Effect of Photorefractive Keratectomy on the Accuracy of Pneumatonometer Readings in Rabbits

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Purpose. To determine whether measurement of intraocular pressure (IOP) using a pneumatonometer is reliable after myopic 5 or 15 D excimer laser photoablation in rabbits.

Methods. Ten rabbits underwent 5 D myopic photorefractive keratectomy (PRK) of the left eye. Another seven rabbits underwent 15 D PRK. The right eye served as a control. The diameter of each PRK was 5 mm. Rabbits were examined 2.5 to 3 months later under general anesthesia. Eyes were cannulated, and the IOP was maintained at 5 to 40 mm Hg and measured using an intracameral manometer and a pneumatonometer at each pressure level; approximately 50 pressure points were formed. Readings of the two techniques were compared.

Results. Linear regression analysis comparing manometric and pneumatonometric readings revealed the following data in eyes with 5 D corrections (n = 10): correlation coefficient (r) = 0.926, slope = 1.058, and intercept = —3.133. The values of the unoperated control eyes were: r = 0.900, slope = 0.962, and intercept = —1.010. The following results were obtained in eyes with 15 D photoablation (n = 7): r = 0.876, slope 1.133, and intercept —3.147. Values for the control eye were: r = 0.885, slope = 1.175, and intercept = —3.497. When the manometer and pneumatonometer readings of all animals were compared, the adjusted squared correlation coefficient was 79%. When the variabilities associated with the animals and the PRK procedure (pooled 5 and 15 D corrections) were taken into account, adjusted squared correlation coefficient increased from 8% to 87%.

Conclusions. Photorefractive keratectomy as high as 15 D/5 mm had only a minor effect on pneumatonometer readings in rabbits, indicating that the elastic properties of the cornea related to the accuracy of pneumatonometry were not significantly altered. Postoperative IOP monitoring with tonometers, based on flattening of the cornea under pressure, is accurate after PRK.

Excimer laser photorefractive keratectomy (PRK) for surgical correction of myopia, astigmatism, or hyperopia has become favored throughout the world. Although the procedure is safe and relatively accurate, some side effects do occur, and haze is one of the most important. Thick central corneal haze may have an impact on the reliability of tonometer readings and may impair the visualization of the optic nerve head.

Despite some controversy, postoperative steroids appear to reduce postoperative haze and myopic regression, although the need for such treatment is questionable in PRK for low and moderate myopia. Elevation of the intraocular pressure (IOP) because of prolonged corticosteroid treatments (prevalence, 13% to 25%) has been reported after PRK; hence, pressure-induced optic nerve damage with visual field loss, presumably caused by prolonged use of postoperative topical steroids, is one of the concerns of PRK surgeons. Nonsteroidal anti-inflammatory drugs do not cause a rise in IOP and may be useful in the control of postoperative pain as well as in the reduction of postoperative myopic regression. However, there is some controversy about the latter effect. Nevertheless, patients with glaucoma probably are good subjects for PRK because contact lens wear is not recommended for patients under standard topical antiglaucoma regimens.

Photorefractive keratectomy removes the Bowman’s layer and as much as one third of the corneal...
stoma, depending on the amount of myopic refractive error to be corrected. It was thought that this would lead to additional problems, such as keratocorneal thickening or permanent alteration of corneal rigidity. The latter may lead to bulging of the central cornea and, hence, to unpredictable refraction.15

Consequently, the reliability of the IOP measurements after PRK has been questioned.16 To clarify this, we performed 5 or 15 D PRKs (diameter, 5 mm) on rabbits. The IOP was measured with a pneumotonometer at various IOP levels and simultaneously recorded with an intracameral manometer 2.5 and 3 months after surgery.

MATERIAL AND METHODS

Animals

Seventeen New Zealand White rabbits of both sexes, each weighing 1 to 2 kg at the time of PRK, were used in the current study. The animals were treated in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. The design of the experiment was approved by the Experimental Animal Committee of Helsinki University Eye Hospital.

Laser Procedure

Each operation was performed under combined general and topical anesthesia. Intravenous anesthesia was induced with a mixture of ketamine hydrochloride (Ketalar; Parke-Davis, Barcelona, Spain) and xylazine hydrochloride (Rompun Veterinary; Bayer, Leverkusen, Germany). Oxybuprocaine eye drops (Oftan Ocu-cain; Leiras, Tampere, Finland) were administered several times before and during the operation. Ten of the animals underwent 5 D PRK, and an additional seven underwent 15 D PRK. The diameter of each photoablation was 5 mm, and each was performed on the right eye, whereas the left eye served as a control. Ablation depth was 122 μm—comparable to 9.5 D PRK using a diameter of 6 mm. A 15 D/6 mm PRK would require an ablation of 165 μm. On the other hand, the thickness of the central stroma of a rabbit is approximately 20% thinner than that of humans (0.35 mm versus 0.42 mm).

