The effects of delivery type and gender on intraocular pressure and central corneal thickness in newborns

Os efeitos do tipo de parto e sexo sobre a pressão intraocular e espessura corneana central em recém-nascidos

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ABSTRACT

Purpose: To analyze intraocular pressure (IOP) and central corneal thickness (CCT) in newborns during the first 12 h of life.

Methods: Forty-three newborns born by vaginal delivery (VD) and 30 newborns born by cesarean section (CS) were evaluated. IOP and CCT were measured using Tono-Pen and handheld pachymeter, respectively, at both the 5th minute after delivery and at the 12th h of life.

Results: The mean IOP for the VD group was significantly higher than that of the CS group at both the 5th minute and 12th h (p=0.042 and p=0.018, respectively). In both groups, the IOP decreased by the 12th h, but the decrease was only significant for the CS group (p=0.020). The decrease in CCT over the 12 h was significant for both groups (p<0.001). In the VD and CS groups, the IOP values of the males were significantly higher than those of the females at the fifth minute only (p=0.024 and p=0.043, respectively). No other values were significantly different between the genders.

Conclusions: Newborn IOP is affected by the mode of delivery and gender. A higher IOP was found in vaginally delivered newborns than in CS newborns for at least 12 h postpartum. CCT showed a significant decline within 12 h. Male newborns have significantly higher IOP values in the first minutes of life.

Keywords: Cesarean section; Delivery, obstetric; Intraocular pressure; Cornea/anatomy & histology; Infant; Newborn

RESUMO

Objetivos: *Analisar a pressão intraocular (IOP) e a espessura corneana central (CCT) em recém-nascidos durante as primeiras 12 horas de vida.*

Método: *Quarenta e três recém-nascidos nascidos por parto vaginal (VD) e 30 recém-nascidos nascidos após cesariana (CS) foram avaliados. IOP e CCT foram medidos com Tono-Pen e Handheld Pachymeter no quinto minuto após o parto e na décima segunda hora de vida.*

Resultados: *A média de IOP para o grupo VD foi significativamente maior do que o grupo CS tanto no quinto minuto quanto na décima segunda hora (p=0,042, p=0,018, respectivamente). Em ambos os grupos, a IOP diminuiu na décima segunda hora, mas a redução foi significativa apenas para o grupo CS (p=0,020). A diminuição da CCT nas doze horas foi significativa para ambos os grupos (p<0,001). Nos grupos VD e CS os valores de IOP dos homens foram significativamente maiores do que das mulheres apenas no quinto minuto (p=0,024 e p=0,043, respectivamente). Outros valores não foram significativamente diferentes entre os sexos.*

Conclusões: *A IOP em recém-nascidos é afetada pela via de parto e pelo sexo. A IOP é maior em recém-nascidos de parto normal durante pelo menos 12 horas. A CCT mostra queda significativa no prazo de 12 horas. Recém-nascidos do sexo masculino têm valores de IOP significativamente mais elevados nos primeiros minutos de vida.*

Descritores: *Cesárea; Parto obstétrico; Pressão intraocular; Córnea/anatomia & histologia; Recém-nascido*

INTRODUCTION

Intraocular pressure (IOP) and central corneal thickness (CCT) have been measured in term and pre-term newborns in previous studies, and are well-documented[1-5]. However, no data are available on the effect of the mode of delivery on IOP and CCT or on the changes in these in the first hours of life. Birth itself, and particularly the duration of active labor until vaginal delivery (VD), is the main stressor for the infant during the peripartum period[6]. This stress results in higher plasma catecholamine levels, grades of excitability, and heart rates in vaginally delivered infants[7-9]. In previous adult and animal studies, physical and emotional stress have also been shown to induce elevation in IOP[10-11]. Thus, IOP in vaginally-delivered infants might also be affected by delivery stress.

