Correlation between ocular perfusion pressure and estimated translamina cribrosa pressure difference in healthy young adults

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ABSTRACT

Introduction and Aim: Glaucoma is a chronic optic neuropathy which is the leading cause of irreversible blindness across the globe. It is known that Intraocular pressure is responsible for these altered changes but recent experimental and clinical studies have reported that cerebrospinal fluid pressure (CSFP) and trans-lamina cribrosa pressure difference (TLCPD), may be an important cause of glaucomatous optic nerve damage, especially in subjects with normal-tension glaucoma. To assess the correlation between ocular perfusion pressure (OPP) and TLCPD in healthy young adults.

Materials and Methods: One hundred healthy young adult volunteers comprising of 50 obese (25 males and 25 females) and 50 non-obese (25 males and 25 females) in the age group of 18-19 years among MBBS Phase I students of JSS Medical College, JSSU, Mysore were the subjects for the study. Blood Pressure and Intra Ocular Pressure were recorded. Mean arterial pressure (MAP), OPP, CSFPand TLCPD were calculated.

Results: There exists a positive correlation (0.50) between OPP and TLCPD. There was a statistically significant difference in OPP, CSFP and TLCPD between obese and non-obese groups.

Conclusion: The present study provides information on the relationship of TLCPD with CSFP and OPP that are higher in obese individuals.

Keywords: Ocular perfusion pressure; trans-lamina cribrosa pressure difference; body mass index; glaucoma.

INTRODUCTION

The trans-lamina cribrosa pressure difference (TLCPD) is defined as the difference between cerebrospinal fluid pressure(CSFP) minus intraocular pressure (IOP).There is growing evidence that TLCPD as compared with the IOP may be a more important factor in the pathophysiology of the optic nerve head disorders including the development of glaucomatous optic neuropathy(1).

The optic nerve is said to be exposed not only to IOP in the eye, but also to Intra-Cranial Pressure (ICP), as it is surrounded by cerebrospinal fluid (CSF) in the subarachnoid space. The lamina cribrosa demarcates (2) these two pressurized zones and the pressure difference between them is called translaminar pressure difference (TPD) (TPD= IOP – ICP).

It has been assumed that both the TLCPD and the translamina cribrosa pressure gradient may be of importance in pressure-related optic nerve head diseases (3).

The CSFP is the counter-pressure against the IOP across the lamina cribrosa and is part of the equation of the TLCPD as IOP – CSFP (4).

Recent experimental and clinical studies have reported that CSFP may play an important role in the pathogenesis of glaucomatous optic neuropathy.

Moreover, several studies have demonstrated that glaucomatous optic nerve damage may develop in subjects with normal IOP due to abnormally low CSFP (5).

OPP is defined as arterial blood pressure (BP) minus IOP. Mean ocular perfusion pressure is generally calculated as two-thirds of mean arterial pressure minus IOP. Occasionally, OPP is further divided into systolic perfusion pressure (SBP minus IOP) and diastolic perfusion pressure (DBP minus IOP). Large population-based studies have determined that reduced OPP is strongly associated with increased prevalence of glaucoma (6).Low DPP has the strongest correlation with the development of glaucoma.

MATERIALS AND METHODS

The study was conducted at department of Physiology, JSS Medical College (JSSMC), Mysuru. The study was done after obtaining an ethical clearance from ethical committee of JSSMC. MBBS phase-I students were requested to complete a questionnaire that included inclusion and exclusion criteria and 100 subjects were recruited for the study after obtaining informed consent. The weight, height, Waist Circumference (WC) and Hip Circumference (HC) were recorded. BMI was calculated by dividing weight in kgs by the square of height in meter and Waist Hip Ratio (WHR) was computed. IOP and BP were measured and OPP was calculated for each subject. Subjects with pre-existing refractive errors, acute or chronic conjunctivitis, glaucoma, migraine, and diabetes mellitus were excluded from the study. As per WHO guidelines, those with BMI 18-22.9 were grouped as control and those with BMI >25 as study group. The study was carried out in a quiet room, by a single examiner between 3pm to 5pm to minimize the bias of examiners and diurnal variations of IOP. Subjects were briefed about the study procedure before the test was done and was assured that the procedure was painless. Subjects were asked to relax for 15 minutes in supine position. Resting BP was measured using Mercury Sphygmomanometer and mean arterial pressure was calculated using the formula,

MAP = DBP+1/3 PP (PP=pulse pressure).