The epithelium was removed with the laser using the phototherapeutic keratectomy mode and 55-μm ablation depth, and the photoablation subsequently was performed. Surgery was performed with a VisX 20/20 (VisX, Sunnyvale, CA) excimer laser equipped with 4.01 software. The fluence was set at 160 mJ/cm², and the repetition rate was at 5 Hz.

Postoperative medication included gentamycin (Garamycin; Schering-Plough, Kenilworth, IL) or chloramphenicol ointment (Oftan Chloral; Leiras) twice daily for 3 days, after which tobramycin ointment (Tobrex; Alcon, Fort Worth, TX) drops were administered twice daily for 1 week. Epithelial wounds healed in 2 to 4 days, but 5 of 10 rabbits in the 5 D group and 4 of 7 rabbits in the 15 D group exhibited one or more recurrent erosions. Postoperative haze developed 3 to 5 weeks after surgery and persisted in all eyes until the end of the study.

Intraocular Pressure Measurement

Animals were anesthetized 2.5 to 3 months after the PRK with an intramuscular combination of ketamine hydrochloride and xylazine hydrochloride (see above), and they were maintained under anesthesia with an intravenous infusion of sodium pentobarbital (Mebumol; Orion-Farmos, Turku, Finland). Local anesthesia was induced with oxybuprocaine hydrochloride. Eyes were cannulated with two 27-gauge needles connected to polyethylene tubings; one cannula was used for IOP monitoring with a manometer (Grass 79 D Polygraph; Grass Instrument, Quincy, MA), and one was used for infusion of sodium chloride (Natrosteril 0.9%; Medipolar, Oulu, Finland) used for maintaining different (5 to 40 mm Hg) IOP levels. Both manometer and pneumotonometer (Mentor Modular One Pneumonometer; Mentor O & O, Norwell, MA) readings were registered at approximately 50 different pressure points per eye. After completing the experiments, the rabbits were killed by overdoses of sodium pentobarbital.

Statistical Methods

Slope, intercept, and correlation coefficient values were obtained using a Sigmaplot SPW 2.01 program. Multiple regression analysis comparing manometric and pneumotonometer measurements was used to assess the adjusted squared correlation coefficient with a SPSS/PC 4.01 program. Confidence intervals (CI) were determined using the Confidence Interval Analysis program.

RESULTS

5 D Corrections

Control eyes (n = 9) and eyes that underwent 5 D PRK (n = 10; Fig. 1) showed good correlation between pneumotonometer and manometric IOP values. The variability of measurements increased slightly and in parallel with IOP, but the curves were linear and showed reasonably high correlation coefficients (control eyes, r = 0.900; 5 D PRK eyes, r = 0.926). The 95% CI were 0.880 to 0.917 and 0.912 to 0.937, respectively. The intercept in the control group was −1.010 (CI = 1.860 to −0.163), and in experimental eyes it was −3.133 (CI = −3.820 to −2.450); slope values

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were 0.962 (CI = 0.918 to 1.010) and 1.058 (CI = 0.880 to 0.917), respectively. Only relatively minor interindividual variations were observed.

**15 D Corrections**

Results showed no significant change in the IOP pneumatonometer reading curve (Fig. 2). The correlation coefficient was now 0.885 (CI = 0.859 to 0.907) in the contralateral control eye and 0.876 (CI = 0.850 to 0.898) in the operated eye, indicating sufficient accuracy of the measurement. The intercept in the control group was −3.497 (CI = −4.780 to −2.210), and in the 15 D PRK group it was −3.147 (CI = −4.290 to −2.010); slope values were 1.175 (CI = 1.110 to 1.240) and 1.133 (CI = 1.070 to 1.200), respectively.

The adjusted squared correlation coefficient value among the pneumatonometer and manometer readings of all animals (controls and PRK eyes) was 79%. When possible sampling errors were adjusted and both 5 D and 15 D corrections were all taken into account, the adjusted squared correlation coefficient rose from 8% to 87%. Moreover, when the IOP values obtained were situated in the regression equation at 15, 20, or 25 mm Hg manometric pressure levels, the pneumatonometer reading always deviated <2.3 mm Hg (5 D PRK at 15 mm Hg) from the manometric pressure.

