Bruno Pimentel de Figueiredo

ANÁLISE COMPARATIVA DA AMPLITUDE DO PULSO OCULAR E PRESSÃO DE PERFUSÃO OCULAR EM GLAUCOMATOSOS, HIPERTENSOS OCULARES E INDIVÍDUOS NORMAIS

Orientador: Prof. Dr. Sebastião Cronemberger

Faculdade de Medicina
Universidade Federal de Minas Gerais
Belo Horizonte
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Tese apresentada ao Programa de Pós-graduação em Ciências Aplicadas à Cirurgia e à Oftalmologia da Faculdade de Medicina da Universidade Federal de Minas Gerais, como requisito parcial para obtenção do título de Doutor em Medicina.

Área de Concentração: Oftalmologia

Orientador: Prof. Dr. Sebastião Cronemberger

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Belo Horizonte
2012

Figueiredo, Bruno Pimentel de.
F475a Análise comparativa da amplitude do pulso ocular e pressão de perfusão ocular em glaucomatosos, hipertensos oculares e indivíduos normais [manuscrito]. / Bruno Pimentel de Figueiredo. - - Belo Horizonte: 2012.
110f.
Orientador: Sebastião Cronemberger Sobrinho.
Área de concentração: Ciências Aplicadas à Cirurgia e à Oftalmologia.
Tese (doutorado): Universidade Federal de Minas Gerais, Faculdade de Medicina.

1. Glaucoma. 2. Pressão Intra-Ocular. 3. Tonometria Ocular. 4. Dissertações Acadêmicas. I. Cronemberger Sobrinho, Sebastião. II. Universidade Federal de Minas Gerais, Faculdade de Medicina. III. Título.
NLM: WW 290

Ficha catalográfica elaborada pela Biblioteca J. Baeta Vianna – Campus Saúde UFMG

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ATA DA DEFESA DE TESE DE DOUTORADO DE **BRUNO PIMENTEL DE FIGUEIREDO,** nº de registro 2008670583.

Às quatorze horas do dia 23 de agosto de dois mil e doze, reuniu-se na Faculdade de Medicina Universidade Federal de Minas Gerias, a Comissão Examinadora de tese indicada pelo Colegiado do Programa, para julgar, em exame final, o trabalho intitulado: **"ANÁLISE COMPARATIVA DA AMPLITUDE DO PULSO OCULAR E PRESSÃO DE PERFUSÃO OCULAR EM GLAUCOMATOSOS, HIPERTENSOS OCULARES E INDIVÍDUOS NORMAIS."**, requisito final para a obtenção do grau de Doutor em Ciências Aplicadas à Cirurgia e à Oftalmologia, pelo Programa de Pós-Graduação em Ciências Aplicadas à Cirurgia e à Oftalmologia. Abrindo a sessão, o Presidente da Comissão, Prof. Sebastião Cronemberger Sobrinho, após dar a conhecer aos presentes o teor das normas regulamentares do trabalho final passou a palavra ao candidato para apresentação de seu trabalho. Seguiu-se a arguição pelos examinadores, com a respectiva defesa do candidato. Logo após, a Comissão se reuniu sem a presença do candidato e do público para julgamento e expedição do resultado final. Foram atribuídas as seguintes indicações:

Prof. Sebastião Cronemberger Sobrinho/Orientador	Instituição: UFMG	Indicação: APROVADO
Prof. Galton Carvalho Vasconcelos	Instituição: UFMG	Indicação: APROVADO
Prof. Homero Gusmão de Almeida	Instituição: UFMG	Indicação: APROVADO
Prof. Adroaldo Alencar Costa Filho	Instituição: UFRJ	Indicação: APROVADO
Prof. Marcelo Palis Ventura	Instituição: UFF	Indicação: APROVADO

Pelas indicações, o candidato foi considerado APROVADO.

O resultado final foi comunicado publicamente ao candidato pelo Presidente da Comissão. Nada mais havendo a tratar, o Presidente encerrou a sessão e lavrou a presente ATA, que será assinada por todos os membros participantes da Comissão Examinadora. Belo Horizonte, 23 de Agosto de 2012.

Prof. Sebastião Cronemberger Sobrinho/Orientador _____

Prof. Galton Carvalho Vasconcelos _____

Prof. Adroaldo Alencar Costa Filho _____

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DECLARAÇÃO

A Comissão Examinadora abaixo assinada, composta pelos Professores Doutores, Sebastião Cronemberger Sobrinho, Galton Carvalho Vasconcelos, Homero Gusmão de Almeida, Adroaldo Alencar Costa Filho, Marcelo Palis Ventura, aprovou a defesa da Tese intitulada: **"ANÁLISE COMPARATIVA DA AMPLITUDE DO PULSO OCULAR E PRESSÃO DE PERFUSÃO OCULAR EM GLAUCOMATOSOS, HIPERTENSOS OCULARES E INDIVÍDUOS NORMAIS."**, apresentada pelo Doutorando **BRUNO PIMENTEL DE FIGUEIREDO,** para obtenção do título de Doutor em Ciências Aplicadas à Cirurgia e à Oftalmologia, pelo Programa de Pós-Graduação em Ciências Aplicadas à Cirurgia e à Oftalmologia da Faculdade de Medicina da Universidade Federal de Minas Gerais, realizada em 23 de Agosto de 2012.

Prof. Sebastião Cronemberger Sobrinho
Orientador

Prof. Galton Carvalho Vasconcelos

Prof. Homero Gusmão de Almeida

Prof. Adroaldo Alencar Costa Filho

Prof. Marcelo Palis Ventura

Ao meu pai e à minha mãe,
meus grandes exemplos,
por me fazerem acreditar na minha capacidade.

AGRADECIMENTOS

Ao meu pai, pela honra de tê-lo como exemplo diário na minha prática médica e pelo incentivo incondicional na realização deste trabalho.

À minha mãe, por ter me ensinado a ter garra, autoestima e principalmente perseverança para alcançar meus objetivos.

À Brenda, amor da minha vida, exemplo de companheirismo, cumplicidade e carinho.

Aos amigos Fabio Nishimura Kanadani e Nikias Alves da Silva pelas valiosas opiniões sobre os artigos científicos desta tese.

Ao Dr. Wagner Duarte Batista, por aceitar e encorajar os meus períodos de ausência da Santa Casa de Belo Horizonte durante a execução deste trabalho.

Ao Dr. Ivan Haeflinger, pelo incentivo e por ampliar os meus horizontes na área da pesquisa.

Ao Dr. Konstantin Gugleta, meu maior exemplo de pesquisador clínico em oftalmologia, sempre presente quando solicitado, compartilhando gentilmente o seu vasto conhecimento.

Ao Dr. Alexandre Simões Barbosa, pelos conselhos sobre os rumos desta pesquisa.

Ao Dr. Marcelo Militão Abrantes e sua equipe da META estatística, pelo profissionalismo impecável dos seus relatórios.

Aos Profs. Marcelo Dias Sanches e Ivana Duval de Araújo, pela dedicação de ambos ao programa de pós-graduação.

Aos meus amigos e familiares, pelo apoio incondicional, dando-me forças nas horas boas e nas ruins.

Ao meu orientador, Prof. Sebastião Cronemberger, por ter aceitado o desafio de me acompanhar nesta pesquisa.

À Mari do CPG, pela excelência no exercício das suas funções e por estar sempre genuinamente disposta a ajudar.

Aos pacientes, que ao aceitarem participar desta pesquisa contribuíram de forma plena em prol da ciência.

"Se quisermos alcançar resultados nunca antes alcançados,

devemos empregar métodos nunca antes testados."

Francis Bacon

1561 - 1626

LISTA DE ABREVIATURAS E SIGLAS

APO	Amplitude do pulso ocular
BP	*Blood pressure*
BPF	Bruno Pimentel de Figueiredo
CCT	*Central corneal thickness*
CI	*Confidence interval*
COAG	*Chronic open-angle glaucoma*
Coef.	Coeficiente
CPG	Centro de Pós-graduação
DBP	*Diastolic blood pressure*
DCT	*Dynamic contour tonometry*
ECC	Espessura corneana central
EGPS	*European Glaucoma Prevention Study*
FSO	Fluxo sanguíneo ocular
GAT	*Goldmann applanation tonometry*
GHT	*Glaucoma Hemifield Test*
GON	*Glaucomatous optic neuropathy*
GPN	Glaucoma de pressão normal
HFA	*Humphrey field analyzer*
HO	Hipertenso ocular
IC	Intervalo de confiança
IOP	*Intraocular pressure*
MAP	*Mean arterial pressure*
MD	*Mean deviation*
mmHg	Milímetro de mercúrio
µm	Micrômetro
n	Tamanho da amostra
n.s.	*non significant*
NTG	*Normal tension glaucoma*
OBF	*Ocular blood flow*
OH	*Ocular hypertensive*

OHTS	*Ocular hypertensive treatment study*
OPA	*Ocular pulse amplitude*
OPP	*Ocular perfusion pressure*
P	valor-*P*, *P-value*
PA	Pressão arterial
PAD	Pressão arterial diastólica
PAM	Pressão arterial média
PAS	Pressão arterial sistólica
PIO	Pressão intraocular
POAG	*Primary open angle glaucoma*
PP	*Pulse pressure,* pressão de pulso arterial
PPD	Pressão de perfusão diastólica
PPO	Pressão de perfusão ocular
PPS	Pressão de perfusão sistólica
pRNFL	*Peripapillary retinal nerve fiber layer*
PSD	*Pattern Standard Deviation*
Q_1	Primeiro quartil, *first quartile*
Q_3	Terceiro quartil, *third quartile*
r	Coeficiente de correlação de Pearson
ρ	Coeficiente de correlação de Spearman
SD	*Standard deviation*
SBP	*Systolic blood pressure*
TAG	Tonometria de aplanação de Goldmann
TDC	Tonometria dinâmica de contorno
UFMG	Universidade Federal de Minas Gerais
VF	*Visual field*

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RESUMO

Objetivos: correlacionar pressão de perfusão ocular e amplitude do pulso ocular em três grupos: glaucomatosos, hipertensos oculares e normais; e avaliar a relação de parâmetros de pressão arterial com a pressão intraocular. **Métodos:** foram recrutados 90 indivíduos para a pesquisa, sendo 30 recém-diagnosticados com glaucoma, sem história prévia de tratamento antiglaucomatoso; 30 apresentavam hipertensão ocular (HO) sem sinais característicos de glaucoma na avaliação do disco óptico e no exame de campo visual; e 30 voluntários com pressão intraocular (PIO) dentro dos valores de referência da normalidade (< 21 mmHg) e sem glaucoma. A PIO foi medida pela tonometria de aplanação de Goldmann (TAG) e tonometria dinâmica de contorno (TDC). Foi medida pressão arterial (PA), feito exame oftalmológico completo além de campo visual computadorizado e gonioscopia em cada paciente. A espessura corneana central (ECC) foi medida por paquimetria ultrassônica. A pressão de perfusão ocular (PPO) foi calculada pela diferença entre a pressão arterial média (PAM) e a PIO. A amplitude do pulso ocular (APO) foi fornecida pela TDC. **Resultados:** a PIO média na TAG foi de 19,0 ± 5,1 mmHg no grupo do glaucoma, 22,4 ± 2,1 mmHg nos HOs e 12,9 ± 2,2 mmHg nos indivíduos normais. Já a PIO média medida pela TDC foi de 22,7 ± 4,3 mmHg nos glaucomatosos, 22,3 ± 2,8 mmHg nos HOs e 14,3 ± 1,6 mmHg nos normais. A PPO média no glaucoma foi de 46,3 ± 7,9 mmHg, nos HOs 41,5 ± 5,2 mmHg e nos indivíduos normais 50,2 ± 7,0 mmHg. A APO média foi de 3,4 ± 1,2 mmHg no grupo glaucoma, 3,5 ± 1,2 mmHg nos HOs e 2,6 ± 0,9 mmHg nos normais. Avaliando o conjunto dos grupos, a APO média foi de 3,2 ± 1,2 mmHg. A ECC média foi de 529,1 ± 41,4 µm, 569,1 ± 30,0 µm e

553,6 ± 28,6 µm nos grupos glaucoma, HO e normais, respectivamente. A pressão arterial sistólica (PAS) média no conjunto dos grupos foi de 125,8 ± 14,3 mmHg e nos grupos glaucoma, HO e normal de 131 ± 16,7 mmHg, 125 ± 12,3 mmHg e 121,5 ± 12,1 mmHg, respectivamente. A pressão arterial diastólica (PAD) foi de 82,2 ± 11,3 mmHg, 81,2 ± 6,9 mmHg e 81,5 ± 9,0 mmHg nos grupos glaucoma, HO e normal, respectivamente, e no total foi 81,6 ± 9,1 mmHg. A pressão de pulso (diferença entre PAS e PAD) teve média de 44,2 ± 10,7 mmHg no conjunto dos grupos e 48,8 ± 10,5 mmHg, 43,8 ± 11,1 mmHg e 40,0 ± 8,7 mmHg nos grupos glaucoma, HO e normal, respectivamente. Não houve correlação entre APO e PPO nos grupos glaucoma, HO e normal *(P/r* = 0,865/-0,032, 0,403/-0,156 e 0,082/-0,307, respectivamente). Confirmou-se forte correlação entre PIO aferida pela TAG e TDC (*P/r* = <0,001/0,858). APO correlacionou-se à PIO medida pela TAG (*P/r* = <0,001/0,430) e DCT e (*P/r* = <0,001/0,399). Obteve-se correlação moderada entre APO e pressão de pulso arterial (*P/r* = 0,017/0,245) na avaliação do conjunto dos grupos. Na avaliação isolada de cada grupo, apenas o HO apresentou correlação com a APO (*P/r* = 0,005/0,496). **Conclusões:** não houve correlação entre pressão de perfusão ocular e amplitude do pulso ocular em indivíduos com glaucoma, HO e normais. A PIO medida pela TAG correlacionou-se à PIO da TDC. A ECC exerceu mais influência à TAG do que à TDC. A amplitude do pulso ocular apresentou apenas correlação moderada à pressão de pulso arterial, ressaltando mecanismos vasculares de regulação da perfusão sanguínea ocular.

Palavras-chave: Glaucoma. Pressão de perfusão ocular. Amplitude do pulso ocular. Tonometria dinâmica de contorno. Pressão arterial sistêmica.

ABSTRACT

Objectives: To correlate ocular perfusion pressure and ocular pulse amplitude in three different groups: Glaucoma patients, ocular hypertensives, and normal individuals. As well as assess the relation between blood pressure parameters with intraocular pressure. **Material and Methods:** Ninety patients were enrolled for the study. Among them: 30 were recently diagnosed with glaucoma, with no previous history of ocular hypotensive medications; 30 presented ocular hypertension (OH) and no specific signs of glaucoma, either by optic nerve examination or visual field; and 30 volunteers with intraocular pressure (IOP) within normal values (< 21 mmHg) and no evidence of glaucoma. IOP was measured by two different methods, Goldmann applanation tonometry (GAT) and dynamic contour tonometry (DCT). Arterial blood pressure (BP) was taken, automated visual field (VF) and gonioscopy a complete ophthalmic exam was also performed. Central corneal thickness (CCT) was measured by ultrasound pachymetry. Ocular perfusion pressure (OPP) was calculated by the difference between mean arterial pressure (MAP) and IOP. Ocular pulse amplitude (OPA) was directly given by DCT. **Results:** Mean IOP measured by TAG was 19.0 ± 5.1 mmHg in glaucoma, 22.4 ± 2.1 mmHg in OH, and 12.9 ± 2.2 mmHg in the normals. Mean DCT IOP was 22.7 ± 4.3 mmHg in glaucoma, 22.3 ± 2.8 mmHg in the OH, and 14.3 ± 1.6 mmHg in the normal participants. Mean OPP in the glaucoma group was 46.3 ±7.9 mmHg, in the OH was 41.5 ± 5.2 mmHg, and in the normals 50.2 ± 7.0 mmHg. Mean OPA was 3.4 ± 1.2 mmHg in glaucoma, 3.5 ± 1.2 mmHg in OH, and 2.9 ± 0.9 mmHg in the normals. Analyzing the three groups together, mean OPA was 3.2 ± 1.2 mmHg. Pachymetry revealed a mean CCT of

529.1 ± 41.4 µm, 569.1 ± 30.0 µm, and 553.6 ± 28.6 µm, in the glaucoma group, OH, and normals, respectively. Mean systolic blood pressure (SBP) for all patients was 125.8 ± 14.3 mmHg and in the glaucoma, OH, and normal groups, was 131.1 ± 16.7 mmHg, 125 ± 12.3 mmHg, and 121.5 ± 12.1 mmHg, respectively. Mean diastolic blood pressure (DBP) was 82.2 ± 11.3 mmHg, 81.2 ± 6.9 mmHg, and 81.5 ± 9.1 mmHg in the glaucoma, OH, and normal groups, respectively and including all three groups it was 81.6 ± 9.1. Arterial pulse pressure (PP), which is the notation of SBP minus DBP, had mean values of 44.2 ± 10.7 mmHg for all patients, and 48.8 ± 10.5 mmHg, 43.8 ± 11.1 mmHg, and 40.0 ± 8.7 mmHg in the glaucoma, OH, and normal groups, respectively. No correlation between OPA and OPP was found neither in glaucoma (*P/r* = 0.865/-0.032), OH (*P/r* = 0.403/-0.156), or normals (*P/r* = 0.082/-0.307). IOP measured by TAG appeared strongly correlated to DCT (*P/r* = <0.001/0.858). OPA was correlated with TAG (*P/r* = <0.001/0.403) and DCT (*P/r* = <0.001/0.399), showing that OPA closely linked to IOP. A moderate correlation was observed between OPA and PP (*P/r* = 0.017/0.245) when all groups were analyzed together. The analysis for each group separately, only OH showed a positive correlation between OPA and PP (*P/r* = 0.005/0.496). **Conclusions:** No correlation was observed between OPP and OPA analyzing glaucoma patients, OH, and normal individuals. GAT values were strongly correlated to DCT values, although GAT tended to be lower than DCT, especially in individuals with low CCT. OPA showed only a moderate correlation with PP, drawing the attention to vascular mechanisms regulating ocular perfusion.

