Systematic Review

Complications Related to Implants Used in Anterior Bleb Forming Glaucoma Surgery: A Systematic Review of the Literature

Alejandra Salinas, MD1; Fabián Rodríguez, MD, MSc2; Javier Bardavío, MD, FRCSeD3

1Department of Ophthalmology, Hospital Universitario de Torrevieja, Spain
2Department of Ophthalmology, Hospital Verge de la Cinta, Tortosa, Spain
3St Mary’s Treatment Centre, Portsmouth, UK

*Corresponding author
Alejandra Salinas, MD
Ophthalmologist, FEBO, Department of Ophthalmology, Hospital Universitario de Torrevieja, Spain; E-mail: san.salinas.ss@gmail.com

Article information
Received: September 17th, 2019; Revised: October 3rd, 2019; Accepted: October 4th, 2019; Published: October 11th, 2019

Cite this article

ABSTRACT

Purpose
To make an account of published implant-related complications (IRC) by a systematic review of the literature.

Methods
A systematic search of Pubmed and Scopus databases and Google Scholar engine was performed with selection criteria to detect papers on IRC. We excluded unrelated papers and reviewed selected ones. We considered papers that did not explicitly state about occurrence or not occurrence of IRC as non-IRC reporting. Main outcome measures were the number of papers reporting on complications, IRC, and types of IRC.

Results
After the search, selection, and addition, we studied 109 papers. Incidence of IRC was 4.5%, half required explantation. While 26 implant studies found IRCs (23%), 13 case reports on surgical complications, 8 (61.5%) of them reported IRC. Frequent complications were conjunctival erosion, blockage of the tube, migration to anterior chamber or damage to surrounding tissues.

Conclusion
Most papers did not report on IRC. Length or nature of studies may skew finding IRC. The incidence of IRC was 4.5%. Hard and sharp implants carry a greater risk of IRC and explantation.

Keywords
Implant-related complications (IRC); Glaucoma surgery; Anterior bleb forming.

INTRODUCTION

Glaucoma is a chronic progressive optic neuropathy that may cause severe visual loss and affect the quality of life. The front line of treatment consists of reducing intraocular pressure. Most patients achieve good medical control: some require one or more surgical procedures. Although conventional filtering surgery is effective it has only moderate success and are subject to risks. Some devices have been designed and introduced to improve success and risks. Some of these implants are associated with classical conventional fistulizing surgery or to newer filtering procedures that intend the construction of a paralimbal bleb (subconjunctival, Subtenon's or intra-scleral). Regulatory bodies have studied the security and effectiveness of these implants and authorized for human application. Some systematic reviews or meta-analysis show that support for the use of these devices may be limited.1-4 This study aimed to make an account of published implant-related complications (IRC), this is complications directly caused by the implant, by a systematic review of the literature up to April 2015. Only implants that contribute to creating a paralimbal bleb were considered since those are the ones that are used as an alternative to trabeculectomy or non-penetrating deep sclerectomy and are

ABSTRACT

Purpose
To make an account of published implant-related complications (IRC) by a systematic review of the literature.

Methods
A systematic search of Pubmed and Scopus databases and Google Scholar engine was performed with selection criteria to detect papers on IRC. We excluded unrelated papers and reviewed selected ones. We considered papers that did not explicitly state about occurrence or not occurrence of IRC as non-IRC reporting. Main outcome measures were the number of papers reporting on complications, IRC, and types of IRC.

Results
After the search, selection, and addition, we studied 109 papers. Incidence of IRC was 4.5%, half required explantation. While 26 implant studies found IRCs (23%), 13 case reports on surgical complications, 8 (61.5%) of them reported IRC. Frequent complications were conjunctival erosion, blockage of the tube, migration to anterior chamber or damage to surrounding tissues.

Conclusion
Most papers did not report on IRC. Length or nature of studies may skew finding IRC. The incidence of IRC was 4.5%. Hard and sharp implants carry a greater risk of IRC and explantation.

Keywords
Implant-related complications (IRC); Glaucoma surgery; Anterior bleb forming.
potentially avoidable. We excluded equator bleb creating implants, angular devices or anterior chamber to supraciliary space shunts from the scope of this study. We were also interested to know how many of the papers referred to complications related to the implants.

