Long-term Surgical Outcome of Eleven Patients with Glaucoma Secondary to the Iridocorneal Endothelial Syndrome

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Abstract

**Purpose:** To report the long-term outcome of patients with iridocorneal endothelial syndrome (ICE) who required surgery for glaucoma.

**Materials & Methods:** This retrospective, noncomparative case series was conducted on 11 patients with ICE who underwent surgery to control their glaucoma between 1992 and 2004 in Farabi Eye Hospital. The first surgery was trabeculectomy with Mitomycin C except in one patient in whom Mitomycin C was not used. If intraocular pressure was not controlled, redo trabeculectomy and alternative procedures such as Molteno tube implantation, bleb revision, and cyclodestructive procedures were performed.

**Results:** Nine patients were female and two were males. The mean age of the patients was 39.4±11.2 years and they were followed for a median of 22 months (minimum: 6, maximum: 146 months). The first surgery in all patients was trabeculectomy with adjunctive Mitomycin C except in one for whom trabeculectomy was carried out without Mitomycin C. Seven (63.7%) patients had intraocular pressure less than 21 mm Hg; only one of them was on topical medications. Four (36.4%) of the patients had intraocular pressure less than 21 mm Hg after the first surgery at the last follow up. The IOP was controlled in one patient after the second trabeculectomy and in two other cases it was controlled following other procedures such as bleb revision and cyclodestructive procedures (following the second trabeculectomy). The surgical intervention failed in four patients; two of them had intraocular pressure>21 mm Hg after the first surgery and the other two developed no light perception vision despite Molteno tube implantation. Seven (63.7%) of the patients had visual acuity of ≥20/200 at the last visit. In one patient due to corneal decompensation penetrating keratoplasty was done.

**Conclusion:** Glaucoma associated with ICE syndrome can be managed successfully surgically in the majority of cases, however multiple procedures are often needed.

**Key words:** Glaucoma, Iridocorneal endothelial syndrome, Molteno tube, Trabeculectomy.


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Introduction
Iridocorneal endothelial (ICE) syndrome is a spectrum of ocular disease (essential iris atrophy, Chandler syndrome, and Cogan-Reese syndrome) characterized by corneal endothelial abnormalities, unilateral glaucoma, and iris stromal abnormalities.\(^1,2\) This disorder is usually diagnosed in early adulthood and is more common in females than in males.\(^3\) The spectrum of this syndrome includes the following features to a variable degree: unilaterality, iris stromal abnormalities, abnormal corneal endothelium with proliferation and secondary glaucoma caused by formation of membranes composed of endothelial-like cells and a Descemet's-like structure, as well as closure of the angle by broad-based peripheral anterior synechiae.\(^4\)

The etiology of this syndrome is unknown although some studies implicated the possible role of viruses in the pathogenesis.\(^1,5,6\) The rate of glaucoma associated with ICE syndrome has been reported to range from 46\% to 82\%.\(^7-10\) The natural history of the disease is progressive and there is no known means of arresting its progression.\(^4\) The glaucoma associated with ICE syndrome often is difficult to treat.\(^7,9,11\) Medical therapy is usually limited to aqueous suppressants and often becomes ineffective.\(^7,11-13\) Laser trabeculoplasty is ineffective.\(^3,14\) The success rate of filtering surgery is also believed to be lower than that with most other forms of glaucoma.\(^7,10,11\) A few studies of secondary glaucoma in ICE patients have looked at the outcomes since the introduction of antifibrotic agents and glaucoma drainage implant (GDI) surgery\(^{4,14,15}\), The purpose of the current study was to report the long term outcome of patients who underwent surgery for glaucoma secondary to the ICE syndrome.

Materials and Methods
We retrospectively reviewed the medical records of 11 consecutive patients who underwent glaucoma surgeries at the glaucoma service of the Farabi Eye Hospital (Tehran, Iran) between 1992 and 2004 due to the uncontrolled glaucoma secondary to ICE syndrome.

The subtype of ICE was determined by the examining physician. Patients with a diagnosis of ICE and iris holes were categorized as essential iris atrophy, Figure 1, those with iris nodule were categorized as cogan-Reese syndrome, and those without iris findings but corneal changes typical of ICE syndrome were categorized as Chandler syndrome.