Keywords: Glaucoma. Ocular perfusion pressure. Ocular pulse amplitude. Dynamic contour tonometry. Systemic blood pressure.

SUMÁRIO

INTRODUÇÃO

INTRODUÇÃO

O glaucoma crônico de ângulo aberto é uma doença multifatorial no nervo óptico, que tem a pressão intraocular (PIO) elevada como principal fator de risco (KOTECHA *et al*., 2010). O tratamento atual do glaucoma restringe-se à redução da PIO, mesmo sabendo que alguns pacientes persistem com a progressão da doença após atingirem valores da PIO estatisticamente normais. Existem também pessoas que desenvolvem o glaucoma com PIO em valores baixos. Para estas, é dado o diagnóstico de glaucoma de pressão normal (GPN) (ABEGÃO PINTO *et al*., 2011; KIM *et al*., 2010). Está sendo cada vez mais estudada a existência de fatores de risco, que não a PIO elevada, no desenvolvimento do glaucoma. Alguns destes fatores de risco, como aterosclerose, enxaqueca, fenômeno de Raynaud e disfunção vasoespástica já foram identificados como tendo influência na etiopatogenia do glaucoma (GOLDBERG *et al*., 1981; PHELPS; CORBETT, 1985; GASSER; DRANCE *et al*., 1988; FLAMMER, 1991; WALDMANN *et al*., 1996).

Uma maneira de avaliar a quantidade de sangue que está chegando a determinado tecido é através da medida da pressão de perfusão. A fórmula para o cálculo da pressão de perfusão é a partir da diferença entre pressão arterial média (PAM) e pressão venosa. A PAM é obtida por: PAD + [1/3 X (PAS-PAD)], onde PAS = pressão arterial sistólica e PAD = pressão arterial diastólica. No olho, a pressão venosa é igual ou ligeiramente mais alta que a PIO (COSTA; ARCIERI; HARRIS, 2009). A pressão arterial (PA) na artéria oftálmica é 2/3 da PA braquial e com isso a fórmula para obtenção da pressão de perfusão ocular (PPO) é 2/3 da PAM menos a PIO (GROVER; BUDENZ, 2011). A medida da PPO é uma das

formas de investigação da porção vascular do glaucoma. Alguns estudos associaram baixos valores de PPO com a presença do dano glaucomatoso (HAYREH, 2001; TIELSCH *et al*., 1995; WEINREB, 2009).

Além do estudo da PPO e sua importância na etiopatogenia do glaucoma, foram investigados alguns outros fatores que têm na sua fórmula a associação de parâmetros da PA e PIO (CAPRIOLI; COLEMAN, 2010; COSTA; ARCIERI; HARRIS, 2009). Entre eles, a pressão de perfusão diastólica (PPD) e pressão de perfusão sistólica (PPS) que, em vez de utilizar a PAM, leva em consideração a PA diastólica e PA sistólica, respectivamente. A relação entre PPD baixa e glaucoma foi descrita em vários estudos (BONOMI *et al*., 2000; COSTA *et al*., 2010; HULSMAN *et al*., 2007; ORZALESI *et al*., 2007).

Deve ser levado em consideração o fato de que a PIO exerce grande influência na PPO. Quando se busca um método de avaliação da circulação sanguínea ocular, tal método deveria ser independente do valor da PIO, especialmente porque o estudo do componente vascular tem mais importância nos pacientes com glaucoma de pressão normal (GPN).

A influência da PA como fator de risco independente no glaucoma foi alvo de vários estudos. O resultado foi que tanto a hipertensão arterial sistêmica (BONOMI *et al*, 2000; MITCHELL *et al*. 2004; ORZALESI *et al*., 2007) quanto a hipotensão arterial sistêmica (COLLIGNON *et al*., 1998; GRAHAM; DRANCE, 1999; TOPOUZIS *et al*., 2006) foram demonstradas como possíveis fatores de risco associados ao glaucoma. A variação circadiana da PA e o seu efeito na etiopatogenia do glaucoma também foram exaustivamente investigados, com resultados ressaltando associação do descenso noturno acentuado da PA nos indivíduos com glaucoma, quando comparados com pessoas sem a doença

(CHOI *et al*., 2006; COLLIGNON *et al*., 1998; DETRY *et al*., 1996; GRAHAM *et al.*, 1995; KASHIWAGI *et al*., 2001; TOKUNAGA *et al*., 2004).

A tonometria de aplanação de Goldmann (TAG), método padrão-ouro para medida da PIO, precisa gerar uma aplanação da região central da córnea no momento de sua aferição. Desta forma, indivíduos com a córnea fina tendem a ter a PIO subestimada pela TAG, haja visto que a força necessária para gerar a aplanação é menor nesses casos. O contrário também é verdadeiro, pessoas com maior espessura corneana tendem a ter a PIO superestimada. A influência da espessura corneana na acurácia da TAG vem sendo alvo de estudo há algumas décadas (DOUGHTY; ZAMAN, 2000; EHLERS; BRAMSEN; SPERLING, 1975). O próprio Hans Goldmann, idealizador da TAG, já destacava a influência da espessura corneana na medida de PIO (GOLDMANN, 1970), mas a consolidação desse conceito só ocorreu após o advento da cirurgia refrativa (BAYRAKTAR; BAYRAKTAR, 2005; CRONEMBERGER *et al*., 2009) e da publicação do estudo multicêntrico dos hipertensos oculares (*Ocular Hypertension Treatment Study* - OHTS) (GORDON *et al*., 2002). A avaliação da espessura corneana ajuda, portanto, a entender alguns casos de GPN quando a PIO está subestimada devido a córnea ser mais fina, assim como a tendência de hipertensos oculares (HO) a ter a PIO superestimada devido a córnea ser mais espessa.

Nem sempre o indivíduo com GPN tem a córnea fina, assim como nem sempre o HO tem a córnea espessa. Alguns fatores como hidratação corneana (SIMON *et al*., 1993) e propriedades biomecânicas da córnea (LIU; ROBERTS, 2005) também foram atribuídos como potenciais causadores de interferências na TAG.

A tonometria dinâmica de contorno (TDC) é um método alternativo de medida da PIO. Esse aparelho funciona por meio de uma ponteira côncava que se posiciona no contorno da córnea e não necessita aplaná-la para fazer a sua aferição (KANNGIESSER; KNIESTEDT; ROBERT, 2005). Assim, a TDC tende a sofrer menos influência de fatores como espessura central e propriedades biomecânicas da córnea (DOYLE; LACHKAR, 2005; FRANCIS *et al*., 2007; KOTECHA *et al*., 2005).

Além de medir a PIO com menos exposição aos fatores de interferência corneanos, a TDC é capaz de fornecer a amplitude do pulso ocular (APO). A PIO varia ritmicamente de acordo com a fase do ciclo cardíaco e durante a própria TAG é possível notar, em alguns casos, a oscilação dessa pressão. Na TDC a PIO é medida de maneira contínua e o resultado é uma curva com picos e vales, sendo que o pico denota a PIO máxima ou sistólica e o vale denota a PIO mínima ou diastólica (KAUFMANN *et al*., 2006). A diferença entre os valores da PIO sistólica e PIO diastólica é a APO. Ainda não se sabe ao certo qual a real importância da APO no glaucoma (KAUFMANN *et al*., 2006; PUNJABI *et al*., 2006; WEIZER *et al*., 2007), mas alguns estudos a identificam como um possível método de avaliação da perfusão ocular (MCKEE; SALDAÑA; AHAD, 2004; SCHWENN *et al*., 2002) .

O acompanhamento de pacientes portadores de glaucoma cuja doença evolui mesmo na vigência de PIO dentro dos valores de referência da normalidade é um desafio constante para o oftalmologista. A investigação da amplitude do pulso ocular e pressão de perfusão ocular é uma possível forma de se avaliar a porção vascular do glaucoma e entender de forma mais plena a etiopatogenia da doença.

OBJETIVOS

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A presente tese teve como objetivo estudar a correlação entre a amplitude da pressão intraocular (PIO) e fatores de avaliação da perfusão ocular. Para tal, foram utilizados indivíduos portadores de glaucoma sem tratamento prévio, hipertensos oculares e normais. Entre os fatores de perfusão ocular, foi considerado inicialmente a pressão de perfusão ocular, que tem em sua fórmula dados referentes à PA e PIO. Em seguida, avaliou-se a correlação da amplitude do pulso ocular com parâmetros da pressão arterial de maneira isolada, dentre eles: PA sistólica, PA diastólica e pressão de pulso arterial. Paralelamente à essas avaliações, observou-se também a correlação entre a PIO medida pela tonometria de aplanação de Goldmann e tonometria dinâmica de contorno, além de estudar a influência da espessura corneana central nesses dois diferentes métodos de aferição da PIO.

O método e os resultados da tese foram descritos em dois artigos científicos:

1) Correlação entre pressão de perfusão ocular e amplitude do pulso ocular em glaucomatosos, hipertensos oculares e normais.
2) A amplitude do pulso ocular pode ser considerada uma forma de medir o fluxo sanguíneo ocular?

Como ambos os artigos foram enviados para publicação em periódicos estrangeiros, os mesmos são apresentados na presente tese em sua versão original, na língua inglesa. A formatação das citações e referências bibliográficas

também está disposta de acordo com as exigências do periódico ao qual o artigo foi submetido.

ANÁLISE DOS TRABALHOS

PRIMEIRO TRABALHO

"Correlation between ocular perfusion pressure and ocular pulse amplitude in glaucoma, ocular hypertension, and normal individuals."

"Correlação entre pressão de perfusão ocular e amplitude do pulso ocular em glaucomatosos, hipertensos oculares e normais."

OBJETIVOS DO PRIMEIRO TRABALHO

O objetivo principal do trabalho foi correlacionar a amplitude do pulso ocular com a pressão de perfusão ocular em portadores de glaucoma, HO e indivíduos normais. Além disso, o trabalho comparou a PIO obtida pela TAG e TDC nos três diferentes grupos e avaliou a influência da espessura corneana central nessas medidas.

O presente artigo foi apresentado na ARVO 2012 em Fort Lauderdale e está submetido à publicação na revista *Graefe's archive for clinical and experimental ophthalmology*.

RESUMO DO PRIMEIRO TRABALHO

Objetivo: investigar a correlação entre pressão de perfusão ocular (PPO) e amplitude do pulso ocular (APO) em portadores de glaucoma, hipertensos oculares e normais. **Método:** foram selecionados 90 olhos de 90 pacientes, sendo 30 recentemente diagnosticados com glaucoma sem tratamento hipotensor ocular prévio; 30 tinham pressão intraocular (PIO) elevada sem evidência de glaucoma e 30 foram incluídos no grupo-controle com PIO dentro dos valores de referência da normalidade (<21 mmHg) e ausência de sinais de glaucoma. Todos os pacientes foram submetidos à avaliação oftalmológica completa, gonioscopia, paquimetria ultrassônica, campo visual computadorizado, tonometria de aplanação de Goldmann (TAG), tonometria dinâmica de contorno (TDC) e pressão arterial (PA). A PPO foi calculada pela diferença entre a pressão arterial média (PAM) e PIO. A APO foi fornecida pela TDC. Foi utilizado o cálculo do coeficiente de correlação de Pearson nos grupos glaucoma e hipertensos oculares (HO), já nos normais a correlação foi testada pelo coeficiente de Spearman. **Resultados:** a TDC mostrou PIO média no grupo do glaucoma de 22,7 ± 4,3 mmHg, nos HOs 22,3 ± 2,8 mmHg e nos normais 14,3 ± 1,6 mmHg. Já a PIO média medida pela TAG foi 19,0 ± 5,1 mmHg (glaucoma), 22,4 ± 2,1 mmHg (HO) e 12,9 ± 2,2 mmHg (normais). A APO média foi de 3,4 ± 1,2 mmHg no grupo do glaucoma, 3,5 ± 1,2 mmHg nos HO e 2,6 ± 0,9 mmHg nos normais. A PPO média foi 46,3 ± 7,9 mmHg, 41,5 ± 5,2 mmHg e 50,2 ± 7,0 mmHg nos grupos glaucoma, HO e normais, respectivamente. Não foi notada correlação significativa da PPO e APO em algum dos grupos [P/r = 0,865/-0,032 (glaucoma); 0,403/-0,156 (HO); 0,082/-0,307 (normais)]. **Conclusão:** os resultados mostraram ausência de correlação entre PPO e APO em pacientes com glaucoma recém-diagnosticado, HO e normais. A PIO medida pela TAG

mostrou boa correlação com a TDC. A espessura corneana central correlacionou-se à TAG, mas não à TDC.

Palavras-chave: Glaucoma. Pressão de perfusão ocular. Amplitude do pulso ocular. Tonometria dinâmica de contorno. Pressão arterial sistêmica.

Correlation between ocular perfusion pressure and ocular pulse amplitude in glaucoma, ocular hypertension, and normal individuals

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Financial Support:

This work was partially funded by a government research support foundation (FAPEMIG, Brazil). The authors have no financial or commercial disclosures to declare.

ABSTRACT

Background: To investigate the correlation between ocular perfusion pressure (OPP) and ocular pulse amplitude (OPA) in individuals with glaucoma, ocular hypertension and normals.

Methods: Ninety eyes from 90 patients were selected in which: 30 were recently diagnosed with glaucoma with no previous history of ocular hypotensive therapy, 30 had elevated intraocular pressure (IOP) without any evidence of glaucoma, and 30 were included in the control group with IOP within normal values (< 21 mmHg) and no detectable glaucoma damage. It was performed in each patient: Goldmann applanation tonometry (GAT), dynamic contour tonometry (DCT), blood pressure (BP) measurement, pachymetry, Humphrey visual field, and routine ophthalmic examination. The ocular perfusion pressure (OPP) was calculated by the difference between mean arterial pressure (MAP) and IOP. The ocular pulse amplitude (OPA) was given by the DCT. The correlation test used in the glaucoma and ocular hypertensive groups was the Pearson coefficient; for the normal group it was used the Spearman's rank correlation coefficient.

Results: Mean IOP by DCT was 22.7 ± 4.3 mmHg in the glaucoma group, 22.3 ± 2.8 mmHg in the ocular hypertensives (OH), and 14.3 ± 1.6 mmHg in the normals. Mean GAT was 19.0 ± 5.1 mmHg (glaucoma), 22.4 ± 2.1 mmHg (OH), and 12.9 ± 2.2 mmHg (normal). Mean OPA in the glaucoma group was 3.4 ± 1.2 mmHg, ocular hypertensive 3.5 ± 1.2 mmHg, and normals 2.6 ± 0.9 mmHg. Mean OPP was 46.3 ± 7.9 mmHg in the glaucoma group, 46.3 ± 7.9 mmHg in the ocular hypertensive, and 50.2 ± 7.0 mmHg in normals. Neither groups showed significant

correlation between OPP and OPA (*P*=0.865, r=-0.032 / *P*=0.403, r=-0.156 / *P*=0.082, ρ=-0.307; glaucoma, OH, and normals, respectively).

Conclusion: There is no significant correlation between OPP and OPA values in individuals with glaucoma, ocular hypertensive or normals. IOP measured by GAT is correlated with DCT. CCT influences GAT, but has no influence with DCT.

Keywords: Glaucoma; Ocular pulse amplitude; Ocular perfusion pressure; Dynamic contour tonometry; Vascular factors

INTRODUCTION

Chronic open-angle glaucoma (COAG) is a multifactorial disorder of the optic nerve and has the elevated intraocular pressure (IOP) as its main risk factor. The current glaucoma treatment aims to reduce the IOP alone, although some glaucoma patients continue to progress, even when the IOP reach the preset target pressure. Also, some individuals develop the disease under low IOP values and are known as normal tension glaucoma (NTG). Therefore, it's reasonable to assume that risk factors other than IOP itself may contribute in a variable manner with glaucoma's etiopathogeny. Among these, the role of vascular disorders such as atherosclerosis, migraine, Raynaud's phenomenon, and other vasospastic conditions have already been linked as potential risk factors for glaucoma [1-8].

The influence of blood pressure (BP) as an independent risk factor for glaucoma is still a controversy. Although some studies have shown a significant positive correlation between systemic hypertension and glaucoma [9,10], Leske et al. found a negative correlation between these two variables [11]. As BP and IOP values tend to fluctuate throughout the day in a circadian manner, the variation span may also be related to the glaucoma progression [12].

There are different ways to assess vascular factors related to glaucoma. One of them is by measuring the ocular perfusion pressure (OPP). A reduced OPP may be considered as an important risk factor for glaucoma [13-15].

Another way to assess the vascular portion in glaucoma is through the ocular pulse amplitude (OPA) given by the dynamic contour tonometry (DCT) [16]. The IOP varies according to each cardiac cycle and this variation can be frequently noticed by a rhythmic oscillation of the semi circles in the Goldmann

applanation tonometry (GAT). DCT measures the amplitude of the IOP variation between the systole and the diastole [17].

The Purpose of this study was to evaluate the correlation between OPP and OPA in glaucoma, ocular hypertension, and normal individuals.

MATERIAL AND METHODS

Ninety eyes of 90 patients were enrolled and they were divided into three groups. The glaucoma group included individuals recently diagnosed with glaucoma and no previous treatment for the disease. The ocular hypertension and normal groups both had no identifiable functional and/or structural glaucoma damage, differentiated according to the IOP value.

This present study was approved by the Ethics Committee of the Federal University of Minas Gerais, Brazil. Written informed consent was obtained from each participant. The research followed the tenets of the Declaration of Helsinki.

The evaluation of the 90 patients was conducted by the same physician (BPF) during the period of September 2008 to May 2010.

Inclusion criteria for all groups were: age >40 years old; gonioscopy revealing an open angle; and best corrected visual acuity of 20/40 or better. To include a patient in the glaucoma group, it was necessary to identify the coexistence of optic disc signs of glaucoma as well as suggestive glaucoma damage in the visual field (VF).

