PRÓ-REITORIA DE PESQUISA E PÓS-GRADUAÇÃO
MESTRADO EM CIÊNCIA ANIMAL

JOÃO VICTOR GOULART CONSONI PASSARELI

COMPARAÇÃO ENTRE OS TONÔMETROS PORTÁTEIS TONOVET, TONOVET PLUS, TONO-PEN AVIA VET E KOWA HA-2 NA MENSURAÇÃO DA PRESSÃO INTRAOCULAR EM CÃES

Presidente Prudente - SP
2019

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Defesa da Dissertação apresentada à Pró-Reitoria de Pesquisa e Pós-Graduação, Universidade do Oeste Paulista, como parte dos requisitos para obtenção do título de Mestre – área de concentração: Ciência Animal.

Orientadora:
Prof.ª. Dra. Silvia Maria C. Franco Andrade

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Presidente Prudente, 29 de novembro de 2019.

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DEDICATÓRIA

Dedico este trabalho primeiramente á Deus que sempre esteve presente, me sustentando e me dando forças para que eu pudesse concluir mais essa etapa na minha vida.

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“Conheça todas as teorias, domine todas as técnicas, mas ao tocar uma alma humana seja apenas outra alma humana”. (Carl G. Jung)

RESUMO

Comparação entre os tonômetros portáteis Tonovet, Tonovet Plus, Tono-Pen Avia Vet e Kowa HA-2 na mensuração da pressão intraocular em cães

O objetivo deste estudo foi comparar a acurácia dos tonômetros Tonovet e Tonovet Plus (rebote), Tono-Pen Avia Vet (aplanação) e Kowa (aplanação Goldmann) em cães. Foram mensurados a pressão intraocular (PIO) em 154 olhos de 77 cães. Através de um estudo *post-mortem* correlacionando os valores da manometria versus tonometria e calculando o coeficiente de correlação (r^2), um estudo *in vivo* comparando a PIO real (manometria) com os tonômetros e um estudo ambulatorial em olhos saudáveis, e em olhos com sinais de glaucoma e uveíte. Os resultados obtidos no estudo *post-mortem* dos valores de (r^2) em ordem decrescente foram: Kowa (0,989), Tonovet Plus (0,984), Tonovet (0,981) e Tono-Pen (0,847). Os valores da PIO em mmHg no estudo *in vivo* foram: manômetro aneroide (16,8 ± 2,5,7), Tonovet (18,1 ± 2,9), Tonovet Plus (20,6 ± 2,3), Tono-Pen (17,1 ± 2,5) e Kowa (16,1 ± 1.7); ambulatorial sadios: Tonovet (16,8 ± 3,8), Tonovet Plus (19,2 ± 2,9), Tono-Pen (16,2 ± 2,4) e Kowa (15,0 ± 1,3); glaucoma: Tonovet (30,2 ± 3,5), Tonovet Plus (35,0 ± 6,1), Tono-Pen (29,5 ± 4,2) e Kowa (23,9 ± 5,0); e uveíte: Tonovet (14,2 ± 1,4), Tonovet Plus (17,6 ± 1,9), Tono-Pen (13,7 ± 2,1) e Kowa (12,6 ± 1,7). Conclui-se que houve uma forte correlação entre os valores da PIO com a manometria em todos os tonômetros. Os valores mais altos de PIO foram com Tonovet Plus e os mais baixos com Kowa HA-2. Todos os tonômetros foram precisos na medição da PIO em cães, incluindo o mais recente, Tonovet Plus, que mostrou um excelente coeficiente de correlação.

Palavras-chave: Tonometria de aplanação, manometria direta, cães, tonometria de Goldmann, tonometria de rebote.

ABSTRACT

Comparison between Tonovet, Tonovet Plus, Tono-Pen Avia Vet and Kowa HA-2 portable tonometers for measuring intraocular pressure in dogs