CCT in newborns decreases during the first days of life[1,2], and the corneal endothelium is primarily responsible for the pump function. Previous studies of mouse corneas have demonstrated that the pump function of the corneal endothelium can be enhanced by dexamethasone[12,13]. During VD, stress increases the plasma levels of catecholamines[14-16]. This increment may also activate the corneal endothelial pump system and result in thinner corneas in vaginally-delivered infants. The effect of gender on CCT in newborns has been evaluated previously, and corneas in male newborns have been found to be thicker than corneas in female newborns[1]. However, the effect of gender on IOP and CCT in the first hours of life has not been analyzed.

The gold standard for IOP measurement is Goldmann applanation tonometry, and in many studies the measured IOP has been demonstrated to vary with CCT[17-19]. In recent studies, Tono-Pen XL and iCare have been recommended for obtaining accurate IOP measurements of edematous corneas[20]. These methods were presumed to be less dependent on CCT due to the smaller area of applanation[21].

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In newborns, corneas are edematous, so the Tono-Pen is a suitable instrument for measuring IOP.

In this study, we prospectively studied the behavior of IOP and CCT in newborns in terms of their delivery type and gender. Our aim was to establish a standard of normality of IOP and CCT of newborns in the first 12 h of their lives.

METHODS

This study was approved by the institutional review board of the hospital, and adhered to the tenets of the Declaration of Helsinki. In this prospective study, 43 right eyes of 43 infants born by VD and 30 right eyes of 30 infants born after elective cesarean section (CS) by epidural anesthesia at Diyarbakir Women's and Children's Diseases Hospital, were evaluated. Parental consent was obtained after the purpose and risks of the study had been fully explained.

The inclusion criteria included: infants with a gestational age between 37 and 41 weeks according to Dubowitz assessment (a method of clinical assessment in newborns from birth until five days old that includes neurological criteria for the infant's maturity and other physical criteria to determine gestational age), and with a birth weight between 2500 g and 4000 g. Further, in the VD group, infants presented cephalically, and in the CS group, infants born after elective operations, were included. The exclusion criteria were as follows: ocular abnormalities resulting in a negative red reflex; corneal and iris alterations; familial congenital glaucoma; maternal major organ dysfunction or a syndrome that can affect IOP; and complicated or assisted deliveries, general anesthesia, and the mother being given anesthetic drugs in addition to epidural anesthesia.

The ophthalmological examination included an external examination, testing of pupil reactivity, and visualization of the red reflex. Measurements were performed using the smallest wire lid speculum under topical anesthesia (proparacaine hydrochloride 0.5%) in a supine position. The right eyes of all the newborns were measured by the same operator. The newborn was given time to become accustomed to the speculum (quiet and still) to avoid a Valsalva-like effect. IOP and CCT were measured centrally immediately after the delivery at the fifth minute and at the 12th h of the postpartum period. IOP was determined using the Tono-Pen AVIA (TPA; Reichert Inc., Depew, NY, USA). The TPA displays the mean of 10 independent readings, along with a statistical confidence index. Each series of measurements was performed three times, and the mean was taken into account. The mean of the measurements was accepted with a confidence index of 95%, which represents very reliable measurements. CCT was determined using the Palm Scan AP2000 Handheld Pachymeter (Micromedical Devices, Inc., Englewood, CO, USA), by determining the mean of four independent readings.

Statistical calculations were performed using the SPSS 15.0 statistical package (SPSS for Windows, Chicago, IL, USA). All data are presented as the mean ± standard deviation. The distribution of the data was analyzed using the Kolmogorov-Smirnov test, and the distributions of IOP and CCT were found to be normal; therefore, parametric tests were used. Qualitative data were evaluated using the paired samples *t*-test and the independent samples *t*-test. The Pearson test was used for correlation analysis, and a *p*-value of <0.05 was regarded as statistically significant.

RESULTS

In this study, 43 right eyes of 43 infants (28 girls, 15 boys, ratio: 1.86) born by VD and 30 right eyes of 30 infants (18 girls, 12 boys, ratio: 1.5) born by CS, were evaluated. In the VD group, the mean gestational age at birth was 38.4 ± 0.63 weeks (range: 37-41 weeks), and the mean birth weight was 3199 ± 329 g (range: 2700-3900 g). In the CS group, the mean gestational age at birth was 38.4 ± 0.62 weeks (range: 37-40 weeks), and the mean birth weight was 3290 ± 349 g (range: 2770-4000 g). Differences between the two groups in terms of gestational age, birth weight, and gender were not statistically significant (p=0.957, p=0.388, and p=0.656, respectively). The mean IOP and CCT values for both groups at the fifth minute and at the 12th h of the postpartum period are shown in table 1. The independent samples *t*-test was used to compare the IOP and CCT values between the VD and CS groups. The IOP values of the VD group were significantly higher than those of the CS group, both at the fifth minute and at the 12th h of the postpartum period (p=0.042 and p=0.018, respectively). In the CS group, the IOPs of five newborns were above 21 mmHg at the fifth minute (range: 31-23 mmHg), and the IOP of two of these infants (40%) remained above 21 mmHg at the 12th h (23 and 28 mmHg). In the VD group, the IOPs of 16 newborns were above 21 mmHg at the fifth minute (range: 43-22 mmHg), and the IOP of five of these infants (31.25%) remained above 21 mmHg at the 12th h (range: 35-22 mmHg). The CCT differences between the two groups were not statistically significant (p=0.188 and p=0.075, respectively). We analyzed the changes in IOP and CCT between the fifth minute and 12th h in both groups, using the paired samples *t*-test. The CCT values for both the VD and CS groups declined significantly (p<0.001 for both groups). In the VD group, the IOP appeared to be decreased, but the difference was not statistically significant (p=0.120). Conversely, IOP decreased significantly in the CS group (p=0.020). We analyzed the correlations between the IOP and CCT values in both delivery groups at both measurement times. In the VD group, a weak correlation was found at the fifth minute and 12th h (p=0.006, r=0.416 and p=0.000, r=0.538, respectively). However, in the CS group, no correlation was found at the fifth minute and 12th h (p=0.870, r=-0.031 and p=0.665, r=0.082, respectively).

In the VD and CS groups, we also evaluated the effect of gender on IOP and CCT both at the fifth minute and at the 12th h of the postpartum period. The VD group values are shown in table 2, while the CS group values are shown in table 3. In the VD and CS groups, the IOP values of the males were significantly higher than those of the females at the fifth minute (p=0.024 and p=0.043, respectively). When the delivery type was not taken into account, at the fifth minute all of the males' IOP was again significantly higher than that of the females (p=0.003). In the VD and CS groups, at the fifth minute, the CCT values of the males were not significantly different to those of the females (p=0.091 and p=0.841, respectively). Further, when the delivery

Table 1. IOP and CCT values of the VD- and CS-delivery groups at the fifth minute and at the 12th hour of the postpartum period

Measurement time	Delivery type	Newborn numbers	Mean IOP ± SD (mmHg)	IOP range (mmHg)	Mean CCT ± SD (µm)	CCT range (µm)
5th min	VD	43	21.6 ± 6.2	13-45	681 ± 55	535-789
	CS	30	18.9 ± 4.6	12-31	703 ± 86	556-916
12th h	VD	43	19.8 ± 5.6	11-35	595 ± 53	510-721
	CS	30	16.9 ± 4.2	9-28	623 ± 80	500-820

IOP= intraocular pressure; CCT= central corneal thickness; VD= vaginal delivery; CS= cesarean section; SD= standard deviation.

Table 2. IOP and CCT values of both genders at the fifth minute and at the 12th h of the postpartum period in the VD group

Measurement time	Gender	Newborn numbers	Mean IOP ± SD (mmHg)	IOP range (mmHg)	Mean CCT ± SD (µm)	CCT range (µm)
5th min	Female	28	20.1 ± 5.1	13-32	670 ± 51	535-752
	Male	15	24.5 ± 7.0	17-43	700 ± 58	584-789
12th h	Female	28	19.3 ± 5.0	11-32	582 ± 42	510-664
	Male	15	20.9 ± 6.8	12-35	619 ± 63	518-721

IOP= intraocular pressure; CCT= central corneal thickness; SD= standard deviation; VD= vaginal delivery.

Table 3. IOP and CCT values of both genders at the fifth minute and at the 12th h of the postpartum period in the CS group

Measurement time	Gender	Newborn numbers	Mean IOP ± SD (mmHg)	IOP range (mmHg)	Mean CCT ± SD (µm)	CCT range (µm)
5th min	Female	18	17.3 ± 3.3	12-25	699 ± 75	556-916
	Male	12	21.1 ± 5.4	16-31	705 ± 94	559-864
12th h	Female	18	15.9 ± 3.6	12-23	626 ± 81	513-820
	Male	12	18.4 ± 4.7	9-28	618 ± 82	500-817

IOP= intraocular pressure; CCT= central corneal thickness; SD= standard deviation; CS= cesarean section.

type was not taken into account, there was no significant difference of the CCT values between the genders (p=0.360). At the 12th h, IOP values between the genders were not significantly different in the VD group, CS group, or in all of the studied newborns (p=0.386, p=0.107, and p=0.155, respectively). Similarly, at the 12th h, the CCT values between the genders were not significantly different in the VD group, CS group, or all of the studied newborns (p=0.055, p=0.811, and p=0.225, respectively).

DISCUSSION

In recent studies, IOP and CCT have been evaluated in pre-term and full-term newborns. However, to the best of our knowledge, CCT and IOP values immediately after birth and after 12 h have not been studied. Therefore, the current study is the first to report the effect of the mode of delivery and gender on IOP and CCT in the first 12 h of life.

Active labor is the main cause of stress for infants during the peripartum period[6]. The final effectors of physical and emotional stresses during birth are glucocorticoids and the main actors are catecholamines such as adrenaline and noradrenaline. Previously published studies have shown that plasma catecholamine levels of infants born by CS are lower than those of infants born by VD[6,7]. Another study identified a significant correlation between a lower plasma level of noradrenaline and poor muscle tone and/or lower grade of excitability in infants born by CS compared to infants born by VD[8]. In the first minutes of life, higher heart rates have also been reported in infants born by VD compared to infants born by CS[9]. Psychological stress is known to induce elevated IOP in adults[10]. In our study, IOP values were significantly higher in the VD group than in the CS group at the fifth minute. The psychological stress of VD may be the cause of the higher IOP.

In the present study, IOP was also measured at the 12th h of the postpartum period. Although the IOP had decreased by the 12th h in both groups, the IOP values of the VD group were still significantly higher than those of the CS group. In a previous study, infant saliva cortisol levels were examined 72 h after birth, and higher levels were observed in the VD group than in the CS group[6]. The study demonstrated that the effects of delivery stress continue for at least 72 h postpartum. Therefore, the higher IOP in the VD group at the 12th h may have been the result of sustained higher cortisol levels.

Fetuses delivered vaginally are at greater risk of head compression than those delivered by CS. The direct physical effect of vaginal birth may be the reason for this increment in IOP. Further, the intracranial major venous system may be affected by the increased pressure around it due to the thin wall structure of the venous vessels. The effect of the mode of delivery on cerebral hemodynamics has been discussed in previous studies[22,23]. Moreover, similar changes of cerebral hemodynamics have been observed in newborns delivered by VD and CS[24]. Additionally, no correlation was found between the duration of labor and venous and arterial Doppler indices and velocities[25]. These data support our theory of hormonal effects on the IOP of newborns.

In our study, at the fifth minute, IOP of males was found to be significantly higher than that of females in both delivery groups. In a previous study, IOP was measured in 150 newborns between 12 and 24 h after birth, and again no significant difference was found between the genders[4]. This result is similar to the results of our study, because in our study the difference between the genders was only significant at the fifth minute. At the 12th h, however, while the males' mean IOP values appeared to be higher than those of the females in both delivery groups, the differences were not statistically significant. As far as we know, none of the studies researching delivery stress, cerebral hemodynamics, and the IOP of newborns have evaluated the effect of gender. Further investigation is necessary to understand the reason for the higher IOP values in males.

Newborn CCT has also been evaluated in recent studies. The earliest measurements in the literature were performed at 6 h postpartum without grouping the newborns according to delivery type. The mean CCT was 647 ± 61 µm at 0-6 h postpartum and 611 ± 72 µm at 7-12 h postpartum[1]. For both groups, our results were higher than those of the previous study at 0-6 h postpartum, most likely due to our earlier measurement time. The effect of gender on the CCT of newborns was evaluated in the same study, at six days postpartum. In males, the mean CCT was 631 ± 67 µm in the right eyes and 630 ± 65 µm in the left eyes, while in females, these values were 601 ± 52 µm in the right eyes and 559 ± 49 µm in the left eyes; the difference between the genders was statistically significant[1]. In another study,

the effect of gender was evaluated again at six days postpartum. The mean CCT of the males was again found to be higher than that of the females, but the difference was not significant[2]. In our study, although the differences did not reach statistical significance, in the VD group the males' mean CCT at both times was higher than that of the females. In the CS group, the differences between the genders were negligible. In the previous studies mentioned above, the delivery type was not taken into account. If the newborns had been grouped according to delivery type, the results could have been more significant in the VD groups.

Previous studies have reported a decline in CCT in newborns during the first days of life[1,2]. In our study, this decrease was highly significant in both the VD and CS groups. This decline is thought to be due to improving control of corneal hydration, evaporation, and corneal remodeling over time[2,5]. Prolonged eye closure may explain the thicker corneas during the first days of life. Infants are known to have physiologic intracellular fluid excess and, after birth, sudden fluid efflux occurs from the intracellular compartment to the extracellular compartment[26]. In addition to prolonged eye closure, physiologic intracellular fluid excess might be the cause of the edematous cornea.

The respiratory outcome in newborns is linked to fetal maturity and the mode of delivery. Infants delivered by CS have a higher incidence of respiratory distress than vaginally delivered infants. Active Na^+ transport across the pulmonary epithelium drives liquid from the lung lumen to the interstitium, and labor is critical for the activation of the Na^+ pump system. There is considerable evidence that high levels of endogenous catecholamines at birth may be important for accelerating alveolar fluid clearance by increasing its activity[27]. In our study, although the differences were not statistically significant, the mean CCT was higher for the CS group than for the VD group both at the fifth minute and at the 12th h. The Na^+- and K^+-dependent ATPase (Na^+/K^+-ATPase) expressed in the basolateral membrane of corneal endothelial cells is primarily responsible for the pump function of the corneal endothelium. In two different studies of mouse corneal endothelial cells, dexamethasone was shown to increase Na^+/K^+-ATPase activity and pump function[12,13]. We suggest that, like the pulmonary epithelium Na^+ transport system, the corneal endothelial pump function may be induced by higher endogenous plasma catecholamine levels in vaginally-delivered infants, causing thinner CCT values in the VD group than in the CS group.

To measure IOP and CCT in newborns, a protocol based on the experiences documented in previous studies was used. A previous study reported that the use of the Alfonso eyelid speculum in children can falsely elevate IOP by 4 mmHg[28]. Further, topical anesthetics have been found to affect IOP and CCT readings[29,30]. Therefore, the use of a speculum and topical anesthetic drops are limitations of our study. The small number of cases involved in our study is another limitation. Since the international gold standard for IOP measurement is Goldmann applanation tonometry, the use of a Tono-Pen in our study could be considered a limitation. However, Tono-Pen XL and iCare have recently been recommended for obtaining accurate IOP measurements of edematous corneas[20]. These methods were presumed to be less dependent on CCT due to the smaller area of applanation[21]. The duration of active labor of the deliveries was not taken into account because, in our region, most pregnant women arrive at hospital after the beginning of active labor, which is another limitation of our study.

In conclusion, IOP remains higher in vaginally-delivered infants than in infants delivered by CS for at least 12 h postpartum. Infant CCT decreases significantly over the 12 h postpartum. Vaginally-delivered infants have thinner CCT values than infants delivered by CS. The present study establishes reference values for IOP and CCT in newborns, which could be used in the early diagnosis of congenital eye disorders. Additionally, these data may be useful for understanding the ocular physiology of newborns. Further studies are needed to clarify the possible effects on IOP and CCT in newborns.

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