Optic Nerve Examination

The optic disc and papillary retinal nerve fiber layer (pRNFL) evaluation was conducted at a slit-lamp using a 78-diopter lens. To identify the glaucomatous optic neuropathy (GON) it was necessary at least two of the following criteria: (1)

cup/disc ratio >0.6; (2) localized rim loss in the superior or inferior quadrants; (3) disc hemorrhage; (4) cup/disc asymmetry >0.2 [11].

Visual Field Examination

The VF was measured by a Humphrey field analyzer (HFA; Carl Zeiss Meditec, Inc., Dublin, CA), program 24-2, SITA standard strategy. The glaucoma damage was defined as the presence of at least two of the following criteria: (1) a cluster of three or more non-edge points, all of which was depressed on the pattern deviation plot at a p <0.05 level and one of which was depressed at a p <0.01 of normal fields; (2) Glaucoma Hemifield Test (GHT) outside normal limits; (3) Pattern Standard Deviation (PSD) at a p <0.05 of normal fields. The VF exam was repeated for each eye to check reproducibility of the findings, if necessary, a third exam was to be performed within a week. In case of incongruity of data between the three exams, the patient was excluded from the study. As for reliability, the criteria were: (1) false-positive <33%; (2) false-negative <33%; (3) fixation loss <20% [18].

The ocular hypertension or normal individuals had no one of the previously mentioned signs of glaucoma in their optic nerve and/or VF exam. The inclusion in each one of these two groups was based on the IOP values. The ocular hypertensive group had individuals with IOP ≥ 21mmHg as the normal group had subjects with IOP <21mmHg. The IOP was measured using a Goldmann applanation tonometer (GAT) between 8 and 9 AM, always repeating the measurement within five minutes. In case the difference between the two values was less than 2mmHg, the lower value was used in the study. If the difference was greater than 2mmHg, a third measurement was taken, and the lower value was to be considered, but still respecting the 2mmHg difference between the

measurements. In case of difference greater than 2mmHg between the three values, the patient was excluded from the study.

Dynamic contour tonometry (DCT) readings were taken employing the Pascal tonometer (Swiss Micro-technology AG, Port, Switzerland) between 8 and 9 AM. The quality level (Q) of the DCT measurement ranges from 1 to 5, 1 being optimal and 5 least optimal; only readings with Q levels of 1 and 2 were included in the study. The ocular pulse amplitude (OPA) given by the DCT stands for the difference between systolic IOP and diastolic IOP.

By definition, perfusion pressure (PP) is calculated as follows: PP = MAP - VP, where MAP is mean arterial pressure and VP is venous pressure. The MAP formula is: MAP = DBP + [1/3 X (SBP - DBP)], where DBP is diastolic blood pressure and SBP is systolic blood pressure. To obtain the ocular perfusion pressure (OPP) one can use the PP formula, substituting VP for IOP. As the BP in the ophthalmic artery is 2/3 of the brachial BP, the final OPP formula is as follows: OPP = 2/3 MAP - IOP.

Blood Pressure (BP) was measured with a brachial Welch Allyn DS66 sphygmomanometer and a Littmann Classic II stethoscope on the upper right arm after the subject had been seated for at least 5 minutes. Caffeine, exercise, and smoking were not allowed for at least 30 minutes prior to the exam. Two measurements with a 5 minute interval were taken and the average recorded [19].

Gonioscopy was performed with a Sussman lens and ultrasound pachymetry was obtained using the DGH 555 (DGH Technology, Inc., Exton, PA).

Were excluded from the study individuals with: previous use of glaucoma medication, history of ocular surgery or laser procedures in the eye, corneal

disorder that could interfere with an optimal TAG or DCT, spherical equivalent > ±4.0 D, advanced cataract, or evidence of ocular infection.

Statistical Analysis

In the glaucoma group, the eye selected for statistical analysis was the one with lower cup/disc ratio, respecting the minimum 0.6 value. In case of equal ratios in both eyes, the lower IOP eye was selected. If IOP was also the same, the right eye was used in the study.

For the eye selection in the ocular hypertensive group, it was considered the one with lower IOP, respecting the 21 mmHg value. In case the patient had the same IOP for both eyes, the right eye was selected. The normal group had always the right eye chosen.

The univariate analysis was performed comparing OPA and OPP to each of the three groups using the F test (ANOVA) in case the variables had a normal distribution. The Kruskal-Wallis test was used in case of a non normal distribution. The verification of the distribution was performed by Shapiro-Wilk test. When the *P*-value was statistically different between the three groups, a *post-hoc* two on two comparison was performed using either Tukey range test (parametric) or Mann-Whitney test with the Bonferroni adjustment (non-parametric). The *P*-value for the two later tests was 0.017 as there were three groups involved (0.05/3).

To evaluate the correlation between APO and OPP it was calculated the Pearson correlation coefficient in case the two variables had a normal distribution or Spearman rank's correlation coefficient if one of the variables had a non-normal distribution. Statistical analysis was performed using R software version 2.14.1.

RESULTS

Mean age of the glaucoma patients was 57.2 ± 9.9 years, the ocular hypertensives (OH) were 49.9 ± 8.7 years, and the normals were 52.3 ± 7.2 years. Fifty-one subjects (56.7%) were white, 30 (33.3%) were brown, and 9 (10%) were African descendants.

There were 48 (53.3%) men and 42 (46.7%) women included in the study. There were 18 (60%) men in the glaucoma group, 14 (46.7%) in the ocular hypertensive, and 16 (53.3%) in the normal group.

TABLE 1. IOP by GAT and DCT

IOP (mmHg) / Group	n	Mean (SD)	Median	Range
IOP - DCT	**90**	**19.8 (5.0)**	**19.7**	**10.2 – 31.9**
Glaucoma	30	22.7 (4.3)	23.2	13.7 - 31.9
Ocular Hypertension	30	22.3 (2.8)	22.2	16.6 - 27.9
Normal	30	14.3 (1.6)	14.3	10.2 - 17.5
IOP - GAT	**90**	**18.1 (5.2)**	**20.0**	**10.0 - 30.0**
Glaucoma	30	19.0 (5.1)	20.5	10.0 - 30.0
Ocular Hypertension	30	22.4 (2.1)	22.0	18.0 - 27.0
Normal	30	12.9 (2.2)	13.0	10.0 - 17.0

All data expressed in mmHg. DCT = dynamic contour tonometry, GAT = Goldmann applanation tonometry, SD = standard deviation.

IOP was measured by GAT and DCT. Mean (SD), median, and range values are shown on table 1. In the present study, mean GAT was 18.1 ± 5.2 mmHg and mean DCT was 19.8 ± 5.0 mmHg. The mean difference between the measurements obtained with both techniques was 1.7 mmHg. Despite the difference between DCT and TAG values, a high positive correlation was found when studying these two variables (r = 0.832; P < 0.01; figure 1).

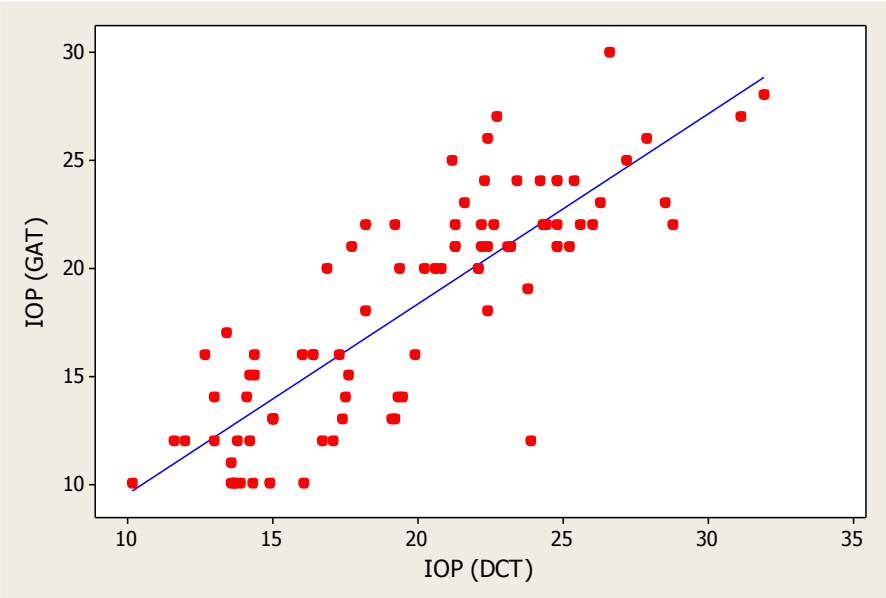

FIGURE 1. Relation between IOP measured by Goldmann applanation tonometry (GAT) and dynamic contour tonometry (DCT).

We also tested the correlation between both measurements of IOP and CCT and the result was a slight positive correlation between GAT and CCT (*r* = 0,230; *P* = 0.029), while no correlation between DCT and CCT (*r* = -0.005; *P* = 0.965).

TABLE 2. OPA and OPP in glaucoma patients, ocular hypertensive, and normals

Group	OPA		OPP	
	Mean (SD)	*P*- value	Mean (SD)	*P*- value
Glaucoma	3.4 (1.2)	**0.002**[1]	46.3 (7.9)	**<0.001**[2]
Ocular hypertensive	3.5 (1.2)		41.5 (5.2)	
Normal	2.6 (0.9)		50.2 (7.0)	

1: F-test (ANOVA); 2: Kruskal-Wallis Test. All data expressed in mmHg. Bold *P* values are statistically significant. OPA = ocular pulse amplitude, OPP = ocular perfusion pressure.

OPA and OPP results concerning mean, SD, and P-values are shown on table 2. In Glaucoma patients, OPA ranged from 1.6 to 6.4 mmHg (Q_1 = 2.5 mmHg; median = 3.2 mmHg; Q_3 = 4.2 mmHg). In OH, it ranged from 0.9 to 6.0 mmHg (Q_1 = 2.8 mmHg; median = 3.5 mmHg; Q_3 = 4.2 mmHg), and for the normal group, OPA ranged from 0.9 to 4.9 mmHg (Q_1 = 2.0 mmHg; median = 2.4 mmHg; Q_3 = 3.2 mmHg; figure 2). As the difference between the three groups was statistically significant (*P* = 0.002; ANOVA F-test), a Tukey range test was applied showing a significant difference between glaucoma and normal (*P* = 0.014), OH and normal (*P* = 0.003). The comparison between glaucoma and OH showed no statistical significance (*P* = 0.887).

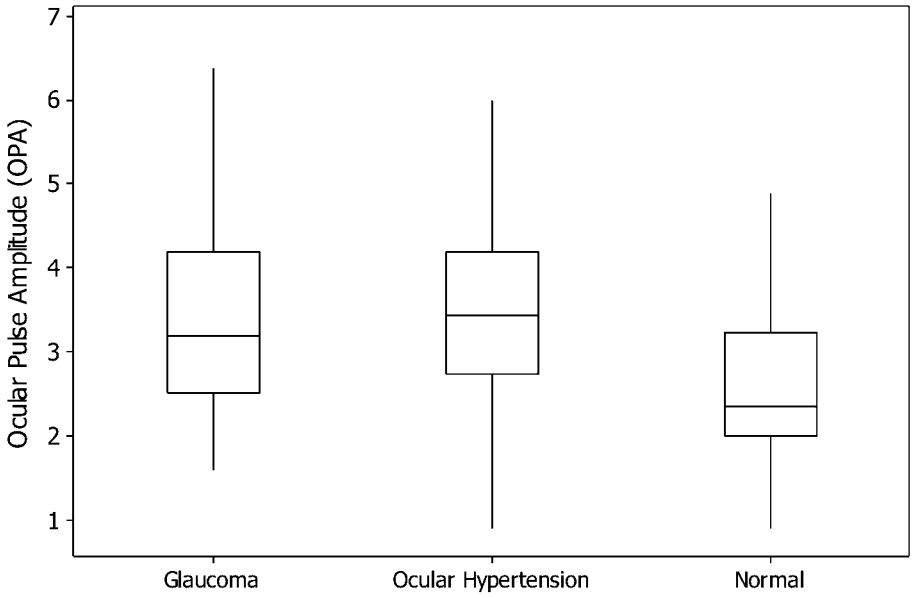

FIGURE 2. Mean OPA in glaucoma, ocular hypertension, and normals

The OPP range in the glaucoma patients was from 32.2 to 63.8 mmHg (Q_1 = 41.1 mmHg; median = 45.3 mmHg; Q_3 = 50.5 mmHg), in the OH it ranged from 27.1 to 54.6 mmHg (Q_1 = 40.0 mmHg; median = 41.2 mmHg; Q_3 = 43.6 mmHg),

and the normal group shown a minimum OPP of 37.3 mmHg and maximum 63.3 mmHg (Q_1 = 45.1 mmHg; median = 50.2 mmHg; Q_3 = 54.5 mmHg; figure 3). To compare the groups in pairs, Mann-Whitney test with Bonferroni adjustment was applied. The result was a significant difference between glaucoma and OH (*P* = 0.010) and OH and normal (*P* < 0.001). The glaucoma/normal comparison showed no statistical significance (*P* = 0.026).

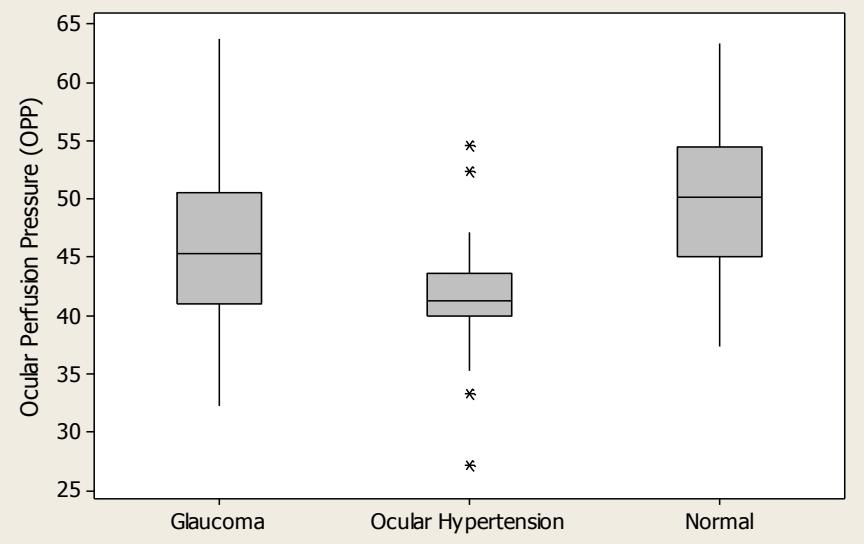

FIGURE 3. Mean OPP in Glaucoma, Ocular hypertensives, and normals. Asterisks = Outliers.

The systolic blood pressure (SBP) was 131.0 ± 16.7 mmHg in the glaucoma group, 125.0 ± 12.3 mmHg in the OH, and 121.5 ± 12.1 mmHg in the normals. Diastolic blood pressure (DBP) was 82.2 ± 11.3 mmHg, 81.2 ± 6.9 mmHg, and 81.5 ± 9.0 mmHg, respectively.

Table 3 presents the correlation between OPA and OPP in the three different groups. It was not observed a significant correlation (*P* < 0.05) between the two variables in neither one of the three groups evaluated separately nor when they were tested the groups together.

TABLE 3. Correlation between OPP and OPA

Ocular Perfusion Pressure (OPP)	Ocular Pulse amplitude (OPA)	
	Coefficient	***P* value**
Groups		
Glaucoma	-0.032	0.865[1]
Ocular hypertension	-0.156	0.403[1]
Normal	-0.307	0.082[2]

1: Pearson correlation coefficient; 2: Spearman correlation coefficient

DISCUSSION

The accurate IOP measurement is a critical parameter to diagnose and treat glaucoma patients. The GAT is the gold standard method to measure the IOP for over 50 years, although the validity of GAT has been questioned since the publication of two studies: ocular hypertensive treatment study (OHTS) and European glaucoma progression study (EGPS). They brought to surface the relation between corneal central thickness (CCT) and IOP [20]. Other studies had confirmed the influence of corneal properties and its biomechanics in the IOP measured by GAT [21-24]. The DCT is an alternative way to measure IOP based on a completely new physical principle that does not distort the corneal anatomy [16]. Thus, DCT seems to be less prone to be affected by factors such as corneal thickness and hysteresis when compared to GAT [25]. In our study, the difference between mean DCT and TAG was 1.7 mmHg. This difference was also observed in other studies ranging from 0.7 to 2.8 mmHg. A positive correlation between DCT and GAT was also in the literature as well as in the present study [26-33]. Doyle and Lachkar [28], presented a study showing that individuals with normal or high central corneal thickness had similar IOP values by GAT and DCT, as the ones

with thin cornea tend to have a higher discrepancy between the two measurements, possibly due to an underestimated IOP from the Goldmann tonometer. DCT measurements tend to be less influenced by CCT than GAT [27,28,34,35], especially in individuals with thin corneas.

Another advantage of the DCT is that by measuring IOP in a continuous manner it captures the IOP variation during the cardiac cycle [16]. The rhythmic oscillation of the IOP is measured by DCT and presented as the ocular pulse amplitude (OPA). The role of OPA in glaucoma is still unclear. Weizer et al. [30] published a study correlating OPA with the severity of glaucoma and concluded that a high OPA seems to be related to a less severe glaucoma. Schwenn et at. [36] showed that low OPA was more present in normal tension glaucoma (NTG) than primary open angle glaucoma (POAG), ocular hypertensive (OHT), or normals. Kynigopoulos et al. [37] found a relation between low OPA and presence of glaucomatous functional and structural damage in POAG. In our study, the mean OPA was significantly lower in the normal group than in the glaucoma or ocular hypertensive (OH) individuals. A possible reason for that is the positive correlation between GAT and OPA, explained by Punjabi et al. [38] and Kaufmann et al. [39]. To include normal tension glaucoma patients in our study, we did not use high IOP (>21 mmHg) as an inclusion criterion for the glaucoma group. Therefore, the mean IOP in the OH group was higher than in the glaucoma patients.

