This publication includes independent authors’ guidelines for the safe use and handling of mitomycin C in ophthalmic practices. Readers should use these guidelines as a resource only. These guidelines should never take precedence over manufacturers’ recommended practices, facilities policies and procedures, or compliance with federal regulations. Information in this publication may assist facilities in developing policies and procedures specific to their needs and practice environment.

American Society of Ophthalmic Registered Nurses

For questions regarding content or association issues contact ASORN at asorn@aoa.org or 1.415.561.8513.

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Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

ACKNOWLEDGMENTS
The development of this educational resource would not have been possible without the knowledge and expertise of the ophthalmologists and ophthalmic registered nurses who wrote the content and the subsequent reviewers who provided valuable input. Their efforts exemplify a diverse knowledge of the use of mitomycin C in ophthalmic surgery, an understanding of quality patient care, and a commitment to safe ophthalmic practice. Each has given of their knowledge, talent and valuable time in order to foster education and excellence for the ophthalmic surgical team.

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Conflict of Interest Disclosure
ASORN received an unrestricted educational grant from Mobius Therapeutics™ to support the development and printing expenses of this learning module. Authors wrote the articles included in this module as a contribution to ASORN’s journal: Insight: The Journal of the American Society of Ophthalmic Registered Nurses, without input and independent of Mobius Therapeutics™.

Off-Label Use Disclosure
At the time of publication the use of mitomycin C for ophthalmic procedures was considered off label. Off-label use is addressed in the individual articles.

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Please review the expiration information noted in the product detail associated with this assessment at www.actioned.org or posted on the ASORN web site at www.asorn.org.
Activity Format
This learning activity is a self-paced, independent learning module consisting of a compilation of articles on the use of mitomycin C in ophthalmology first published in 2010 in Insight: The Journal of the American Society of Ophthalmic Registered Nurses, and a post-test.

Target Audience
The target audience for this material is ophthalmic registered nurses, ophthalmic assistants, technicians and technologists, surgical technologists, and other personnel who may use mitomycin-c in their medical practice.

Audience Level
Intermediate – Advanced

Successful Completion
To receive continuing education credits for this activity the learner should visit www.actioned.org. Upon payment of the registration fee learners will have access to the full text module, evaluation and post-test. Successful completion includes submission of the activity evaluation and post-test, and achievement of a passing score of 80% or higher. At the time of publication nursing contact hours are available; other types of credits may also be available and can be verified through the ASORN office or by reviewing the course catalog description at www.actioned.org. Participants who do not achieve a minimum score of 80% or higher may retake the test once at no charge. Subsequent re-takes will incur a fee. Re-take rules associated with ACTIONED are subject to change. Please verify rules at www.actioned.org.

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2. Locate course in Course Catalog
3. Add to shopping cart and follow instructions
4. Certificate of completion is awarded automatically upon successful completion of the online evaluation and post-test.
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The registration fee to earn continuing education credits for this activity is: $20.00 to individuals with current membership in ASORN, ATPO, CSOMP, OPS, ASOA, current JCAHPO-certificants, and current COEs; $30.00 for non-members.

About ASORN and ACTIONED
About ASORN: Established in 1976, ASORN is a 501(c)(3) not-for-profit organization. ASORN members are comprised of ophthalmic registered nurses and non-RNs active in the field of ophthalmic patient care. The mission of the American Society of Ophthalmic Registered Nurses (ASORN) is to foster excellence in ophthalmic patient care and to support the ophthalmic team through individual development, education, and evidence-based practice.

About ACTIONED: In May 2010, ASORN collaborated with JCAHPO, ATPO, CSOMP, OPS and ASOA to launch ACTIONED, an innovative online educational resource for eye care professionals. Short for Assessment, Certification, an Interactive Ophthalmology Network, ACTIONED provides online educational resources for the entire eye care team. Look for this assessment and other online educational opportunities offered by ASORN and the other ACTIONED partners at www.actioned.org.
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Introduction

Mitomycin C (MMC) is an antimetabolite used in ophthalmic procedures for its antifibrotic effect. MMC is a toxic and potentially hazardous chemotherapeutic drug that must be handled with care to protect healthcare providers and patients.

