Brazilian Journal of Medical and Biological Research (2006) 39: 1249-1253
ISSN 0100-879X

Computerized invasive measurement of time-dependent intraocular pressure

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Abstract

Several methods have been described to measure intraocular pressure (IOP) in clinical and research situations. However, the measurement of time varying IOP with high accuracy, mainly in situations that alter corneal properties, has not been reported until now. The present report describes a computerized system capable of recording the transitory variability of IOP, which is sufficiently sensitive to reliably measure ocular pulse peak-to-peak values. We also describe its characteristics and discuss its applicability to research and clinical studies. The device consists of a pressure transducer, a signal conditioning unit and an analog-to-digital converter coupled to a video acquisition board. A modified Cairns trabeculectomy was performed in 9 *Oryctolagus cuniculus* rabbits to obtain changes in IOP decay parameters and to evaluate the utility and sensitivity of the recording system. The device was effective for the study of kinetic parameters of IOP, such as decay pattern and ocular pulse waves due to cardiac and respiratory cycle rhythm. In addition, there was a significant increase of IOP versus time curve derivative when pre- and post-trabeculectomy recordings were compared. The present procedure excludes corneal thickness and error related to individual operator ability. Clinical complications due to saline infusion and pressure overload were not observed during biomicroscopic evaluation. Among the disadvantages of the procedure are the requirement of anesthesia and the use in acute recordings rather than chronic protocols. Finally, the method described may provide a reliable alternative for the study of ocular pressure dynamic alterations in man and may facilitate the investigation of the pathogenesis of glaucoma.

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Research supported by FAPEMIG, FUNDEP, CNPq, and PRONEX.

Received December 12, 2005
Accepted July 24, 2006

Key words
- Glaucoma
- Intraocular pressure measurement
- Trabeculectomy
- Signal processing
- Computer-assisted measurement

Introduction

Intraocular pressure (IOP) is recognized as the main risk factor in the pathogenesis of glaucoma and is a determinant of ocular perfusion, which might be affected in this disease (1). Moreover, the dynamic properties of time-varying IOP are an important factor in the evaluation of implants, such as those used in glaucoma treatment designed to increase aqueous humor drainage without lowering IOP below physiological levels. While several methods have been described to measure IOP in clinical practice and re-

search, it is still a challenge to perform its measurement continuously over time and/or with high accuracy in specific situations such as corneal swelling, refractive surgeries and scarred corneas (2).

Initial attempts to invasively measure and to continuously record IOP were made in the 1970's. A polygraph was used to study the mathematical and mechanical properties of ocular drainage but setup size caused difficulties in introducing this technology in clinical protocols (3).

Direct assessment of IOP via the anterior chamber may constitute an alternative to eliminate bias related to corneal interference. Variability in central corneal thickness and curvature are considered to be potent confounders for most tonometric techniques, especially the Goldmann applanation (2,4). In addition, many clinical situations, e.g., LASIK surgery and keratoconus, may reduce central corneal thickness leading to underestimation of IOP. The inaccuracy of the Goldmann tonometers while measuring IOP in scarred corneas could compromise its utility in diseases that, due to corneal edema, preclude accurate IOP estimation such as acute glaucoma crises and bullous keratopathy (4,5).

Since vascular dysfunction may play a role in the pathogenesis of open-angle glaucoma, attempts have been made to record ocular pulsatile pressure using specialized tonometers (e.g., pulsatile ocular blood flow) (6). However, due to its low sensitivity, the utility of this recording device could not be validated. Nevertheless, real-time continuous measurement of IOP constitutes a promising approach by permitting the study of IOP dynamical features in special situations (e.g., assessment of the action of hypotensive agents, IOP oscillation during ophthalmic surgeries and vascular parameters such as systolic IOP peak).

Most of the IOP data obtained with currently available methods do not focus on the dynamic properties of oscillating pressure levels since these methods perform steady-state recordings. Parameters derived from the analysis of spontaneous IOP decay after induced anterior chamber hypertension may directly correlate with anterior chamber drainage efficiency and ocular perfusion, among other physiological variables relevant for the diagnosis of glaucoma and for investigative protocols. Therefore, the objective of the present study was to design a computerized system capable of recording the transitory variability of IOP, sensitive enough to reliably detect ocular pulse peak-to-peak values, after controlled anterior chamber pressure clamping.

Material and Methods

Animal preparation

Oryctolagus cuniculus rabbits (N = 9) weighing 2.2-3.25 kg were housed in individual cages with food and water *ad libitum* prior to the experiments. Animals were anesthetized with an intramuscular injection of ketamine (40 mg/kg) and xylazine (5 mg/kg). Topical proxymetacaine was instilled at 5-min intervals during the surgical procedure (7). The right eye was selected for surgery and recording in all experiments. All procedures complied with the Association for Research in Vision and Ophthalmology statement for the use of animals in research (8).