Considering the ocular perfusion pressure (OPP) formula, one has low OPP when the BP is relatively low or the IOP is relatively high. A number of population-based epidemiologic studies have shown the relation between low OPP and glaucoma [11,13,40-42]. There is no consensus on a reference value to

differentiate normal and altered OPP. Leske et al. [11] found that OPP < 42 mmHg had a higher risk in developing glaucoma (RR = 2.2). In the present study, the normal group had a mean OPP ranging from 43.2 to 57.2 mmHg maintaining above the cut-off value of 42 mmHg proposed by the Barbados study's results [11]. In the OH group, we found a low mean OPP that could be explained by a high mean IOP and the fact OPP and IOP are inversely proportional. We assumed the OPP was higher in our glaucoma group because we did not include only high-pressure glaucoma patients.

Assessment of ocular blood flow (OBF) using OPP and/or OPA can be rather limited for two main reasons. First, the fluctuation of the measurements, especially at night, when drastic BP drops can occur in patients defined as non-physiological dippers leading to a poor perfusion of the optic nerve [43,45]. Also, both OPP and OPA are more related to IOP itself than any other factor that could directly influence of the OBF. The association between vascular risk factors, including OPP and OPA, in glaucoma has been the subject of some recent studies and the results were that no significant correlation was found between these two vascular factors [46,47]. Vascular risk factors such as OPP and OPA may have independent roles in glaucoma. There is still much to learn about the complex interaction between these factors. Glaucoma patients with low OPP or high OPA could be at a higher risk of progressing with the disease.

In conclusion, our results showed no correlation between ocular perfusion pressure and ocular pulse amplitude in glaucoma, OH, or normal individuals. We found a strong correlation between GAT and DCT. Corneal thickness was slightly related GAT and not related to DCT.

REFERENCES

1. Drance SM, Douglas GR, Wijsman K, Schulzer M, Britton RJ (1988) Response of blood flow to warm and cold in normal and low-tension glaucoma patients. Am J Ophthalmol 105:35-39

2. Gasser P, Flammer J (1991) Blood-cell velocity in the nailfold capillaries of patients with normal-tension and high-tension glaucoma. Am J Ophthalmol 111:585-588

3. Phelps CD, Corbett JJ (1985) Migraine and low-tension glaucoma. A case-control study. Invest Ophthalmol Vis Sci 26:1105-1108

4. Goldberg I, Hollows FC, Kass MA, Becker B (1981) Systemic factors in patients with low-tension glaucoma. Br J Ophthalmol 65:56-62

5. Waldmann E, Gasser P, Dubler B, Huber C, Flammer J (1996) Silent myocardial ischemia in glaucoma and cataract patients. Graefes Arch Clin Exp Ophthalmol 234:595-598

6. François J, Neetens A (1970) The deterioration of the visual field in glaucoma and the blood pressure. Doc Ophthalmol 28:70-132

7. Drance SM (1996) The concept of chronic open-angle glaucoma: A personal view. Ophthalmologica 210:251-256

8. Hayreh SS, Zimmerman MB, Podhajsky P, Alward WL (1994) Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. Am J Ophthalmol 117:603-624

9. Mitchell P, Lee AJ, Rochtchina E, Wang JJ (2004) Open-angle glaucoma and systemic hypertension: The blue mountains eye study. J Glaucoma 13:319-326

10. Ulrich A, Ulrich C, Barth T, Ulrich WD (1996) Detection of disturbed autoregulation of the peripapillary choroid in primary open angle glaucoma. Ophthalmic Surg Lasers 27:746-757

11. Leske MC, Wu S-Y, Hennis A, Honkanen R, Nemesure B, BESs Study Group (2008) Risk factors for incident open-angle glaucoma: The barbados eye studies. Ophthalmology 115:85-93

12. Demailly P, Cambien F, Plouin PF, Baron P, Chevallier B (1984) Do patients with low tension glaucoma have particular cardiovascular characteristics? Ophthalmologica 188:65-75

13. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC (1995) Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. Arch Ophthalmol 113:216-221

14. Weinreb RN (2009) Ocular blood flow in glaucoma. Kugler Publications.

15. Hayreh SS (2001) Blood flow in the optic nerve head and factors that may influence it. Prog Retin Eye Res 20:595-624

16. Kanngiesser HE, Kniestedt C, Robert YC (2005) Dynamic contour tonometry: Presentation of a new tonometer. J Glaucoma 14:344-350

17. McKee HD, Saldaña M, Ahad MA (2004) Increased ocular pulse amplitude revealing aortic regurgitation. Am J Ophthalmol 138:503

18. Mills RP, Budenz DL, Lee PP, Noecker RJ, Walt JG, Siegartel LR, Evans SJ, Doyle JJ (2006) Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. Am J Ophthalmol 141:24-30

19. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ, National High Blood Pressure Education Program Coordinating Committee (2003) Seventh report of the joint

national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 42:1206-1252

20. Brandt JD (2004) Corneal thickness in glaucoma screening, diagnosis, and management. Curr Opin Ophthalmol 15:85-89

21. Detry-Morel M, Jamart J, Detry MB, Ledoux A, Pourjavan S (2007) Clinical evaluation of the pascal dynamic contour tonometer. J Fr Ophtalmol 30:260-270

22. Hager A, Annette H, Loge K, Kristina L, Schroeder B, Bernd S, Füllhas MO, Mark-Oliver F, Wiegand W, Wolfgang W (2008) Effect of central corneal thickness and corneal hysteresis on tonometry as measured by dynamic contour tonometry, ocular response analyzer, and Goldmann tonometry in glaucomatous eyes. J Glaucoma 17:361-365

23. Morita T, Shoji N, Kamiya K, Hagishima M, Fujimura F, Shimizu K (2010) Intraocular pressure measured by dynamic contour tonometer and ocular response analyzer in normal tension glaucoma. Graefes Arch Clin Exp Ophthalmol 248:73-77

24. Kara N, Bozkurt E, Baz O, Altinkaynak H, Dundar H, Yuksel K, Yazici AT, Demirok A, Candan S (2012) Corneal biomechanical properties and intraocular pressure measurement in marfan patients. J Cataract Refract Surg 38:309-314

25. Mangouritsas G, Mourtzoukos S, Mantzounis A, Alexopoulos L (2011) Comparison of goldmann and pascal tonometry in relation to corneal hysteresis and central corneal thickness in nonglaucomatous eyes. Clin Ophthalmol 5:1071-1077

26. Kaufmann C, Bachmann LM, Thiel MA (2004) Comparison of dynamic contour tonometry with Goldmann applanation tonometry. Invest Ophthalmol Vis Sci 45:3118-3121

27. Kotecha A, White ET, Shewry JM, Garway-Heath DF (2005) The relative effects of corneal thickness and age on Goldmann applanation tonometry and dynamic contour tonometry. Br J Ophthalmol 89:1572-1575

28. Doyle A, Lachkar Y (2005) Comparison of dynamic contour tonometry with Goldman applanation tonometry over a wide range of central corneal thickness. J Glaucoma 14:288-292

29. Schneider E, Grehn F (2006) Intraocular pressure measurement-comparison of dynamic contour tonometry and Goldmann applanation tonometry. J Glaucoma 15:2-6

30. Weizer JS, Asrani S, Stinnett SS, Herndon LW (2007) The clinical utility of dynamic contour tonometry and ocular pulse amplitude. J Glaucoma 16:700-703

31. Lee J, Lee CH, Choi J, Yoon SY, Sung KR, Park SB, Kook MS (2009) Comparison between dynamic contour tonometry and Goldmann applanation tonometry. Korean J Ophthalmol 23:27-31

32. Kotecha A, White E, Schlottmann PG, Garway-Heath DF (2010) Intraocular pressure measurement precision with the Goldmann applanation, dynamic contour, and ocular response analyzer tonometers. Ophthalmology 117:730-737

33. Ito K, Tawara A, Kubota T, Harada Y (2012) IOP measured by dynamic contour tonometry correlates with IOP measured by Goldmann applanation tonometry and non-contact tonometry in japanese individuals. J Glaucoma 21:35-40

34. Sáenz-Francés F, García-Catalán R, Jerez-Fidalgo M, Fernández-Vidal A, Martínez-de-la-Casa JM, Méndez-Hernández C, Santos-Bueso E, Reche-Frutos J, García-Sánchez J, García-Feijoo J (2011) Comparison of Goldmann applanation

and dynamic contour tonometry measurements: Effects of corneal morphometry. Arch Soc Esp Oftalmol 86:287-291

35. Francis BA, Hsieh A, Lai MY, Chopra V, Pena F, Azen S, Varma R, Los Angeles Latino Eye Study Group (2007) Effects of corneal thickness, corneal curvature, and intraocular pressure level on Goldmann applanation tonometry and dynamic contour tonometry. Ophthalmology 114:20-26

36. Schwenn O, Troost R, Vogel A, Grus F, Beck S, Pfeiffer N (2002) Ocular pulse amplitude in patients with open angle glaucoma, normal tension glaucoma, and ocular hypertension. Br J Ophthalmol 86:981-984

37. Kynigopoulos M, Tzamalis A, Ntampos K, Schlote T (2012) Decreased ocular pulse amplitude associated with functional and structural damage in open-angle glaucoma. Eur J Ophthalmol 22:111-116

38. Punjabi OS, Ho HK, Kniestedt C, Bostrom AG, Stamper RL, Lin SC (2006) Intraocular pressure and ocular pulse amplitude comparisons in different types of glaucoma using dynamic contour tonometry. Curr Eye Res 31:851-862

39. Kaufmann C, Bachmann LM, Robert YC, Thiel MA (2006) Ocular pulse amplitude in healthy subjects as measured by dynamic contour tonometry. Arch Ophthalmol 124:1104-1108

40. Bonomi L, Marchini G, Marraffa M, Bernardi P, Morbio R, Varotto A (2000) Vascular risk factors for primary open angle glaucoma: The Egna-Neumarkt study. Ophthalmology 107:1287-1293

41. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R (2001) The prevalence of glaucoma in a population-based study of hispanic subjects: Proyecto VER. Arch Ophthalmol 119:1819-1826

42. Hulsman CA, Vingerling JR, Hofman A, Witteman JC, de Jong PT (2007) Blood pressure, arterial stiffness, and open-angle glaucoma: The Rotterdam study. Arch Ophthalmol 125:805-812

43. Collignon N, Dewe W, Guillaume S, Collignon-Brach J (1998) Ambulatory blood pressure monitoring in glaucoma patients. The nocturnal systolic dip and its relationship with disease progression. Int Ophthalmol 22:19-25

44. Detry M, Boschi A, Ellinghaus G, De Plaen JF (1996) Simultaneous 24-hour monitoring of intraocular pressure and arterial blood pressure in patients with progressive and non-progressive primary open-angle glaucoma. Eur J Ophthalmol 6:273-278

45. Tokunaga T, Kashiwagi K, Tsumura T, Taguchi K, Tsukahara S (2004) Association between nocturnal blood pressure reduction and progression of visual field defect in patients with primary open-angle glaucoma or normal-tension glaucoma. Jpn J Ophthalmol 48:380-385

46. Choi J, Lee J, Park SB, Lee KS, Sung KR, Kook MS (2010) Factors affecting ocular pulse amplitude in eyes with open angle glaucoma and glaucoma-suspect eyes. Acta Ophthalmol [Epub ahead of print]

47. Gugleta K, Polunina A, Kochkorov A, Waldmann N, Portmann N, Katamay R, Flammer J, Orgul S (2012) Association between risk factors and glaucomatous damage in untreated primary open-angle glaucoma. J Glaucoma [Epub ahead of print]

SEGUNDO TRABALHO

"Can ocular pulse amplitude be used as a measure of ocular blood flow?"

"A Amplitude do pulso ocular pode ser considerada uma forma de medir o fluxo sanguíneo ocular?"

OBJETIVOS DO SEGUNDO TRABALHO

O presente trabalho teve como objetivo avaliar se a perfusão sanguínea ocular é influenciada de maneira direta pela pressão arterial. Para tal, foi estudada a associação da amplitude do pulso ocular com parâmetros da pressão arterial, entre eles a pressão arterial sistólica, diastólica e a pressão do pulso arterial em pacientes portadores de glaucoma, hipertensos oculares e normais.

O presente artigo foi apresentado na ARVO 2012 em Fort Lauderdale e está submetido à publicação na revista *American Journal of Ophthalmology*.

RESUMO DO SEGUNDO TRABALHO

Objetivo: determinar o papel da amplitude do pulso ocular (APO) na avaliação do fluxo sanguíneo ocular (FSO). **Método**: foram recrutados 90 olhos de 90 pacientes; 30 tinham glaucoma sem tratamento prévio, 30 eram hipertensos oculares (HO) sem evidência de glaucoma e 30 foram incluídos no grupo de normais, com pressão intraocular (PIO) dentro dos valores de referência de normalidade (<21 mmHg) e sem dano glaucomatoso. A PIO foi medida pela tonometria de aplanação de Goldmann (TAG) e tonometria dinâmica de contorno (TDC). A pressão arterial (PA) e espessura corneana central também foram medidas. A amplitude do pulso ocular (APO) foi fornecida pela TDC e a pressão do pulso arterial foi calculada pela diferença entre PA sistólica e PA diastólica. Foram realizados testes de correlação entre APO e os parâmetros da PA, além de modelo de regressão multivariado para investigar o papel da APO na avaliação do FSO. **Resultados**: a TAG mostrou PIO média de 19,0 ± 5,1 mmHg, 22,4 ± 2,1 mmHg e 12,9 ± 2,2 mmHg nos grupos glaucoma, HO e normais, respectivamente. Já a DCT média foi de 22,7 ± 4,3 mmHg, 22,3 ± 2,8 mmHg e 14,3 ± 1,6 mmHg também nos três grupos, respectivamente. A APO dos três grupos em conjunto variou entre 0,9 e 6,4 mmHg (média 3,2 ± 1,2; mediana 3,1 mmHg) e a pressão do pulso variou de 30 a 80 mmHg (média 44,2 ± 10,7; mediana 40 mmHg). O estudo mostrou discreta correlação positiva entre APO e pressão de pulso quando avaliados os três grupos em conjunto usando o coeficiente de correlação de Pearson (P/r = 0,017/+0,245). **Conclusão**: a discreta correlação positiva entre a APO e a pressão do pulso arterial chamou a atenção para mecanismos vasculares que regulam a perfusão ocular. A PIO medida pela TAG e TDC estão

correlacionadas, mas os valores de TAG tendem a ser mais baixos, especialmente em indivíduos com ECC baixa.

Palavras-chave: Pressão de perfusão ocular. Amplitude do pulso ocular. Tonometria dinâmica de contorno. Pressão arterial sistêmica.

Can ocular pulse amplitude be used as a measure of ocular blood flow?

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Financial Support:

This work was partially funded by a government research support foundation (FAPEMIG, Brazil). The authors have no financial or commercial disclosures to declare.

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ABSTRACT

Purpose: To determine the role of ocular pulse amplitude (OPA) in the assessment of ocular blood flow (OBF).

Patients and Methods: Ninety eyes from 90 patients were enrolled. Thirty had glaucoma with no previous treatment, 30 were ocular hypertensives (OH) without any evidence of glaucoma, and 30 were included in the control group with intraocular pressure (IOP) within normal values (< 21 mmHg) and no detectable glaucoma damage. IOP was measured by Goldmann applanation tonometry (GAT) and dynamic contour tonometry (DCT). Blood pressure (BP) and central corneal thickness (CCT) were also measured. The ocular pulse amplitude (OPA) was given by the DCT. Pulse pressure (PP) was calculated by BP systole minus diastole. Correlation tests between OPA and BP parameters as well as a multiple regression model was used to assess whether or not OPA is able to measure OBF.

Results: Mean GAT in glaucoma, OH, and normals were 19.0 ± 5.1, 22.4 ± 2.1, and 12.9 ± 2.2 mmHg, respectively. Mean DCT were 22.7 ± 4.3, 22.3 ± 2.8, and 14.3 ± 1.6 mmHg, respectively. OPA, in general, ranged from 0.9 to 6.4 mmHg (mean 3.2 ± 1.2, median 3.1 mmHg) and PP ranged from 30 to 80 mmHg (mean 44.2 ± 10.7, median 40 mmHg). We found a slight positive correlation between OPA and PP when the three groups were evaluated together using Pearson correlation coefficient (*P/r* = 0.017/+0.245).

Conclusion: OPA and PP are only slightly correlated, drawing the attention to a vascular mechanism that regulates the ocular perfusion. DCT and GAT are

correlated although GAT values tend to be lower than DCT values, especially in individuals with low CCT.

INTRODUCTION

Glaucoma is an optic neuropathy that usually causes cupping of the optic nerve disc and progressive vision loss, detected by a typical visual field defect. Elevated intraocular pressure (IOP) is still the most important risk factor in glaucoma but when the disease keeps progressing even when low target pressures are reached, one must consider factors other than IOP that are contributing to the glaucoma damage. Among these factors, the idea of a vascular portion in glaucoma and the study of ocular blood flow (OBF) had grown substantially over the last decades.

The mechanism involved in maintaining a relatively constant OBF despite different conditions such as perfusion pressure fluctuation is called autoregulation. This regulatory system is present in several tissue beds, including the eye.[1] An impaired autoregulation leading to a decrease in OBF has been linked to glaucoma.[2]

Dynamic contour tonometry (DCT; SMT Swiss micro-technology AG, Port, Switzerland) measures IOP continuously and the result is a cyclic curve of pressure where the lower value is attributed to the diastolic IOP and the higher value is equivalent to the systolic IOP.[3] Ocular pulse amplitude (OPA) is the difference between systolic IOP and diastolic IOP. The role of OPA in glaucoma is still uncertain, but in theory, it can be used to assess OBF.[4] Variation in OPA is not only dependent on blood pressure (BP) variation, but also depends on choroidal vascular rigidity and scleral rigidity.[5,6]

The purpose of this study was to investigate the relation between OPA and blood pressure parameters in healthy eyes, as well as in glaucoma patients and ocular hypertensives (OH).

PATIENT AND METHODS

Patients

The present study was approved by the Ethics Committee of the Federal University of Minas Gerais, Brazil. Written informed consent was obtained from each participant. The research followed the tenets of the Declaration of Helsinki.