The following series of articles appeared in Insight: The Journal of the American Society of Ophthalmic Registered Nurses (ASORN) in 2010. This series was compiled after a survey of members indicated a need for education regarding the safe use, handling, storage and disposal of mitomycin C (MMC). The results of this survey are documented in the first article, Results of ASORN Mitomycin C Survey.

The series continues with information about the overall care and handling of MMC followed by information specific to use in pterygium, trabeculectomy and refractive procedures.

At the time this series was written MMC was used off label for ophthalmic procedures and each article addresses the off label use as well as issues of compounding and storage of MMC. As an update to this series it should be recognized that MMC is no longer considered off label for three ophthalmic procedures. Subsequent to the publication of this series Mitosol (ophthalmic) has been granted orphan drug status for trabeculectomy, pterygium and surface ablation laser keratectomy procedures.

Though this does not affect the overall handling and disposal recommendations it does change the storage recommendations since Mitosol® is a single use product mixed on the sterile field for immediate use. There is no long term storage, either refrigerated or frozen, of premixed product to consider.

We hope you find these articles both educational and valuable as you promote safety for both patients and personnel when using mitomycin C in ophthalmic procedures.
Educational Objectives

1) Name three ophthalmic procedures which may utilize mitomycin C as part of the procedure.

2) Recall the purpose of mitomycin C use in ophthalmic surgical procedures.

3) Describe the safe handling and disposal of mitomycin C.

4) Identify the roles of the circulating nurse and scrub person during an ophthalmic procedure utilizing mitomycin C.

5) Describe the surgical technique of pterygium removal utilizing mitomycin C.

6) List three possible side effects of mitomycin C used in ophthalmic surgery.

7) Recall three potential hazards associated with the mishandling of mitomycin C.

8) Describe the importance of using personal protective equipment when working with mitomycin C.

9) Describe the trabeculectomy procedure utilizing mitomycin C.

10) Explain the importance of copious irrigation following the topical administration of mitomycin C.

11) Recall appropriate methods for disposal of mitomycin C.

12) Describe the use of mitomycin C in refractive surgical procedures.
Results of ASORN Mitomycin C Survey

by Lancy Gail Broadhurst, RN, MSN

The field of ophthalmology is always changing. It is full of innovators, both in the physician and nursing arenas. When a surgeon decides to try a new procedure or medication and the idea is successful the practice often spreads across the country without formal training for surgeons or staff.

One such innovation was the off-label use of mitomycin C in the trabeculectomy procedure. Use of this medication, which was initially developed for chemotherapy, required nurses to be innovative and formulate safe methods for storage, handling and disposal in the operating room without formal resources. This became increasingly important as additional uses for mitomycin C were identified in other ophthalmic specialties.

ASORN has always been a leader in education for the ophthalmic healthcare team. The ASORN Board of Directors was challenged to determine the extent to which mitomycin C is used in practice by its members and identify the educational needs of the nurse dispensing mitomycin C. A survey was developed by a team of ophthalmic nurses from across the U.S. and the questions were disseminated electronically. ASORN invited ophthalmic staff around the country to complete the questionnaire. The responses to the study were impressive; there were 171 responses within a few days. The intent of this article is to share some of the highlights from the study and to provide a basis for additional educational articles in upcoming Insight issues. The full survey results are available online at www.asorn.org.

The first part of the survey dealt with background information including practice setting, educational background and use of mitomycin C in their practice.

Those responding to the survey came from the following practice settings:

<table>
<thead>
<tr>
<th>ASC</th>
<th>Hospital</th>
<th>Office/Clinic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>55%</td>
<td>28.7%</td>
<td>12.3%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

They identified their educational background as follows: [It should be noted that the number of RNs surveyed was greater than the number of non-RNs.]