Instrument configuration

Basically, the data acquisition system consisted of a pressure transducer, a signal conditioning unit (CYBERAMP TM 380, Axon Instruments, Sunnyvale, CA, USA) and an analog-to-digital converter (BIOPAC MP 100A-CE; Biopac Systems Inc., Santa Barbara, CA, USA). The integration of IOP recordings and live video images from the digital camera attached to the surgical microscope was done using a multipurpose

video card (ATI All-In Wonder Radeon®, Markham, Ontario, Canada). The video card also permitted the integrated image on the computer monitor, together with simultaneous IOP data and surgical procedure, to be transferred to a videocassette recording device. This additional feature of the recording system proved to be important when analyzing data and interpreting IOP noise due to mechanical artifacts. Experiments were recorded on a VHS cassette tape along with IOP recordings saved in digital format for further computational processing and data analysis.

The gain of the signal-conditioning unit was set at 5000X in order to adjust the amplified pressure signal from the transducer to fit the end scale of the analog-to-digital converter, thus enhancing the sensitivity of the recorded signal. The pressure signal was then digitized at a 200-Hz sampling rate, high enough for pulsatile pressure recordings, and saved in the computer. The setup was calibrated before the experiments using a mercury column.

In order to record IOP, a needle (N1, 26.5G) was inserted through the eye limbus into the anterior chamber. A polyethylene tube (PE 20) filled with heparinized saline solution (0.9% NaCl) (Endomed, São Paulo, SP, Brazil) + heparin sodium (Cristália do Brasil S/A, São Paulo, SP, Brazil) connected the pressure transducer to N1. Another polyethylene tube (PE 20) was used to connect a heparinized saline reservoir to a second needle (N2, 27G, butterfly), which, in turn, was placed inside the anterior chamber of the eye. The mean IOP value was externally driven by adjusting the reservoir's height, while a three-way valve was used to interrupt the flow from N2 to the anterior chamber. Therefore, when the three-way valve was in the open position, it stabilized pressure at the desired level (60 mmHg); when it was in the closed position, IOP spontaneously decreased due to trabecular drainage.

Experimental procedure

The baseline IOP was obtained as soon as N1 was inserted into the anterior ocular chamber. After positioning N2, leakage was assessed using fluorescein eye-drops (sodium fluorescein, Allergan, São Paulo, SP, Brazil) to confirm the seal around the needles. Positioning the saline reservoir at approximately 80 cm above the eye level raised the IOP to 60 mmHg. After IOP stabilization at 60 mmHg, the infusion was interrupted by switching the three-way valve to the closed position. IOP decay was recorded until stabilization at physiological levels.

After baseline recordings, a modified Cairns trabeculectomy was performed to obtain changes in IOP decay parameters in order to confirm the utility and the sensitivity of the recording system (9). All surgeries were performed by the same surgeon (SJ). Animals were allowed to recover for 4 days from the first set of measurements before the same recording sequence was executed.

Data analysis

Using commercial software, the pressure versus time curve derivative was calculated at each pressure level (dP/dt versus P). The integral of four successive segments of the IOP decay curve was also obtained, permitting the study of aqueous humor outflow. Data obtained before and four days after trabeculectomy were compared statistically by the paired Student *t*-test.

Results

The reservoir height maneuver successfully stabilized IOP at desired levels without affecting the ability of the system to record oscillations due to arterial pulsatile pressure (PP; Figure 1, inset). Also, the system permitted a clear identification of systolic-diastolic oscillations and of the slow change in baseline PP due to the respiratory incursion.

A common plethysmographic effect was observed, i.e., when mean IOP decreased the peak-to-peak PP recorded also decreased.

Animals displayed a faster decay in the IOP versus time curve after the trabeculectomy procedure (Figure 2A depicts the usual pattern). The derivative of the decay curve varied according to the mean IOP (Figure 2B) and both groups stabilized at baseline levels. On the 4th day after surgery, the derivative of the P versus time curve was significantly higher (-0.03 ± 0.01 s^{-1}) than the pre-surgical value (-0.004 ± 0.001 s^{-1}; Figure 3). The comparison of the four segments from the integral analysis did not reveal a significant difference between surgical and pre-surgical levels.

