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A Study of Prevalence and Distribution of Elevated Intraocular Pressure and Glaucoma in Individuals with Thyroid Related Orbitopathy

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Abstract

Introduction: Patients with thyroid eye disease may have an elevated intra ocular pressure in primary position or on attempted upgaze, which is related to the restrictive myopathy and / or orbital congestion. Increased intra ocular pressure results from pressure of the in-elastic muscle pulling the eye and is most commonly appreciated on attempted upgaze with a tethered inferior rectus muscle. *Methodology:* This prospective, observational study enrolled 30 consecutive patients, visiting to GRH Ophthalmology OPD with proven diagnosis of thyroid related orbitop. Thyroid related orbitopathy was diagnosed on the basis of clinical history of thyroid dysfunction, eye symptoms and signs. Laboratory investigations – serum T3, T4 and TSH, which confirmed the thyroid status to be hyper, hypo or euthyroid and all patients underwent ultra-sonography and few computed tomography as required. *Results:* The Paired sample test and statistics, revealed a significant increase in intraocular pressure, when the gaze is shifted from primary to up gaze (p-value 0.0001). There was a mean difference of 4.57mm in intraocular pressure from primary to up gaze. *Conclusion:* The incidence of glaucoma was not higher than that in the normal general population, as only two patients had glaucoma.

Keywords: Intraocular Pressure; Glaucoma; Thyroid Related Orbitopathy.

Introduction

The intra ocular pressure variation with ocular movements in endocrine exophthalmos was first reported by Weasley in 1918. In 1901, a case series was published by Brailey & Eyre describing the presence of glaucoma in 5 young women suffering from thyrotoxicosis.

In 1920, Friendenberg postulated, endocrine imbalance as the cause of glaucoma. Magitot (1947) postulated hypothalamic disturbance as the cause. In 1958, Braley noted the increase of IOP in upgaze & decrease in downgaze, which he postulated to be helpful in differentiating thyrotoxic from thyrotropic exophthalmos [1].

In 1964, Rogova postulated an observational study which included a sample size of 105 patients with simple goitre and described that 13% has raised IOP which was in proportion to the degree of hypothyroidism. In 1965, Vasilieva described 53 cases of hyperthyroidism with raised IOP.

In 1965, McLenachan and Dawes reported presence of some thyroid dysfunction in 45 out of 100 cases of open angle glaucoma they observed. They postulated that trabecular obstruction by mucopolysaccharides was the cause of open angle glaucoma.

Howard & English (1965) reported 10% incidence of glaucoma in their case series which consisted of 74 cases of acromegaly. This led them to believe thatpituitary dysfunction as an aetiological factor. Vanni and Vozza postulated the aetiological role of venous obstruction in ocular hypertension.

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In 1967, Cheng and Perkins published an observational study comprising 155 cases of thyroid dysfunction. 17 cases had exophthalmos. 56% of them had 4mm Hg IOP raise in upgaze. 25% had 10 mm Hg raise in upgaze. Only 2 cases had features of glaucoma. They observed that IOP distribution did not differ much from the normal population. Also, the IOP distribution did not differ significantly between hypo and hyperthyroid group [2].

McLenachan and Daves did a comparative study between 100 cases each of open angle glaucoma and narrow angle glaucoma. They described the increased incidence of thyroid dysfunction in open angle glaucoma group.

Cartwright and associates reported 30% prevalence of immune disorders in normal tension glaucoma group in their study. Smith et al reported a case of primary open angle glaucoma which reverted to normal on treatment of hypothyroidism. He also found poor outflow facility using tonometry and tonography [3].

Gillow P Shah did a study on 100 cases of primary open angle glaucoma and did not find any association of thyroid dysfunction and glaucoma [4].

PanagiotisKaradinsas et al did an interventional case series comprising 100 hypothyroid patients. They did not find any correlation between intraocularpressure and thyroid stimulating hormone & tri-iodine thyronine levels. No significant difference was found in intra ocular pressure levels before and after the treatment of hypothyroidism. Thus refuting the association between glaucoma and thyroid dysfunction.

Thus there exists a lot of confusion and controversy regarding the association between thyroid dysfunction and glaucoma.

