Continuous Measurement of Intraocular Pressure in Rabbits by Telemetry

Jay W. McLaren, Richard F. Brubaker, and J. Susan FitzSimon

Purpose. Intraocular pressure (IOP) is dynamic and can be influenced by the use of tonometers. The authors developed a technique to implant a telemetric pressure transducer to measure IOP continuously in unrestrained rabbits.

Methods. A commercial telemetric pressure transducer was implanted subcutaneously on the dorsal neck, between the scapulae, of pigmented rabbits. A fluid-filled catheter that conducts pressure to the transducer was routed to the orbit subcutaneously and implanted in the anterior chamber through a limbal opening. The transducer measured pressure and broadcast this information by amplitude modulation radio to a receiver in the animal’s cage. Data were recorded at a rate of 50 or 100 samples per second for 60 seconds to study transient changes in IOP to tonometry, or for 15 seconds every 2.5 minutes to study circadian behavior of IOP.

Results. Intraocular pressure was recorded from seven rabbits for 180 to 370 days. Within 3 to 8 days of implant surgery, IOP began to follow a circadian rhythm: IOP decreased after room lights were turned on at 00:00 CT and increased after they were turned off at 12:00 CT. (The term CT refers to circadian time and begins at 00:00 CT when lights are turned on.) The maximum difference in IOP between light and dark phases ranged from 6.4 mm Hg to 16.6 mm Hg. When the lighting cycle was advanced by 6 hours, the time of nocturnal rise in IOP also advanced, but it did so gradually over 10 to 14 days.

Conclusions. The implanted pressure transducer provides a convenient, preinvasive method to measure and study IOP in unrestrained experimental animals. This technique will be used to study circadian variations in IOP, the effects of environmental stimuli, and the oculohypotensive effects of therapeutic agents.

Intraocular pressure (IOP) is dynamic. It rises and falls from minute to minute as muscle tone and physiologic states of the subject change. In humans, IOP has a repeated diurnal pattern and is often different after awakening a subject from sleep than when the subject has been awake and alert. Investigators have studied this rhythm in patients with glaucoma, and some have suggested that extreme pressures outside the physician’s office contribute to optic neuropathy in low-tension glaucoma. Diurnal changes in IOP have been reviewed recently by Wilensky. Animals trained to a 24-hour lighting cycle also exhibit a well-defined circadian rhythm in IOP synchronized to the onset of light and dark and have been used as an experimental model to study why IOP has the cycle it does.

Although we base many clinical decisions on IOP, measuring it a few times during a day may give only a partial view of how a patient’s IOP behaves. For example, we do not know what happens to IOP when the patient is not approached with a tonometer or after the patient leaves the physician’s office. Intraocular pressure during sleep may be different from IOP before sleep or immediately after awakening. Differences in IOP with time of day and from patient to patient could affect therapeutic decisions if this information were available. Knowing IOP in the absence of the physician or investigator would advance our understanding of ocular dynamics and would provide...
insight into better methods of treating hypertensive eyes.

Ideally, one would measure IOP in the subject's normal environment without the subject's knowing it had been measured. Intraocular pressure should be measured at regular intervals for as long as necessary to study the principle being investigated. A telemetric tonometer would serve this purpose well. This device would be worn or implanted in the eye and would transmit information about IOP to a nearby receiver and recorder.

Several telemetric tonometers have been designed and used in experimental animals, and a few have been tested in humans. These devices were implanted surgically or incorporated into contact lenses; they measured IOP and transmitted this information to a nearby antenna and receiver. Collins34,35 invented a pressure-sensitive radio capsule that he implanted in the vitreous or anterior chambers of rabbits. The resonant frequency of a simple electric circuit in this device changed as the surrounding pressure changed. Resonance was detected from outside the eye with a grid-dip meter and an electronics package that converted this signal to IOP. The capsules were 2 to 5 mm in diameter and were well tolerated by rabbits. Signal strength depended on the orientation of the capsule to the receiver, and the radio range was limited to a few centimeters. Although he measured IOP for several hours at a time, it was not practical to record pressures continuously for 24 hours.