The IOP was recorded using Schiotz indentation tonometer. The instrument was calibrated so as the scale reading was made to coincide at zero before recording the IOP. Ciprofloxacin eye drop was instilled prophylactically in both the eyes to prevent any ocular infections after the procedure. OPP was calculated using the formula,

OPP = 2/3(MAP-IOP).

Estimation of CSFP and TLCPD

The gold standard for ICP evaluation is an invasive measurement of the pressure in the CSF via lumbar puncture or via implantation of a pressure sensor into a cerebral ventricle(7,8).Importantly, this invasiveness includes the potential risk for intracranial haemorrhages and infection.(9).

To overcome these invasive limitations, several approaches have been proposed. Xie and his colleague’s estimated mathematical ICP formula based on three parameters: The algorithm for determining CSFP was constructed based on three parameters, diastolic BP, BMI, and age (10).

Estimated CSFP [mmHg] = 0.44 × BMI [kg/m2] + 0.16 × diastolic blood pressure [mmHg]—0.18 × age [years]—1.91). This formula was applied to groups of subjects by comparing the estimated CSFP with the direct CSFP measurements. The formula was then tested in the independent test group, in which the measured lumbar cerebrospinal fluid pressure (12.6 ± 4.8 mm Hg) then did not differ significantly (p=0.29) from the calculated cerebrospinal fluid pressure (13.3 ± 3.2 mm Hg)and Bland–Altman analysis revealed that 40 of 42 measurements were within the 95% limits of agreement(11). Using the calculated CSFP, TLCPD was calculated as CSFP-IOP.

Statistical analysis

Microsoft Excel and SPSS version 19 software were used for data entry and statistical analyses respectively. Mean and standard deviation were worked out to assess the estimate of various parameters under study. Paired t-test was applied to test the significance of difference between the groups. Pearson's Correlation test was applied to determine the relationship between the parameters.

RESULTS

Table 1: Physiological characteristics of the study and control groups

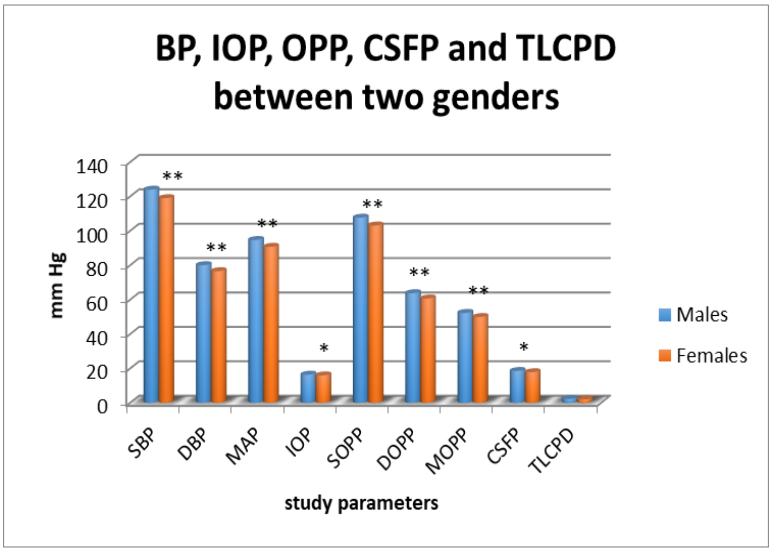
Parameter	Study Group (obese, n = 50)	Control Group (non-obese, n = 50)	p value
Age (Years)	18.26 ± 0.44	18.26 ± 0.44	(≤)1.000
Weight (Kg)	73.56 ± 8.38	56.12 ± 7.61	(≤)0.001*
Height (Cm)	162.72 ± 7.44	162.34 ± 10.83	(≤)0.838
BMI	27.76 ± 2.27	21.28 ± 1.13	(≤)0.001*

