Determination of normal values of intraocular pressure and central corneal thickness in healthy premature infants—a prospective longitudinal study

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PURPOSE To evaluate the longitudinal change of intraocular pressure (IOP) and central corneal thickness (CCT) in healthy premature infants.

METHODS Premature infants born at 28 weeks' gestational age were included in this prospective, single-center longitudinal study. IOP was measured by handheld applanation tonometer (Tono-Pen Avia); CCT measurements were performed by ultrasonic pachymeter. Examinations were held at 32 weeks' gestational age initially and at 2-week intervals thereafter for a total of 5 consecutive measurements by the same ophthalmologist.

RESULTS A total of 110 right eyes of 110 healthy premature infants were analyzed. The mean IOP at 32 weeks' gestational age was 18.28 ± 2.78 mm Hg; mean CCT, 670.56 ± 55.72 μm. Mean IOP and CCT thereafter were 16.13 ± 2.20 mm Hg and 613.67 ± 48.11 μm in week 34, 14.67 ± 2.04 mm Hg and 579.24 ± 43.73 μm in week 36, 13.49 ± 2.08 mm Hg and 551.91 ± 40.75 μm in week 38, and 13.21 ± 1.94 mm Hg and 546.18 ± 38.70 μm in week 40. The longitudinal changes of mean IOP and CCT values between 5 consecutive measurements were statistically significant ($P < 0.001$, for each).

CONCLUSIONS IOP and CCT values decrease longitudinally in healthy premature infants between 32 and 40 weeks' gestational age. Elevated IOP values, which were identified in the early premature period, seem to be associated with higher CCT values. (J AAPOS 2016;20:239-242)

Elevated intraocular pressure (IOP) is the most important risk factor for glaucomatous damage.[1] Although IOP measurements are significantly affected by central corneal thickness (CCT) in adults, the exact role of CCT in preterm infants is still unclear.[2] Determination of normal intervals of these parameters is important for glaucoma diagnosis in premature infants. Various cross-sectional studies have been carried out to measure IOP and CCT in premature and neonatal infants in order to determine the normal ranges.[3-10] In a prospective cross-sectional study, we previously determined a negative linear relationship between postconceptional age (PCA) and IOP and CCT and a significantly positive correlation between IOP and CCT in 470 premature infants.[3] The present study aimed to determine the normative IOP and CCT data in healthy premature infants and to evaluate the *longitudinal* change of these parameters.

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Subjects and Methods

This study was approved by the Ethics Committee of the Zekai Tahir Women's Health Training and Research Hospital. Informed consent of parents was obtained prior to screening examination for premature retinopathy (ROP), in accordance with the Helsinki Declaration. Premature infants who would be screened for ROP at 28 weeks' gestational age were included in this prospective, longitudinal study. In order to form a normative database for healthy premature infants, premature infants with diseases or conditions such as congenital eye abnormalities (pathologies related to cornea, iris and the lens, and glaucomatous optic disc abnormalities), systemic abnormalities (for example, chromosome disorders, visceral anomalies and topical or systemic corticosteroid usage history), genetic anomalies, or diseases and conditions that might affect IOP and CCT were excluded. Because clinical conditions of premature infants show differences in early weeks of the life, initial measurements were made at 32 weeks' gestational age. Premature infants with low birth weight compared to the 28-week average (<550 g for girls, <600 g for boys) and with weight gain problems in follow-up examinations were also excluded.[11] PCA, in weeks, at the time of the examination were recorded for all infants. IOP and CCT measurements were performed by the same experienced ophthalmologist (DEA), as explained in detail previously.[3] In brief, IOP was measured using the Tono-Pen Avia (Reichert Inc, NY). The mean of 3 consecutive measurements was calculated and recorded. CCT was measured using an ultrasonic pachymeter (Compact Touch 3-in-1 Ultrasound System; Quantel