Ninety eyes in 90 patients were selected for the study. They were divided into three different groups of 30 eyes each. The glaucoma group included patients with functional and structural signs of glaucoma with no previous ocular hypotensive treatment, the OH group had patients with high IOP (≥ 21 mmHg) and no identifiable sign of glaucoma, and the normal group included individuals with IOP within normal values (< 21 mmHg) and also no sign of glaucoma.

All participants were over 40 years old and none had history of glaucoma treatment. To be included in the glaucoma group, it was necessary to identify the coexistence of optic disc glaucoma signs as well as suggestive glaucoma damage in the visual field (VF). For the OH and normal groups, none of the structural and/or functional glaucoma criteria were found. The two groups together could be considered as the control group, because they both included non-glaucomatous eyes. The cutting point between the two was the IOP value (21 mmHg). The evaluation of the 90 patients was conducted by the same physician (BPF) between September 2008 and May 2010.

Exclusion criteria were: ocular surgery or laser procedures in the eye, corneal disorder which could interfere with an optimal IOP measure, spherical equivalent > ±4.0 D, lens sclerosis greater than grade II or any evidence of ocular infection.

Optic Nerve Examination

The optic disc and papillary retinal nerve fiber layer (pRNFL) evaluation was conducted at a slit-lamp using a 78-diopter lens. To identify the glaucomatous optic neuropathy (GON) it was necessary at least two of the following criteria: (1) cup/disc ratio >0.6; (2) localized rim loss in the superior or inferior quadrants; (3) disc hemorrhage; (4) cup/disc asymmetry >0.2.[7]

Visual Field Examination

The VF was measured by a Humphrey field analyzer (HFA; Carl Zeiss Meditec, Inc., Dublin, CA), program 24-2, SITA standard strategy. The glaucoma damage was defined as the presence of at least two of the following criteria: (1) a cluster of three or more non-edge points, all of which was depressed on the pattern deviation plot at a P <0.05 level and one of which was depressed at a P <0.01 of normal fields; (2) Glaucoma Hemifield Test (GHT) outside normal limits; (3) Pattern Standard Deviation (PSD) at a P <0.05 of normal fields. The VF exam was repeated for each eye to check reproducibility of the findings, if there were conflicting results, a third exam was to be performed within a week. In case of incongruity of data between the three exams, the patient was excluded from the study. As for reliability, the criteria were: (1) false-positive <33%; (2) false-negative <33%; and fixation loss <20%.[8]

Goldmann applanation tonometry, dynamic contour tonometry, and central corneal thickness

IOP measurement by Goldmann applanation tonometry (GAT) was performed between 8 and 9 AM. Two measurements were taken and the lower

value was used in the study. DCT was taken 15 minutes after GAT. The quality level (Q) of the DCT measurement ranges from 1 to 5, 1 being optimal and 5 least optimal; only readings with Q levels of 1 and 2 were included in the study. The ocular pulse amplitude (OPA) was delivered directly by DCT. Central corneal thickness (CCT) was measured by ultrasound pachymetry using the DGH 555 (DGH Technology, Inc., Exton, PA).

BP measurement

Blood Pressure (BP) was measured with a brachial Welch Allyn DS66 sphygmomanometer and a Littmann Classic II stethoscope on the upper right arm after the subject had been seated for at least 5 minutes. Caffeine, exercise, and smoking were not allowed for at least 30 minutes prior to the exam. Two measurements with a 5 minute interval were taken and the average recorded.[9] Pulse pressure (PP) was calculated as: Systolic BP minus Diastolic BP.

Statistical Analysis

Statistical analysis was performed using R software version 2.14.1. In the glaucoma group, the eye selected for statistical analysis was the one with lower cup/disc ratio, respecting the minimum 0.6 value. In case of equal ratios in both eyes, the lower IOP eye was selected. If IOP was also the same, the right eye was used in the study.

For the eye selection in the OH group, it was considered the one with lower IOP, respecting the cut-off value of 21 mmHg. In case the patient had the same IOP for both eyes, the right eye was selected. The normal group had always the right eye chosen.

ANOVA F-test was used to compare the groups when all of them presented a normal distribution. In case of a significant difference, a *post-hoc* Tukey range test was performed to compare the groups in pairs and the significance value in this case was 0.017. Kruskal-Wallis test was chosen when at least one of the groups showed a non-normal distribution. *Post-hoc* Mann-Whitney test with Bonferroni adjustment ($P = 0.017$) was performed to compare the groups in pairs if the difference between them was statistically significant. The verification of the distribution was performed by Shapiro-Wilk test.

Correlation was tested using Pearson correlation coefficient for the parametric variables and Spearman rank's correlation as a non-parametric test.

A multiple regression analysis was performed using OPA as the dependent variable and PP, GAT, DCT, and CCT as the independent variables. Initially, all the independent variables with P values ≤ 0.25 were included in the model. Then, the variables were excluded in a stepwise process leaving the final model only with variables statistically significant ($P < 0.05$).

RESULTS

Ninety patients, including 30 with glaucoma (mean age 57.2 ± 9.1 years; 18 males), 30 with OH (mean age 49.9 ± 8.7 years; 16 males), and 30 normals (mean age 52.3 ± 7.2 years; 16 males) were examined. We observed a significant difference between the group ages ($P = 0.009$). Bonferroni adjustment was performed and the result was that the mean age in the glaucoma group was higher than in the OH (Mann-Whitney test; $P = 0.005$). No significant difference was found between normal and glaucoma groups, nor when comparing normal and OH.

TABLE 1. IOP and CCT

	All	Glaucoma	OH	Normal	P-value
GAT (mmHg)	18.1 ± 5.2	19.0 ± 5.1	22.4 ± 2.1	12.9 ± 2.2	**<0.001[2]**
DCT (mmHg)	19.8 ± 5.0	22.7 ± 4.3	22.3 ± 2.8	14.3 ± 1.6	**<0.001[2]**
CCT (µm)	550.6 ± 37.3	529.1 ± 41.4	569.1 ± 30.0	553.6 ± 28.6	**<0.001[1]**

Note: Data are expressed as the mean ± SD. IOP, intraocular pressure; CCT, central corneal thickness; OH, ocular hypertensive; GAT, Goldmann applanation tonometry; DCT, dynamic contour tonometry. Bold P-values are statistically significant. 1: Kruskal-Wallis; 2: ANOVA F-test.

IOP was measured by GAT and DCT. Mean ± SD values are shown on table 1. A paired comparison between groups using the Tukey range test was then performed. GAT presented a significant difference between normal and OH (P < 0.001), normal and glaucoma (P < 0.001), and OH and glaucoma (P = 0.001). DCT post-hoc comparison showed significant difference between normal and OH (P < 0.001), normal and glaucoma (P < 0.001) but when comparing OH and glaucoma we did not find a statistically significant difference (P = 0.827).

Mean central corneal thickness (CCT) in the glaucoma groups was 529.1 ± 41.4 µm (Q_1: 500; median: 523,5; Q_3: 548,3; range: 450 - 648 µm), in the OH mean CCT was 569.1 ± 30.0 (Q_1: 551,5; median: 577; Q_3: 592,8; range: 500 - 624 µm), and in the normals it was 553.6 ± 37.3 µm (Q_1: 533,8; median: 543,5; Q_3: 580,3; range: 512 - 616 µm; Figure 1). The *post-hoc* paired comparison using Bonferroni correction showed a significant difference between normal and glaucoma (P = 0.003), OH and glaucoma (P < 0.001). No significant difference was found when comparing normal and OH (P = 0.028).

A positive correlation between GAT and DCT was found in our study (*P/r* = <0.001/0.858; Pearson correlation coefficient). When comparing each IOP method with CCT, a slight correlation was found between GAT and CCT (*P/ρ* = 0.029/0.230) but no correlation between DCT and CCT (*P/r* = 0.965/-0.05).

Mean OPA in the glaucoma eyes was 3.4 mmHg (SD, 1.2; median 3.2; range, 1.6-6.4 mmHg), in the OH was 3.5 mmHg (SD, 1.2; median, 3.5; range, 0.9-6.0 mmHg) and in the normal group was 2.6 mmHg (SD, 0.9; median, 2.4; range, 0.9-4.9 mmHg).

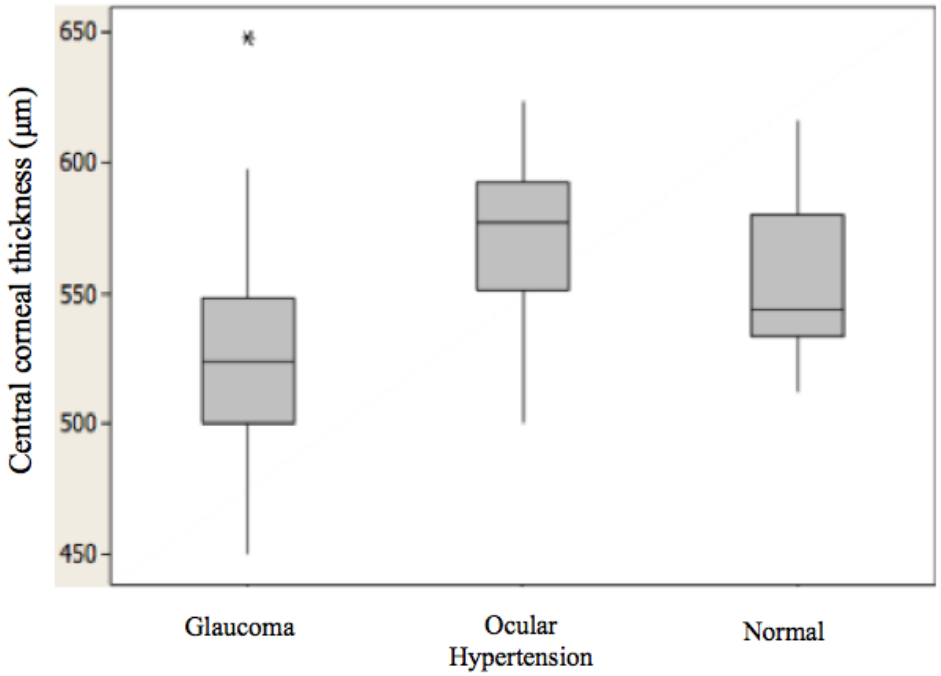

FIGURE 1. Central corneal thickness in glaucoma patients, ocular hypertensive, and normals

Blood pressure parameters assessed were systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP). Mean SBP in the glaucoma patients was 131.0 mmHg (SD, 16.7; median 130; range 110-180mmHg), in the OH was 125.0 mmHg (SD, 12.3; median, 120; range 100-160

mmHg), and in the normal participants 121.5 mmHg (SD, 12.1; median, 120; range, 110-140 mmHg) The difference between the three groups was not statistically significant (*P* = 0.072; Kruskal-Wallis test). Mean DBP in glaucoma was 82.2 (SD, 11.3; median, 80; range 60-110 mmHg), in OH was 81.2 mmHg (SD, 6.9; median, 80; range 60-100 mmHg), and in normals was 81.5 mmHg (SD, 9.0; median, 80; range 70-100 mmHg). No significant difference was found between the groups (P = 0.913; ANOVA F-test). The blood pressure amplitude, or PP was calculated by SBP minus DBP and mean PP in the glaucoma group was 48.8 mmHg (SD, 10.5; median, 50; range 30-70 mmHg), in OH was 43.8 mmHg (SD, 11.1; median, 40; range 30-80 mmHg), and in normals was 40.0 mmHg (SD, 8.7; median, 40; range 30-60 mmHg). A statistically significant difference was found between the three groups. Tukey test was then performed to compare the pair of groups and a significant difference found only between glaucoma and normals (P = 0.004). Mean ± SD and P-values of SBP, DBP, and PP are shown in Table 2.

TABLE 2. BLOOD PRESSURE PARAMETERS

	All	Glaucoma	OH	Normal	P-value
SBP	125.8 ± 14.3	131.0 ± 16.7	125.0 ± 12.3	121.5 ± 12.1	0.072[1]
DBP	81.6 ± 9.1	82.2 ± 11.3	81.2 ± 6.9	81.5 ± 9.0	0.913[2]
PP	44.2 ± 10.7	48.8 ± 10.5	43.8 ± 11.1	40.0 ± 8.7	**0.006[2]**

Note: Data expressed as the mean ± SD. All values are in mmHg. OH, ocular hypertensive; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure. Bold P-values are statistically significant. 1: Kruskal-Wallis; 2: ANOVA F-test.

A positive correlation was found between SBP and OPA (*P*/ρ = 0.029/0.224), PP and OPA (*P/r* = 0.017/0.245), GAT and OPA (*P*/ρ = <0.001/

0.430), and DCT and OPA (*P/r* = <0.001/0.399). DBP and CCT were not significantly correlated to OPA (Table 3).

A multivariate regression model was created to evaluate OPA as the dependent variable. When including all the patients in the analysis, the final model had only GAT as an independent variable (P < 0.001; slope, 0.103; SE, 0.02; 95%CI, 0.06-0.15). In the OH model, PP was the only variable present in the model (P = 0.015; slope, 0.05; SE, 0.02; 95%CI, 0.01-0.08).

TABLE 3. OPA correlations

Variables	Ocular Pulse Amplitude (OPA)	
	Coefficient	***P* value**
Systolic blood pressure	0.224	**0.029**[2]
Diastolic blood pressure	0,052	0.619[1]
Pulse pressure	0,245	**0.017**[1]
Goldmann applanation pressure	0.430	**<0.001**[2]
Dynamic contour pressure	0.399	**<0.001**[1]
Central corneal thickness	-0.076	0.466[1]

Note: Bold P-values are statistically significant. 1: Pearson correlation coefficient; 2: Spearman correlation coefficient.

DISCUSSION

After the advent of DCT not only a new method of IOP measurement was available but also a new way to interpret how IOP varies according to the cardiac cycle.[3] Significant number of studies compared IOP values obtained by DCT and GAT, the gold standard method.[10-13] A positive correlation between GAT and DCT was found in the literature and also in our study. Boehm et al.[14] compared DCT with intracameral IOP measurement and concluded that there is a strong concordance between these two variables. Another study aimed to compare GAT

and DCT in cadaver eyes and their results showed that DCT was significantly closer to manometric IOP than GAT.[15] Our study also points out this difference in IOP values, being higher with GAT than with DCT, especially in the glaucoma and normal groups (Table 1). This may reflect that IOP with GAT tend to be lower than the true IOP, or manometric IOP.

The discrepancy between GAT and DCT values is also related to CCT. Individuals with thin corneas are prone to have a larger difference between IOP measured by GAT and DCT, probably due to an underestimate of IOP measured by GAT.[16] Our results showed a slight correlation between CCT and GAT but no correlation between CCT and DCT. Punjabi et al.[17] studied IOP measured by GAT and DCT in patients with glaucoma, OH, and normal individuals. Their results showed a significantly lower GAT than DCT in glaucoma and normal individuals but not in OH. A reason for that outcome is the fact that OH individuals tend to present higher CCT than glaucoma patients and normals.

As mentioned earlier, DCT not only measures IOP but it also shows how IOP fluctuate between systole and diastole; the amplitude of this fluctuation is termed OPA. The role of OPA in glaucoma is still unclear and it is not certain whether is good to have a high or a low OPA. Weizer et al.[4] concluded in their study that a high OPA apparently correlate with a milder glaucoma, but from that we cannot say that it is beneficial for a patient to have a high OPA. There seems to be correlation between OPA and IOP measturements.[17] We found such correlations for both IOP measured by GAT and DCT. That shows an IOP influence on OPA and, as a result, there is a possible bias when considering OPA as a method to assess the vascular portion of glaucoma.

Measurements from DCT tend to be at least less influenced by corneal parameters, such as CCT.[19] Our results showed no correlation between OPA and CCT. Grieshaber et al.[20] also found no correlation between OPA and anterior segment parameters.

A linkage between arterial BP parameters and glaucoma damage has been the aim of numerous studies.[21-29] In the present study, we observed SBP, DBP, and PP in patients with glaucoma, OH, and normal individuals. Orzalesi et al.[30] found a mean SBP of 139.2 mmHg in the glaucoma patients and 137.1 mmHg in the control group. Mean SBP in our study was 131.0 ± 16.7 mmHg and 121.5 ± 12.1 mmHg in glaucoma and normal groups, respectively. That difference between the results in the two studies could be due to differences in age or use of systemic hypotensives in the samples. In the Orzalesi study, mean DBP in the glaucoma and control group were 82.4 and 81.5 mmHg, respectively. As for our study the values were similar (82.2 and 81.5 mmHg, respectively). Despite the different values between groups, SBP and DBP were not significantly different in our study.

Considering OPA is the IOP variation according to the arterial BP, a correlation between these two variables has been tested by some studies.[20, 29,31,32] The results of those studies were not in agreement. Detry-Morel et al.[31] showed a correlation between OPA and BP parameters (SBP, positive correlation; DBP, negative correlation). Grieshaber et al.[20] presented data showing the opposite. A third study recently published by Ito et at.[32] showed a slightly positive correlation between OPA and SBP and no correlation between OPA and DBP. Our results were similar to the ones found by Ito with a positive correlation between OPA and SBP and no correlation between OPA and DBP when analyzing all individuals together. Grieshaber attributed the different outcomes to the heterogeneity in the

sample of Detry-Morel study, including glaucoma and normal individuals, and the fact that DCT and BP were measured separately. Our study showed a similar result to the one found by Grieshaber and Ito, even though our sample was also heterogeneous, with glaucoma, OH, and normal individuals, and we measured OPA and BP in the same manner as in the study by Detry-morel. That draws the attention to other factors acting in the ocular circulation that might be influencing these results.