Others have used external sensors to monitor IOP continuously by telemetry. Wolbarsht et al36 and Flower et al37 designed and implanted a band that resembled a scleral buckle and contained a strain gauge. As IOP changed, tension in the band was sensed and recorded. Other devices have been suggested or designed around contact lenses to measure IOP by applanating the sclera38,39 or cornea.40-42 Others43 have suggested that electronic circuits to sense and transmit IOP be built into haptics of intraocular lenses.

Prototypes of many of these devices have measured some basic properties of IOP in the laboratory. All were custom built and required specialized equipment and technical and engineering skills to operate. They have not been used to study IOP in humans or experimental animals during sleep, during a complete circadian cycle, or after administration of oculohypotensive drugs. In many instruments, the range between receiver and transducer was limited to a few centimeters, limiting the freedom of the animal. None has been developed commercially, and none is generally available.

In contrast, telemetric monitor systems for use in experimental animals have been developed extensively to measure other physiologic variables, such as blood pressure, temperature, and bioelectric potentials.44-46 These devices were designed to be implanted in large body compartments and are much larger than would fit in an eye. They are, however, readily available and easy to use.

In this study, we developed a method to implant a commercial telemetric pressure transducer in rabbits to measure IOP. The body of the transducer was placed subcutaneously on the back of the neck, and a catheter that conducts pressure to the transducer was implanted in the anterior chamber. This preparation allowed us to monitor IOP in unrestrained animals continuously, 24 hours a day, for several months.

**METHODS**

**Telemetric Pressure Transducers**

The implantable pressure monitors (Model TA11PA-C40; Data Sciences International, St. Paul, MN) are cylindrical, measure 25 mm in length and 15 mm in diameter, and weigh approximately 9 g. They contain a pressure transducer, a short-range amplitude modulation radio transmitter, and a battery in a biocompatible case. Pressure is conducted to the transducer through a fluid-filled polyurethane catheter that is 15 cm long and 0.7 mm in diameter. The 3-mm distal tip of the catheter couples the transducer to the surrounding fluid; it is modified with a thin flexible wall, and the end is filled with a biocompatible gel. The thin wall conducts transient pressure changes, whereas the gel prevents mixing of the fluid in the catheter with the surrounding biologic fluid and conducts slow pressure changes. Transducers were supplied in sterile packages. Although these devices originally were designed to monitor blood pressure, they are well suited for measuring intraocular pressure. They have a dynamic range of 0 to 300 mm Hg, and, when exposed to room air, the range of spontaneous noise is 0.2 mm Hg. They have a frequency response from direct current to 70 Hz.

The transmitter broadcasts an amplitude modulation radio signal to two antenna and receiver assemblies (33 cm long × 22 cm wide × 3.8 cm thick) mounted inside the animal's cage. As many as 12 transducers can be monitored through a multiplexer called a consolidation matrix, although in this experiment we measured from a maximum of six transducers (Fig. 1). The consolidation matrix also monitors atmospheric pressure (through a dedicated transducer), ambient light, ambient sound, and user-defined switch closures (e.g., opening or closing of a door) and transfers data to a laboratory computer for storage and analysis. All telemetered pressures were corrected for changes in atmospheric pressure.
Figure 1. System for recording intraocular pressure (IOP) by telemetry. The implanted capsule transmits IOP information to two antenna-receiver assemblies mounted in the cage. Signals from both receivers are combined (IOP monitors) and routed to the "consolidation matrix," a multiplexer that sequentially polls pressure monitors from six animals and three environment sensors. The operating program records IOP from each animal at 50 samples/second for 15 seconds and saves the average IOP. This cycle was repeated every 2.5 minutes; 576 IOP measurements from each rabbit were stored every 24 hours.