The aim of this study was to compare the accuracy of Tonovet and Tonovet Plus (rebound), Tono-Pen Avia Vet (applanation) and Kowa (Goldmann applanation) tonometers in dogs. Intraocular pressure (IOP) was measured in 130 eyes of 65 dogs. A *post-mortem* study was performed comparing manometry versus tonometry values and calculating the correlation coefficient (r2), an in vivo study comparing actual IOP (manometry) with tonometers and an outpatient study in healthy eyes and eyes with signs of glaucoma and uveitis. The results obtained in the postmortem study of (r2) values in decreasing order were: Kowa (0.989), Tonovet Plus (0.984), Tonovet (0.981) and Tono-Pen Avia Vet (0.847). The IOP values in mmHg in the in vivo study were: aneroid manometer (16.8 ± 2.5.7), Tonovet (18.1 ± 2.9), Tonovet Plus (20.6 ± 2.3), Tono Pen Avia Vet (17.1 ± 2.5) and Kowa (16.1 ± 1.7); healthy outpatients: Tonovet (16.8 ± 3.8), Tonovet Plus (19.2 ± 2.9), Tono-Pen Avia Vet (16.2 ± 2.4) and Kowa (15.0 ± 1.3); glaucoma: Tonovet (30.2 ± 3.5), Tonovet Plus (35.0 ± 6.1), Tono-Pen Avia Vet (29.5 ± 4.2) and Kowa (23.9 ± 5.0); and uveitis: Tonovet (14.2 ± 1.4), Tonovet Plus (17.6 ± 1.9), Tono-Pen Avia Vet (13.7 ± 2.1) and Kowa (12.6 ± 1.7). We can conclude that there was a strong correlation between IOP values and manometry in all tonometers. The highest values were with Tonovet Plus and the lowest with Kowa HA-2. All tonometers were accurate in measuring IOP in dogs, including the latest Tonovet Plus, which showed an excellent correlation coefficient.

Keywords: Applanation tonometry, direct manometry, dogs, Goldmann tonometry rebound tonometry.

SUMÁRIO

1 ARTIGO CIENTÍFICO

Comparison among Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2® portable tonometers for measuring intraocular pressure in dogs

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Running Title: Tonovet®, Tonovet Plus®, Tono-Pen® and Kowa® Tonometers

Abstract

Objective To compare the accuracy of Tonovet® and Tonovet Plus® (rebound), Tono-Pen Avia Vet® (applanation) and Kowa® (Goldmann applanation) tonometers in dogs.

Animals Intraocular pressure (IOP) was measured in 154 eyes from 77 dogs. A postmortem study was performed comparing manometry vs. tonometry values and calculating the correlation coefficient (r^2), an in vivo study comparing real IOP (manometry) among the tonometers, an outpatient study in healthy eyes and eyes with signs of glaucoma and uveitis.

Results In the postmortem study, the values of (r^2) in descending order were Kowa® (0.989), Tonovet Plus® (0.984), Tonovet® (0.981) and Tono-Pen Avia Vet® (0.847). The IOP values in mmHg in the in vivo study were: aneroid manometer (16.8 ± 2.5.7), Tonovet® (18.1 ± 2.9), Tonovet Plus® (20.6 ± 2.3), Tono Pen Avia Vet® (17.1 ± 2.5) and Kowa® (16.1 ± 1.7); in outpatient clinics: Tonovet® (16.8 ± 3.8), Tonovet Plus® (19.2 ± 2.9), Tono-Pen Avia Vet® (16.2 ± 2.4) and Kowa® (15.0 ± 1.3); glaucoma: Tonovet® (30.2 ± 3.5), Tonovet Plus® (35.0 ± 6.1), Tono-Pen Avia Vet® (29.5 ± 4.2) and Kowa® (23.9 ± 5.0); and uveitis: Tonovet® (14.2 ± 1.4), Tonovet Plus® (17.6 ± 1.9), Tono-Pen Avia Vet® (13.7 ± 2.1) and Kowa® (12.6 ± 1.7).

Conclusions There was a strong correlation between IOP values and manometry in all tonometers. The highest values were with Tonovet Plus® and the lowest with Kowa HA-2®. All tonometers were accurate in measuring IOP in dogs, including the latest Tonovet Plus, which showed an excellent correlation coefficient.

Key words: applanation tonometry, direct manometry, dogs, Goldmann tonometry rebound tonometry

INTRODUCTION

Tonometers are an important tool for measuring intraocular pressure (IOP) for the diagnosis of eye diseases that can lead to irreversible blindness, including those that causing increased of IOP, such as glaucoma, which can lead to optic neuropathy and is characterized by the death of retinal ganglion cells and their axons with accompanying vision loss, or those that reduce IOP, such as uveitis, which are usually due to secondary causes such as infections, inflammation, trauma or tumoral processes.[1-6] Early determination of an increase in IOP in glaucoma and a decrease in uveitis represents an important treatment success factor and provides a more favorable prognosis for these diseases, as they are ophthalmopathies with great potential to induce irreversible blindness.[7,8]

IOP measurements can be performed by manometry or tonometry. The most accurate considered the golden method is direct or ocular manometry, which measures actual IOP in mmHg and consists of anterior chamber cannulation and measurement with a digital instrument or a mercury column.[9-11]

Tonometers use different techniques to measure IOP and may be contact or not, fixed or portable. [1,2,7] In veterinary medicine, the most commonly used tonometers are of contact and portable, using the applanation method (Tono-Pen®),[7,8] or more recently, the rebound method (Tonovet® and Tonovet Plus®).[12-14] Other methods used are indentation (Schiötz®)[7,8] and applanation tonometry using the Goldmann prism (Perkins® and Kowa HA-2®).[15-18]