Another way to assess the relation between OPA and OBF is by correlating the BP amplitude (PP), and IOP amplitude (OPA). To our knowledge, two studies correlated these two variables. The results were contradictory as well. Grieshaber et al.[20] found no correlation between PP and OPA, while Ito el at.[32] found a positive correlation between the two. Our results showed a positive correlation when analyzing all patients together. However, when placed in the multivariate regression model with the mean GAT level, this correlation was no longer significant. In fact, the analysis of each group separately showed that after correction for the mean GAT level, the influence of PP on OPA was present only in the OH group. Apparently, OBF may not be directly transmitted from the arterial BP to the IOP. It seems that the main defining parameter for the OPA is the mean IOP level. It was only in the OH group, where the mean IOP level was high, where the actual BP amplitude played a role in defining the OPA. In other groups, based on the missing PP vs. OPA correlation even after the correction for mean IOP, it is possible that individual local vascular regulatory mechanism determine the volume of blood (scleral rigidity was not assessed in this study) traversing the eye during the cardiac cycle and are hence reflected in the OPA.

The autoregulatory system is responsible for maintaining a stable flow and therefore supply the eye with the necessary metabolic demand despite changes in the ocular perfusion pressure.[33] When impairment in autoregulation takes place in the eye, it becomes more sensitive to IOP variations and OBF does not meet its metabolic needs, causing ischemia and leading to the glaucomatous neural loss. The vascular dysregulation caused by the disturbance in the regulatory system seems to play an important role in the progression of glaucoma, especially the ones within normal IOP values.[23,29,33-35]

One must always keep in mind that not only normal tension glaucoma (NTG) patients are prone to be affected by vascular dysregulation and other impairments to the adequate OBF. The health of the vascular system is what might influence how high an IOP can go without causing damage to the optic nerve.[35] This concept can help explain why some patients have high IOP without glaucoma and others progress with low IOP values.

In conclusion, although OPA and PP are correlated in our general sample, we could not define for certain if OPA is a reliable method to measure OBF. The results of the present study indicate that IOP cyclic variation is not a mere reflection of BP cyclic variation. DCT and GAT showed to be correlated although GAT values tend to be lower than DCT values, especially in individuals with low CCT.

REFERENCES

1. Liang Y, Downs JC, Fortune B, et al. Impact of systemic blood pressure on the relationship between intraocular pressure and blood flow in the optic nerve head of nonhuman primates. Invest Ophthalmol Vis Sci 2009;50:2154-60.

2. Flammer J, Orgül S, Costa VP, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res 2002;21:359-93.

3. Kanngiesser HE, Kniestedt C, Robert YC. Dynamic contour tonometry: Presentation of a new tonometer. J Glaucoma 2005;14:344-50.

4. Weizer JS, Asrani S, Stinnett SS, et al. The clinical utility of dynamic contour tonometry and ocular pulse amplitude. J Glaucoma 2007;16:700-3.

5. Georgopoulos GT, Diestelhorst M, Fisher R, et al. The short-term effect of latanoprost on intraocular pressure and pulsatile ocular blood flow. Acta Ophthalmol Scand 2002;80:54-8.

6. Bayerle-Eder M, Kolodjaschna J, Wolzt M, et al. Effect of a nifedipine induced reduction in blood pressure on the association between ocular pulse amplitude and ocular fundus pulsation amplitude in systemic hypertension. Br J Ophthalmol 2005;89:704-8.

7. Leske MC, Wu SY, Hennis A, et al. BESs Study Group. Risk factors for incident open-angle glaucoma: The Barbados eye studies. Ophthalmology 2008;115:85-93.

8. Mills RP, Budenz DL, Lee PP, et al. Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. Am J Ophthalmol 2006;141:24-30.

9. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 2003;42:1206-52.

10. Barleon L, Hoffmann EM, Berres M, et al. Comparison of dynamic contour tonometry and Goldmann applanation tonometry in glaucoma patients and healthy subjects. Am J Ophthalmol 2006;142:583-90.

11. Salvetat ML, Zeppieri M, Tosoni C, et al. Comparisons between pascal dynamic contour tonometry, the tonopen, and Goldmann applanation tonometry in patients with glaucoma. Acta Ophthalmol Scand 2007;85:272-9.

12. Halkiadakis I, Patsea E, Chatzimichali K, et al. Comparison of dynamic contour tonometry with Goldmann applanation tonometry in glaucoma practice. Acta Ophthalmol 2009;87:323-8.

13. Grammenandi E, Detorakis ET, Pallikaris IG, et al. Differences between Goldmann applanation tonometry and dynamic contour tonometry in pseudoexfoliation syndrome. Clin Experiment Ophthalmol 2010;38:444-8.

14. Boehm AG, Weber A, Pillunat LE, et al. Dynamic contour tonometry in comparison to intracameral IOP measurements. Invest Ophthalmol Vis Sci 2008;49:2472-7.

15. Kniestedt C, Nee M, Stamper RL. Accuracy of dynamic contour tonometry compared with applanation tonometry in human cadaver eyes of different hydration states. Graefes Arch Clin Exp Ophthalmol 2005;243:359-66.

16. Park SJ, Ang GS, Nicholas S, et al. The effect of thin, thick, and normal corneas on Goldmann intraocular pressure measurements and correction formulae in individual eyes. Ophthalmology 2012;119:443-9.

17. Punjabi OS, Ho HK, Kniestedt C, et al. Intraocular pressure and ocular pulse amplitude comparisons in different types of glaucoma using dynamic contour tonometry. Curr Eye Res 2006;31:851-62.

18. Kac MJ, Solari HP, Velarde GC, et al. Ocular pulse amplitude in patients with asymmetric primary open-angle glaucoma. Curr Eye Res 2011;36:727-32.

19. Siganos DS, Papastergiou GI, Moedas C. Assessment of the pascal dynamic contour tonometer in monitoring intraocular pressure in unoperated eyes and eyes after LASIK. J Cataract Refract Surg 2004;30:746-51.

20. Grieshaber MC, Katamay R, Gugleta K, et al. Relationship between ocular pulse amplitude and systemic blood pressure measurements. Acta Ophthalmol 2009;87:329-34.

21. Tielsch JM, Katz J, Sommer A, et al. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. Arch Ophthalmol 1995;113:216-21.

22. Gugleta K, Polunina A, Kochkorov A, et al. Association between risk factors and glaucomatous damage in untreated primary open-angle glaucoma. J Glaucoma 2012 [Epub ahead of print].

23. Costa VP, Arcieri ES, Harris A. Blood pressure and glaucoma. Br J Ophthalmol 2009;93:1276-82.

24. Hulsman CA, Vingerling JR, Hofman A, et al. Blood pressure, arterial stiffness, and open-angle glaucoma: The rotterdam study. Arch Ophthalmol 2007;125:805-12.

25. Graham SL, Drance SM, Wijsman K, et al. Ambulatory blood pressure monitoring in glaucoma. The nocturnal dip. Ophthalmology 1995;102:61-9.

26. Bonomi L, Marchini G, Marraffa M, et al. Vascular risk factors for primary open angle glaucoma: The Egna-Neumarkt study. Ophthalmology 2000;107:1287-93.

27. Graham S. Are vascular factors involved in glaucomatous damage? Aust N Z J Ophthalmol 1999;27:354-6.

28. Choi J, Jeong J, Cho HS, et al. Effect of nocturnal blood pressure reduction on circadian fluctuation of mean ocular perfusion pressure: A risk factor for normal tension glaucoma. Invest Ophthalmol Vis Sci 2006;47:831-6.

29. Caprioli J, Coleman AL, Blood Flow in Glaucoma Discussion. Blood pressure, perfusion pressure, and glaucoma. Am J Ophthalmol 2010;149:704-12.

30. Orzalesi N, Rossetti L, Omboni S, CONPROSO (Collegio Nazionale dei Professori Ordinari di Scienze Oftalmologiche). Vascular risk factors in glaucoma: The results of a national survey. Graefes Arch Clin Exp Ophthalmol 2007;245:795-802.

31. Detry-Morel M, Jamart J, Detry MB, et al. Clinical evaluation of the Pascal dynamic contour tonometer. J Fr Ophtalmol 2007;30:260-70.

32. Ito K, Tawara A, Kubota T, et al. IOP measured by dynamic contour tonometry correlates with IOP measured by Goldmann applanation tonometry and non-contact tonometry in japanese individuals. J Glaucoma 2012;21:35-40.

33. Anderson DR. Introductory comments on blood flow autoregulation in the optic nerve head and vascular risk factors in glaucoma. Surv Ophthalmol 1999;43(suppl.1):S5-9.

34. Flammer J, Haefliger IO, Orgül S, et al. Vascular dysregulation: A principal risk factor for glaucomatous damage? J Glaucoma 1999, Jun;8(3):212-9.

35. Flammer J, Mozaffarieh M. Autoregulation, a balancing act between supply and demand. Can J Ophthalmol 2008;43:317-21.

DISCUSSÃO

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A redução da PIO é ainda o único tratamento cientificamente comprovado para impedir a progressão do dano glaucomatoso (AGIS INVESTIGATORS, 2002; LESKE *et al*., 2003; MALERBI *et al*., 2005). Embora exista expressivo número de pacientes que continuam apresentando piora do glaucoma, mesmo tendo a sua PIO reduzida a valores dentro da referência de normalidade. Outros desenvolvem a doença sem nunca apresentar qualquer evidência de PIO elevada. Mesmo diante de glaucoma evoluindo com valores de pressão dentro da normalidade o tratamento consagrado é a redução, até de forma rigorosa, da PIO (ANDERSON *et al*., 2003). Ainda assim, uma parcela desses pacientes ainda piorava mesmo com a doença apresentando valores da PIO extremamente baixos, o que indica a existência de outros fatores de risco que talvez estejam contribuindo na etiopatogenia do glaucoma.

O método padrão-ouro de medida da PIO é a partir da tonometria de aplanação de Goldmann (TAG). A influência dos fatores corneanos na acurácia da TAG foi vastamente abordada na literatura (BRANDT, 2004; DAMJI; MUNI; MUNGER, 2003; DOUGHTY; ZAMAN, 2000; EHLERS; BRAMSEN; SPERLING, 1975; LIU; ROBERTS, 2005; WHITACRE; STEIN, 1993), haja vista que esse aparelho foi desenvolvido baseado em córneas de espessura central (ECC) de 520 µm (GOLDMANN, 1970). Na presença de córneas de espessura muito abaixo desse valor de referência, a PIO poderia estar hipoestimada devido a menos força para gerar a aplanação central. O oposto também ocorre com córneas espessas, tendendo a apresentar valores hiperestimados da PIO.

A tonometria dinâmica de contorno (TDC) é um método mais recente e uma alternativa para medida da PIO. Na TDC não é necessário aplanar a córnea ou causar qualquer tipo de deformação da mesma para se obter a sua aferição (KANNGIESSER; KNIESTEDT; ROBERT, 2005). O resultado é uma medida da PIO com menor influência dos fatores corneanos, como ECC e histerese corneana, quando comparado com a TAG (DETRY-MOREL *et al*., 2007; HAGER *et al*., 2008; MANGOURITSAS *et al*., 2011; MORITA *et al*., 2010). O presente trabalho mostrou leve correlação positiva entre TAG e ECC (*P/ρ* = 0,029/0,230), já a TDC não apresentou correlação com a ECC (*P/r* = 0,965/-0,005).

O valor da PIO medido na TAG tende a ser mais baixo que na TDC, sendo que essa diferença varia de 0,7 a 2,8 mmHg (DOYLE; LACHKAR, 2005; ITO *et al*., 2012; KAUFMANN; BACHMANN; THIEL, 2004; KOTECHA *et al*., 2005; KOTECHA *et al*., 2010; LEE *et al*., 2009; SCHNEIDER; GREHN, 2006; WEIZER *et al*., 2007). Nossos resultados revelaram um delta entre os dois métodos de medida da PIO de 1,7 mmHg. Apesar de não haver uma boa concordância, o presente trabalho confirmou a correlação positiva entre a PIO medida pela TAG e TDC, reforçando os resultados obtidos na literatura (DOYLE; LACHKAR, 2005; ITO *et al*., 2012; KAUFMANN *et al*., 2006; KOTECHA *et al*., 2005; KOTECHA *et al*., 2010; LEE *et al*., 2009; SCHNEIDER; GREHN, 2006).

A menor influência dos fatores corneanos na TDC quando comparada com a TAG pode explicar a diferença dos valores absolutos da PIO obtida por cada um dos métodos. Este estudo mostrou discreta correlação positiva entre TAG e ECC enquanto a nenhuma correlação entre TDC e ECC. A diferença entre os valores da PIO pela TAG e TDC se mostra mais significativa em indivíduos com a ECC baixa. Pela lógica, os indivíduos com a córnea espessa deveriam apresentar

valores de TDC mais baixos que os da TAG, mas na verdade os valores se mostram semelhantes nesses casos, sugerindo possível limitação da TDC em pacientes com córnea espessa ou presença de algum outro fator corneano de interferência nesses casos.

A TDC mede a pressão de forma contínua e, com isso, é capaz de aferir a oscilação da PIO de acordo com a fase do ciclo cardíaco (KANNGIESSER; KNIESTEDT; ROBERT, 2005). Sendo assim, a TDC desmembra a PIO em duas: PIO máxima ou sistólica e PIO mínima ou diastólica. A APO é obtida pela diferença entre a PIO sistólica e diastólica. Ainda não há fortes evidências a respeito do real papel da APO na etiopatogenia do glaucoma. Estudo mostrou resultados compatíveis com correlação entre APO elevada e baixa gravidade do glaucoma (WEIZER *et al*., 2007).

A APO mostrou-se mais baixa em indivíduos com glaucoma de pressão normal (GPN) do que em portadores de glaucoma primário de ângulo aberto, hipertensos oculares e normais (SCHWENN *et al*., 2002). Trabalho mostrou a relação entre baixa APO e existência de dano estrutural e funcional de glaucoma (KYNIGOPOULOS *et al*., 2012).

No presente estudo, a média da APO foi significativamente menor no grupo dos normais do que nos grupos do glaucoma e hipertensos oculares. Tal resultado pode ser explicado a partir da correlação positiva entre TAG e APO (KAUFMANN *et al*., 2006; PUNJABI *et al*., 2006). Para incluir indivíduos portadores de glaucoma de pressão normal no estudo, não foi utilizado o critério de PIO elevada (>21 mmHg) para inclusão no específico grupo. Assim, a PIO média no grupo do glaucoma ficou relativamente menor, baixando a média da APO nesse grupo.

A correlação de pressão arterial (PA) e glaucoma é ainda um tema bastante controverso. A hipertensão arterial sistêmica foi considerada por alguns autores um fator de risco independente no glaucoma (BONOMI *et al*., 2000; GOLDBERG *et al*., 1981; KASHIWAGI *et al*., 2001; LEIGHTON; PHILLIPS, 1972; LEVENE, 1980; ROUHIAINEN; TERÄSVIRTA, 1990). Em contrapartida, outros estudos referiram a hipotensão arterial como fator relacionado à progressão do dano glaucomatoso (COLLIGNON *et al*., 1998; DEMAILLY *et al*., 1984; GRAHAM; DRANCE, 1999; GRAHAM *et al*., 1995; HAYREH *et al*., 1994; KAISER; FLAMMER; BURCKHARDT, 1993). Na presente investigação, a PA sistólica média no grupo do glaucoma foi mais alta que nos grupos hipertensos oculares e normais, porém esta diferença não foi estatisticamente significativa. As médias da PA diastólica nos três grupos se mantiveram muito próximas e também não apresentaram diferença significativa.

Considerando que a APO representa a variação da PIO de acordo com a fase do ciclo cardíaco, as correlações entre APO e parâmetros da PA foram alvo de alguns estudos (DETRY-MOREL *et al*., 2007; GRIESHABER *et al*., 2009; ITO *et al*., 2012). Detry-Morel *et al*. (2007) salientaram a correlação positiva entre APO e PA sistólica e negativa entre APO e PA diastólica. Já Grieshaber *et al*. (2009) apresentaram resultados opostos. Um terceiro estudo recentemente publicado por Ito *et al*. (2012) enfatizou discreta correlação entre APO e PAS e nenhuma correlação entre APO e PA diastólica. Nossos resultados foram similares aos encontrados pelo grupo de Ito *et al.* (2012), verificando correlação positiva entre APO e PAS e nenhuma correlação entre APO e PAD quando avaliados os três grupos em conjunto. A divergência nos resultados indica fatores da circulação ocular que podem estar influenciando a APO.

Na interpretação da pressão de perfusão ocular (PPO), o indivíduo pode ter baixa PPO devido à baixa PA e/ou elevada PIO. Estudos epidemiológicos populacionais reportaram a relação entre baixa PPO e glaucoma (BONOMI *et al*., 2000; HULSMAN *et al*., 2007; LESKE *et al*., 2008; QUIGLEY *et al*., 2001; TIELSCH *et al*., 1995). Não há, todavia, consenso sobre um valor de referência para diferenciar a PPO entre normal e alterada. Leske *et al*. (2008) concluíram que portadores de PPO < 42 mmHg tinham risco relativo aumentado ao desenvolvimento do glaucoma (RR=2,2). Na presente pesquisa, a média da PPO foi de 46,3 ± 7,9 mmHg no grupo do glaucoma, 50,2 ± 7,0 mmHg nos normais e 41,5 ± 5,2 mmHg nos hipertensos oculares. A PPO no grupo do glaucoma está elevada devido à não inclusão do critério de PIO elevada para a seleção desse grupo. O grupo normal manifestou variação de 43,2 a 57,2 mmHg, mantendo-se sempre o ponto de corte de 42 mmHg proposto pelo grupo de Leske *et al*. (2008).

Um fator que precisa ser levado em conta quando se avalia o fluxo sanguíneo ocular a partir da PPO ou pela APO é que ambas são influenciadas diretamente pela PIO. A existência de um fator de risco vascular no glaucoma independente da PIO seria mais valiosa no entendimento da doença, principalmente em se tratando de glaucomas que progridem na vigência de PIO normal. Outro aspecto importante que precisa ser considerado é a variação circadiana dessas medidas, principalmente no que diz respeito às quedas da PA no período noturno. O descenso noturno não fisiológico da PA foi atribuído como causa de baixa perfusão do nervo óptico (COLLIGNON *et al*., 1998; DETRY *et al*., 1996; TOKUNAGA *et al*., 2004).