Methodology

This prospective, observational study enrolled 30 consecutive patients, visiting to GRH Ophthalmology OPD with proven diagnosis of thyroid related orbitop.

Thyroid related orbitopathy was diagnosed on the basis of clinical history of thyroid dysfunction, eye symptoms and signs.

Laboratory investigations – serum T3, T4 and TSH, which confirmed the thyroid status to be hyper, hypo or euthyroid and all patients underwent ultra-sonography and few computed tomography as required.

Definition of Thyroid – Related Orbitopathy

A combination of any of thefollowing eyelid retraction, with lagophthalmos, lid lag, conjunctival injection, chemosis, eyelid swelling, unexplained proptosis or myopathy (enlarged extra ocular muscle) as a sequelae of thyroid gland dysfunction.

Diagnostic Criteria for Thyroid Associated Orbitopathy

Eyelid retraction withor without other clinical signs of inflammation and with or without evidence of thyroid dysfunction (or) proptosis, extra ocular muscle enlargement, orbital congestion or inflammation accompanied by either eyelid retraction with lagophthalmos or evidence of thyroid dysfunction.

Serum T3,T4,TSH levels used to determine the thyroid status and patients who had significant thyroid disease were examined in detail and treated accordingly by endocrinologist.

All patients were examined by two observers one of whom is a senior consultant, who confirmed the diagnosis of thyroid related orbitopathy and other was me; and all patients were personally seen by both of us.

Ocular examination included assessment of best corrected visual acuity (BSVA) for distance by Snellen's chart. Colour vision was evaluated by Ishihara's pseudo isochromatic chart. Afferent papillary function was assessed by pen torch and swinging flash light test of levatin and slit lamp. Central 30 degreefield was charted in each eye with best corrected vision , using Octopus automated perimetry.

Detailed ocular motility was checked with pen torch and graded between – 4 to 0 to +4 based on degree of under action to normal to grades of over action respectively.

Fundus was examined initially by direct ophthalmoscopy and subsequently dilated with tropicamide. Stereo bio-microscopic evaluation was done with 90D condensing lens and slit lamp for assessing optic disc parameters, nerve fibre layer and other abnormalities.

Proptosis evaluation and documentation was done using Hertel'sexophthalmometer. Myopathy was evaluated using motility parameter's as described earlier with additional confirmation by imaging studies. Ultrasonography or computed tomography, to document the characteristic spindle shaped thickening of extra-ocular muscle bellies

with sparing of tendons. The intra ocular pressure was measured first by Goldmannapplanation tonometer and then by Schiotz's indentation tonometer.

Results

There is no influence of thyroid status on the variation of IOP between gazes.

Table 1: Thyroid status and differential intraocular pressure

	Thyroid status	Mean	N	Std. Deviation	Minimum	Maximum
Difference from	Hyperthyroidism	5.02	41	2.90	4.17	5.87
primary to up gaze	Hypothyroidism	3.27	11	1.85	1.45	5.09
(absolute increase)	Euthyroidism	4	8	2.39	1.74	6.26
p: 0.265	Total	4.57	60	2.73	3.87	5.27
Difference from	Hyperthyroidism	2.49	41	1.91	1.92	3.06
primary to down gaze	Hypothyroidisim	1.82	11	1.40	0.61	3.03
(absolute decrease)	Euthyroidism	1.5	8	1.41	-0.01	3.01
p: 0.441	Total	2.23	60	1.84	1.76	2.70

Table 2: Proptosis and Differential Intraocular Pressure

	Proptosis	Mean	N	Std. Deviation	Minimum	Maximum
Difference from prime	Present	5.38	48	2.41	4.66	6.10
to up increase) p<0.0001	Absent	1.33	12	0.99	- 0.25	2.91
	Total	4.57	60	2.73	3.93	5.21
Difference from prime	Present	2.38	48	1.92	1.85	2.91
To down (absolute	Absent	1.67	12	1.44	0.50	2.84
decrease) p: 0.49	Total	2.23	60	1.84	1.75	2.71

Proptosis has a significant influence on the variation of IOP between primary to up gazes.