Applanation tonometry is based on the principle that a force required to flatten a given area of a sphere is equal to the pressure within that sphere (Imbert-Fick Law).[7] The first applanation tonometer used in human medicine was the Goldmann (fixed to the slit lamp). Portable applanation tonometers that facilitated the examination of bedridden patients and children were later developed and are represented by those using the Goldmann prism

(Perkins® and Kowa HA-2®), as well as others with different methodologies such as the Draeger® and MacKay-Marg® that are no longer sold, and the Tono-Pen, which is a portable digital applanation tonometer widely used in veterinary medicine.[1,2,7,8,16-19]

Recently, the rebound method, in which a light probe is used to make momentary corneal contact, has been introduced, and software analyzes the probe's deceleration and contact time as it touches the cornea. In simpler terms, the faster it slows down, the shorter the time that the probe contacts the cornea and the greater the intraocular pressure. The probe used is disposable, avoiding microbiological contamination, and the measurements are performed without the need for topical anesthesia, making it a good alternative for ocular examination. Rebound tonometry is well tolerated and causes minimal stress and discomfort. It is marketed under the name of Tonovet®; for laboratory animals Tonolab®, and more recently Tonovet Plus® was developed.[12-15]

Since the cornea of most animals differs from the human cornea, for the validation of a human tonometer for use in animals, it is mandatory to perform direct postmortem manometry to calibrate the device using a calibration curve and equation of linear regression with various manometer versus tonometer IOP measurements and with validation by in vivo study of real IOP versus tonometer IOP measurements.[9-11,20] Direct manometry versus tonometry has been studied in several species to validate, calibrate or confirm the efficacy and accuracy of measuring IOP with various types of tonometers, in dogs we can cite: Mackay-Marg®, TonAir and EMT-20® in 1977,[9] Mackay-Marg®, Tono-Pen® and Challenger® in 1990,[21] Mackay-Marg® and Tono-Pen® in 1992,[22] Tonovet® in 2005,[13] Perkins® in 2009,[16] and Kowa HA-2® in 2016.[18]

To date, there have been no studies in the literature that have compared the main tonometry methodologies such as rebound (Tonovet® and Tonovet Plus®), applanation (Tono-

Pen Avia Vet®) and applanation with the Goldmann prism (Kowa HA-2®) in dogs. Thus, the present study aimed to evaluate and compare the accuracy of these tonometers with different methodologies for measuring IOP in dogs.

MATERIALS AND METHODS

This study was approved by the Ethical Committee on Animal Use of UNOESTE (Protocol No. 4177) and was conducted according to the ARVO Guidelines (*Association for Research in Vision and Ophthalmology for the use of animals in ophthalmic and visual research)*. To determine the minimum sample size required to estimate the mean IOP measurements, we used the formula described by Pagano et al,[23] with a standard deviation value based on the results obtained by Tofflerine et al.[24] Based on these parameters, we concluded that a minimum of 130 eyes would be needed for the present study. The actual sample size (154 eyes) used in the study was larger than the minimum in order to improve reliability. All eyes included in the study initially underwent a slit lamp examination (SL-15®, Kowa, Tokyo, Japan) and indirect ophthalmoscopy (Pocket Jr®, Welch Allyn, New York, USA) to rule out any ophthalmic conditions that could affect the IOP or the ocular surface. All the owners of the animals signed an informed consent form before participating in the research.

A total of 154 eyes were used from 77 dogs, aged 1 to 10 years, weight between 4 and 35 kg, without breed preference, being the most prevalent: 46.8% mixed breed, 7.8% Lhasa Apso, 5.2% Poodle, 5.2% Shih Tzu, 3.9% English Bulldog, 3.9% Blue Heeler, 3.9% French Bulldog and other breeds. The dogs were divided into 3 groups: postmortem study (20 healthy eyes of 10 dogs, animals with mortis caused by various reasons) at the Veterinary Hospital of the UNOESTE and authorized for autopsy examination (postmortem up to 24 hours); in vivo study (20 healthy eyes of 10 healthy dogs from the University kennel, by normal laboratory, clinical and ophthalmic examinations) and outpatient study (114 eyes of 57 dogs) of routine eye care at the UNOESTE Veterinary Teaching Hospital were the first time of the animals in consultations, without prior eye treatment: 68 healthy eyes of 34 healthy dogs were submitted on clinical and laboratory examinations to confirm that 20 eyes from 10 dogs with clinical signs of glaucoma were healthy (congested episcleral vessels, blepharospasm, visual impairment, corneal edema, buphthalmia, fixed dilated pupil, anterior chamber changes, lens dislocation, retinal degeneration, and optic disc excavation), and 24 eyes from 12 dogs with clinical signs of uveitis (photophobia, blepharospasm, pain, epiphora, aqueous flare, keratic precipitates, hypopion, hyphema, ciliary injection, corneal edema, miosis and anterior or posterior synechia), the measurements were all done in the afternoon from 01:30-04:30 pm.

