Dynamics of Compliance in Glaucoma Progression a Cross-Sectional Study Comparing Intraocular Pressure/IOP/ and Central Corneal Thickness/CCT/ Devices Followed by a Longitudinal Intraocular Pressure/IOP/ and Cup-to-Disc Ratio Analysis

Abstract
Glaucoma is a group of conditions defined by a progressive optic neuropathy associated with visual field changes. Higher intra-ocular pressure is classified as a main risk factor. The most important role in the diagnosis, monitoring, and treatment of glaucoma is the accurate measurement of intraocular pressure. Currently, Goldmann applanation tonometry is the gold standard for the evaluation of intraocular pressure. The concept of cup to disc ratio /CDR/ was developed by Armaly in 1967 as a standardized way of documenting disc appearance in order to address glaucoma progression. Unlike intraocular pressure, cup to disk ratio does not fluctuate from day to day and it has the potential therefore to be the most useful indicator of the long-term observation of the disease. However, patient compliance and the progression in visual field loss may be correlated.

Purpose
An observational study by a single investigator was conducted to evaluate the glaucoma progression during adequate therapy and excellent patient compliance. A quantitative analysis was conducted to establish the accuracy and correlation between two widely used ultrasound and non-contact central corneal thickness devices. A qualitative analysis was performed to determine the fluctuations of intraocular pressure and glaucoma excavation over a period of 25 weeks.

Methods
During the first part of the study - the quantitative analysis, a cross-sectional study was performed. Each patient had their central corneal thickness measured using Ocuscan RxP Ophthalmic Ultrasound System and intraocular pressure using Goldman Applanation Tonometer, and then compared to intraocular pressure and central corneal thickness /CCT/ measured with Nidek NT-530P Combination Non-contact Tonometer, Non-contact Pachimeter. The second part of the study - the qualitative analysis, includes a longitudinal intraocular pressure and cup-to-disc ratio analysis. At the baseline: intraocular pressure was measured by Goldmann application tonometry and cup-to-disc ratio was examined by stereoscopic indirect ophthalmoscopy with high plus 78D condensing lens. At the follow-up: intraocular pressure was measured using Goldmann application tonometry (after 12 and 25 weeks) and cup-to-disc ratio was examined after 25 weeks in a similar manner. A two-tailed t-test and Pearson’s correlation were performed for statistical analysis. All participants in this study were asked to complete a questionnaire regarding the relevant side effects of the prescribed eye drops, such as Hyperemia, Foreign body sensation, Dry eye, etc. A daily drop reminder was also circulated along with the questionnaire in order to further improve patient compliance (Figure 1-3).

Figure 1: Here are some pictures of the applied equipment: Goldmann applanation tonometer.
Participants

I. 70 eyes from 35 patients were examined
II. Among them, there were 7 men and 28 women
III. whose age ranged from 51 to 85, and the mean age was 65.9
IV. Prior to this investigation, all participants were clinically diagnosed to have glaucomatous eyes (POAG) (Table 1&2).

Table 1: Symptom list.

| Symptom         | Right | Left |
|-----------------|-------|------|
| Red eye         |       |      |
| Stare eye       |       |      |
| Itching         |       |      |
| Burning         |       |      |
| Watering        |       |      |
| Pressure of vision |     |      |
| Dizzyness       |       |      |
| Anorexia of breath |     |      |
| Nausea          |       |      |
| Mood change     |       |      |
| Other           |       |      |

Table 2: Medication list.

| Medication | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| L          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Please record genuinely and honestly each time you take your eye drops / medication.
Mark a tick if you remembered, or a cross if you did not take your medication as prescribed that day.

Day of the month:

Results

At baseline each patient had their intraocular pressure measured by Goldmann applanation tonometry and Nidek tonometer and the mean measurements are Goldmann applanation tonometry: 16.31±3.03 mmHg; Nidek: 15.2±3.74 mmHg. Intraocular pressure values are recalculated in order to account for the central corneal thickness/CCT/ measurements. The calculations reveal the following results:

Goldmann applanation tonometry with central corneal thickness (Ocuscan) 16.65±2.99 mmHg; Nidek intraocular pressure-IOP with central corneal thickness-CCT (NT-530P) 16.23±3.69 mmHg. The correlation plot between central corneal thickness (Ocuscan) and (Nidek) revealed a statistically significant positive correlation (r=0.9; p=0.036). The graph shows that central corneal thickness /CCT/ measurements ranged between approximately 450 and 650 and the mean standard deviation measured with Ocuscan is 539.06±40.35 m and respectively with Nidek is 524.43±40.27 m. The correlation plot between the two devices revealed a statistically significant positive correlation –p=0.036. The plot between Goldmann applanation tonometer and Goldmann applanation tonometry/ central corneal thickness showed a weak correlation (r=0.47; p=0.51).