**METHODS**

### Search Strategy

Three different search engines were used: Pubmed, Google Scholar and Scopus in April 2015. The search was performed over all fields of bibliographic references. We applied three levels of search restriction and combined controlled Mesh and natural languages. Language filters were applied. Inclusion criteria: any series of patients, whether prospective or retrospective and case reports in English, Spanish or French (filtered) found introducing the selected keywords. The word “complication” was extended to the abstract search also. Exclusion criteria: reports on other glaucoma drainage devices like Ahmed or Krupin Valve, Baerveldt or Molteno drainage devices. Any anterior chamber to supraciliary or suprachoroidal shunts like Gold Micro Shunt or Esnoper V-2000. Papers in any other languages. Keywords: “prostheses and implants/ complications”, “glaucoma drainage implants”, implant, ex press, esnoper, SK gel, aqua flow, collagen implant, Hem Acrylic, reticulated hyaluronic acid, T flux, thiobarbituric acid-reactive (T BAR), filtering surgery, filtering surgeries, deep sclerectomy, non-penetrating deep sclerectomy, viscoanalostomy, trabeculectomy, sclerotomy. Mendele reference manager (www.mendeley.com, Elsevier) detected duplications. Refer to Table 1 for search strategy.

### Initial Revision Strategy: The Selection of Papers for Revision

All papers’ titles were reviewed by a team of trained or in training ophthalmologist in search of papers that reported on paralimbal bleb forming surgical procedures with the implantation of a device. When in doubt, we reviewed the abstract. We excluded papers reporting on surgical procedures without an implant, different pro-