IOP measurements with the tonometers were obtained by the same examiner: (JVGCP) for Tonovet® (Icare, Vantaa, Finland), Tonovet Plus® (Icare, Vantaa, Finland) and Tono-Pen Avia Vet® (Reichert, New York, USA) and (SFA) for Kowa HA-2® (Kowa, Tokyo, Japan). The tonometers were used according to the manufacturer's instructions. Table 1 describes the main characteristics of the tonometers. In addition, the main advantages and disadvantages of each tonometer were evaluated at the end of the experiment by the researchers involved in this study, analyzing the following requirements of each device: accuracy, training required for adequate IOP measurements, need for topical anesthesia, probe (size, price and safety), battery cost benefit and tonometer price.

To study the accuracy of the tonometers at different IOP values, a postmortem study was performed comparing real IOP values among the tonometers by ocular direct manometry. The methodology was based on other previously published studies.[16-18] The eyelids were separated with a blepharostat, and the anterior chamber was cannulated with a 23-gauge scalp 2 mm posterior to the lateral limb for 10 h in the right eye and 2 h in the left eye. Cyanoacrylate glue was applied around the needle to prevent the leakage of aqueous humor.

The needle was connected to a polyethylene tube that was connected to a three-way stopcock that connected through another polyethylene tube to a 0.9% saline reservoir on one side and an aneroid manometer (Missouri, São Paulo, Brazil) on the other side. The aneroid manometer was in the zero position relative to the center of the eye. The calibration curve for manometry vs. tonometry was determined by artificially raising the IOP in 5 mmHg increments up to 60 mmHg (10 - 60 mmHg). Three readings were taken at each IOP level with the tonometers, and the average was calculated. Following an order for tonometer use, starting with Tonovet®, followed by Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2®, the first instillation of 1% fluorescein eye drops was performed for the formation of the fluorescein semicircle.

To evaluate the accuracy of the tonometers, an in vivo study was performed to compare the actual IOP with direct manometry in dogs anesthetized, and the IOP was obtained with the tonometers. The animals were anesthetized with the following protocol: preanesthetic medication with 0.2% acepromazine (Acepran®, Vetnil, São Paulo, Brazil) at a dose of 0.05 mg/kg IV followed by induction with 10 mg/ml propofol (Propovan®, Cristalia, São Paulo, Brazil) at a dose of 5 mg/kg IV and intubation via an endotracheal tube for anesthetic maintenance with 1.5% isoflurane (Isoflurano®, Biochimico, Rio de Janeiro, Brazil). For centralization of the eyeball, we used 10 mg/ml of the neuromuscular blocker atracurium besylate (Tracur®, Cristalia, São Paulo, Brazil) at a dose of 0.1 mg/kg IV. To reverse the possible effects of atracurium besylate, 0.5 mg/ml neostigmine (Normastig®, Union Química, São Paulo, Brazil) at a dose of 0.01 mg/kg plus 0.25 mg atropine sulfate (Pasmodex®, Isofarma, São Paulo, Brazil) at a dose of 0.04 mg/kg was used. After the animals were anesthetized, the eyelids were separated with blepharostat, three readings of the IOP were taken with the tonometers, and the mean was calculated in the following sequence: Tonovet, Tonovet Plus, Tono-Pen Avia Vet and Kowa HA-2 tonometers. Prior to the use of Tono-Pen

Avia Vet, a topical anesthetic was used with 1 drop of eye drops based on 1% tetracaine hydrochloride + 0.1% phenylephrine hydrochloride (Anestésico®, Allergan, São Paulo, SP, Brazil); prior to reading with the Kowa HA-2 tonometer, 1 drop of 1% fluorescein eye drops (Fluoresceína®, Allergan, São Paulo, SP, Brazil) was instilled for the formation of fluorescein semicircles. For the prevention of transmissible eye diseases, the protocol of each tonometer after use was as follows: Tonovet® and Tonovet Plus® probe change (Icare tonometer probe®, Icare, Vantaa, Finland), Tono-Pen Avia Vet film® change (Ocu-Film®, Reichert, New York, USA), and Kowa HA-2 Goldmann prism® (Kowa, Tokyo, Japan) in a 0.9% physiological solution, maintained for 5 minutes immersed in a 3% hydrogen peroxide solution and dried with a sterile gauze.[25] After tonometer IOP readings, direct manometry was performed as previously described in the postmortem study. After the IOP measurement was read with the aneroid manometer, the needle was removed from the anterior chamber, and then the cyanoacrylate glue was instilled using a 25x7 needle at the puncture site to seal the perforation and prevent extravasation of the aqueous humor.[26] Following this procedure, the animals were treated with the instillation of 1 drop 3x/day of tobramycin antibiotic eye drops (Tobrex®, Novartis, Sao Paulo, Brazil) and diclofenac anti-inflammatory eye drops (Still®, Allergan, São Paulo, Brazil) for 1 week and assessed by daily ophthalmic examination.