![Ocular findings in a patient with essential iris atrophy](image)

Surgery was indicated when the level of intraocular pressure (IOP) was considered too high on maximal medical therapy. All of the surgeries were performed by one of the authors (H.A) or under his direct supervision. The first surgery in all of the patients was trabeculectomy and if IOP was not controlled the second trabeculectomy also was done. After the second trabeculectomy if IOP was not controlled bleb revision, Molteno tube implantation or cyclodestructive procedures (Diode laser cyclophotocoagulation and cyclocryotherapy) were performed.

Trabeculectomy operation was performed by both fornix-based and limbus-based methods. Mitomycin C (MMC) was used with 2-4 mg/ml concentration for 2-4 minutes. Molteno tube implantation was performed as described elsewhere.\(^16\)

Success was defined as an IOP of 21 mm Hg or lower, with or without glaucoma medications, at the last follow up visit. Failure was defined as IOP more than 21 mm Hg with medications, loss of vision to no light perception (NLP), or phthisis bulbi.

Results
The clinical characteristics, surgeries, and clinical course of 11 patients of ICE syndrome with glaucoma are summarized in Table 1. Nine patients were females and two were males. The mean age, mean preoperative IOP, and mean number of preoperative glaucoma medications were 39.4±11.2 years, 32.5±3.9 mm Hg, and 2.8±1.4 medications, respectively.
Base line visual acuity ranged from 20/25 to HM. All eyes were phakic. Median follow-up of the patients after surgical intervention was 22 months (minimum: 6; maximum: 146 months).

A correct diagnosis of the ICE syndrome was made at presentation in 73% (8) of the patients. The initial and the final diagnosis are shown in Table 2.

### Table 1. Demographic data, clinical course and surgeries of 11 patients with iridocorneal endothelial syndrome

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Preoperative IOP</th>
<th>Final IOP</th>
<th>Preoperative drugs</th>
<th>Postoperative drugs</th>
<th>Surgeries after first trabeculectomy with Mitomycin C (Mon)</th>
<th>Total length of follow up (Mon)</th>
<th>Preoperative visual acuity</th>
<th>Final visual acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EIA*</td>
<td>40</td>
<td>F</td>
<td>35</td>
<td>6</td>
<td>3</td>
<td>-</td>
<td>Trab+MMC还要(30), TSCPC&gt;70, CCT&gt;90</td>
<td>146</td>
<td>20/70</td>
<td>2mFC</td>
</tr>
<tr>
<td>2</td>
<td>EIA</td>
<td>32</td>
<td>F</td>
<td>28</td>
<td>20</td>
<td>3</td>
<td>2</td>
<td>Penetrating keratoplasty (65)</td>
<td>123</td>
<td>20/25</td>
<td>20/40</td>
</tr>
<tr>
<td>3</td>
<td>EIA</td>
<td>51</td>
<td>F</td>
<td>32</td>
<td>16</td>
<td>3</td>
<td>-</td>
<td>Bleb Revision (12), Trab+MMC (18)</td>
<td>36</td>
<td>20/25</td>
<td>20/30</td>
</tr>
<tr>
<td>4</td>
<td>EIA</td>
<td>34</td>
<td>F</td>
<td>40</td>
<td>15</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>13</td>
<td>20/50</td>
<td>20/50</td>
</tr>
<tr>
<td>5</td>
<td>EIA</td>
<td>36</td>
<td>F</td>
<td>26</td>
<td>6</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>11</td>
<td>20/40</td>
<td>20/70</td>
</tr>
<tr>
<td>6</td>
<td>INS &gt;&gt;</td>
<td>28</td>
<td>F</td>
<td>35</td>
<td>30</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>6</td>
<td>20/25</td>
<td>20/25</td>
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<tr>
<td>7</td>
<td>Chandler syndrome</td>
<td>22</td>
<td>F</td>
<td>30</td>
<td>26</td>
<td>3</td>
<td>3</td>
<td>-</td>
<td>22</td>
<td>20/200</td>
<td>20/200</td>
</tr>
<tr>
<td>8</td>
<td>INS</td>
<td>37</td>
<td>F</td>
<td>35</td>
<td>14</td>
<td>3</td>
<td>-</td>
<td>Trab+MMC (18)</td>
<td>14</td>
<td>20/70</td>
<td>20/200</td>
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<tr>
<td>9</td>
<td>EIA</td>
<td>57</td>
<td>M</td>
<td>35</td>
<td>16</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>11</td>
<td>HM</td>
<td>LP</td>
</tr>
<tr>
<td>10</td>
<td>EIA</td>
<td>56</td>
<td>M</td>
<td>30</td>
<td>18</td>
<td>2</td>
<td>-</td>
<td>Trab+MMC (6), Molteno tube (40), Bleb Revision (65)</td>
<td>120</td>
<td>20/25</td>
<td>NLP</td>
</tr>
<tr>
<td>11</td>
<td>EIA</td>
<td>41</td>
<td>F</td>
<td>32</td>
<td>40</td>
<td>3</td>
<td>4</td>
<td>Trab + MMC (14), Molteno tube (36), CCT (60)</td>
<td>72</td>
<td>20/25</td>
<td>NLP</td>
</tr>
</tbody>
</table>