<table>
<thead>
<tr>
<th>RN</th>
<th>LVN/LPN</th>
<th>CST</th>
<th>COMT</th>
<th>COT</th>
<th>COA</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.6%</td>
<td>2.9%</td>
<td>2.3%</td>
<td>0.6%</td>
<td>4.1%</td>
<td>2.3%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

The majority of the respondents to the survey said they use mitomycin C in their practice.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.5%</td>
<td>6.5%</td>
</tr>
</tbody>
</table>

For those that indicated that mitomycin C is not used in their practice, the reasons were varied:

<table>
<thead>
<tr>
<th>Cost prohibitive</th>
<th>Lack proper training</th>
<th>Lack protocols for use</th>
<th>Surgeons have not requested</th>
<th>Not readily available</th>
<th>Do not perform applicable procedures</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1%</td>
<td>11.1%</td>
<td>22.2%</td>
<td>44.4%</td>
<td>22.2%</td>
<td>44.4%</td>
<td>22.2%</td>
</tr>
</tbody>
</table>
The second part of the survey dealt with usage and availability. The volume of cases done per week using mitomycin C varied but confirmed the drug is still used regularly in ophthalmic surgery.

<table>
<thead>
<tr>
<th>1-5 times/week</th>
<th>6-10 times/week</th>
<th>11-15 times/week</th>
<th>16-20 times/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>89%</td>
<td>9.1%</td>
<td>1.3%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Availability of the drug was assessed by asking if the drug was difficult to obtain and whether or not the respondents had ever encountered a backorder of the medication.

Is the product difficult to obtain?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Did not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.7%</td>
<td>55.8%</td>
<td>19.5%</td>
</tr>
</tbody>
</table>

Has mitomycin C ever been on backorder or unavailable?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Did not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.8%</td>
<td>38.3%</td>
<td>14.9%</td>
</tr>
</tbody>
</table>

The third part of the survey referred to policies and procedures for the safe use of mitomycin C. Since mitomycin C has toxicity issues, it was important to determine if it is being handled properly.

Are the standards for mixing and handling chemotherapeutic agents, such as donning personal protective wear and chemoresistant gloves, strictly adhered to in your facilities?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Did not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>60.3%</td>
<td>25.3%</td>
<td>14.4%</td>
</tr>
</tbody>
</table>

The next question asked if chemo-spill kits are readily accessible:

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Did not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>63.7%</td>
<td>22.6%</td>
<td>13.7%</td>
</tr>
</tbody>
</table>

Are the materials that are used to handle mitomycin C discarded in the proper chemotherapeutic/biohazard receptacle?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Did not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>87.7%</td>
<td>6.2%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

Finally it was asked if the respondents’ facilities had policies in place to cover mitomycin C use.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Do not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>64.4%</td>
<td>18.5%</td>
<td>17.1%</td>
</tr>
</tbody>
</table>

While the majority responded that they do have a policy in place more than one third indicated that they did not or were unaware. Based on the responses to this question it is clear that more education is needed to help ophthalmic staff understand the process of using mitomycin C in the safest way.

The final part of the survey inquired about the need for educational resources for the use of mitomycin C. 94.7% of the respondents stated they would like more education on this topic including:

<table>
<thead>
<tr>
<th>Ophthalmic use</th>
<th>Safe handling</th>
<th>Proper storage</th>
<th>Proper disposal</th>
<th>Nurse/Tech role</th>
</tr>
</thead>
<tbody>
<tr>
<td>89.5%</td>
<td>92.1%</td>
<td>74.3%</td>
<td>88.8%</td>
<td>86.2%</td>
</tr>
</tbody>
</table>

With budget cuts throughout the industry it was not surprising to see that the majority of respondents preferred educational methods that did not require travel or meeting registration fees.