Table 3: Elevation and Differential Intraocular Pressure

	Elevation	Mean	N	Std. Deviation	Minimum	Maximum
Difference from primary	Normal	3.4	40	1.77	2.67	4.19
to up gaze P<0.0001	Abnormal	6.9	20	2.86	5.75	8.06
	Total	4.57	60	2.73	3.93	5.21
Difference from primary	Normal	1.95	40	1.54	1.34	2.54
to down gaze. P:0.24	Abnormal	2.8	20	2.29	1.94	3.66
	Total	2.23	60	1.84	1.76	3.70

There is significant influence of elevation status on the variation of intraocular pressure between gazes. This is of lesser significance in down to primary gaze.

Table 4: Depression and Differential Intraocular Pressure

	Depression	Mean	N	Std. Deviation	Minimum	Maximum
Difference from primary	Normal	4.61	56	2.81	3.87	5.35
to up gaze. P:0.91	Abnormal	4	4	1.63	- 0.37	8.37
	Total	4.57	60	2.73	3.86	5.28
Difference from primary	Normal	2.25	56	1.87	1.76	2.74
to down gaze. P:0.97	Abnormal	2	4	0.63	-0.92	4.92
	Total	2.23	60	1.84	1.76	2.70

Table 5: Ultrasonography and Differential Intraocular Pressure

	USG	Mean	N	Std. Deviation	Minimum	Maximum
Difference from primary	Normal	3.55	44	1.77	2.80	4.30
to up gaze. P<0.0001	Abnormal	7.38	16	2.99	6.07	8.69
	Total	4.57	60	2.73	3.93	5.21
Difference from down	Normal	1.91	44	1.49	1.36	2.46
To primary gaze. P:0.07	Abnormal	3.13	16	2.42	2.17	4.09
	Total	2.23	60	1.84	1.76	2.70

Table 6: Ocular Hypertension (OHT)status between gaze shifts

	OHT status in primary gaze		OHT status in UP gaze		OHT status in down gaze	
	Count	%	Count	%	Count	%
No	55	91.67	28	46.67	57	95
OHT	5	8.33	32	53.33	3	5
Total	60	100	60	100	60	100

Table 7: OHT status in primary gaze (Up)

		OHT	Normal	Total
OHT	OHT	3	29	32
status in	Normal	2	26	28
up gaze	Total	5	55	60

Proportions of OHT
Upgaze 32/60 = 0.533
Primary gaze 5/60 = 0.083
P <0.0001
There is significant shift from normal to OHT, when there is a shift of gaze from primary to up gaze.

Table 8: OHT status in primary gaze (down)

		OHT	Normal	Total
OHT	OHT	0	3	3
Status in down gaze	Normal	5	52	57
	Total	5	55	60

Proportions:
Down gaze 3/60 = 0.05
Primary gaze 5/60 = 0.083
P: 0.727

There is no significant change normal to OHT when there is shift of gaze from primary to down gaze. In fact eyes became normal when the gaze is shifted downwards.

Discussion

7 eyes (11.66%)had rise of intraocular pressure >6mm of mercury, while 14 eyes (23.33%) had rise in intraocular pressure between 4mm and 6mm of mercury and (65%) i.e., 39 eyes had a variation between 0mm and 4mm of mercury.

It is believed widely that a greater than 6mm of mercury rise is significant, while some consider a rise of greater than 4mm to be significant.

The Paired sample test and statistics , revealed a significant increase in intraocular pressure, when the gaze is shifted from primary to up gaze (p-value 0.0001). There was a mean difference of 4.57mm in intraocular pressure from primary to up gaze. Which correlates with study by Khurana AK, which observed a significant increase of IOP on upgaze in 53% and 87% of cases with early and late GO, respectively. The positional IOP changes may have significant role to play under circumstances like; in diagnosis of early GO when either eye has no exophthalmos, establishing bilateral involvement in patients with unilateral exophthalmos and monitoring the progression or response to therapy [5].

Down gaze to primary gaze 3 eyes had a rise in intraocular pressure greater than 6mm of mercury and in two eye the rise was between 4mm and 6mm of mercury. Remaining 55 patients had intraocular pressure difference between 0mm and 4mm ofmercury.