**DISCUSSION**

The central rabbit corneal stroma is approximately 20% thinner (0.35 versus 0.42 mm) than human stroma, and, according to our experience, the epithelium also heals more slowly. Consequently, we chose to perform a 15 D/5 mm PRK on our young (1.5 kg) rabbits. The ablation depth (122 μm) was approximately 25% less than that of a 15 D/6 mm PRK (165 μm). The latter is standard for human PRK in VisX 20/20 excimer lasers. However, 5 mm PRKs have also been performed by older excimer lasers.

Liwin et al., using human postmortem eyes, observed the formation of central corneal bulging after deep PRK. This could compromise the accuracy of tonometer readings. It is assumed that if the increased corneal flaccidity produced the observed change in corneal curvature, a deep photoablation also would have caused a change in the elastic properties of the cornea and, hence, have an impact on the accuracy of tonometer readings. This type of PRK also could induce the development of irregular astigmatism known to impair the accuracy of the measurement of IOP.

The current results, however, showed that 5 or 15 D PRK did not lead to significantly less accurate pneumatonometer readings 3 months after the procedure. A relatively good correlation existed between electronic, Goldmann, and pneumatonometer values. The observed good correlation, also shown in the current study, between the pneumatonometer and manometer IOP readings obtained in the operated and control eyes shows that the Modular One (Mentor) pneumatonometer was relatively accurate throughout the pressure range tested.
Our results on control and operated eyes correspond well with those reported by Menage et al., who compared the accuracy of an electronic Tono-Pen tonometer (Mentor O & O), minified Goldmann tonometer, and the current Model 30 R (Mentor O & O) pneumatonometer after PRK performed on postmortem human eyes. The ProTon electronic tonometer recently was reported to correlate well with the standard Goldmann tonometer in a study of 196 human eyes. With regard to the comparison between the current electronic tonometers, Midelfart and Wiggers also found in a study with human patients that the ProTon electronic tonometer (Tomey Technology, Santa Ana, CA) was slightly more accurate than the TonoPen when compared with the standard Goldmann tonometer. The ProTon electronic tonometer, on the other hand, has been reported to be slightly more accurate than the pneumatonometer. The latter tends to overestimate the intraocular pressure in grafted or normal postmortem human eyes, although the differences have generally been less than or equal to 2 to 4 mm Hg. In the current study, the pneumatonometer (Modular One; Mentor) gave even more reliable results and correlated well with the manometric values. A tendency to minor underestimation (negative intercepts) may have occurred, and it could be because live rabbits were used rather than postmortem human eyes.

The relatively minor interindividual variation among the animals suggests that only a minimal change occurred in physical elastic properties of the cornea even after a 5 mm-wide 15 D PRK. This conclusion is supported by Hjortdal and Ehlers, who reported that photoablation of as much as 70% of the stroma induced only insignificant elastic changes in the central corneal radius of enucleated human globes. Consequently, we propose that PRK at its usual range (2 to 10 D) does not disturb clinical monitoring of IOP with a pneumatonometer. Because there is a relatively good correlation between the current tonometers (pneumatonometer, Goldmann applanation tonometer, and electronic tonometers) with manometric IOP measurements, the concern that a standard Goldmann tonometer would not be a clinically reliable means of detecting patients with elevated IOP after PRK may be exaggerated.

Recently, Schipper et al. reported a decrease of 2 to 3 mm Hg in central corneal Goldmann tonometer readings after 3 to 10 D PRKs (mean, 6.40 ± 1.90 D) performed on 35 human eyes. They compared Goldmann tonometer readings obtained from central and peripheral cornea before and after PRK. Although this setup might have caused a minor bias (the elastic properties of the limbal cornea may be different), the results do not necessarily contradict ours because of the relatively small decrease in tonometer readings reported by them. We were unable, however, to detect any statistical difference between the pneumatonometer and manometer readings either before or after 5 or 15 D PRK (diameter 5 mm) performed on rabbits. The final answer to this question, however, can only be obtained when a large series of patients who un-
ndergo PRK has been monitored by modern visual field and/or optic nerve head laser scanning techniques and compared with their matched cohorts.

Key Words
corneal biomechanics, excimer laser, intraocular pressure, pneumatonometry, rabbit cornea.

References