Original Article

Burden of acute attack of angle closure on corneal endothelium-a study from Eastern India

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Abstract

Background: To compare the endothelial cell count among eyes with acute attack of angle closure and unaffected fellow eyes. **Materials and methods:** Prospective, Institutional, comparative and interventional trial. Specular microscopy, intraocular pressure and best corrected vision were tested in a total cohort of 60 eyes (30 with acute attack and 30 unaffected fellow eyes as control).Duration of attack was noted in each case. After the corneal oedema subsides, Nd-YAG iridotomy was performed by a single surgeon in both the groups.IOP and specular microscopy was done in both the groups one and three months after iridotomy. Results were documented and compared. **Result:** The mean age of patients with acute attack of primary angle closure glaucoma was 67.2+/-7.44 years and females outnumbered the males. The mean duration of disease was 75.8+/-95.43 hours (range: 3+/-4 days, r=+0.80). The average cell count of affected eyes with duration of attack greater than 72 hours was 1185.625 cells/mm^2 and the average cell count of affected eyes with duration of attack less than 72 hours was 2411.273 cells/mm^2. The affected eyes with visual acuity less than 6/60 had mean endothelial cell count of 1533.71+/-893.66 cells/mm^2 and the eyes with visual acuity greater than 6/60 had mean endothelial cell count of 2252±556.10 cells/mm^2 ($p>0.05$). The mean endothelial cell count in affected eyes before YAG PI was 2084.20±613.13 cells/mm^2 and 1month after YAG PI it was 1719.63±613.13 cells/mm^2 ($p< 0.05$). The mean endothelial cell count 3 months after YAG PI was 1694.22±449.48 cells / mm^2 ($p >0.1$). The mean endothelial cell count of control eyes before YAG PI was 2394±359.27 cells/mm^2 and the mean endothelial cell count 1 month after YAG PI was 2185±348.60 ($p< 0.05$) and the mean endothelial cell count 3 months after YAG PI was 1694.22±449.48 cells / mm^2 ($p >0.1$). **Conclusion:** A linear positive correlation exists between duration of attack and loss of endothelial cells. The cell loss mainly takes place if duration of attack lasts more than 72 hours. Both acute attack of angle closure and Nd YAG iridotomy cause depletion of endothelial cells at statistically significant level.

Several factors influence the effects of a raised IOP on the anterior segment tissues. Following acute attack of angle closure glaucoma the bio-chemical abnormalities that accompany reflex ischemia, acidosis or reflex vasodilatation with plasma leakage, may cause serious and often irreparable damage to cells exposed to these insults. The resistance of the tissues to these insults also depends on the viability of the cellular constituents and their innate capacity for repair. The corneal endothelium is the principal target for their harmful mechanisms. Corneal oedema is a common clinical manifestation of the raised IOP. With this background this study was undertaken to evaluate the effect of acute attack of angle closure in an Eastern Indian cohort.

Material and methods

Total sixty eyes (30 eyes with primary angle closure glaucoma with acute attack and 30 fellow eyes as control) who presented to our Institute between March 2007 to August 2009 were recruited for the study. Patients having corneal pathology, history of ocular trauma, active surface and intraocular inflammation, past history of intraocular surgery, contact lens use were excluded from the study. Patients suffering from diabetes mellitus, chronic renal failure, high myopia (>6D), history of past attack of angle closure, use of any form of steroid therapy, use of tricyclic anti Depressants and anti Parkinsonian drugs were excluded at the outset.

On recruitment each of the patients underwent routine ocular evaluation including recording of best corrected visual acuity and slit lamp bio microscopy of both the eyes. IOP was measured in the control eyes by applanation technique. Angle of anterior chamber was measured in the fellow eye by Goldman three mirror gonio lens and

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was graded according to Schffares' grading. Specular microscopy of the fellow eye was performed using SP-2000P specular microscope (Topcon, Japan). Fundus examination of both the eyes was done by direct ophthalmoscope through undilated pupil.

After admission each patient received intra-venous Mannitol, oral acetazolamide and topical pilocarpine therapy in both eyes. Specular microscopy, Gonioscopy and IOP measurement of the affected eye were performed as soon as corneal edema disappeared.All the patients undergone Nd:YAG laser iridotomy after corneal edema disappeared in the affected and in the fellow eye in the superonasal quadrant using energy level in the range of 5-15 mj , pulse duration around 12 nanoseconds with 1-3 pulses per burst. Written Informed consent was taken at recruitment level and prior to laser therapy separately. Laser therapy was performed by a single surgeon (TR). Permission from Institutional ethical committee was obtained before recruitment of first patient. All the patients were re-examined next day after laser iridotomy and also one month and three months after iridotomy using previous parameters. Specular microscopy done on one month and three months visit only.