- The first surgery in all of the patients was trabeculectomy with MMC except case 10 that was without MMC.
- EIA: Essential Iris Atrophy
- Trab + MMC: Trabeculectomy with Mitomycin C
- TSCPC: Transscleral cyclophotocoagulation
- CCT: Cyclocryotherapy
- INS: Iris Nevus Syndrome

### Table 2. The initial and final diagnosis in eleven patients with iridocorneal endothelial syndrome

<table>
<thead>
<tr>
<th>Initial diagnosis (No. of the patients)</th>
<th>Final diagnosis (No. of the patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential iris atrophy (5)</td>
<td>Essential iris atrophy (8)</td>
</tr>
<tr>
<td>Juvenile glaucoma (2)</td>
<td></td>
</tr>
<tr>
<td>Chandler syndrome (1)</td>
<td></td>
</tr>
<tr>
<td>Iris nevus syndrome (2)</td>
<td>Iris nevus syndrome (2)</td>
</tr>
<tr>
<td>Chandler syndrome (1)</td>
<td>Chandler syndrome (1)</td>
</tr>
</tbody>
</table>
In 3 patients upper lid ptosis was seen on the same side of ocular involvement before any surgical intervention, Figure 2.

Figure 2. Left upper lid ptosis in a patient with essential iris atrophy

Seven (63.7%) of the patients had IOP less than 21 mm Hg, only one of them was on topical antiglaucoma medications. Four (36.4%) of them (case 2, 4, 5, 9) had IOP less than 21 mm Hg after the first surgery, trabeculectomy with adjunctive MMC, in the last follow-up visit. The IOP was controlled in one patient (case 8) after the second trabeculectomy and in two others (case 1, 3) after further procedures such as bleb revision and cyclodestruction that were done consequent to the second trabeculectomy. The surgical intervention failed in four patients. Two of them had IOP more than 21 mm Hg with medications after the first trabeculectomy with MMC (case 6, 7) and were scheduled for further surgical intervention. The two others (case 10, 11) developed NLP vision even with Molteno tube implantation.

At the last visit seven (63.7%) patients had visual acuity equal or more than 20/200. One of the patients (case 2) underwent penetrating keratoplasty after the first glaucoma surgery due to decompensated cornea, and had clear grafted cornea and controlled IOP at the last visit (123 months). The corneal decompensation occurred 60 month after trabeculectomy and seemed to be related to the natural course of ICE syndrome.

Discussion

Medical treatment generally proved ineffective at reducing the IOP in the long term in patients with ICE syndrome, in accordance with previous reports. In our series none of the patients were controlled with medical therapy, so they underwent surgical intervention. Four (36.4%) of our patients after the first trabeculectomy with adjunctive MMC operation had IOP less than 21 mm Hg in the last follow up visit (median: 22; range: 6-14 months). In Wright et al's study; 4 (44%) of nine patients with ICE syndrome who underwent trabeculectomy with postoperative 5-Fluorouracil injection had IOP less than 21 mm Hg with a mean follow-up of 25 months. In another study by Lanzl et al, it was reported that 8 of 10 patients with ICE syndrome had adequate IOP control after filtering surgery with adjunctive MMC with a mean follow-up of 14.9 months. This high success rate may be attributed to the lower duration of follow-up. In Langanowski et al's research on 22 patients with ICE syndrome who underwent trabeculectomy without antimetabolite operation a success rate of 60% at 1 year and 40% at 2 years was obtained. Kid et al reported 64% success of trabeculectomy at 1 year and 39% at 3 years in 37 patients of ICE syndrome.