Implant surgery

Transducers were implanted in 13 pigmented rabbits weighing between 2 and 3.5 kg by using aseptic procedures. A protocol of this experiment was approved by the Institutional Animal Care and Use Committee at Mayo Clinic; the experiment conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Animals were anesthetized with intramuscular ketamine (50 mg/kg) 20 minutes after intramuscular xylazine (10 mg/kg). Anesthesia was maintained by giving supplementary doses of ketamine (50 mg/kg) or xylazine (5 mg/kg) as needed. Each animal was prepared for aseptic surgery and covered with a clear plastic surgical drape (Steri-drape; 3M Health Care, St. Paul, MN). A 4-cm midline incision was made on the dorsal neck and connective tissue, and muscle over the vertebral column and between the scapulae were blunt dissected to form a pocket to contain the transducer capsule. This area was covered with moist gauze while the eye was prepared to receive the catheter.

The right eye was used in all experiments. Eyelids were retracted with an infant lid speculum, and a 7-0 silk suture was placed through the mid-corneal stroma approximately 3 mm from the superior limbus (Fig. 2). The two ends were weighted to maintain downward rotation of the globe. The conjunctiva was opened 2 to 3 mm behind the limbus and 2 mm temporal to the superior rectus muscle and gently dissected free of the sclera back to the superotemporal orbital rim.

A 10-cm, 17-gauge catheter needle (inner needle of 14g4, number 6765; Becton Dickinson, Rutherford, NJ) was inserted through the conjunctival opening, advanced to the orbital rim, and pushed through the orbital fascia into the subcutaneous space just behind the orbital rim. It was advanced carefully under the skin to the top of the skull and back between the ears until the tip emerged from the opening at the back of the neck. The needle was flushed with sterile saline to remove any tissue or blood it had collected.

The transducer was dipped in an antibiotic solution (1000 U/ml bacitracin and 10 mg/ml neomycin in Ringer's solution) and was placed in the pocket formed earlier on the neck. The tip was then inserted into the bore of the 17-gauge needle and advanced carefully as far as possible. The needle was withdrawn and removed from the conjunctival opening, leaving the transducer catheter along its path. Approximately 2 cm of the catheter was left extending through the conjunctival opening and, if necessary, was temporarily tied out of the way while an opening was made into the anterior chamber.

The anterior edge of the conjunctival flap was reflected forward, and the sclera over the trabecular

Figure 2. Placement of transducer catheter in rabbit anterior chamber. (A) The incised conjunctiva was reflected forward, the sclera over the trabecular meshwork was thinned, an opening was made into the anterior chamber, and the catheter was inserted and advanced to the mid-anterior chamber. During the operation, the globe was rotated downward by a weighted 7-0 silk suture placed through a half-thickness of the cornea. (B) The catheter was fixed to the sclera with three 90 nylon sutures. One 80 silk suture (braided) also was tied around the catheter as an anchor point for granulation (reproduced by permission of the Mayo Foundation).
The body of the transducer was implanted on the dorsal neck between the scapulae; its catheter lies subcutaneously between the ears and over the superotemporal orbital rim. The entire implant was internal (reproduced by permission of the Mayo Foundation).

meshwork was scraped with a sharp, rounded blade (microsurgery knife model 681.01; Grieshabar & Co. AG, Schafhausen, Switzerland) until the trabecular meshwork was visible as a dark streak. A 21-gauge needle was inserted through this thinned tissue into the anterior chamber and withdrawn, and the anterior chamber was refilled through the same opening with Healon (Pharmacia Ophthalmics, Monrovia, CA). The catheter was grasped with a tube forceps and was inserted through the opening into the anterior chamber. The tip was advanced to approximately mid pupil (4 to 5 mm); care was taken not to touch the corneal endothelium.

The catheter was secured to the sclera with three 9-0 or 10-0 nylon sutures. Each was tied securely around the catheter three times and its ends passed through the sclera before they were tied together (Fig. 2B). One 8-0 silk suture was also tied tightly three times around the catheter to promote formation of granulation tissue. The catheter was pulled gently back toward the transducer to remove the excess loop in the orbit. In some animals, a glycerated scleral patch was sutured directly over the catheter. The conjunctiva was closed with 9-0 nylon suture, and the traction suture was removed from the cornea.