<table>
<thead>
<tr>
<th>Journal article</th>
<th>Self-paced independent learning module</th>
<th>CD-ROM</th>
<th>Webinar with audio-visual</th>
</tr>
</thead>
<tbody>
<tr>
<td>74.3%</td>
<td>58.8%</td>
<td>39.5%</td>
<td>32.2%</td>
</tr>
</tbody>
</table>

The results of this study clearly demonstrate that ophthalmic staff would benefit from more education on proper use, storage, and disposal of mitomycin C. In this issue of Insight are two articles which are the first in a series about the use of mitomycin C in ophthalmic procedures. ASORN is committed to following up on this topic by offering more articles and information that will lead to a safer environment for those involved in the administration of this medication. [View full survey results at www.asorn.org]
Mitomycin C—Care and Handling

by Lori Pacheco, RN, CRNO

Mitomycin C (MMC) is a chemotherapeutic agent commonly known for its off-label use in ophthalmology. Its antifibrotic effect makes its use essential for procedures such as glaucoma filtration and pterygium surgeries. Corneal refractive surgery has seen the benefits of MMC in the prevention of corneal haze. MMC may also be used in other ophthalmic procedures such as cicatricial eye disease, conjunctival neoplasia, and allergic eye disease.

Risks and Complications

Patients must consent to treatment with MMC and the off-label use in ophthalmic procedures. Risks and complications for use of MMC in the ophthalmic patient, although rare, include secondary glaucoma, corneal edema, corneal or scleral thinning or perforation requiring corneal transplants, permanent stem cell deficiency, sudden onset mature cataract, corneal decompensation, corectopia (displacement of the pupil from its normal position), iritis, scleral calcification, scleral melt, retinal vascular occlusion, conjunctival irritation (redness of the eye), and incapacitating photophobia and pain.

Storage

MMC may be stored frozen or refrigerated. The type of storage is dependent upon whether the supplier is local or out of state and how it is shipped. Check with your supplier for the proper storage requirements. The temperature in the refrigerator and/or freezer should be checked daily and results logged to assure the proper guidelines have been met.

MMC syringes should each be labeled with the drug name, dose (concentration), expiration date, and packaging information. Verify that the information on the syringe and the information on the package are consistent. Verify that the dose is correct and that you are storing that concentration in the correct place. The dose used in glaucoma procedures may differ from that of corneal refractive procedures. If you have a refrigerator in the operating room and one in the LASIK suite, make sure you are storing the correct concentration in each to avoid a possible medication error.

Administration and Safety Concerns

MMC is a very potent and potentially toxic drug, and the low dose of MMC used in ophthalmic procedures may make one underestimate the possible toxic effects of this powerful antimetabolite.

The handling of MMC should be met with caution. Employers should develop, implement, and maintain at the workplace a written hazard communication program for employees handling or otherwise exposed to chemicals, including drugs that represent a health hazard to employees.

Gloves should always be worn when handling or administering MMC. Mitomycin is a vesicant, a chemical that causes extensive tissue damage. If skin contact occurs, immediately wash with soap and water.
MITOMYCIN C--CARE AND HANDLING

Emergency procedures to cover hazardous spills should be included in the facility’s safety program. If a spill should occur, the area in which the spill occurred should be identified with a warning sign and access to the area limited. An incident report should be filed to document the spill and persons exposed. The American Society of Hospital Pharmacists (ASHP) considers small spills to be those less than 5 ml. Spills less than 5 ml outside a biological safety cabinet should be cleaned up immediately by personnel wearing a gown, double latex gloves, and splash goggles. Liquid should be wiped with absorbent gauze pads. The spill area should be cleaned three times using a detergent, followed by clean water. These items can be found in a spill kit. Spill kits should be kept near preparation and administrative areas. The MSDS for MMC includes sections on emergency procedures, including personal protective equipment.

Disposal

Commercial waste disposal should be handled by a licensed company. Hazardous drug–related waste should be handled separately from other hospital trash and disposed of in accordance with the Environmental Protection Agency (EPA), state, and local regulations for hazardous waste. This disposal occurs at either an incinerator or a licensed sanitary landfill for toxic wastes, as appropriate.