Paired sample test and statistics, revealed no significant increase in intraocular pressure, when gaze is shifted from down to up gaze. P = 0.06, mean elevation was only 2.23, which is not clinically significant.

Thyroid Status and Its Influence on Intraocular Pressure

There is no influence of thyroid status (hyperthyroid, hypothyroid or euthyroid) on differential intraocular pressure as evidenced below. This correlates with the study done by Khurana which concludes that, there is no correlation between positional IOP changes and biochemical thyroid status of patients [5].

- Hyperthyroid patients, showed a mean rise of 5.02mm and 2.49 for primary to up and down gaze

to primary gaze respectively.

- The hypothyroid group, revealed a 3.27mm and 1.82mm mean rise respectively for gaze variation.
- The euthyroidgroup, reveals a 4mm and 1.5mm variation respectively. However these are not statistically significant with the p-value:0.265 and p-value :0.441 respectively.

Proptosis and its Influence on Intraocular Pressure

A significant influence of proptosis on the differential intraocular pressure was noted.

- The variation is high (mean 5.38±2.41mm) among those with proptosis, from primary to up gaze.
- Difference from primary to up gaze, was only 1.33mm in those without proptosis which is statistically significant (p-value<0.0001), whereas the difference from down to primary gaze was 2.38mm and 1.67mm in those with and without proptosis respectively, which is statistically not significant with p-value: 0.49

Elevation Restriction Versus Differential Intraocular Pressure

We found significant influence of elevation restriction, on variation of intraocular pressure between gazes. There was a 6.9±2.86mm increase in intraocular pressure in eyes with restricted elevation as compared to a 3.4±1.77mm in eyes with no restriction of elevation.

- We also found that restricted depression does not influence significantly intraocular pressure changes between gazes.

Ultrasonography

There was a significant influence of muscle thickening as determined by ultrasonography on intraocular pressure variation with different gazes. The thickened group by imaging showed an elevation in intraocular pressure of 7.38 mm of mercury, as compared to the 3.55mm of mercury in normal group, on shifting from primary to up gaze and 3.13mm of mercury and 1.91mm of mercury, respectively from down to primary gaze. which correlates with study by Khurana AK which states ultrasonography is useful in diagnosing early cases without manifest clinical proptosis and in picking up bilateral changes in apparently unilateral cases is unequivocal [5].

Ocular Hypertension Status between Gaze Shifts

Only 8.33% patients were ocular hypertensives in primary gaze. This number increased to 53.33% on up gaze. McNemar's chi square test test (p-value<0.0001) revealed a significant shift from normal to ocular hypertensive status, when there is shift from primary to up gaze.

However no significant change in ocular hypertensive status was found on shifting gaze from down to primary. This correlates with the study done by Peele Cockerhan K which inferred the increased prevalence of ocular hypertension in thyroid related orbitopathy [6].

Conclusion

- The measurement of intraocular pressure on up gaze, does serve as an index of muscle restriction and it correlates well with the muscle involvement as evidenced by imaging.
- We found no correlation between the systemic thyroid status (hyperthyroid, hypothyroid and euthyroid) and the ocular hypertension or intraocular pressure variation.

References

1. Braley AE. Malignant exophthalmos. Am J Ophthalmol 1958;36:1286-90.
2. Cheng H, Perkins, ES. Thyroid disease and glaucoma. Br J Ophthalmol 1967;51:547-53.
3. Cartwright MJ, Grajewski AJ, Fridelberg ML, Anderson DR, Richards DW. Immune-related disease and normal-tension glaucoma. Am J Ophthalmol 1992;110:500-2.
4. Gillow JT, Shah P.O, Neill EC. Primary open-angle glaucoma and hypothyroidism: chance or true association? Eye. 1997;11(pt 1):113-4.
5. Khurana AK, Sunder S, Ahluwalia BK, Malhotra KC, Gupta S. A clinico-investigative profile in Graves' ophthalmopathy. Indian J Ophthalmol 1992;40:56-8.
6. Peele Cockerham K. Pal C, Jani B, et al. The Prevelance and implication of ocular hypertension and glaucoma in thyroid – associated oorbitopathy. Ophthalmology 1997;104:914-7.