<table>
<thead>
<tr>
<th>Table 1. Search Strategy Details</th>
<th># Searches on Google Scholar</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(((implant OR collagen implant OR collagen implants OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”)) AND (complication) AND (glaucoma))</td>
<td>11600</td>
</tr>
<tr>
<td>2</td>
<td>(implant OR esnoper OR sk gel OR aquaflow OR “ex-press” OR “collagen implant” OR “collagen implants” OR “Hemacrylic” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) AND (complication) AND (Glaucoma-“Moltena Implants”-Molteno-Ahmed-“Krupin valve”-“kru pin valves”-Baerveldt)</td>
<td>2300</td>
</tr>
<tr>
<td>3</td>
<td>(“Filtering Surgery” OR “Trabeculectomy” OR “Filtering Surgeries” OR “deep sclerectomy” OR “Sclerostomy” OR “deep sclerectomies” OR viscocanalostomy) AND (implant OR esnoper OR sk gel OR aquaflow OR “ex-press” OR “collagen implant” OR “collagen implants” OR “Hemacrylic” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) AND (complication) AND (Glaucoma-“Molteno Implants”-Molteno-Ahmed-“Krupin valve”-“kru pin valves”-Baerveldt)</td>
<td>1572</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># Searches on Scopus</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>(TITLE.implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) OR ABS.(implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar” AND (TITLE(complication)) AND (TITLE(glaucoma) OR ABS(glaucoma)) AND LIMIT(TO(LANGUAGE,”English”)) OR LIMIT(TO(LANGUAGE,”French”)) OR LIMIT(TO(LANGUAGE,”Spanish”))</td>
</tr>
<tr>
<td>5</td>
<td>(TITLE.implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) OR ABS.(implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar” AND (TITLE(complication)) AND (TITLE(glaucoma) OR ABS(glaucoma)) AND NOT TITLE-ABS-KEY(“Molteno” OR Ahmed OR “Krupin valve” OR “baerveldt”) AND LIMIT(TO(LANGUAGE,”English”)) OR LIMIT(TO(LANGUAGE,”French”)) OR LIMIT(TO(LANGUAGE,”Spanish”))</td>
</tr>
<tr>
<td>6</td>
<td>(TITLE “Trabeculectomy” OR “Filtering Surger*” OR “deep sclerectomy” OR “Sclerostomy” OR viscocanalostomy) OR ABS (“Trabeculectomy” OR “Filtering Surger*” OR “deep sclerectomy” OR “Sclerostomy” OR viscocanalostomy) AND (TITLE.implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) OR ABS.(implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) AND (TITLE(complication) OR ABS(complication)) AND (TITLE(glaucoma) OR ABS(glaucoma)) AND NOT TITLE-ABS-KEY(“Molteno” OR Ahmed OR “Krupin valve” OR “baerveldt”) AND LIMIT(TO(LANGUAGE,”English”)) OR LIMIT(TO(LANGUAGE,”French”)) OR LIMIT(TO(LANGUAGE,”Spanish”))</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># Searches on Pubmed/medline</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>(TITLE.implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) OR ABS.(implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) AND (TITLE(complication)) OR ABS(complication) AND (TITLE(glaucoma) OR ABS(glaucoma)) AND NOT TITLE-ABS-KEY(“Molteno” OR Ahmed OR “Krupin valve” OR “baerveldt”) AND LIMIT(TO(LANGUAGE,”English”)) OR LIMIT(TO(LANGUAGE,”French”)) OR LIMIT(TO(LANGUAGE,”Spanish”))</td>
</tr>
<tr>
<td>9</td>
<td>(TITLE “Trabeculectomy” OR “Filtering Surger*” OR “deep sclerectomy” OR “Sclerostomy” OR viscocanalostomy) OR ABS (“Trabeculectomy” OR “Filtering Surger*” OR “deep sclerectomy” OR “Sclerostomy” OR viscocanalostomy) AND (TITLE.implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) OR ABS.(implant OR esnoper OR sk gel OR aquaflow OR “express implant” OR “collagen implant” OR “Hemacrylic Metha Stealth” OR “reticulated hyaluronic acid” OR “T flux” OR “T bar”) AND (TITLE(complication) OR ABS(complication)) AND (TITLE(glaucoma) OR ABS(glaucoma)) AND NOT TITLE-ABS-KEY(“Molteno” OR Ahmed OR “Krupin valve” OR “baerveldt”) AND LIMIT(TO(LANGUAGE,”English”)) OR LIMIT(TO(LANGUAGE,”French”)) OR LIMIT(TO(LANGUAGE,”Spanish”))</td>
</tr>
</tbody>
</table>
cedures all together (posterior forming blebs, angular surgery, anterior chamber to supraciliary or suprachoroidal shunts), different languages or animal studies. We included systematic reviews and meta-analysis of implanting surgical procedures studies to secure relevant studies that our search could have missed out, but carefully made sure we did not duplicate the study papers by doing so.

Full text of all included papers was requested for revision. New references were found during revision and added under the same criteria.

Ethical Committee approval was not requested as no patient information was searched at any time.

Outcome Measures

The following outcomes were measured: total number of papers after exclusions, number of papers that report complications, number of papers that report IRC, type of implant, type of IRC found as extrusion, migration, damage to surrounding tissue, dysfunctional implants, explanted cases, relocated cases, other (Table 2).

Papers’ revision was directed to find a statement on complications within the method and the results sections of the article. We did not look for complications reports within the discussion section nor conclusions of the papers. Since the presence or absence of complications report is not interpretable, only one reviewer read through every paper. A paper was considered to report on IRC if the actual complication was reported or it explicitly stated that no IRC was found during the study. Papers that did not state one thing or the other were considered not to report on IRC. In case of doubt, the paper was consulted with the senior ophthalmologist in the study group.

A register of complications was established to include both studies with and without complications’ reports.

RESULTS

The result from the search of the three engines was 253 papers from Scopus, 314 from Pubmed and 1572 from Google Scholar that were reduced to 1102 after removing redundant papers. All titles of those papers were reviewed to discard unrelated ones when in doubt the abstract was used. Finally, 120 full-text articles were requested for review. From systematic revisions and meta-analysis, we found 28 new unknown references that were also requested. From a total of 148 papers, 23 were excluded due to belonging to animal or experimental implants studies, reporting on the different procedure, German language, or unfound full text. Of the 125 reviewed papers, 9 were systematic reviews, and 7 were meta-analysis that included studies already reviewed by this research team. Therefore, the final number of papers considered for study purposes was 109 (Figure 1).