Refer to your state and local regulations, licensed medical waste disposal company, and the EPA for guidelines regarding proper disposal of MMC.

References


Ophthalmic Mutual Insurance Company, Addendum Mitomycin-C (MMC) with Refractive Surgery, version 6.30.05.
Pterygium Surgery with Mitomycin C: A Nursing Perspective

by Pamela J. Schultz, RN, CRNO

Educational needs for the ophthalmic health care team in the use of mitomycin C (MMC) were evaluated by an ASORN survey in late 2009. More than 70% of the respondents indicated that a journal article would be a valuable learning tool. This article will review the surgical use of MMC during a pterygium excision procedure in a hospital setting where the pharmacy department prepares the requested MMC dose.

Mitomycin C is classified as an antineoplastic or cytotoxic drug. Its use in ophthalmology is considered an unlabeled use or off-label use of a drug. According to Federal Drug Administration (FDA) regulations, off-label use allows physicians to use or “prescribe an approved medication” for a purpose other than that for which it was originally intended.

Cytotoxic drugs are in a high-risk category and exposure to them may be carcinogenic or mutagenic. Safe handling is essential for the welfare of patients, healthcare workers, and ancillary staff.

MMC is indicated in pterygium excision because of frequent recurrence. Although a pterygium is a non-malignant lesion of the conjunctiva, a patient may present with cosmesis complaints or decreased vision. Visual loss is related to astigmatic changes in the cornea or to an obstructed visual axis caused by the pterygium encroaching onto the cornea.

The patient elects to undergo surgery after an examination and diagnosis by the ophthalmologist. Surgical preparation begins at this time. The physician’s staff provides information to the patient and coordinates the following activities:

- selection of the date for surgery
- confirmation of the physician’s anesthetic choice
- provision of verbal and written preoperative instructions
- scheduling the procedure with the facility
- obtaining required laboratory findings including history and physical, blood chemistries, and X-ray and EKG when indicated
- submitting a separate, written order form 24 hours before surgery for the MMC; signed or co-signed by the attending physician

When the patient arrives at the pre-surgical area of the hospital or ambulatory surgery center the day of surgery, the patient is greeted, identified, and given an identification band (ID) with a patient-specific number. A preoperative checklist (Table 1) is completed before the patient is transported to the operating room (OR).

On the day of surgery, the OR staff assesses the surgical instrumentation, supplies, equipment, and medications necessary for the procedure. In cases scheduled with MMC, a separate cytotoxic waste receptacle is ordered for disposing of the items exposed to the agent. Pharmacy is called to verify the dose and availability of MMC before the patient is transported to the OR suite (Table 2). A spill kit for cytotoxic material clean-up needs to be in the Safety Station of the facility.
Typically, this kit (Table 3) is necessary for spills over 5 mL, which exceeds the dosage amount of MMC used for this procedure.

Once the patient arrives outside the OR, hand-off communication is exchanged. The preoperative data is confirmed. At this point, the patient's operative eye has been marked by the physician (Table 1). The patient is positioned for the procedure and the entire OR team participates in the procedural time-out, verifying the availability and strength of the MMC.

During the surgery, the circulating nurse dispenses the MMC into a labeled cup onto the sterile field. The scrub person (scrub) is responsible for monitoring the instruments and supplies touched by the agent during the procedure. Upon completion of the surgery, instruments are rinsed with distilled water before sending to the processing area. Waste materials that have been in contact with the MMC are placed in a separate, labeled container and removed by environmental services/housekeeping.

The patient is transferred to the recovery area with a pressure patch in place on the operative eye. Hand-off communication for the patient's surgical experience is completed. The patient is released accompanied by a responsible adult after meeting the discharge criteria. Written and verbal discharge information, which includes an emergency contact number and follow-up physician appointment, is provided.

In the event of an accidental exposure to MMC by the patient or employee, immediately flush the area with copious amounts of water for 15 minutes. For a patient exposure, complete an Incident Form after the exposure. Include the attending physician's written comment, evaluation, and follow-up plan for the patient. For an employee contact with the agent, complete an Employee Incident Form and have the employee report to employee/occupational health services. After work hours, report to the emergency department. Return all forms to the supervisor on duty. (Refer to specific facility policies.)