The intraocular pressure fluctuations measured using Goldmann applanation tonometry and intraocular pressure recalculated in accordance with the central corneal thickness values measured with Ocuscan demonstrated a weak statistical correlation. P=0.51. The next graph illustrates the correlation between Goldmann applanation tonometry and Nidek intraocular pressure measurements. The mean standard deviation of
intraocular pressure values with Goldmann applanation tonometry is 16.31±3.03 mmHg and 15.2±3.74 mmHg using Nidek. No significant correlation between Goldmann applanation tonometry and Nidek intraocular pressure measurements was established (r=0.54; p=0.06). Intraocular pressure measured with Nidek showed a distinct correlation to Nidek intraocular pressure/central corneal thickness values. p=0.1. Intraocular pressure was also measured using Goldmann applanation tonometry /GAT/ on both eyes of each patient at follow up in 12 and 25 weeks (Graph 1-4). I would like to remind you that the mean Goldmann applanation tonometry /GAT/ at baseline was: 16.31±3.03 mmHg.

i. Mean GAT 12 weeks OD: 15.8±1.8 mmHg
ii. Mean GAT 12 weeks OS: 15.9±1.9 mmHg
iii. Mean GAT 25 weeks OD: 15.4±1.8 mmHg
iv. Mean GAT 25 weeks OS: 15.5±2.0 mmHg

As you probably notice, there is a declining trend in intraocular pressure values which confirms excellent patient compliance with the prescribed therapy. Results between Goldmann applanation tonometry 12/25 weeks OD were statistically significant with very high positive correlation (p=0.006; r=0.90). The bar chart on this slide provides Goldmann applanation tonometry measurements for the right eyes at follow-up: after 12 weeks (in blue lines) and 25 weeks (in red lines). The results were statistically significant with extremely high positive correlation p=0.006. The results were identical for the left eyes with extremely high positive correlation (p=0.008). Results between Goldmann applanation tonometry 12/25 weeks OS also were statistically significant and demonstrated very high correlation (p=0.008; r=0.91). In order to evaluate the glaucoma progression, cup to disk ratio /CDR/ was assessed as a functional parameter. Cup to disk ratio was measured at baseline and follow-up after 25 weeks in order for any changes to be observed and to record the respective progress. The bar chart here provides data for the right eyes about c/d ratio at baseline (in blue lines) and after 25 weeks (in red lines).

The result clearly showed extremely high correlation and was statistically significant, p=0.096. The derived data from c/d-baseline OD and c/d-25 weeks OD clearly showed extremely high correlation and were statistically significant (p=0.096; r=0.97). Similar data about c/d ratio at the baseline and after 25 weeks for the left eyes proved extremely high correlation and also were statistically significant, p=0.019.

The radar graph for right eyes further illustrates that the rates at baseline (in blue) and follow up (in red) are crucial to evaluating the patients’ compliance. For those who rate at lower values, the cup to disc ratio is smaller and the visual field is preserved. The results show identical levels for the majority of the patients therefore the damage to the optic nerve hasn’t progressed (Graph 5-10).
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Discussion

The intraocular pressure and central corneal thickness differences between the applied methods suggest that intraocular pressure is highly dependent on corneal parameters. Goldmann applplanation tonometry and Nidek provide clinically different intraocular pressure values, indicating that they should not be used interchangeably. The follow-up intraocular pressure measurements using Goldmann applplanation tonometry showed that there is no statistically significant change over a long period of time which suggests adequate therapy and compliance. Cup-to-disc ratio analysis clearly demonstrates that there is no progression in the appearance of the optic disc which confirms that patients adhere to the prescribed therapy. Enhanced compliance and adequate therapy are the most important prerequisites for visual field loss to be retained and current patients’ sight preserved.

Conclusion

It is crucial that the most appropriate intraocular pressure measuring technique is used during all examinations in order to assess over time the functional changes in the appearance of the optic disc. The accuracy of intraocular pressure data should be taken into account when non-contact devices are used. Central corneal thickness should be an inseverable part of each intraocular pressure measurement.
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