Results

The mean age of patients with acute attack of primary angle closure glaucoma was 67.2±7.44 years and number of females with acute attack of primary angle closure glaucoma was higher than males (Table 1).

Table 1:- Age and sex distribution of the patients of primary angle closure glaucoma with acute attack.

Age groups (years)	Male	Female	Total
50-55	1	0	1
56-60	1	4	5
61-65	2	6	8
66-70	2	2	4
71-75	3	4	7
76-80	2	2	4
81-85	0	1	1
Total	11	19	30

Table 2:- Affected eye endothelial cell count and duration of disease.

Affected eye cell count(cells/mm^2)	Duration of disease (hours)
585	96
2145	24
2766	24
2794	12
2565	24
2525	48
830	360
2645	12
2380	24
2298	14
2715	12
2448	36
2162	10
2143	24
2622	36
689	288
1366	192
2484	192
1981	48
2110	24
2016	36
2416	24
2827	48
2766	48
1827	24
682	72
833	312
2016	168
2792	18
2105	24

The mean duration of disease was 75.8±95.43 hours (range: 3+/-4 days).Regression analysis was done to find out any relationship between the duration of attack and difference in the endothelial cell count between the affected and control eyes. The r value was +0.80; showing a linear

positive correlation between duration of attack and loss of endothelial cells. It means that if duration of attack increases, endothelial cell loss increases. The average cell count of affected eyes with duration of attack greater than 72 hours was 1185.625 cells/mm^2 and the average cell count of affected eyes with duration of attack less than 72 hours was 2411.273 cells/mm^2. It means that cell loss mainly took place if duration of attack lasts more than 72 hours (Table 2).

The affected eyes with visual acuity less than 6/60 had mean endothelial cell count of 1533.71±893.66 cells/mm^2 and the eyes with visual acuity greater than 6/60 had mean endothelial cell count of 2252±556.10 cells/mm^2.

Statistical test did not found any significant difference between these two groups (p>0.05).It means that visual acuity has no relation with endothelial cell count (Table 3).

The mean endothelial cell count in affected eyes before YAG PI was 2084.20±613.13 cells/mm^2 and 1month after YAG PI it was 1719.63±613.13 cells/mm^2. To compare the cell count before YAG PI and 1 month after YAG PI in the affected eye, Student 't' test was applied and found significant(p< 0.05).It means that the cell count is significantly lower 1 month after YAG PI in affected eyes. The mean endothelial cell count 3 months after YAG PI was 1694.22±449.48 cells / mm^2. Cell count 1 month and 3 months after YAG PI was compared and found that there was no statistically significant difference between these two groups (p >0.1). It means that the cell count did not differ significantly 3 months after YAG PI compared with the cell count 1 month after YAG PI in affected eyes (Table 4).

The mean endothelial cell count of control eyes before YAG PI was 2394±359.27 cells/mm^2 and the mean endothelial cell count 1 month after YAG PI was 2185±348.60. Students' t test was applied to compare the endothelial cell count of these two groups and found statistically significant (p< 0.05). The mean endothelial cell count 3 months after YAG PI in control eyes was 2081±364.26 cells/mm^2. Students't test was used to compare the cell count 1 month after YAG PI with 3 months after YAG PI and found that there was no significant difference in between these two groups (p> 0.1).It means that the cell count 1month and 3 months after YAG PI did not differ significantly (Table 5).

Most of the patients showed improvement of visual acuity 1month after YAG PI in the affected eyes. Patients with presenting visual acuity counting finger close to face or less, did not show any improvement. Around 30% patients showed further improvement in visual acuity at 3 months after YAG PI in affected eyes and around 3.33% patients showed deterioration (Table 6).

Table 3:- Endothelial cell count and visual acuity of both affected and control eyes.

Endothelial Cell Count(cells/Mm^2)		Best Corrected Vusual Acuity	
Affected	Fellow	Affected	Fellow
585	1576	1/60	6/36
2145	2234	6/60	6/12
2766	2790	6/60	6/6
2794	2765	6/24	6/9p
2565	2665	6/18	6/6
2525	2569	6/60	6/6p
830	2170	FC 4ft,PRacc	6/12
2645	2697	6/18	6/6
2380	2415	6/18	6/6
2298	2326	6/24p	6/9
2715	2742	6/24	6/6
2448	2330	6/36p	6/6
2162	2224	6/18	6/9
2143	2236	6/24	6/12
2622	2668	6/36	6/9
689	1906	NO PL	6/24
1366	2567	FCCF,PRacc	6/6
2484	2892	FCCF, PRacc	6/12
1981	2187	6/60	6/18
2110	2262	6/24	6/12
2016	2120	6/36	6/6
2416	2531	6/18	6/9
2827	2916	6/60	6/12
2766	2889	5/60	6/9
1827	1919	6/36	6/6
682	1678	6/60	6/9
833	2155	6/60	6/12
2016	2368	FC 4ft,PRacc	6/18
2792	2856	6/24	6/6
2105	2167	6/36	6/9

Table 4:- Endothelial cell count in the affected eye before YAG PI,1month after PI and 3 months after PI.