In conclusion, safe handling of cytotoxic drugs is an important goal for patient care and employee health. Accidental exposure is minimized by practicing universal precautions and using personal protective equipment properly. Remember the following points:

- know the procedure and steps for ordering MMC and the proper handling and disposal of exposed items

Table 1
Preoperative Checklist
- Verify the patient by checking name, procedure, birth date, or identification number
- Verify the consent
- Verify the surgical site
- Note allergy(ies) to food or drugs
- Check the chart—laboratory findings/history and physical
- (Surgeon) Mark the operative site; verify the mark in the OR

Table 2
Mitomycin C Process
- Physician orders the MMC at least 24 hours ahead of the surgery
- Pharmacy prepares per specific patient and MD order; the patient name and dosage are attached to the syringe and outer plastic bag
- Pharmacy technician/designate transports the MMC to the OR in the enclosed double set of self-sealing sturdy plastic bags, which also contain two pairs of gloves and safety labels
- RN circulator verifies the drug, dosage, the patient name, and ID
- RN circulator dons gloves to dispense the MMC into a labeled cup onto the sterile field, verifying with the scrub person; then she removes the gloves and discards the syringe and gloves into the hazardous waste container; following, she washes her hands with soap and water
- Scrub person monitors the drug at all times on the sterile field, keeping instruments and disposable items that have been used with the drug in a separate location
- Physician verifies the MMC with the scrub before applying to the surgical site using forceps and surgical spears, then irrigates the site with balanced salt solution
- Scrub person collects all disposable items used with the drug including the cup, spears, surgical drapes, gowns, and gloves; she then places all items into the hazardous waste container. She rinses the forceps with distilled water before returning them with other instruments to the processing area
- Environmental services/housekeeping removes the labeled, hazardous waste garbage

Table 3
Spill Kit Contents
- Gloves, 4 pairs, powder-free, non-vinyl
- Safety glasses, 2 pairs
- Shoe covers, 2 pairs
- Gown, non-permeable
- Respiratory mask
- OR scrubs, if a change of clothing is necessary
- Spill towels
- Waste bags
- Cytotoxic labels
PTERYGIUM SURGERY WITH MITOMYCIN C: A NURSING PERSPECTIVE

- review frequently the existing policies and procedures in all departments including nursing, pharmacy, infection control, occupational safety, materials management, and environmental services/housekeeping
- keep all employees updated on the Safety Station, the location of the spill kit, available forms and Material Safety Data Sheet (MSDS) information
- post these phone numbers: emergency services, employee health services, occupational safety, pharmacy, and environmental services

More information on safe handling of cytotoxic drugs can be found on the following websites:

American Journal of Nursing (AJN)
nursingworld.org

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Use of Mitomycin C in Pterygium Surgery

by Gaston O. Lacayo, III, MD

What Is a Pterygium?

A pterygium (from the Greek word pterygium for wing) is an elastotic degeneration of the conjunctiva, which produces fibrovascular subepithelial tissue and invades the superficial cornea. It is commonly a wedge-shaped interpapillary lesion that extends from the bulbar conjunctiva over the limbus onto the cornea. It has a higher prevalence along the periorbital regions, supporting a possible association with ultraviolet exposure along with dust and wind.\textsuperscript{1}

Indications for pterygium removal include excessive foreign body sensation, decreased visual acuity from the pterygium invading the visual axis, decreased vision from induced astigmatism, chronic or recurrent inflammation, and recurrent pterygium.