To evaluate the routine clinical use of the tonometers, an outpatient IOP measurement study was performed in normal eyes of healthy dogs, and in eyes with clinical signs of glaucoma and uveitis. Tonometer readings were performed with the following order of use: 1st Tonovet®, 2nd Tonovet Plus®, 3rd Tono-Pen Avia Vet® after the previous instillation of 1 drop of anesthetic eye drops and 4th Kowa HA-2® instillation of 1 drop of 1% fluorescein eye drops for the formation of fluorescein semicircles. Previous studies reported that the use interval between tonometers can be 2 minutes[12] or 1 minute.[27] In the present study, a 2-minute interval between the use of each tonometer was used.

In the postmortem study, regression lines were constructed for the measured values of manometry versus tonometry, and the coefficient of determination (r^2) and the linear regression equation were calculated as well as the Bland-Altman agreement analysis to compare the two methods of measuring IOP (manometry vs. tonometry). A series of agreements was defined as the mean bias of ± 2 standard deviations. In the in vivo and outpatient studies, the mean and standard deviation of the measured IOP values were calculated and compared statistically with analysis of variance (ANOVA). A significance level of 5% (P<0.05) was adopted.

RESULTS

The main advantages and disadvantages observed during this study by the authors with the use of each tonometer are described in Table 2.

In the postmortem study, the correlation coefficient (r^2) values (Fig. 1) in descending order were Kowa HA-2® (0.989), Tonovet Plus® (0.984), Tonovet® (0.981) and Tono-Pen Avia Vet® (0.847). The linear regression equation was y = 1.017x - 0.8886 (Tonovet), y = 0.9969x + 0.1194 (Tonovet Plus), y = 0.773x - 0.6835 (Tono-Pen Avia Vet) and y = 0.9397x + 0.1954 (Kowa HA) -2). The Bland-Altman plot comparing the various tonometers with the manometry results is described in Figure 2.

All IOP values (mean ± standard deviation and minimum and maximum range) in the in vivo study are described in Table 3, and the outpatient study is described in Table 4. In the in vivo study, there was no significant difference (p> 0.05) between the IOP values measured between the manometry and Tonovet®, Tono-Pen Avia Vet® and Kowa HA-2® tonometers, with Tonovet Plus being the only tonometer that presented significantly higher IOP values (p <0.05) than the manometry and the other tonometers. In the outpatient study, again, the only tonometer that showed a significant difference (p <0.05) between the measured IOP values and the other tonometers in all studied groups (healthy, with signs of glaucoma and uveitis) was Tonovet Plus®. In all the groups studied, IOP values measured with Tonovet Plus® averaged 3 to 5 mmHg higher than those measured with the other tonometers.

DISCUSSION

This is the first study in the field of veterinary medicine that compares the main tonometers used in dogs to measure IOP with different types of methodology: rebound (Tonovet® and Tonovet Plus®) and applanation (Tono-Pen Avia Vet®) with the applanation methodology of Goldmann (Kowa HA-2®). According to the authors, Tonovet® and Tonovet Plus® generally have more advantages in terms of their daily use, but all tonometers showed excellent accuracy for measuring IOP in dogs (Tab. 2). The IOP values that came closest to the IOP values measured by manometry (in vivo study) were, in decreasing order, Kowa HA-2®, Tono-Pen Avia Vet® and Tonovet®; Tonovet Plus® differed statistically (p>0.05) with higher values than with manometry (Tab. 3).

In the outpatient study (Tab. 4), measuring IOP in healthy eyes with clinical signs of glaucoma and uveitis, Tonovet Plus® had significantly higher IOP values ($p < 0.05$) than the values measured with the other tonometers. In both the in vivo and outpatient studies, the IOP values measured by Tonovet Plus averaged 3 to 5 mmHg higher than those measured with the other tonometers, which is consistent with some recent studies, such as those of Muirhead and Ben-Shlomo (2018)[28] who compared IOP values in healthy dogs with Tonovet® (15.0 ± 3.2 mmHg; range 7-22 mmHg); Tonovet Plus® (19.2 ± 3.1 mmHg; range 11-25 mmHg) and Tono-Pen Avia Vet® (12.8 ± 2.9 mmHg; range 6-19) and concluded that Tonovet Plus® had significantly higher IOP values than Tonovet® and Tono-Pen Avia Vet®.