*Statistically significant (p<0.05)

Table 2: Mean± SD BP, IOP, OPP, CSFP and TLCPD of study and control groups

Parameter	Study Group (obese, n = 50)	Control Group (non-obese, n = 50)	p value
SBP (mm Hg)	124.44 ± 6.06	118.44 ± 4.44	(≤)0.001*
DBP (mm Hg)	78.680± 4.94 2	77.840 ± 2.881	(≤)0.302
MAP (mm Hg)	93.93±4.75	91.37±2.71	(≤)0.001*
IOP(mm Hg)	16.71±1.07	16.170± 0.969	(≤)0.010*
SOPP (mm Hg)	105.73±5.20	100.38±4.26	(≤)0.05*
DOPP (mm Hg)	59.97±4.10	61.26±3.37	(≤)0.61
MOPP (mm Hg)	51.48±3.227	50.14 ±1.574	(≤)0.010*
CSFP (mm Hg)	18.97±1.22	16.56±0.90	(≤)0.0001*
TLCPD (mm Hg)	3.26±1.52	0.45±1.10	(≤)0.0001*

*Statistically significant (p<0.05)



*Statistically significant (p<0.05), **highly significant (p<0.001)

Fig. 1: Mean of BP, IOP, OPP, CSFP and TLCPD between two genders

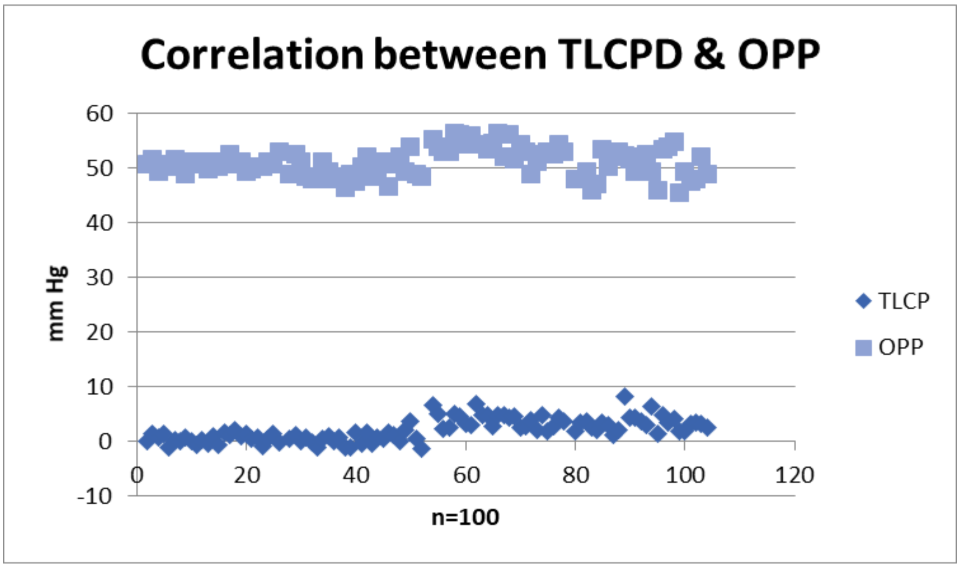


Fig. 2: Graph showing positive correlation between TLCPD and OPP in obese and non-obese groups (sex-independent). (r = 0.501)

DISCUSSION

The aim of this work was to study the relationship between OPP and TLCPD in healthy young adults. This study involved 100 young adults aged between 18-19 years. Study group allocation was done based on WHO guidelines, depending on their BMI as obese and non-obese.