Endothelial cell count in affected eyes (cells/mm²)		
Before YAG PI	1month after PI	3months after PI
578	480	424
2145	1823	1603
2766	2145	2076
2794	2215	2013
2565	2100	1867
2525	2122	2121
830	565	Not came for follow up
2645	2213	2056
2380	2100	1892
2298	1900	1722
2715	2109	1903
2448	2003	2001
2162	1800	1572
2143	1813	1768
2622	2119	1879
689	456	Trabeculectomy
1366	1000	975
2484	2100	1907
1981	1654	1603
2110	1812	1581
2016	1755	1445
2416	2102	1862
2827	2412	2200
2766	2400	2116
1827	1589	1444
682	437	Trabeculectomy
833	513	500
2016	1730	1546
2792	2310	2109
2105	1812	1559

Table 5:- Endothelial cell count of control eyes before YAG PI, 1month after PI and 3 months after PI.

Endothelial cell count in control eyes(cells/mm²)		
Before YAG PI	1month after PI	3months after PI
1576	1366	1355
2234	2022	2003
2790	2456	2421
2765	2534	2512
2665	2444	2324
2569	2377	2008
2170	2008	Not came for follow up
2697	2545	2504
2415	2210	2100
2326	2117	2110
2742	2532	2265
2330	2125	1985
2224	2109	2004
2236	2112	2326
2668	2448	2397
1906	1707	1654
2567	2338	2226
2892	2715	2688
2187	1988	1870
2262	2046	1816
2120	1833	1686
2531	2322	2212
2916	2700	2553
2889	2667	2579
1919	1607	1430
1678	1553	1503
2155	1939	1744
2368	2166	2022
2856	2633	2366
2167	1956	1706

Table 6:-Visual acuity of patients affected and non affected control eyes on presentation, 1 month after YAG PI and 3 months after YAG PI.

Best Corrected Visual Acuity					
Affected Eyes			Control Eyes		
On presentation	1 month after PI	3 months after PI	On presentation	1 month after PI	3 months after PI
1/60	3/60	5/60	6/36	6/36	6/36
6/60	6/36p	6/36	6/12	6/12	6/12
6/60	6/36p	6/36p	6/6	6/6	6/6
6/24	6/9	6/9p	6/9p	6/9p	6/9p
6/18	6/9p	6/9p	6/6	6/6	6/6
6/60	6/24	6/18	6/6p	6/6	6/6
FC 4 ft,PRacc	FC 5ft,PRacc	Not attended	6/12	6/12	Not attended
6/18	6/9p	6/9	6/6	6/6	6/6
6/18	6/9	6/9	6/6	6/6	6/6
6/24p	6/9	6/9	6/9	6/9	6/9
6/24	6/6p	6/6p	6/6	6/6	6/6
6/36p	6/18p	6/12	6/6	6/6	6/6
6/18	6/9	6/9	6/9	6/9	6/9
6/24	6/12p	6/12p	6/12	6/12	6/12
6/36	6/18	6/12	6/9	6/9	6/9
NO PL	NO PL	NO PL (Trab)	6/24	6/24	6/24
FCCF,PRacc	FCCF,PRacc	FCCF,PRacc	6/6	6/6	6/6
FCCF,PRacc	FCCF,PRacc	FCCF ,PRacc	6/12	6/12	6/12
6/60	6/36	6/36	6/18	6/18	6/18
6/24	6/12p	6/12p	6/12	6/12	6/12
6/36	6/18	6/12p	6/6	6/6	6/6
6/18	6/9	6/9	6/9	6/9	6/9
6/60	6/36	6/24	6/12	6/12	6/12
5/60	6/36p	6/36	6/9	6/9	6/9
6/36	6/18p	6/18p	6/6	6/6	6/6
6/60	6/24	6/36 after Trab	6/9	6/9	6/9
6/60	6/60	6/60	6/12	6/12	6/12
FC 4 ft,PRacc	FC 5 ft,PRacc	FC 6ft,PRacc	6/18	6/18	6/18
6/24	6/12	6/9	6/6	6/6	6/6
6/36	6/18	6/9p	6/9	6/9	6/9

Discussion

Several factors influenced the effects of a raised IOP on the anterior segment tissues, the most important of which are the duration, as well as the rate and magnitude of the increase in IOP. The gradual increase in IOP occurring in