The capsule was anchored in the pocket on the neck; again, care was taken not to nick or make any sharp bends in the catheter. The muscle layer was closed with 3-0 vicryl sutures, with several sutures placed through the fabric anchor ridge on the capsule. The skin was closed with 3-0 vicryl sutures, and the animal was allowed to recover and was returned to its home cage. At the end of surgery, the entire transducer and catheter assembly was internal (Fig. 3).

Measurements of IOP began 1 or 2 days after recovery. The animal room was lighted by overhead fluorescent lights that were cycled on for 12 hours and off for 12 hours. The front of the cages was illuminated with between 100 and 300 foot-candles (depending on the position of the cage) when the lights were on and with less than 0.02 foot-candle when they were off. When desired, this cycle was shifted or reversed or lights were continuously on or off for several days. During part of the study, the light cycle was reversed for 7 days and was followed by continuous darkness for 7 days. The original light cycle was then restored for 7 days and was followed by 7 days of continuous light. In another part of the study, several months later, the light cycle was advanced by 6 hours. When lights were off continuously, animal husbandry services were performed under a red photographic safelight (wavelength >600 nm).

Intraocular Pressure Recordings

The software supplied by Data Sciences International measures pressure from all transducers at regular intervals. We programmed the system to record IOP from each animal (maximum of six animals in our experiments) at 50 measurements per second for 15 seconds every 2.5 minutes. A programmable low-pass filter limited frequency response to 10 Hz. The average IOP during each 15-second interval was calculated and saved with the starting time of the interval. When slow changes in IOP were of interest, measurements from 30-minute intervals (12 measurements) were averaged.

We also recorded IOP continuously at 50 or 100 Hz for 60 seconds at a time. The low-pass cutoff frequency was set to 20 Hz when recording at 100 Hz. This mode was used to examine fast IOP variations and IOP during tonometry and to check calibration in vivo.

Day-to-day and week-to-week changes in amplitude of the diurnal rhythm were examined by calculating mean IOP during 2 hours of the light phase, from 3:00 CT to 5:00 CT, and during 2 hours of the dark phase, 14:00 CT to 16:00 CT. The term CT refers to circadian time and begins at 00:00 CT when lights are turned on. In these experiments, the room was darkened between 12:00 CT and 24:00 CT.

Calibration Check

Transducers were calibrated by the manufacturer. We checked calibration in vivo near the end of the experiment (150 to 320 days after implant) by recording while setting IOP with a manometer. Each rabbit was anesthetized with ketamine and xylazine (50 mg/kg and 10 mg/kg), and a 25-gauge butterfly needle connected to a column of sterile irrigation solution (0.9% sodium chloride) was inserted through the cornea, 1 to 2 mm from the limbus, into the mid-anterior cham-
Intraocular pressure (IOP) was measured by the implanted transducer while pressure was set by a water manometer. Transducers were linear, although sometimes they were offset from IOP. This curve was measured 234 days after the transducer was implanted.

We also examined linearity of the transducers between 102 and 177 days after implant by placing the anesthetized animal in a hyperbaric chamber and raising ambient pressure in steps of 5 mm Hg to 45 mm Hg. Changes in IOP measured through the transducer were compared to changes in air pressure. Although this method does not give an absolute calibration, it verifies the linearity and gain of the transducer.

RESULTS

We successfully recorded IOP for 180 to 370 days from 7 of the 13 rabbits implanted with transducers. In these animals, the useful life of the preparation was limited by the battery life of the transducer. As the batteries ran down, signal strength of the transmitter decreased, and large offsets in the measured pressure developed.

Positioning the catheter tip away from the corneal endothelium was critical for stable long-term measurements. In four animals, the catheter rubbed the corneal endothelium during insertion or remained against the cornea, and fibrous tissue grew around and encased the tip during the 2 to 4 weeks that followed surgery. During this time, the pressure recorded by the transducer decreased and became negative. In one animal, the catheter slipped out of the anterior chamber within the first week of surgery. One animal died of causes unrelated to the implant.