There were no significant differences between the two groups in terms of age, height and DBP. The mean SBP, CSFP and TLCPD was significantly higher in the obese and there exists a positive correlation between TLCPD and OPP (r = 0.501).

Humans evolved with gravity, and gravity affects human physiology—CSF pools in the caudal spinal canal and CSF pressure at eye level is much lower than CSF pressure in the caudal spinal column in the upright position (12, 13).However in microgravity environment, CSF is distributed throughout the sub-arachnoid space tending to equalize pressure in all compartments and negate any posture-induced flow, resulting in higher than normal CSF pressure at eye level (14). The standard body position for ICP measurement is said to be lateral decubitus/supine (15).

Given that humans sleep in the supine or prone position but are upright during the day, it is important to note that IOP and ICP are dynamic parameters and vary according to changes in body position or individual activities (16).Therefore we assessed these parameters in the standard ICP measuring state – a supine position.

However, all these variations are insignificant to young healthy adults as they have intact homeostasis and ability of a vascular bed to maintain its blood flow despite changes in perfusion pressure. The association between higher cerebrospinal fluid pressure and younger age, higher body mass index, and higher blood pressure had also been reported in other studies (17, 18).

Compared with previous population-based studies that used the same estimation formula, the weighted mean TLCPD value in the normal population (2.31 ± 0.06 mmHg), as well as the weighted mean CSFP value, was also very similar. Moreover, the ranges from minimum to maximum value for the CSFP and TLCPD were much greater (-1.80–23.91 mmHg and 14.61–19.11 mmHg, respectively) than that of IOP (6.00–21.00 mmHg) (10).

Fleischman *et al.* analysed CSFP in five different age groups and found that BMI was positively correlated with CSFP in every age group (19). Positive BMI and CSF pressure associations were found by various prospective and retrospective studies (20).

In our study we analysed young healthy adults and found that mean CSFP was about 2.01 mmHg. Several studies that have examined CSF pressure and age failed to find a relationship of significance (21, 22), while Fleischman *et al.,* in their retrospective analysis of 33,922 patients who had lumbar puncture revealed that CSF pressure decreases with older age. This study found that CSF pressure was stable for the first 50 years of life (2.8 mmHg) after which there was a steady decline by 2.5% at age 50-54 and by 26.9% at age 90-95.

In the Meiktila Eye Study from Myanmar, body height and weight were significantly correlated with age, gender, corneal curvature, axial length, anterior chamber depth, and vitreous chamber length (23).

In this study, it was found that there was a significant difference in baseline MAP and OPP between two genders and these values were higher in males to that of females. A study comprising 72 women and 68 men, showed higher values for ocular blood flow in men compared to women. While estrogen had positive effects on ocular blood flow, the opposite was the case with testosterone (24). These findings were statistically significant only in the younger age group (< 40Yrs). A study investigating choroidal blood flow in men and women also found significant differences. While age had no effect on choroidal blood flow in men, choroidal blood flow was significantly higher in women younger than 40 years compared to women older than 55 years. Although little data is available, oestrogen, progesterone and testosterone are most likely important regulators of blood flow in the retina and choroid, because they are key regulators of vascular tone in other organs. Oestrogen seems to play a protective role since it decreases vascular resistance in large ocular vessels. Some studies indicate that hormone therapy is beneficial for ocular vascular disease in post-menopausal women.

Lee in his landmark study on 6828 healthy Korean population concluded that mean IOP was significantly higher in males when compared with females (25). They also concluded IOP was increased significantly with increasing SBP, DBP and BMI.

CONCLUSION

The present study provides information on the relationship of TLCPD with CSFP and OPP, which are higher in obese individuals. Further prospective studies have to be carried out to investigate these parameters in glaucoma patients to understand if fluctuations in CSFP, OPP and TLCPD can contribute to the disease process. Estimated CSFP and TLCPD may play a significant role in pathogenesis of glaucoma, which may be deemed a misbalance between IOP, CSFP and blood pressure.

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