Pterygium Surgery

Simple pterygium excision with bare sclera technique is associated with high recurrence rates of between 29.2% and 88.9%.\textsuperscript{2} Over the years, various techniques have evolved to try to reduce these recurrence rates because recurrent pterygia are commonly more aggressive and difficult to treat compared to a primary pterygium. Primary closure of conjunctiva, rotational autografts, free conjunctival autografts, and amniotic membrane grafts are all used with varying amounts of success.\textsuperscript{3} Combining conjunctival autografts with use of mitomycin C (MMC) has shown to significantly reduce recurrent rates to as low as 2%, significantly better than prior techniques.\textsuperscript{4}

Mitomycin C is a Federal Drug Administration (FDA) approved anti-neoplastic agent used to treat certain cancers. It is an alkylating agent that inhibits DNA-dependent RNA synthesis. It is essentially an antimetabolite, which modulates healing by inhibiting fibroblastic proliferation. Over the past twenty years it has become a popular off-label adjunctive treatment for a variety of ophthalmic conditions. The most common use of MMC is as an antifibrotic agent in the prevention of scarring after glaucoma trabeculectomy surgery. However, the use of MMC has become increasingly common in a variety of corneal conditions including pterygium surgery and corneal haze prophylaxis in refractive surgery.\textsuperscript{5} Postoperative use of MMC in the treatment of pterygium was first reported in 1963. Over the years, intraoperative use of MMC has become more common than postoperative use for pterygium management.

Standard intraoperative ophthalmic MMC concentrations are from 0.01% to 0.04% (0.1 mg/mL to 1.4 mg/mL) with a duration time of 1 to 5 minutes. The concentration and duration are determined by the surgeon based on surgeon preference. Longer durations and higher concentrations are more common for recurrent or aggressive pterygia. Commonly, 0.02% is used for two minutes on primary cases and four to five minutes for recurrent pterygia. Extreme care is warranted on dosage, duration, and location of use of MMC due to serious side effects including scleral thinning, scleral melting, corneal epithelial toxicity, and early cataract formation even years after its original use.\textsuperscript{6}
USE OF MITOMYCIN C IN PTERYGIUM SURGERY

Figure 1. Intraoperative view of pterygium.

Figure 2. Placement of MMC-soaked sponge below leading edge of host conjunctiva.

Figure 3. Placement of fibrin glue on bare sclera.

Figure 4. Conjunctival autograft adhered to bare sclera with fibrin glue.

Technique

Local anesthesia (lidocaine 2% mixed with bupivacaine 0.75%) is given in a peribulbar fashion. Topical 2% lidocaine jelly is used on the ocular surface. A lid speculum is used to expose the surgical field (Figure 1). One percent lidocaine with 1:100,000 epinephrine is used on a 30-gauge needle to balloon up a subconjunctival wheal under the pterygium. 7-0 Vicryl sutures are used for traction at the 6 o’clock and 12 o’clock positions of the corneal limbus to help rotate the globe and improve exposure to the pterygium. Sharp Westcott scissors are then used to excise the pterygium head from the limbus and cornea. The head is truncated and sent to pathology for review. Blunt Westcott scissors are then used to remove tenons insertions from the sclera.

Balanced salt solution (BSS) is injected into the subconjunctival space to help inflate and delineate the fibrovascular matrix within the subtenons tissue. The subtenons tissue is carefully excised away from the conjunctiva and recti muscles. Limited electrocautery is used to help with hemostasis and limit scleral scarring and ischemia. A diamond burr is used to polish the cornea and create a smooth transition from limbus to cornea.

Surgical spear sponges are cut into small pieces and soaked in 0.02% MMC. Individual pledgets are then placed below the leading edge of the remaining conjunctiva (Figure 2). Careful attention should be taken to not expose the bare sclera to the MMC and to limit the exposure over the rectus muscle. These pledgets are then removed after the determined time
(1 to 5 minutes) and the eye is thoroughly irrigated with BSS to remove any amount of residual MMC from the ocular surface. A free conjunctival autograft may be harvested from the superior temporal aspect of the globe or an amniotic membrane graft may be placed on the ocular surface to cover the bare sclera. Tisseel™ fibrin sealant (Baxter Healthcare Corp., Deerfield, IL) is then used to fixate the graft onto the globe. Many surgeons find it easier to apply each element (thrombin and fibrinogen) separately in order to control the amount placed on the surface (Figure 3). Once both elements are combined, the graft is slid across the cornea onto the bare sclera and a muscle hook is used to smooth out the graft. Fixation is usually completed within 30 seconds (Figure 4). The remaining three sides of the conjunctiva are similarly attached with application of the fibrin glue, muscle hook, and light pressure. The graft is tucked below the host conjunctiva to provide a smooth transition zone for the epithelial cells to migrate onto the graft.

