and outcome of labor in pregnant women receiving glaucoma medication and followed in the same center.

In seven of our eight patients (87.5%) the disease remained stable throughout pregnancy. Six of eight women required medication during pregnancy to control IOP. The most commonly used medication was timolol.

Delayed intrauterine growth in the only patient under fixed combination timolol–dorzolamide treatment was observed. There have been several reports of fetal complications from topical beta-blockers including bradycardia and arrhythmia⁵ although case reports have also described the use of these drops throughout pregnancy without any

Table 1 Glaucoma type, age at the time of pregnancy, and surgical procedures before pregnancy

Patient	Age	Glaucoma type	Prior surgery
1	33	Ocular hypertension OU	None
2	36	Developmental glaucoma OD	Trabeculectomy (n = 2)
3	31	Developmental glaucoma OU	Trabeculectomy (OD n = 2; OS n = 1)
4	30	Post-keratoplasty glaucoma OD	Penetrating keratoplasty (n = 1), cataract extraction (n = 1), Ahmed valve (n = 1),
5	17	Primary congenital glaucoma OU	Goniotomy (n = 1 OU), trabeculectomy (n = 1 OS), keratoplasty (n = 2 OS), phacoemulsification OS, Ahmed valve (n = 1 OS)
6	29	Primary congenital glaucoma OU	Trabeculectomy (OD n = 3; OS n = 2), Ahmed valve (OD n = 1; OS n = 2)
7	35	Primary congenital glaucoma OU	Trabeculectomy (OU n = 3), cataract extraction OU, evisceration OD
8	34	Pigmentary glaucoma OU	Trabeculectomy (OU n = 1)

Abbreviations: OD, right eye; OS, left eye; OU, both eyes.

Table 2 Visual acuity, IOP, number and nature of the medications used during pregnancy and visual field loss progression

Patient	Eye	Visual acuity	Visual field progression	IOP (mmHg)	Number of medications taken									
					Prepregnancy	1st trimester	2nd trimester	3rd trimester	Postpartum	Postpartum				
1	OD	20/20	No	18	21	17	16	21	1 (L)	0	0	0	0	0
	OS	20/20	No	18	21	15	14	20	1 (L)	0	0	0	0	0
2	OD	20/200	Yes	14	11	21	44	42	2 (L, T)	1 (T)	1 (T)	1 (T)	1 (T)	3 (L-T, AZ)
3	OD	20/30	No	18	17	22	24	23	2 (T, B)	1 (T)	1 (T)	1 (T)	1 (T)	1 (T)
	OS	20/40	No	16	20	18	25	23	2 (T, B)	1 (T)	1 (T)	1 (T)	1 (T)	1 (T)
4	OD	20/200	No	16	-	-	16	20	2 (L, T)	2 (L, T)	2 (L, T)	1 (T)	1 (T)	1 (T)
	OD	20/50	No	12	12	10	12	14	0	0	0	0	0	0
	OS	CF	-	17	10	12	11	17	1 (T)	0	0	0	0	0
6	OD	HM	-	22	20	23	24	16	2 (T, DZ)	2 (T, DZ)	1 (T)	2 (T, DZ)	2 (T, DZ)	2 (T, DZ)
	OS	20/40	No	26	26	20	23	26	2 (T, DZ)	2 (T, DZ)	1 (T)	2 (T, DZ)	2 (T, DZ)	2 (T, DZ)
7	OS	LP	-	16	16	23	16	13	1 (T)	1 (T)	1 (T)	1 (T)	1 (T)	1 (T)
8	OD	20/20	No	18	-	-	23	28	1 (L)	1 (L)	1 (L)	1 (T)	2 (T, BZ)	2 (T, BZ)
	OS	20/20	No	14	-	-	15	17	0	0	0	0	0	0

Abbreviations: IOP, intraocular pressure; L, latanoprost; T, timolol; T,DZ, timolol-dorzolamide, fixed combination; T,BZ, timolol-brinzolamide, fixed combination; T,B, timolol-brimonidine, fixed combination; AZ, acetazolamide; HM, hand movements; LP, light perception; CF, count fingers; OD, right eye; OS, left eye OU, both eyes.

adverse effects.¹ Use of acetazolamide during late pregnancy has been associated with sacrococcygeal teratoma and renal tubular acidosis in the newborn,^{6,7} however, there are no reported cases of adverse effects during pregnancy from topical carbonic anhydrase inhibitors.

Delayed intrauterine growth has not been described as an adverse effect of beta-blockers or carbonic anhydrase inhibitors during pregnancy although high doses of dorzolamide and brinzolamide have been reported to reduce weight gain in the offspring of lactating rats.^{8,9}

In conclusion, good glaucoma control was achieved in most of our patients despite a reduction in the number of hypotensive agents required. Delayed intrauterine growth in one patient under fixed combination timolol-dorzolamide treatment was observed. No other adverse effects were detected neither in our patients nor in their newborns.

Disclosures

Each author declares that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with this work. No financial support was received for this work.

References

- Brauner SC, Chen TC, Hutchinson BT, Chang MA, Pasquale LR, Grosskreutz CL. The course of glaucoma during pregnancy: a retrospective case series. *Arch Ophthalmol.* 2006;124:1089-1094.
- Vaideanu D, Fraser S. Glaucoma management in pregnancy: a questionnaire survey. *Eye.* 2007;21:341-343.
- De Santis M, Lucchese A, Carducci B, Cavalieri A, De Santis L, Merota A. Latanoprost exposure in pregnancy. *Am J Ophthalmol.* 2004;138:305-306.
- Johnson SM, Martinez M, Freedman S. Management of glaucoma in pregnancy and lactation. *Surv Ophthalmol.* 2001;45:449-454.
- Wagenvoort AM, van Vugt JM, Sobotka M, van Geijn HP. Topical timolol therapy in pregnancy: is it safe for the fetus? *Teratology.* 1998;58:258-262.
- Ozawa H, Azuma E, Shindo K, Higashigawa M, Mukouhara R, Komada Y. Transient renal tubular acidosis in a neonate following transplacental acetazolamide. *Eur J Pediatr.* 2001;160:321-322.
- Worsham F Jr, Beckham EN, Mitchell EH. Sacrococcygeal teratoma in a neonate. *JAMA.* 1978;240:251-252.
- Alcon Ophthalmics. *Manufacturer's Information: Azopt Product Monograph.* Fort Worth, TX: Alcon Ophthalmics; 1998.
- Merck and Co, Inc. *Manufacturer's Information: Trusopt Product Monograph.* West Point, PA: Merck and Co, Inc; 1999.

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