All these papers correspond to studies or case reports that report on glaucoma implant surgery and also on surgical complications (100% of the 109 papers reviewed). Out of the 109 papers reviewed, 75 (68.8%) did not report on IRC, 34 (31.2%) reported on IRC, 6 (17.6%) of the IRC reporting papers) explicitly reporting an absence of IRC (4 prospective and 2 retrospective studies). Of the 59 prospective studies (54.1%, of 109), 17 reported on IRC (28.8%, of 59). Of the 37 retrospective studies (33.9%, of 109), 9 (24.3%, of 37) reported IRC. Thirteen of the papers (11.9%, of

<table>
<thead>
<tr>
<th>Table 2. Definition of Outcomes to be Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes to be Measured</strong></td>
</tr>
<tr>
<td>• Number of papers found once the non-related are excluded</td>
</tr>
<tr>
<td>• Number of papers that report complications</td>
</tr>
<tr>
<td>• Number of papers that report implant-related complications</td>
</tr>
<tr>
<td>• Type of implant-related complications found with every implant</td>
</tr>
<tr>
<td>• Extrusion</td>
</tr>
<tr>
<td>• Migration</td>
</tr>
<tr>
<td>• Damage of surrounding tissue</td>
</tr>
<tr>
<td>• Obstructed</td>
</tr>
<tr>
<td>• Explanted cases</td>
</tr>
<tr>
<td>• Relocated cases</td>
</tr>
<tr>
<td>• Other</td>
</tr>
</tbody>
</table>


Figure 1. Final Number of Papers Considered for Study Purposes

28 further references found in the initial papers

Studies for final revision: 109 + 9 Reviews + 7 meta-analysis that included reviewed studies

23 papers further excluded as in German, animal studies, experimental implants, different surgical procedures or full text missing

SCOPUS: 253
PubMed: 314
Google Scholar: 1572
Unrelated papers: 982
Total after cross match: 1102
After initial revision: 120
28 further references found in the initial papers
were case reports, 8 (61.5%, of 13) reported IRC. The total population of eyes considered in this study was 5831 (population range per study: 1-345), 4576 of which had been implanted (78.4%), the others belonging to control groups. The population of eyes with an implant included in studies that reported on IRC was 1479. Of those, the number of eyes that suffered an IRC was 67 (4.5%). Table 3 shows the implants understudied, the number of IRC reporting papers, the number of study eyes and the number of complicated cases.

A summary of the complications is in Table 4. The most common IRC was conjunctival erosion; 20 cases after Express implantation (15 through a full-thickness scleral incision, four under a partial-thickness scleral flap and one unreported technique) that required implant removal, and one case of SK-gel that healed under observation. Obstruction of Express tube occurred in 14 cases. Four Express tubes migrated postoperatively into the anterior chamber (AC) and another one was introduced in the AC during the procedure. Another Express tube migrated to the subconjunctival space, as it occurred to an SK gel implant, and a further Express tube was found misplaced. A T flux implant migrated into the patient’s anterior chamber. A fragment of Ethicon 1/0 chromic catgut, placed under a deep sclerectomy flap, migrated into the AC also. Sixteen cases of damage to surrounding tissues were found, 5 Descemet membrane detachments and one corneal abrasion after collagen implant, five iris touch, two endothelial touches, one corneal abrasion, one crystalline lens touch that induced a white cata-

<table>
<thead>
<tr>
<th>Table 3. Understudy Implants, IRC Reporting Papers, Number of Study Eyes (Eyes with Implants in IRC Reporting Papers) and Number of Complicated Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant</td>
</tr>
<tr>
<td>Express (Steel)</td>
</tr>
<tr>
<td>Collagen Implant</td>
</tr>
<tr>
<td>SK-gel (Hyaluronic acid)</td>
</tr>
<tr>
<td>T-flux (Acrylic)</td>
</tr>
<tr>
<td>Ethicon 1/0 Chromic Catgut</td>
</tr>
<tr>
<td>PMMA</td>
</tr>
<tr>
<td>ePTFE</td>
</tr>
<tr>
<td>Ologen (Collagen)</td>
</tr>
<tr>
<td>HEALA Flow</td>
</tr>
<tr>
<td>Aquaflo (Collagen)</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