POAG more easily permits reflex vasomotor adjustments than the rapid and extreme ocular hypertension associated with PACG. In the later situation, the bio-chemical abnormalities that accompany reflex ischemia and acidosis, or reflex vasodilatation and plasma leakage, may cause serious and often irreparable damage to cells exposed to these unfavourable environment.[1] The resistance of the tissues to these insults also depend on the viability of the cellular constituents and their innate capacity for repair. The corneal endothelium is a principal target for their harmful mechanism. Corneal oedema is a common clinical manifestation of the raised IOP, although there is a marked variation in individual response to a given pressure level. Hence, it presumed that the functional integrity of the corneal endothelium is better preserved in some individual than in others.

Our study found reduction of endothelial count following acute attack of ACG.This had been supported in the following studies. Zarnowski et al[2] examined 159 patients (233 eyes) with glaucoma in medical university of Lubin in between 2000-2004. They found a significant reduction in PACG (2136±620/ mm^2). Kee CW et al[3] studied that as compared to the normal eyes the glaucomatous eyes (POAG and PACG) and ocular hypertensive eyes showed a statistically significant decrease of central corneal endothelial cell density ($p< 0.005$) and there was a reverse correlation between the IOPs and endothelial cell counts. Setala K et al[4] examined 25 patients with unilateral acute glaucoma. Specular microscopy was performed as soon as (average 6-12 hours) the IOP had been lowered and cornea had become clear. He showed that high IOP lasting 3 days or more lowered the central endothelial cell density. The average endothelial cell count in the affected eye was 2161+/-633 cells /mm^2 and in the fellow eye it was 2392±346 cells / mm^2 . The mean difference was 9.7%. The mean IOP in the affected eye was 65.3 mmHg. He found no correlation between the level of IOP and the difference in endothelial cell density. In his study, endothelial cell loss did not correlate to visual acuity. He reported an average of 5% corneal endothelial cell loss after surgical iridectomy. Oslen T et al[5] studied endothelial cell count of 23 patients. He compared the eyes with acute attack with fellow eyes and found that the endothelium of the affected side showed a mean difference in cell density of 23.1% , range (4.82-68%, $p<0.001$) ; but in his study, he did not mention the length of glaucoma attack. Francis Bigar et al[6] examined 20 patients with acute attack of angle closure glaucoma by specular microscopy. The mean endothelial cell density in the affected eye was 1534 and in the fellow eye 2243 cells / mm^2 (mean decrease 33% , $p=0.002$) .The amount of cell loss correlates with the duration of the IOP rise. The mean increase in IOP at admission was 55 (32-70) mmHg. The pressure was normalized within an average of 47 hours (5-192) . The mean cornea cleared up within 4.8 days (range 2-12 days) sufficiently so that specular microscopy could be performed before any surgery. All corneas had a normal thickness after attack. Tham CC et al[7] in an animal model also showed that the duration of elevated IOP was the most important factor affecting the endothelial cell count. Sihota R et al[8] in a prospective study showed that angle closure glaucoma constituted 45.9% of all primary adult glaucomas and 24.8% of these had acute angle closure glaucoma. They found that the mean endothelial cell count in eyes with acute PACG is 1597±653 cells /mm^2 and the mean endothelial cell count in fellow eye is 2388±266 cells /mm^2 . The acute PACG patients had significantly lower endothelial cell count. De Cavallos E et al[9]compared 44 eyes with acute attack of angle closure glaucoma with 174 control eyes and concluded that endothelial cell count is statistically lower in the affected eye.

Our study found statistically significant reduction in cell count both in the affected and control eyes one month post YAG-PI.Though the cell count does not differ significantly 3 months after YAG PI as compared to one month post YAG PI in the affected and control eyes. Gagnon M M et al [10]performed a prospective study to examine the long term effect of Nd:YAG laser iridotomy on the corneal endothelium . 31 eyes of 21 patients underwent complete follower for 1 year. Patients with narrow and occludable angles or fellow eye of acute angle closure glaucoma attack were treated with Nd: YAG laser iridotomy. Endothelial cell count performed before iridotomy and also 1, 3, 6 and 12 months after iridotomy. They found statistically significant decrease in endothelial cell count at 1($p=0.036$) , 6 ($p=0.004$) , 12($p=0.000$) months; but the decrease was not statistically significant at 3 months ($p=0.467$) .

Loss of corneal endothelial cells was reported in association with various types of glaucomas including POAG. Our study also concluded that a linear positive correlation exists between duration of attack and loss of endothelial cells. The mean loss of endothelial cell count was significant both in affected as well as control eyes one month post YAG PI. This probably reflects indirect insult of ongoing intraocular inflammation on the vital layer of cornea.

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