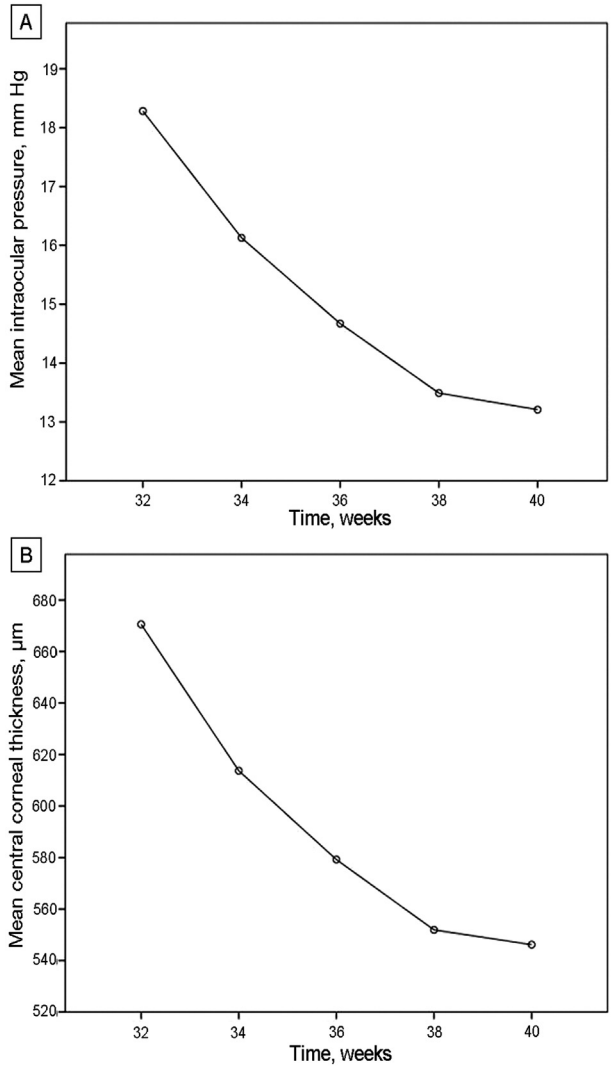

FIG 1. A, Intraocular pressure (IOP) and B, Central corneal thickness (CCT) changes with postconceptional age in premature infants.

Medical, Cournon d'Auvergne, France). The pachymeter probe was placed on the center of the cornea and the mean of 5 consecutive measurements was calculated and recorded. We ensured that infants were calm and relaxed during measurements. These measurements were taken initially at 32 weeks' gestational age and thereafter at 2-week intervals (weeks 34, 36, 38, 40). Data obtained from right eyes of infants were used for statistical analysis.

Statistical Analysis

Mean and standard deviation values were used to describe the quantitative variables. Frequency and percentages were calculated for the nominal data. Normality assumption was checked using the Shapiro-Wilk test, and the data were found to be consistent with a normal distribution. The repeated measures analysis of variance test was used to assess changes over time for IOP and CCT. Bonferroni adjusted *P* values were used for multiple comparisons over time. Pearson correlation coefficients were calculated for values of IOP and CCT. SPSS Statistics for Windows,

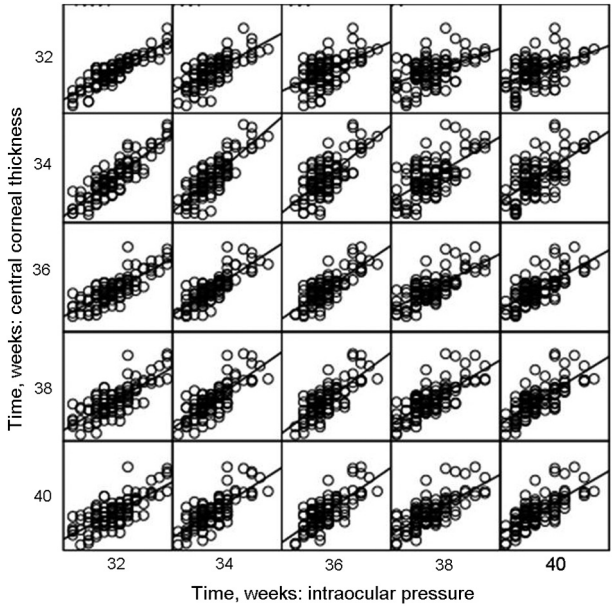

FIG 2. Correlation graph of IOP and CCT in premature infants. (Pearson's $r = +0.798$, $P < 0.001$).

version 21.0 (IBM Corp, Armonk, NY). Statistical significance was set at $P < 0.05$.

Results

A total of 110 right eyes of 110 infants were enrolled at gestational age of 28 weeks. At 32 weeks' gestational age, the mean IOP was 18.28 ± 2.78 mm Hg; the mean CCT was 670.56 ± 55.72 µm. At week 34, mean IOP was 16.13 ± 2.20 mm Hg; mean CCT, 613.67 ± 48.11 µm. At week 36, mean IOP was 14.67 ± 2.04 mm Hg; mean CCT, 579.24 ± 43.73 µm. At week 38, mean IOP was 13.49 ± 2.08 mm Hg; mean CCT, 551.91 ± 40.75 µm. At week 40, mean IOP was 13.21 ± 1.94 mm Hg; mean CCT, 546.18 ± 38.70 µm. The decrease of IOP and CCT values in time were statistically significant ($P < 0.001$, for each; Figure 1). There was a statistically significant positive linear relationship between IOP and CCT values (Pearson's $r = +0.798$, $P < 0.001$; Figure 2).

Discussion

This study investigated the longitudinal change of IOP and CCT normative values in 110 healthy premature infants by performing 5 consecutive measurements beginning at 32 weeks' gestational age and found that IOP and CCT values were decreasing significantly. There are few studies that evaluate the longitudinal change of IOP.[12-14] Ricci[12] made 5 consecutive IOP measurements in 40 eyes of 20 preterm infants at gestational ages ranging between 26-32 weeks and who were in the first postnatal month. He performed the first IOP measurement on the day 1 or 2 and then on days 7, 14, 21, and 28 using a handheld applanation tonometer (Pro-Ton); he reported that the