*Twelve papers tested two or three implant devices; **One paper tested two devices PMMA and Collagen implant

<table>
<thead>
<tr>
<th>Table 4. Reported Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant</td>
</tr>
<tr>
<td>Migration or malposition</td>
</tr>
<tr>
<td>Extrusion</td>
</tr>
<tr>
<td>Damage to surrounding tissues</td>
</tr>
<tr>
<td>Obstructed</td>
</tr>
<tr>
<td>Explanted</td>
</tr>
<tr>
<td>Explanted as treatment of complication</td>
</tr>
<tr>
<td>Repositioned</td>
</tr>
</tbody>
</table>

109) were case reports, 8 (61.5%, of 13) reported IRC.

The total population of eyes considered in this study was 5831 (population range per study: 1-345), 4576 of which had been implanted (78.4%), the others belonging to control groups. The population of eyes with an implant included in studies that reported on IRC was 1479. Of those, the number of eyes that suffered an IRC was 67 (4.5%). Table 3 shows the implants understudied, the number of IRC reporting papers, the number of study eyes and the number of complicated cases.

A summary of the complications is in Table 4. The most common IRC was conjunctival erosion; 20 cases after Express implantation (15 through a full-thickness scleral incision, four under a partial-thickness scleral flap and one unreported technique) that required implant removal, and one case of SK-gel that healed under observation. Obstruction of Express tube occurred in 14 cases. Four Express tubes migrated postoperatively into the anterior chamber (AC) and another one was introduced in the AC during the procedure. Another Express tube migrated to the subconjunctival space, as it occurred to an SK gel implant, and a further Express tube was found misplaced. A T flux implant migrated into the patient's anterior chamber. A fragment of Ethicon 1/0 chromic catgut, placed under a deep sclerectomy flap, migrated into de AC also. Sixteen cases of damage to surrounding tissues were found, 5 Descemet membrane detachments and one corneal abrasion after collagen implant, five iris touch, two endothelial touches, one corneal abrasion, one crystalline lens touch that induced a white cata-
Soft and absorbable implants tend to be more respect cases. Also, non-absorbable acrylic T flux tends to migrate if left press accounts for most cases of explanted, extruded or migrated complications, mainly extrusion. In our study, the steel implant Ex-er and sharper implants that remain longer, increase the risk of extrusion. The physical properties of the implant are relevant: hard-

DISCUSSION

The market offers implants in an attempt to improve post-operative survival, efficacy or safety for patients requiring glaucoma surgery. Some studies, however, suggest that traditional trabeculectomy or newer deep sclerectomy without implants might be just as effective in reducing intraocular pressure. Devices, therefore, attempt to improve prognosis, but its mere physical presence may also increase risks. This study aimed to make an account of published IRC by a systematic review of the literature up to April 2015. We only studied implants that contribute to creating a paralimbal bleb. Equator bleb creating implants, angular devices or anterior chamber to suprachiliary space shunts are not within the scope of this study.

Sixty-seven cases of IRC of 1479 (4.5%) patients were found, of which 31 required implant removal. Our estimation of IRC incidence might be biased by the search or the selection method. The incidence of Express removal was 3% before the tube was guarded under a scleral flap: that reduced the risk but did not eliminate it. The initial design of the technique may show that of 13 case reports dealing with complications, 8 (61.5%) were about IRC. We suspect that the discrepancy in IRC incidence reported in retrospective and prospective studies compared to case reports might be related to the length of the studies and although inconclusive, could be relevant. Issues related to reporting could justify further research.

An IRC incidence of 4.5% resulted from this study, of which about a half required removal. Harder and sharper implants carry a higher risk. It is worth considering the implant’s function and shape of the material are relevant and worth bearing in mind that an implant might induce complications by itself. Also, the type and shape of the material are relevant and worth bearing in mind at the time of assessing the purpose and usefulness of the implant. Further, the importance of considering IRC at the time of designing studies to make them sensible to complication detection and reporting.

ACKNOWLEDGEMENTS

The authors are thankful to Ms. Noemi Aluja for her contribution towards the bibliography.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES