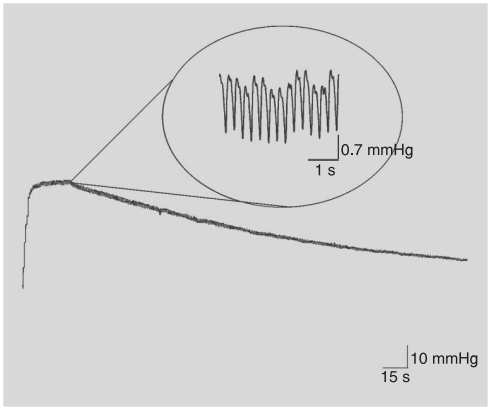

Figure 1. Example of intraocular pressure (IOP) output from the sensor. The applied pressure was raised to 60 mmHg and then reduced by closing the three-way valve, leading to IOP stabilization at physiological levels. The zoom of the IOP curve segment shows the shape of the pulse rate oscillation.

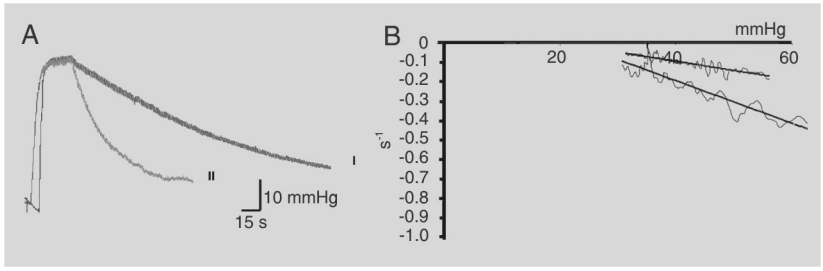

Figure 2. Example of derivative analysis of intraocular pressure (IOP) recording before and 4 days after surgery. *A*, Pressure x time graph showing IOP rise, stabilization and decay: I) rabbit eye prior to surgery; II) the same eye four days after trabeculectomy. IOP decay rate was more pronounced after trabeculectomy than before the surgical procedure. *B*, IOP x decay curve derivative, extracted from data shown in the Figure 2A. Note that curve derivative was greater at higher IOP levels.

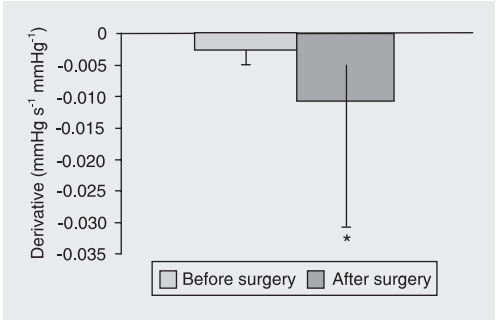

Figure 3. Derivative analysis of the intraocular pressure decay curve. *P < 0.05 compared to before surgery (paired Student *t*-test).

Discussion

The instrument described here identified the kinetic parameters of IOP, such as decay pattern and ocular pulse waves due to the cardiac cycle rhythm. The pulse oscillations detected displayed a peak-to-peak value not exceeding 2 mmHg, as described in the literature, oscillating around the mean IOP level (3,10). These findings provide evidence of the accuracy and sensitivity of the recording system since even on a very enlarged IOP scale the noise is hardly perceptible and baseline levels have almost no detectable movement artifact.

The faster decay after trabeculectomy was most likely due to a decreased resistance to the aqueous humor outflow (Figure 2A). The computational tools available allowed a more refined and faster extraction of parameters for comparing the IOP decay patterns (Figure 2B), and may be used to compare glaucomatous with normal subjects or to detect differences between treated and control subjects (e.g., efficacy of drainage devices) in forthcoming research and clinical protocols.

As compared to conventionally used methods, digital acquisition excludes corneal thickness influences and errors related to operator ability. These factors have been extensively discussed and recent studies with servo-null measurement systems have been conducted in order to minimize their influence. The system described here, however, is a direct measure of IOP and does not require the feedback loop of the servo-null setup (11). Telemetric studies (7) have obvious advantages for continuous long-term

recordings but are not as cost-effective as the high-performance system presented here.

Among the disadvantages of the system described here, is the requirement of an anesthetized state which may interfere with IOP kinetics and physiological response and compromise the pharmacokinetics of drugs used for treatment. Another limitation is its use only for acute recording procedures rather than for chronic data acquisition along extended periods of time (12).

The system described here may be transferred to clinical practice to be incorporated into routine biomicroscopic examination under topical anesthesia, since sterility requirements do not represent a methodological limitation. The biomicroscopic evaluation of the animals did not reveal clinical complications due to the recording procedure, saline infusion, pressure overload, or surgery (13-16). Finally, the method described here may constitute a reliable alternative for the study of dynamic changes in ocular pressure due to different hypotensive agents used in ophthalmologic practice and may facilitate the investigation of the pathogenesis of glaucoma (17).

Acknowledgments

We would like to acknowledge Darcy Ferreira dos Santos and Jose Eustaquio de Oliveira for technical assistance.

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