A correlação entre fatores de risco vasculares no glaucoma, em especial entre PPO e APO, foi testada em dois estudos recentes (CHOI *et al*., 2010;

GUGLETA *et al*., 2012). Ambos mostraram ausência de correlação entre as duas variáveis em questão. Nosso estudo também detectou ausência de correlação entre PPO e APO em pacientes com glaucoma, hipertensos oculares e normais. Quando avaliados os grupos de hipertensos oculares e normais em conjunto, correlação limítrofe foi constatada, mas a razão para tal resultado não ficou clara.

A avaliação da correlação da APO com o fluxo sanguíneo ocular pode ser feita também com base no estudo entre a pressão de pulso arterial (PA sistólica menos PA diastólica) e APO (PIO sistólica menos PIO diastólica). Da literatura consultada, foram selecionados dois recentes trabalhos que correlacionaram essas duas variáveis (GRIESHABER *et al*., 2009; ITO *et al*., 2012) e os resultados também foram contraditórios. Grieshaber *et al*. (2009) não acharam correlação entre APO e pressão de pulso, enquanto Ito *et al.* (2012) encontraram tal correlação. Na presente pesquisa foi detectada discreta correlação quando se avaliou os três grupos em conjunto. Na análise dos três grupos de maneira isolada a correlação se manteve presente apenas no grupo dos hipertensos oculares. Aparentemente, o fluxo sanguíneo ocular não é transmitido de maneira direta da PA para a PIO. A influência de mecanismos vasculares regulatórios pode atuar de maneira individualizada.

O sistema de autorregulação é responsável pela manutenção de um fluxo sanguíneo estável, suprindo o olho com a demanda metabólica necessária, mesmo diante de flutuações na PPO. Na vigência de desregulação desses mecanismos vasculares, o olho fica mais susceptível às variações da PIO e o fluxo sanguíneo ocular torna-se inferior ao necessário, causando isquemia e perda neuronal característica do glaucoma (ANDERSON, 1999). Essa degeneração vascular parece exercer importante papel na progressão do

glaucoma, especialmente no GPN (COSTA; ARCIERI; HARRIS, 2009; CAPRIOLI; COLEMAN, 2010; FLAMMER *et al*., 1999; FLAMMER; MOZAFFARIEH, 2008).

É importante lembrar que não apenas o paciente com GPN está exposto à desregulação vascular e demais alterações de fluxo sanguíneo ocular. A saúde do sistema vascular no olho influencia a maneira na qual a PIO poderá ou não causar o dano glaucomatoso. Esse conceito pode ajudar a explicar por que determinados indivíduos desenvolvem glaucoma com PIO mais baixa e outros não a desenvolvem com PIO mais elevada.

CONCLUSÕES

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Os resultados desta pesquisa levaram às seguintes conclusões:

- A amplitude do pulso ocular não está correlacionada à pressão de perfusão ocular em pacientes glaucomatosos, hipertensos oculares e normais.
- A amplitude do pulso ocular e pressão do pulso arterial estão discretamente correlacionadas, não podendo, portanto, definir a amplitude do pulso ocular como método confiável de mensuração do fluxo sanguíneo ocular.

A PIO medida pela tonometria dinâmica de contorno mostrou-se correlacionada à medida pela tonometria de aplanação de Goldmann. Entretanto, não houve boa correspondência entre esses dois métodos, principalmente em indivíduos com baixa espessura corneana, nos quais a tonometria de Goldmann tendeu a mostrar valores inferiores à tonometria dinâmica de contorno.

REFERÊNCIAS

REFERÊNCIAS

ABEGÃO PINTO, L. *et al*. Intraocular pressure correlates with optic nerve sheath diameter in patients with normal tension glaucoma. **Graefe's archive for clinical and experimental ophthalmology**, Dec. 2011.

AGIS INVESTIGATORS. The Advanced Glaucoma Intervention Study (AGIS): 12. Baseline risk factors for sustained loss of visual field and visual acuity in patients with advanced glaucoma. **American Journal of Ophthalmology***,* United States, v. 134, n. 4, p. 499-512 , Oct. 2002.

ANDERSON, D.R. *et al*. Factors that predict the benefit of lowering intraocular pressure in normal tension glaucoma. **American Journal of Ophthalmology***,* United States, v. 136, n. 5, p. 820-9 , Nov. 2003.

ANDERSON, D.R. Introductory comments on blood flow autoregulation in the optic nerve head and vascular risk factors in glaucoma. **Survey of Ophthalmology***,* United States, v. 43, Suppl 1, p. S5-9, Jun. 1999.

BAYRAKTAR, S.; BAYRAKTAR, Z. Central corneal thickness and intraocular pressure relationship in eyes with and without previous LASIK: comparison of Goldmann applanation tonometer with pneumatonometer. **European Journal of Ophthalmology,** Italy, v. 15, n. 1, p. 81-8, 2005.

BONOMI, L. *et al*. Vascular risk factors for primary open angle glaucoma: the Egna-Neumarkt Study. **Ophthalmology***,* United States, v. 107, n. 7, p. 1287-93, Jul. 2000.

BRANDT, J.D. Corneal thickness in glaucoma screening, diagnosis, and management. **Current Opinion in Ophthalmology***,* United States, v. 15, n. 2,85-9 , Abr 2004.

CAPRIOLI, J.; COLEMAN, A.L. Blood pressure, perfusion pressure, and glaucoma. **American Journal of Ophthalmology***,* v. 149, n. 5, p. 704-712, 2010.

CHOI, J. *et al*. Effect of nocturnal blood pressure reduction on circadian fluctuation of mean ocular perfusion pressure: a risk factor for normal tension glaucoma. **Investigative Ophthalmology & Visual Science***,* United States, v. 47, n. 3, p. 831-6, Mar. 2006.

CHOI, J. *et al*. Factors affecting ocular pulse amplitude in eyes with open angle glaucoma and glaucoma-suspect eyes. **Acta Ophthalmologica***,* epub ahead of print, Jun. 2010.

COLLIGNON, N. *et al*. Ambulatory blood pressure monitoring in glaucoma patients. The nocturnal systolic dip and its relationship with disease progression. **Int Ophthalmol***,* Netherlands, v. 22, n. 1, p. 19-25, 1998.

COSTA, V.P.; ARCIERI, E.S.; HARRIS, A. Blood pressure and glaucoma. **The British Journal of Ophthalmology***,* England, v. 93, n. 10, p. 1276-82, Oct. 2009.

COSTA, V.P. *et al*. Twenty-four-hour ocular perfusion pressure in primary open-angle glaucoma. **The British Journal of Ophthalmology***,* England, v. 94, n. 10, p. 1291-4, Oct. 2010.

CRONEMBERGER, S. *et al*. Intraocular pressure and ocular rigidity after LASIK. **Arquivos Brasileiros de Oftalmologia***,* Brazil, v. 72, n. 4, p. 439-43 , 2009.

DAMJI, K.F.; MUNI, R.H.; MUNGER, R.M. Influence of corneal variables on accuracy of intraocular pressure measurement. **Journal of Glaucoma***,* United States, v. 12, n. 1, p. 69-80, Fev. 2003.

DEMAILLY, P. *et al*. Do patients with low tension glaucoma have particular cardiovascular characteristics? Ophthalmologica. Journal International

D'ophtalmologie. International **Journal of Ophthalmology**. Zeitschrift für Augenheilkunde*,* Switzerland, v. 188, n. 2, p. 65-75, 1984.

DETRY, M. *et al*. Simultaneous 24-hour monitoring of intraocular pressure and arterial blood pressure in patients with progressive and non-progressive primary open-angle glaucoma. **European Journal of Ophthalmology***,* Italy, v. 6, n. 3, p. 273-8, 1996.

DETRY-MOREL, M. *et al*. Clinical evaluation of the Pascal dynamic contour tonometer. **J Fr Ophtalmol***,* France, v. 30, n. 3, p. 260-70, Mar. 2007.

DOUGHTY, M.J.; ZAMAN, M.L. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. **Survey of Ophthalmology***,* United States, v. 44, n. 5, p. 367-408, 2000.

DOYLE, A.; LACHKAR, Y. Comparison of dynamic contour tonometry with Goldman applanation tonometry over a wide range of central corneal thickness. **Journal of Glaucoma***,* United States, v. 14, n. 4, p. 288-92, Aug. 2005.

DRANCE, S.M. *et al*. Response of blood flow to warm and cold in normal and low-tension glaucoma patients. **American Journal of Ophthalmology***,* United States, v. 105, n. 1, p. 35-9, Jan. 1988.

EHLERS, N.; BRAMSEN, T.; SPERLING, S. Applanation tonometry and central corneal thickness. **Acta Ophthalmologica***,* Denmark, v. 53, n. 1, p. 34-43, Mar. 1975.

FLAMMER, J. *et al*. Vascular dysregulation: a principal risk factor for glaucomatous damage? **Journal of Glaucoma***,* United States, v. 8, n. 3, p. 212-9, Jun. 1999.

FLAMMER, J.; MOZAFFARIEH, M. Autoregulation, a balancing act between supply and demand. Canadian Journal of Ophthalmology. **Journal Canadien D'ophtalmologie***,* Canada, v. 43, n. 3, p. 317-21, Jun. 2008.

FRANCIS, B.A. *et al*. Effects of corneal thickness, corneal curvature, and intraocular pressure level on Goldmann applanation tonometry and dynamic contour tonometry. **Ophthalmology***,* United States, v. 114, n. 1, p. 20-6, Jan. 2007.

GASSER, P.; FLAMMER, J. Blood-cell velocity in the nailfold capillaries of patients with normal-tension and high-tension glaucoma. **American Journal of Ophthalmology***,* United States, v. 111, n. 5, p. 585-8, May. 1991.

GOLDBERG, I. *et al.* Systemic factors in patients with low-tension glaucoma. **The British Journal of Ophthalmology,** England, v. 65, n. 1, p. 56-62 , Jan. 1981.

GOLDMANN, H. Factors influencing intraocular pressure. **Bibliotheca Ophthalmologica: Supplementa ad Ophthalmologica***,* Switzerland, v. 81, p. 97-105, 1970.

GORDON, M.O. *et al*. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. **Archives of Ophthalmology***,* United States, v. 120, n. 6, p. 714-20; discussion 829-30, Jun. 2002.

GRAHAM, S.L.; DRANCE, S.M. Nocturnal hypotension: role in glaucoma progression. **Survey of ophthalmology***,* United States, v. 43 Suppl 1, S10-6, Jun. 1999.

GRAHAM, S.L. *et al*. Ambulatory blood pressure monitoring in glaucoma. The nocturnal dip. **Ophthalmology***,* United States, v. 102, n. 1, p. 61-9, Jan. 1995.

GRIESHABER, M.C. *et al*. Relationship between ocular pulse amplitude and systemic blood pressure measurements. **Acta Ophthalmologica***,* England, v. 87, n. 3, p. 329-34, May, 2009.

GROVER, D.S.; BUDENZ, D.L. Ocular perfusion pressure and glaucoma. **International Ophthalmology Clinics***,* United States, v. 51, n. 3, p. 19-25 , 2011.

GUGLETA, K. *et al*. Association Between Risk Factors and Glaucomatous Damage in Untreated Primary Open-angle Glaucoma. **Journal of Glaucoma***,* epub ahead of print, Jan. 2012.

HAGER, A. *et al*. Effect of central corneal thickness and corneal hysteresis on tonometry as measured by dynamic contour tonometry, ocular response analyzer, and Goldmann tonometry in glaucomatous eyes. **Journal of Glaucoma***,* United States, v. 17, n. 5, p. 361-5, Ago. 2008.

HAYREH, S.S. Blood flow in the optic nerve head and factors that may influence it. **Prog Retin Eye Res***,* England, v. 20, n. 5, p. 595-624, Sep. 2001.

HAYREH, S.S. *et al*. Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. **American Journal of Ophthalmology***,* United States, v. 117, n. 5,p. 603-24, Mai 1994.

HULSMAN, C.A.A. *et al*. Blood pressure, arterial stiffness, and open-angle glaucoma: the Rotterdam study. **Archives of Ophthalmology***,* United States, v. 125, n. 6, p. 805-12, Jun. 2007.

ITO, K. *et al*. IOP measured by dynamic contour tonometry correlates with IOP measured by Goldmann applanation tonometry and non-contact tonometry in Japanese individuals. **Journal of Glaucoma***,* United States, v. 21, n. 1, p. 35-40, Jan. 2012.

KAISER, H.J.; FLAMMER, J.; BURCKHARDT, D. Silent myocardial ischemia in glaucoma patients. **Ophthalmologica***,* Switzerland, v. 207, n. 1, p. 6-7, 1993.

KANNGIESSER, H.E.; KNIESTEDT, C.; ROBERT, Y.C.A. Dynamic contour tonometry: presentation of a new tonometer. **Journal of Glaucoma***,* United States, v. 14, n. 5, p. 344-50, Oct. 2005.

KASHIWAGI, K. *et al*. Systemic circulatory parameters. comparison between patients with normal tension glaucoma and normal subjects using ambulatory monitoring. **Jpn J Ophthalmol***,* United States, v. 45, n. 4, p. 388-96, 2001.

KAUFMANN, C.; BACHMANN, L.M.; THIEL, M.A. Comparison of dynamic contour tonometry with goldmann applanation tonometry. **Investigative Ophthalmology & Visual Science***,* United States, v. 45, n. 9, p. 3118-21, Sep. 2004.

KAUFMANN, C. *et al*. Ocular pulse amplitude in healthy subjects as measured by dynamic contour tonometry. **Archives of Ophthalmology***,* United States, v. 124, n. 8, p. 1104-8, Aug. 2006.

KIM, Y-d, *et al*. Risk factors associated with optic disc haemorrhage in patients with normal tension glaucoma. **Eye**, England, v. 24, n. 4, p. 567-72, Apr. 2010.

KOTECHA, A. *et al*. Intraocular pressure measurement precision with the Goldmann applanation, dynamic contour, and ocular response analyzer tonometers. **Ophthalmology***,* United States, v. 117, n. 4, p. 730-7, Apr. 2010.

KOTECHA, A. *et al*. The relative effects of corneal thickness and age on Goldmann applanation tonometry and dynamic contour tonometry. **The British Journal of Ophthalmology***,* England, v. 89, n. 12, p. 1572-5, Dec. 2005.

KYNIGOPOULOS, M. *et al*. Decreased ocular pulse amplitude associated with functional and structural damage in open-angle glaucoma. **European journal of ophthalmology***,* Italy, v. 22, n. 1, p. 111-6, 2012.

LEE, J. *et al*. Comparison between dynamic contour tonometry and Goldmann applanation tonometry. **Korean J Ophthalmol, Korea** (South), v. 23, n. 1, p. 27-31, Mar. 2009.

LEIGHTON, D.A; PHILLIPS, C.I. Systemic blood pressure in open-angle glaucoma, low tension glaucoma, and the normal eye. **The British Journal of Ophthalmology***,* England, v. 56, n. 6, p. 447-53, Jun. 1972.

LESKE, M.C. *et al*. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. **Archives of Ophthalmology***,* United States, v. 121, n. 1, p. 48-56 , Jan. 2003.

LESKE, M.C. *et al*. Risk factors for incident open-angle glaucoma: the Barbados Eye Studies. **Ophthalmology***,* United States, v. 115, n. 1, p. 85-93, Jan. 2008.

LEVENE, R.Z. Low tension glaucoma: a critical review and new material. **Survey of Ophthalmology***,* United States, v. 24, n. 6, p. 621-64, 1980.

LIU, J.; ROBERTS, C.J. Influence of corneal biomechanical properties on intraocular pressure measurement: quantitative analysis. **Journal of Cataract and Refractive Surgery***,* United States, v. 31, n. 1, p. 146-55, Jan. 2005.

MALERBI, F.K. *et al*. Intraocular pressure variability in patients who reached target intraocular pressure. **The British Journal of Ophthalmology***,* England, v. 89, n. 5, p. 540-2 , Mai 2005.

MANGOURITSAS, G. *et al*. Comparison of Goldmann and Pascal tonometry in relation to corneal hysteresis and central corneal thickness in nonglaucomatous eyes. **Clinical ophthalmology***,* New Zealand, v. 5, p. 1071-7, 2011.

MCKEE, H.D.R.; SALDAÑA, M.; AHAD, M.A. Increased ocular pulse amplitude revealing aortic regurgitation. **American Journal of Ophthalmology***,* United States, v. 138, n. 3, p. 503, Sep. 2004.

MITCHELL, P. *et al*. Open-angle glaucoma and systemic hypertension: The Blue Mountains eye study. **Journal of Glaucoma***,* United States, v. 13, n. 4, p. 319-26, Aug. 2004.

MORITA, T. *et al*. Intraocular pressure measured by dynamic contour tonometer and ocular response analyzer in normal tension glaucoma. **Graefe's archive for clinical and experimental ophthalmology**, Germany, v. 248, n. 1,73-7 , Jan. 2010.

ORZALESI, N. *et al*. Vascular risk factors in glaucoma: the results of a national survey. **Graefe's archive for clinical and experimental ophthalmology**, Germany, v. 245, n. 6, p. 795-802, Jun. 2007.

PHELPS, C.D; CORBETT, J.J. Migraine and low-tension glaucoma. A case-control study. **Investigative Ophthalmology & Visual Science***,* United States, v. 26, n. 8, p. 1105-8, Aug. 1985.

PUNJABI, O.S. *et al*. Intraocular pressure and ocular pulse amplitude comparisons in different types of glaucoma using dynamic contour tonometry. **Curr Eye Res***,* England, v. 31, n. 10, p. 851-62, Oct. 2006.

QUIGLEY, H.A. *et al*. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. **Archives of Ophthalmology***,* United States, v. 119, n. 12, p. 1819-26, Dec. 2001.

ROUHIAINEN, H.J; TERÄSVIRTA, M.E. Hemodynamic variables in progressive and non-progressive low tension glaucoma. **Acta Ophthalmologica***,* Denmark, v. 68, n. 1, p. 34-6, Feb. 1990.