In another recent study[29] comparing the Schiotz® tonometer with the Tono-Pen Avia Vet® tonometer, the IOP values with the Schiotz® tonometer were in the range of 12 to 24 mmHg, with an average of 16.3 ± 2.1 mmHg, and those with the Tono-Pen Avia Vet® tonometer were in the range of 11 to 25 mmHg, with an average of 18.1 ± 3.8 mmHg, with the results between the two tonometers differing statistically by 1.79 mmHg. In our study, the average IOP with Tono-Pen Avia Vet® was slightly low (16.2 ± 2.4 mmHg), and the variation was quite similar, from 13 to 23 mmHg. The correlation coefficient found with Tono-Pen Avia Vet® in the previous study was 0.894, which is close to the correlation coefficient found in our research of 0.847.

Nagata et al (2011)[30] compared the Tonovet and Tono-Pen XL® tonometers in the measurement of IOP in dogs and found that the values measured by Tonovet® were underestimated values compared to those measured by Tono-Pen XL® when the measurements were 5-15 mmHg, and the inverse occurred when the pressure was above 25 mmHg when Tono-Pen XL® was used to measure values below Tonovet, differing from our study comparing Tonovet® with Tono-Pen Avia Vet® as, throughout the study, Tono-Pen Avia Vet® values were lower than those found with Tonovet. Kulualp et al (2017)[31] also compared Tonovet® and Tono-Pen Vet® in clinically normal Turkish Shepherd dogs, and the IOP measurements were very close to those found in our study, with 17.63 ± 3.34 mmHg and 16.8 ± 3.2 mmHg measured with Tonovet® and 14.95 ± 2.92 mmHg and 16.2 ± 2, 4 mmHg measured with Tono-Pen Vet®, respectively.

The correlation coefficient (r^2) observed in our study with the Kowa HA-2® tonometer was 0.989, and the average was 14.2 ± 1.6 for the measurements of healthy eyes, 23.9 ± 5.0 for eyes with glaucoma and 12.8 ± 1.9 for eyes with uveitis. These results were very close to the values found by Andrade et al (2016)[18] with a correlation coefficient 0.993, 15.1 ± 1.8 for healthy eyes, 25.2 ± 4.0 for eyes with glaucoma and 10.1 ± 2.3 for eyes with uveitis.

The Bland-Altman graph shows that all underestimated IOP tonometers relative to high IOP manometry (30-60 mmHg) in the postmortem study. This is in line with the study by Minella et al (2018) 32, who validated Tonovet Plus® and Tono-Pen Avia Vet® in normal canine eyes and observed this at values of 30-70 mmHg.

We can conclude that there was a strong correlation between IOP values with manometry and Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2®, demonstrating the high accuracy of all tonometers. The highest IOP values were measured with Tonovet Plus® and the lowest with Kowa HA-2®, which reinforces the need for a differentiated IOP value table for each type of tonometer. All tonometers were accurate in measuring IOP in dogs, including the latest Tonovet Plus, which showed an excellent correlation coefficient.