Calibration

The relation between IOP as measured with the implanted transducer and IOP as set by the manometer in one experiment is shown in Figure 4. In six animals, the relation between measured and actual IOP was linear, with a slope of 0.91 ± 0.05 (mean ± SD). The offset (Y-intercept of the fitted line) depended on the individual animal and the time since implant surgery. In all animals, the offset increased near the end of the transducer’s battery life, and in all except one, the offset made the measurements more negative.

Telemetered IOP increased linearly with ambient pressure in the hyperbaric chamber and had a slope of 1 ± 0.02 in 6 animals (mean ± SD). The y-intercept depended on the IOP of the animal during anesthesia.

In one animal, the average IOP reported by the transducer was approximately 40 mm Hg, although tonometrically, IOP was approximately 20 mm Hg. We do not know why the transducer in this animal indicated 20 mm Hg higher pressure than it should have.

Intraocular Pressure at Rest

In alert, resting animals, IOP was not constant but drifted up and down through 3 to 5 mm Hg (Fig. 5). A fast, regular pressure pulse with an amplitude of approximately 0.5 mm Hg and a frequency of 4 to 5 Hz was superposed on IOP in most recordings. This pulse was present when the rabbits were awake and when they were anesthetized, and it usually increased as IOP increased. Its rate corresponded to heart rate. When animals were anesthetized, the spontaneous drift disappeared. Others have demonstrated similar patterns of IOP in resting animals.

Intraocular Pressure During Tonometry

Pressure increased when the eye was massaged gently through a closed lid or when the cornea was touched.

FIGURE 4. Intraocular pressure (IOP) measured by the implanted transducer while pressure was set by a water manometer. Transducers were linear, although sometimes they were offset from IOP. This curve was measured 234 days after the transducer was implanted.

FIGURE 5. Intraocular pressure (IOP) in an alert rabbit. IOP was not constant but varied through several mm Hg. A pulse of approximately 1 mm Hg at the heart rate (approximately 5 Hz) was present on most recordings.
Intraocular Pressure by Telemetry

**FIGURE 6.** Intraocular pressure (IOP) increased approximately 5 mm Hg in this animal during contact with a pneumatonometer. In many recordings, IOP transiently increased after the last contact with the tonometer probe, as it did here (peak at 46 seconds).

with a tonometer. Intraocular pressure increased 2 to 6 mm Hg during contact with a pneumatonometer (Fig. 6). The pressure pattern recorded by the pneumatonometer was similar to the pattern recorded from the implanted transducer.

When the cornea was touched with the rigid tip of the Tonopen (Mentor O & O, Norwell, MA), IOP increased by 20 to 30 mm Hg, although this increase lasted only for the duration of the contact, typically less than 0.5 second (Fig. 7). Readings from the Tonopen corresponded to IOP at the inflection point as pressure began to increase.

**Circadian Changes in Intraocular Pressure**

Within 3 to 8 days of surgery, IOP began to follow a circadian rhythm; IOP increased after the lights were turned off and decreased after they were turned on (Fig. 8). Typically, IOP was highest between 2 and 4 hours after the onset of darkness and remained high or gradually decreased through the night. With the onset of light, IOP dropped and remained low until the return of darkness. Pressure was lowest between 3 and 6 hours after the onset of light.

This circadian rhythm continued day after day for as long as the light cycle remained unchanged (Figs. 9, 10). The absolute IOP and difference between AM (light) and PM (dark) IOP varied over several months (Fig. 11). The maximum light–dark difference ranged from 6.4 to 16.6 mm Hg, and the average difference ranged from 0.2 to 7.2 mm Hg. In one animal, the difference slowly decreased from 5 mm Hg at 50 days after implant to zero and eventually reversed, so that in the light IOP was 2 mm Hg greater than in the dark. All other animals had greater IOP in the dark than in the light, although the difference varied with time.