SCHNEIDER, E.; GREHN, F. Intraocular pressure measurement-comparison of Dynamic contour tonometry and Goldmann applanation tonometry. **Journal of glaucoma***,* United States, v. 15, n. 1, p. 2-6, Feb. 2006.

SCHWENN, O. *et al*. Ocular pulse amplitude in patients with open angle glaucoma, normal tension glaucoma, and ocular hypertension. **The British Journal of Ophthalmology***,* England, v. 86, n. 9, p. 981-4, Sep. 2002.

SIMON, G. *et al*. Effect of corneal hydration on Goldmann applanation tonometry and corneal topography. **Refractive & Corneal Surgery***,* United States, v. 9, n. 2, p. 110-7, 1993.

TIELSCH, J.M. *et al*. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. **Archives of Ophthalmology,** United States, v. 113, n. 2, p. 216-21, Feb. 1995.

TOKUNAGA, T. *et al*. Association between nocturnal blood pressure reduction and progression of visual field defect in patients with primary open-angle glaucoma or normal-tension glaucoma. **Jpn J Ophthalmol***,* Japan, v. 48, n. 4, p. 380-5, 2004.

TOPOUZIS, F. *et al*. Association of blood pressure status with the optic disk structure in non-glaucoma subjects: the Thessaloniki eye study. **American Journal of Ophthalmology***,* United States, v. 142, n. 1, p. 60-67, Jul. 2006.

WALDMANN, E. *et al*. Silent myocardial ischemia in glaucoma and cataract patients. **Graefe's archive for clinical and experimental ophthalmology,** Germany, v. 234, n. 10, p. 595-8, Oct. 1996.

WEINREB, R.N. **Ocular Blood Flow in Glaucoma**. Amsterdam, The Netherlands: Kugler Publications, 2009.

WEIZER, J.S. *et al*. The clinical utility of dynamic contour tonometry and ocular pulse amplitude. **Journal of Glaucoma***,* United States, v. 16, n. 8, p. 700-3, Dec. 2007.

WHITACRE, M.M.; STEIN, R. Sources of error with use of Goldmann-type tonometers. **Survey of Ophthalmology***,* UNITED STATES, v. 38, n. 1, p. 1-30, 1993.

APÊNDICES

APÊNDICE A - Termo de Consentimento Livre e Esclarecido (TCLE)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

PROJETO: Análise Comparativa da Pressão de Perfusão Ocular e Amplitude do Pulso Ocular em Indivíduos Normais, Hipertensos Oculares e Glaucomatosos

O glaucoma é uma doença que cursa, na maior parte das vezes, sem sintoma algum para o paciente, até a fase avançada da doença quando a visão se torna irreversivelmente baixa. A lesão causada pelo glaucoma ocorre no nervo Óptico que é responsável por levar a imagem captada no olho para o cérebro. A pressão intra-ocular elevada é um importante fator de risco para o glaucoma e pode ser reduzida através de uma variedade de colírios anti-glaucomatosos. Porém, nem sempre a redução da pressão intra-ocular é o bastante para controlar o glaucoma. Existem outros fatores que atuam juntamente com a pressão para causar esta doença. Dentre estes fatores, nós temos os fatores vasculares. A quantidade de sangue que entra no olho para nutrir o seu tecido nervoso é de fundamental importância para o estudo do glaucoma, haja vista que o tecido acometido pelo dano glaucomatoso é extremamente sensível à baixa oxigenação.

O objetivo principal do presente projeto é avaliar através das medidas da pressão intra-ocular, pressão arterial e amplitude do pulso ocular, dois diferentes métodos para a verificação do aporte de sangue para o olho (perfusão ocular). Comparando os dois métodos em diferentes tipos de indivíduos: normais, hipertensos oculares sem dano glaucomatoso e glaucoma recém diagnosticado, estaremos avaliando o comportamento dessas duas variáveis nos diferentes grupos e com isso, talvez possamos conduzir melhor pacientes glaucomatosos com uma baixa perfusão ocular.

O exame oftalmológico e a avaliação com os diferentes tonômetros serão realizados sem ônus para os pacientes que se dispuserem a colaborar com este projeto. Tampouco, haverá qualquer compensação financeira por sua participação no estudo. Além disto, fica garantido a todos o sigilo sobre os dados clínicos e de exames complementares, e a proteção de sua identidade, em caso de publicação na imprensa científica ou leiga.

Cabe ao participante, ou ao responsável, decidir sobre a opção de participar do projeto. O participante deve ter ciência de que, mesmo após a assinatura deste termo, ele pode se desligar do projeto, a qualquer momento, sem acarretar prejuízo ao seu atendimento.

Emergência / contato com a Comissão de Ética:

Durante o estudo, se você tiver qualquer dúvida ou apresentar qualquer problema médico, contate o Serviço de Glaucoma do Hospital São Geraldo Fone: (31) 3409-9583 ou Dr. Bruno Pimentel de Figueiredo - Fone: (31) 32872624 ou Dr. Sebastião Cronemberger - Fone: (31) 33356218.

ASSINATURAS

Eu pessoalmente expliquei ao paciente o propósito desse estudo cientifico, bem como seus detalhes, os procedimentos a serem realizados, os termos do consentimento e os tratamentos alternativos disponíveis no momento.

_____

Investigador responsável

Sebastião Cronemberger Sobrinho
Serviço de Glaucoma do Hospital São Geraldo – Hospital das Clínicas/UFMG
Endereço: Av. Prof. Alfredo Balena, 190
Área Hospitalar
Telefones: (31) 3409-9583 (31)33356218

_____

Investigador (Aluno de Doutorado)

Bruno Pimentel de Figueiredo
Telefones: (31) 32872624 (31)88972624

Comitê de Ética em Pesquisa da UFMG (COEP)
Av. Pres. Antônio Carlos, 6627
Unidade Administrativa II
2º andar sala 2005
Campus Pampulha
Telefone: (31) 3409-4592

Eu,_____, ____ anos, tendo lido o termo acima e esclarecidas eventuais dúvidas, declaro minha decisão em participar do projeto de pesquisa.

Data:____/____/_____ Assinatura:_____

Eu,_____, pessoalmente expliquei ao paciente o propósito deste estudo científico, bem como seus detalhes, os procedimentos a serem realizados, os termos do consentimento e os tratamentos disponíveis no momento.

Data:____/____/_____ Assinatura:_____

APÊNDICE B - Formulário de coleta de dados

Grupo ( ) NORMAL ( ) HIPERTENSO ( ) GLAUCOMA Prontuário:_____

Nome:

Data de nascimento: / / Idade: _____ anos Gênero: M ( ) F ( )

Raça: ( ) melano ( ) faio ( ) leuco

HPP: ( )HAS _____ ( ) DM _____

( ) outros _____

HF: ( ) glaucoma _____

Melhor AV: OD:

OE:

Bio:

Pressão intra-ocular:

Goldmann: _____ hrs

OD:_____ mmHg

OE:_____ mmHg

PA: _____hrs

_____X_____ mmHg

Pressão de Perfusão Ocular: PPO= 2/3(PBD+ 1/3[PBS - PBD]) – PIO

PPO OD:

PPO OE:

PASCAL: _____hrs

OD: _____IOP

_____OPA

_____ Q

OE: _____IOP

_____OPA

_____Q

Paquimetria

OD:_____µm

OD:_____µm

Gonioscopia:

OD:

OE:

Campo Visual Computadorizado:

OD: MD: _____ PSD: _____

OE: MD: _____ PSD: _____

Biomicroscopia de fundo:

Cd:

Dr. Sebastião Cronemberger Sobrinho

Dr. Bruno Pimentel de Figueiredo

ANEXOS

ANEXO A - Parecer do Comitê de Ética em Pesquisa (COEP) da Universidade Federal de Minas Gerais (UFMG)

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Parecer nº. ETIC 150/08

Interessado(a): Prof. Sebastião Cronemberger Sobrinho
Departamento de Oftalmologia/Otorrinolaringologia
Faculdade de Medicina - UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 15 de maio de 2008, após atendidas as solicitações de diligência, o projeto de pesquisa intitulado **"Análise comparativa da pressão de perfusão ocular e amplitude de pulso ocular em indivíduos normais, hipertensos oculares e glaucomatosos"** bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto.

Profa. Maria Teresa Marques Amaral
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2° andar – Sala 2005 – Cep:31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

ANEXO B - Aprovação do Parecer Consubstanciado de Projeto de Pesquisa

Parecer Consubstanciado de Projeto de Pesquisa

Título do Projeto: ANÁLISE COMPARATIVA DA PRESSÃO DE PERFUSÃO OCULAR E AMPLITUDE DO PULSO OCULAR EM INDIVÍDUOS NORMAIS, HIPERTENSOS OCULARES E GLAUCOMATOSOS.

Pesquisador Responsável Prof. Sebastião Cronemberger Sobrinho

Data da Versão | **Cadastro** | **Data do Parecer** 17/03/2008

Grupo e Área Temática | **Classificação utilizada pela CONEP**

Objetivos do Projeto

1. Mensurar a perfusão sanguínea ocular através de dois métodos: amplitude do pulso ocular e pressão de perfusão ocular em indivíduos normais, hipertensos oculares e glaucomatosos.
2. Avaliar o comportamento da perfusão ocular nos três grupos distintos.

Sumário do Projeto

Sabe-se que a pressão intra-ocular elevada é o principal fator de risco para o glaucoma, entretanto, a baixa pressão arterial sistêmica e a perda da regulação vascular podem atuar como fatores adjuvantes da lesão glaucomatosa. A auto-regulação vascular é a capacidade que um tecido tem de ajustar a sua própria perfusão com base nas suas necessidades e de fazê-lo sem depender da pressão de perfusão. A pressão de perfusão é a diferença entre as pressões arterial e venosa. No olho, para que os vasos não colabem, é necessário que a pressão venosa seja de valor semelhante ao da pressão intra-ocular. Isto significa que a pressão de perfusão ocular é a diferença entre a pressão arterial e a pressão intra-ocular. Quando a auto-regulação funciona apropriadamente, não existem alterações na perfusão retiniana ou do nervo óptico desde que a pressão intra-ocular respeite determinados limites. Por outro lado, quando a auto-regulação está alterada, a perfusão ocular torna-se mais sensível às flutuações tanto da pressão intra-ocular como da pressão arterial. A amplitude do pulso ocular (APO) demonstra o componente pulsátil do fluxo sanguíneo ocular podendo servir como forma alternativa para medir a perfusão ocular independente da pressão intra-ocular. O Tonômetro de Contorno de Pascal além de medir dinamicamente a pressão intra-ocular, mede também amplitude do pulso ocular a cada ciclo cardíaco.
Este projeto visa mensurar e correlacionar a pressão de perfusão ocular e a amplitude do pulso ocular em pacientes normais, hipertensos oculares e glaucomatosos.

Itens Metodológicos e Éticos	Situação
Título	Adequado
Autores	Adequados
Local de Origem na Instituição	Adequado
Projeto elaborado por patrocinador	Não
Aprovação no país de origem	Não necessita
Local de Realização	Própria instituição
Outras instituições envolvidas	Não
Condições para realização	Adequadas

Comentários sobre os itens de Identificação

Introdução	Adequada

Comentários sobre a Introdução

Objetivos	Adequados

Comentários sobre os Objetivos

Pacientes e Métodos	
Delineamento	Adequado
Tamanho de amostra	Total : 90 Local : 90
Cálculo do tamanho da amostra	Adequado
Participantes pertencentes a grupos especiais	Não
Seleção eqüitativa dos indivíduos participantes	Adequada

Critérios de inclusão e exclusão	Adequados
Relação risco- benefício	Adequada
Uso de placebo	Não utiliza
Período de suspensão de uso de drogas (wash out)	Não utiliza
Monitoramento da segurança e dados	Adequado
Avaliação dos dados	Adequada - quantitativa
Privacidade e confidencialidade	Adequada
Termo de Consentimento	Adequado
Adequação às Normas e Diretrizes	Sim

Comentários sobre os itens de Pacientes e Métodos

Cronograma	Adequado
Data de início prevista	Após aprovação do COEP
Data de término prevista	31/12/2011
Orçamento	Adequado
Fonte de financiamento externa	Não

Comentários sobre o Cronograma e o Orçamento

Referências Bibliográficas	Adequadas

Comentários sobre as Referências Bibliográficas

Recomendação

Aprovar

Comentários Gerais sobre o Projeto

Trata-se de um projeto de pesquisa que poderá demonstrar a diferença do comportamento da perfusão sanguínea ocular em indivíduos normais, hipertensos oculares e glaucomatosos.

ANEXO C - Apresentação de parte do projeto em pôster no Congresso da ***Association of Research in Vision and Ophthalmology*** **(ARVO)** em Fort Lauderdale, Flórida (maio 2012)

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Program#/Poster#: 255/A496

Abstract Title: **Correlation Between Ocular Pulse Amplitude And Arterial Pulse Pressure In Glaucoma, Ocular Hypertension ,And Normal Individuals**

Presentation Start/End Time: Sunday, May 06, 2012, 8:30 AM -10:15 AM

Session Number: 108

Session Title: Glaucoma Progression Studies and Blood Flow

Location: Hall B/C

Reviewing Code: 200 glaucoma: ocular blood flow - GL

Author Block: *Bruno P. Figueiredo[1], Fabio N. Kanadani[2], Nubia V. Lima[3], Sebastiao Cronemberger[4], Syril Dorairaj[5].* 1Glaucoma, Cataract, Santa Casa - Belo Horizonte / UFMG, Belo Horizonte, Brazil; 2Ophthalmology/Glaucoma, Hospital Universitário São José, Belo Horizonte, Brazil; 3Ophthalmology, University Federal of Minas Gerais, Belo Horizonte, Brazil; 4Ophthalmology, Federal Univ of Minas Gerais, Belo Horizonte, Brazil; 5Glaucoma, New York Eye & Ear Infirmary, New York, NY.

Keywords: 567 intraocular pressure, 436 blood supply

Abstract Body: **Purpose:** To study the existence of a correlation between ocular pulse amplitude (OPA) and arterial pulse pressure (PP) in individuals with glaucoma, ocular hypertension and normals.
Methods: Ninety eyes from 90 patients were selected in which: 30 were recently diagnosed with glaucoma before starting on any hypotensive medications, 30 had elevated intraocular pressure (IOP) without any evidence of glaucoma, and 30 were included in the control group with IOP within normal range and without any evidence of glaucoma. They all underwent Goldmann applantion tonometry, dymanic contour tonometry (Pascal tonometer), blood pressure (BP), pachymetry, Humphrey visual field, and routine ophthalmologic examination. The OPA was recorded by the Pascal tonometer. Pulse pressure was calculated by systolic blood pressure minus diastolic blood pressure.
Results: Mean OPA in the glaucoma group was 3.4 ± 1.2 mmHg, ocular hypertensive 3.5 ± 1.2 mmHg, and normals 2.6 ± 0.9 mmHg. Mean PP was 48.8 ± 10.5 mmHg in the glaucoma patients, 43.8 ± 11.1 mmHg in the ocular hypertensives, and 40.0 ± 8.7 mmHg in the normals. There was a positive correlation when the three groups were evaluated together using Pearson correlation coefficient (r = 0.245).
Conclusions: The difference between systolic IOP and diastolic IOP, which is the ocular pulse amplitude, had a positive correlation with the difference between systolic and diastolic blood pressure.

CommercialRelationships: **Bruno P. Figueiredo**, None; **Fabio N. Kanadani**, None; **Nubia V. Lima**, None; **Sebastiao Cronemberger**, None; **Syril Dorairaj**, None

Support: None

ANEXO D - Apresentação de parte do projeto em pôster no congresso da ***Association of Research in Vision and Ophthalmology*** **(ARVO)** em Fort Lauderdale, Flórida (maio 2012)

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Presentation Abstract

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Program#/Poster#:	243/A484
Abstract Title:	**Correlation Of Ocular Perfusion Pressure And Ocular Pulse Amplitude In Glaucoma, Ocular Hypertensive And Normal Individuals**
Presentation Start/End Time:	Sunday, May 06, 2012, 8:30 AM -10:15 AM
Session Number:	108
Session Title:	Glaucoma Progression Studies and Blood Flow
Location:	Hall B/C
Reviewing Code:	200 glaucoma: ocular blood flow - GL
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Keywords:	625 optic flow, 436 blood supply, 630 outflow: trabecular meshwork
Abstract Body:	**Purpose:** To investigate a possible correlation between ocular perfusion pressure (OPP) and ocular pulse amplitude (OPA) in individuals with glaucoma, ocular hypertension and normals. **Methods:** Ninety eyes from 90 patients were selected in which: 30 were recently diagnosed with glaucoma before starting any ocular hypotensive medications, 30 had elevated intraocular pressure (IOP>mention the number) without any evidence of glaucoma, and 30 were included in the control group with normal IOP and without any evidence of glaucoma. They underwent Goldmann applantion tonometry, dymanic contour tonometry (Pascal), blood pressure (BP), pachymetry, Humphrey visual field (except the control group), and routine ophthalmologic examination. The OPP was calculated by the difference between mean arterial blood pressure and IOP. The OPA was measured by the Pascal tonometer. **Results:** Mean OPA in the glaucoma group was 3.4 ± 1.2 mmHg, ocular hypertensive 3.5 ± 1.2 mmHg, and normals 2.6 ± 0.9 mmHg. Mean OPP was 46.3 ± 7.9 mmHg in the glaucoma group, 46.3 ± 7.9 mmHg in the ocular hypertensive, and 50.2 ± 7.0 mmHg in the normals. Neither groups showed significant correlation (p-value > 0.05) between OPP and OPA. Pearson coefficient test was used for corelation between glaucoma and ocular hypertensive groups , while Spearman's rank coefficient correlation was used to test for the normal group. **Conclusions:** OPP and OPA values do not correlate with each other in individuals with glaucoma, ocular hypertensive and normals.
CommercialRelationships:	**Fabio N. Kanadani**, None; **Bruno P. Figueiredo**, None; **Sebastiao Cronemberger**, None; **Carlos R. Figueiredo**, None; **Tereza C. Kanadani**, None; **Syril Dorairaj**, None; **Nubia V. Lima**, None
Support:	None