Patients with ICE syndrome undergoing filtering surgery are believed to have a lower success rate than those with most other types of glaucoma. Medical treatment generally proved ineffective at reducing the IOP in the long term in patients with ICE syndrome, in accordance with previous reports. In our series none of the patients were controlled with medical therapy, so they underwent surgical intervention. Four (36.4%) of our patients after the first trabeculectomy with adjunctive MMC operation had IOP less than 21 mm Hg in the last follow up visit (median: 22; range: 6-14 months). In Wright et al's study; 4 (44%) of nine patients with ICE syndrome who underwent trabeculectomy with postoperative 5-Fluorouracil injection had IOP less than 21 mm Hg with a mean follow-up of 25 months. In another study by Lanzl et al, it was reported that 8 of 10 patients with ICE syndrome had adequate IOP control after filtering surgery with adjunctive MMC with a mean follow-up of 14.9 months. This high success rate may be attributed to the lower duration of follow-up. In Langanowski et al's research on 22 patients with ICE syndrome who underwent trabeculectomy without antimetabolite operation a success rate of 60% at 1 year and 40% at 2 years was obtained. Kid et al reported 64% success of trabeculectomy at 1 year and 39% at 3 years in 37 patients of ICE syndrome.

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Glaucoma drainage implant surgery conceptually is appealing in patients with ICE syndrome because it may bypass the chief hazard of filtrations procedure: the regrowth of an ICE membrane over the ostium for filtration and subconjunctival fibrosis over the filtration site. Kim et al reported a survival rate of 70% at 1 year and 40% at 3 years for GDI in 10 patients with ICE syndrome and glaucoma. In Doe et al's study in which GDI surgery was done for 21 patients of ICE, 14 (66%) of them...
had controlled IOP without further glaucoma surgery. One of the patients developed NLP vision, the eye was enucleated due to painful eye, and another one developed LP vision at the last follow up visit (50 months). Thirty percent of these patients did not have any surgery prior to GDI's operation. This may be a factor for increasing their success rate.

We performed single plate Molteno tube implantation in 2 of our patients whose IOP was not controlled by two previous filtering procedures. Unfortunately both of them lost their vision. Although this result is not similar to the previous mentioned studies, but it may be related to the long-term follow-up (6 and 10 years) of these patients. Both of these patients had essential iris atrophy and according to the previous studies glaucoma secondary to this variant of ICE syndrome has a more refractory glaucoma than others. It has been suggested that the GDI surgical technique be modified for patients with ICE by lengthening the tube to allow further repositioning, and the excess tubing can be routed along the sclera. Additionally, the tube tip should be kept well away from potential source of the ICE cells such as the iris and the cornea; entry through the pars plana can be used in pseudophakic vitrectomized eyes.

The initial diagnosis was correct in 8 (73%) patients. This is not unusual for this rare disease which does not have the typical picture of the syndrome at presentation, so the glaucoma is attributed to some other causes. In Laganowski et al. study on 25 patients with glaucoma secondary to ICE syndrome, the diagnosis of this syndrome was overlooked initially in 17 (68%) patients. Hence, in all patients with unilateral glaucoma, particularly if they are young the ICE syndrome should be considered and confirmed by specular microscopy.

In three of our patients upper lid ptosis was detected on the same side of ocular involvement. To the best of our knowledge, there is no previous report of ptosis on the same side of ocular involvement in the ICE syndrome. For defining any relationship, detailed examination of these patients and further studies for this entity is warranted.

Considering the results of our study multiple glaucoma procedures may be required to achieve successful outcome, and trabeculectomy with an antifibrotic agent works well for a certain percentage of patients. Although in our series we did not have a good result of GDI procedures, in those that trabeculectomy fails, early consideration should be given to these procedures because the success rate of filtering surgery declines with each subsequent procedure.

References