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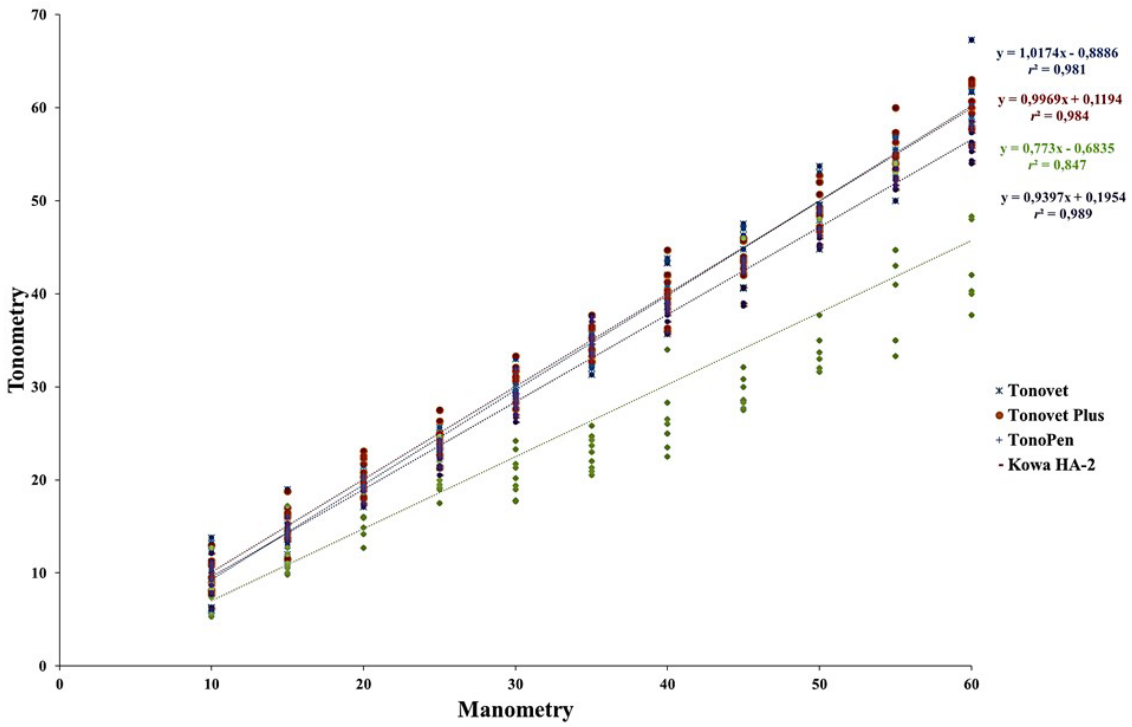

Figure 1 Comparison of intraocular pressure (IOP) measurements in mmHg between manometry (aneroid manometer) vs. tonometry (Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2®) in 10 dogs (*n* = 20 eyes) in a postmortem study. The solid line is the calculated regression line. r^2 (correlation coefficient)

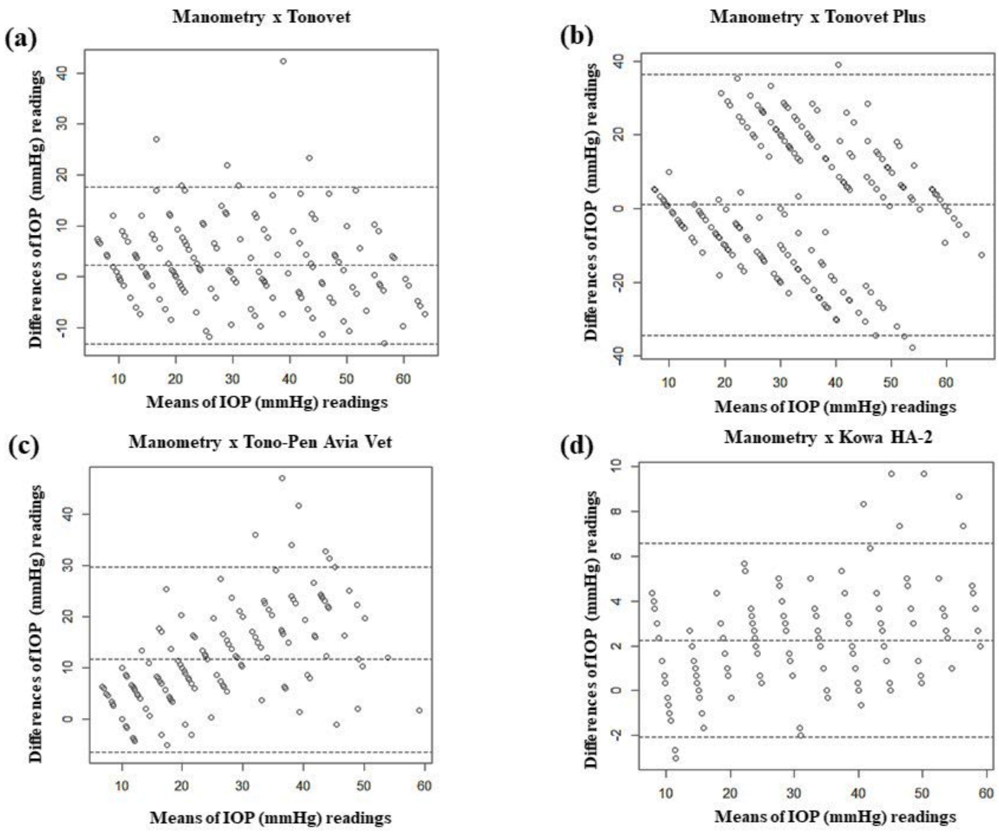

Figure 2 Bland-Altman plot comparing intraocular pressure (IOP) in mmHg in dogs (*n* = 20 eyes): (a) Tonovet® tonometer and manometer, (b) Tonovet Plus® tonometer and manometer, (c) Tono-Pen Avia Vet® tonometer and manometer, and (d) tonometer Kowa HA-2® and manometer.