**FIGURE 8.** Diurnal intraocular pressure (IOP) in one rabbit. Each point represents IOP averaged over 15 seconds; measurements were spaced at 2.5-minute intervals. The solid horizontal line is the 24-hour average. IOP was highest in the dark and lowest in the light.

**FIGURE 7.** Intraocular pressure increased by 30 to 40 mm Hg during contact with the Tonopen tonometer. The pressure increase lasted for the duration of contact, typically less than 1 second.

**FIGURE 9.** The diurnal cycle in intraocular pressure (IOP) was consistent from day to day. Each point represents the average IOP on a 30-minute interval. IOP from 6 consecutive days were superposed (one animal). The solid horizontal line represents the 6-day mean IOP.
FIGURE 10. Thirty-day average and standard deviation of circadian intraocular pressure (IOP) in one rabbit. The pattern of IOP was consistent over many days. The solid horizontal line represents the 24-hour average of the pressures graphed.

The diurnal pressure cycle was synchronized with the cycle of room lighting. When the light cycle was shifted, the time of IOP change also shifted, although the IOP cycle often required several days to realign with the light cycle. After the light cycle was reversed (12-hour advance), the IOP cycle reversed during the next 5 days in four of the five animals that showed a circadian rhythm in IOP. (The sixth animal had been implanted only 6 days earlier and did not show a consistent circadian rhythm at this time.) In the fifth animal, the circadian rhythm diminished when lights were reversed and IOP differences between light and dark were small and inconsistent. The reversed IOP cycles continued during the 7 days of continuous darkness that followed the reversed light cycle. When lights were on continuously, the circadian cycle was inconsistent between animals. In three animals, the difference between morning and night IOP began to diminish after 5 to 7 days. In one animal the difference was maintained, and in two others, no clear cycle was apparent from the beginning of the week. Changes in the circadian rhythm of IOP in one animal can be seen in Figure 11.

FIGURE 11. Daily morning intraocular pressure (IOP) (averaged between 3:00 circadian time [CT] to 5:00 CT) and night IOP (averaged between 14:00 CT to 16:00 CT) in one rabbit through life of implant. The horizontal bar at the bottom indicates changes in lighting schedule. During the normal circadian light cycle labeled 1, lights were on between 00:00 CT and 12:00 CT and off between 12:00 CT and 24:00 CT. On days labeled 2, the light-dark cycle was reversed, on days labeled 3 the room was under continuous dark, and on days labeled 4 the room was under continuous light (times of day and night IOP were determined by the original schedule). IOP was higher in the dark than it was in the light. When the light cycle was reversed, the IOP cycle also reversed; daytime IOP was greater than nighttime IOP. This continued through the dark period that followed but quickly reverted to the original cycle when lights were returned to their original schedule. In this animal, the IOP cycle was diminished after 6 days of continuous light. The lighting cycle was advanced by 6 hours on day 144 and was followed by an apparent loss of the IOP cycle (times of day and night IOP were determined by a new schedule). In fact, the IOP cycle shifted gradually during the next 10 days (Fig. 12). After day 230, IOP as measured through the implant decreased and eventually became negative. This offset continued until the transmitter failed near 280 days.

The diurnal pressure cycle was readjusted slowly after onset of dark was advanced by 6 hours. Each day, the IOP cycle advanced by approximately 25 minutes until after 15 days it was again synchronized with the light cycle. Time of the drop in IOP after onset of light changed immediately.

FIGURE 12. The onset of elevated intraocular pressure (IOP) readjusted slowly after onset of dark was advanced by 6 hours. Each day, the IOP cycle advanced by approximately 25 minutes until after 15 days it was again synchronized with the light cycle. Time of the drop in IOP after onset of light changed immediately.
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trast, the IOP decrease that followed onset of light shifted immediately after the light cycle was shifted.