Table 1 Main characteristics of Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2 tonometers.

Tonometers		Scale / Manufacturer	Methodology	Source / Weight	Species	Characteristics
Tonovet®		5 – 80 mmHg Icare Finland	Rebound 1.0 mm probe	4 AA batteries 250g	Dog Cat Horse	LCD display, error codes, 2 settings: dog/cat and horse. Does not require daily calibration.
Tonovet Plus®		10 – 60 mmHg Icare Finland	Rebound 1.0 mm probe	4 AA batteries 230g	Dog Cat Rabbit Horse	Oled in colours display, positioning assistant lights for correct aligment, error messages with pictures, option for one-press-measurement (take all six readings by one press only). Does not require daily calibration.
Tonopen Avia Vet®		1 – 99 mmHg Reichert USA	Applanation 1.02mm probe	Powercell batterie Pack 70g	Dog Cat	LCD display with number of applanations collected, statistical confidence indicator, and battery life status. Does not require daily calibration
Kowa HA-2®		0 – 60 mmHg Kowa Japan	Goldmann applanation 3.06 mm prism	2 AA batteries 240g	Dog Cat	Display that visualizes fluorescein semicircles. Does not require daily calibration.

Table 2 Advantages (X) and disadvantages (-) observed by the authors in this study using Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2® tonometers.

Characteristics	Tonometers			
	Tonovet	Tonovet Plus	Tono-Pen Avia Vet	Kowa HA-2
Accuracy	X	X	X	X
Training (facility)	X	X	X	-
No topical anesthesia	X	X	-	-
Probe (smaller size)	X	X	-	-
Probe (Disposable)	X	X	X	-
Battery (cost/benefit)	X	X	-	X
Price	-	-	-	X

Table 3 Means and standard deviations for the IOP values obtained in the in vivo study in 20 eyes from 10 dogs of manometry versus tonometry with Tonovet®, Tonovet Plus®, Tono-Pen Avia Vet® and Kowa HA-2® tonometers.

Animal	**Manometer**	**Tonovet®**	**Tonovet Plus®**	**Tono-Pen Avia Vet®**	**Kowa HA-2®**
1	15.5	22.0	22.0	18.3	18.0
2	15.5	16.0	22.0	15.8	15.3
3	19.0	20.5	21.3	15.5	18.2
4	20.0	22.7	24.0	19.5	17.0
5	14.0	14.0	17.2	17.0	13.5
6	14.5	18.0	21.2	14.0	13.5
7	16.5	18.0	21.8	22.7	16.8
8	15.5	16.5	17.0	15.7	16.2
9	16.0	15.0	18.3	15.5	15.3
10	21.5	18.5	21.3	16.8	16.8
Mean±SD*	16.8±2.5**[a]	18.1±2.9[a]	20.6±2.3[b]	17.1±2.5[a]	16.1±1.7[a]
Range	14.0-21.5	14.0-22.7	17.0-24.0	14.0-22,7	13.5-18.2

* Mean ± standard deviation.
** Different superscript letters indicate significant differences (*P* <0.05) ANOVA.

Table 4 Means and standard deviations of IOP values obtained with Tonovet®, Tonovet Plus®, Tono-Pen Avia® and Kowa HA-2® tonometers in the outpatient study of 112 eyes from 56 dogs (66 healthy eyes, 20 eyes with glaucoma and 26 eyes with uveitis) in dogs treated at the ophthalmology department of UNOESTE Veterinary Hospital, Presidente Prudente, SP, Brazil.

Group	Tonovet®	Tonovet Plus®	Tono-Pen Avia Vet®	Kowa HA-2®
Health				
Mean±SD*	16.8±3.2[a]	19.2±2.9[b]	16.2±2.4[a]	15.0±1.3[a]
Range	11.7-24.5	14.7-25.0	13.3-23.0	12.5-18.0
Glaucoma				
Mean±SD*	30.2±3.5[a]	35.0±6.1[b]	29.5±4.2[a]	23.9±5.0[a]
Range	26.0-34.6	29.5-44.8	26.0-37.7	20.0-33.7
Uveitis				
Mean±SD*	14.2±1.4[a]	17.6±1.9[b]	13.7±2.1[a]	12.6±1.7[a]
Range	12.0-15.5	15.5-20.5	11.0-16.5	10.0-14.8

* Mean ± standard deviation.
** Different superscript letters indicate significant differences ($P < 0.05$).

ANEXO

QRCode to watch video of tonometers Tonovet, Tonovet Plu, Tono-Pen Avia Vet e Kowa HA-2 in ambulatory use (use your cell phone or tablet to watch).

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