DISCUSSION

The implanted pressure transducer provides a convenient and preinvasive technique to measure and study IOP in unrestrained experimental animals. Intraocular pressure can be measured continuously for as long as is needed to study normal physiological responses to environmental and pharmacologic stimuli. This is not the first attempt to measure IOP by telemetry, but it is the first time a readily available commercial device has been implanted to measure intraocular pressure.

Investigators should be aware of two conditions that can affect the IOP reported by the implanted transducer. First, eyes with implanted transducers have been operated on and contain the tip of the catheter, a foreign body. The tip can rotate through the anterior chamber and irritate the cornea and iris; in some animals, corneas became scarred from this movement. Often, a bleb formed around the wound during the days that followed implant surgery and dissipated over the next several weeks. When measured by tonometry, IOP in the operated eye was lower than in the unoperated eye, although in some animals this difference gradually disappeared. Experiments that would be affected by altered outflow kinetics and lower than normal IOPs may be misleading.

Second, the offset that often developed gives an error in absolute IOP. Telemetered pressure was usually less than 4 or 5 mm Hg different from tonometric pressure when the transducer had been implanted for less than 100 days. Differences between the tonometer, IOP in the operated eye was lower than in the unoperated eye, although in some animals this difference gradually disappeared. Experiments that would be affected by altered outflow kinetics and lower than normal IOPs may be misleading.

It is not clear why the average gain of the transducer was 0.91 when IOP was set with the manometer, whereas it was 1 when measured in the hyperbaric chamber. The hyperbaric chamber experiment was considerably earlier than the water column experiment (mean time after implant surgery, 129 days versus 245 days, respectively). Perhaps aging of the transducer contributed to this difference.

The diurnal rhythm in IOP is consistent with measurements by others.17,19,22–28 Clearly, IOP rises with the onset of darkness and falls with the onset of light. Because animals were not disturbed during our measurements, we know that the diurnal cycle was not influenced by any physiologic response to the presence of an investigator or to handling. By using this method, one could easily perform many of the classical experiments to explore the relationship between IOP and lighting patterns,19,22,26 sympathetic stimulation and denervation,24,25,31,49 endogenous substances and kinetics,22,26,28,30–33 and administration of specific neuroreceptor agonists and antagonists7,29,46–53 to learn how and why IOP follows a circadian pattern.

Unfortunately, one cannot perform a paired test between right and left eyes because the transducers measure through only one channel. In studies that compare two treatments, each animal must be used as its own control. The power of a test between IOP on 2 days, one with treatment and one without, depends on the number of animals and the variance of the difference in IOP between the 2 days. For example, the 30-minute average IOP on a drug day could be compared to the 30-minute average IOP at the same time on a placebo day. In our six animals, the standard deviation of the difference in IOP measured 7 days apart was 2.9 mm Hg (66 to 202 days after implant; mean = 132 days). If this variance does not change when a drug is applied, there would be a 90% chance of finding a difference of 4.7 mm Hg in our sample of six animals, if such a difference existed. A slightly smaller difference would be detectable if IOP were averaged over 60 minutes. This difference is approximately equal to the average diurnal change in IOP and would be a reasonable minimal goal in ocular hypertensive therapy.

Measuring IOP by telemetry has many advantages, the greatest of which is the absence of the investigator during the measurement. With conventional tonometry, the probe must be brought to and must contact the cornea. In most experiments, the animal is removed from its cage, and anesthetic drops are instilled in the eyes. When rabbits are frightened or uncooperative, they often withdraw and squeeze their eyelids closed to avoid the tonometer. Dragging the animal out of its cage in the dark aggravates the situation.

With a telemetric implant, the animal will not be aware of the measurement, and IOP can be measured at all times, under opened or closed eyelids. Data can be sampled at a high or low rate as required by the experiment. The investigator need only be present to administer the test solution; all data are recorded by the computer. The number of studies that can be designed around measuring IOP by telemetry is limited only by the imagination of the investigators.

Key Words

circadian rhythm, intraocular pressure, rabbits, telemetry, tonometer

References

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