Postoperatively, each patient is treated with a topical antibiotic and steroid 4 times daily. The antibiotic is discontinued once the corneal epithelium is healed, and the steroid is tapered off and discontinued over a period of one to three months.

Summary

The role of MMC continues to expand in ophthalmology. Current studies indicate that MMC is a viable and safe adjunctive treatment in pterygium surgery. Although both intraoperative and postoperative topical applications of mitomycin C are effective at preventing pterygium recurrence, intraoperative use has several advantages. The main benefit is that the surgeon has control over the concentration and duration of the application, thereby obviating problems of patient compliance and toxicity, which increases dramatically with cumulative doses. While longer follow-up is needed to validate the future role of MMC in ophthalmic surgery, recent developments have corroborated past findings and shown great promise in its continued success.

References

Preparation for the Use of Mitomycin C in a Trabeculectomy Procedure

by Annquinetta F. Dansby-Kelly, RN, CRNO

Mitomycin C is considered by the FDA as an anti-neoplastic agent used to treat certain cancers. Mitomycin C is used off-label in trabeculectomy filtration procedures to treat glaucoma. There isn't a universal standard operating procedure (SOP) for the use of mitomycin C in surgical procedures. However, there are basic principles that are observed throughout the ophthalmic community regarding the use and contraindications of mitomycin C.

Mitomycin C is considered a hazardous drug that can potentially cause health risks to the health care worker. It is prudent that anyone involved with the care and handling of mitomycin C should have the appropriate training. They should demonstrate a high level of competence before proceeding with handling this toxic drug. Videos such as "Safe Handling of Hazardous Drugs" can be helpful in understanding the importance of exercising caution while using mitomycin C in a trabeculectomy procedure. The misuse of mitomycin C can cause birth defects, leukemia, organ toxicity and other illnesses.

Personal protective equipment (PPE) should be worn before using mitomycin C. Examples of PPE are gloves, lab coat/gown, safety glasses, etc. The Occupational Safety and Health Administration (OSHA) has published guidelines for the safe handling of these medications since 1986. These guidelines, if implemented, will protect the health care worker from possible injury which could lead to mortality. Chemotherapy gloves are available for facilities that require their staff to wear them.

Mitomycin C should be prepared in a biological safety cabinet (BSC). A BSC has vertical airflow that moves the toxic fumes away from the preparer that are emitted when mixing the medications. Air from the BSC flows into a HEPA (high-efficiency particulate air) filter. This filter is capable of trapping the hazardous toxic emissions. Mitomycin C preparation is usually done in a pharmacy. The pharmacist usually dispenses mitomycin C in containers with a tamper-proof seal, chemotherapy-specific cap and in a yellow chemotherapy bag.

When handling mitomycin C during a trabeculectomy procedure, members of the surgical team should take extreme caution to avoid injury from needle sticks, skin exposure and when transferring the medication to the sterile field. Mitomycin C should be labeled immediately after it is drawn up. The circulating nurse should wear gloves during the transfer of medication. Once received, the scrub nurse should place the syringe in a remote area on the back table. This is an additional step to avoid confusing mitomycin C with other medications. Mitomycin C should not be placed in an open container, as toxic fumes can escape into the air.

During the procedure, care should be taken to ensure that mitomycin C is applied to the incision site only! This is done to prevent the unintended destruction of adjacent tissues. Should this occur, copious irrigation of the site is recommended. Pledgets must be placed in a container or medicine cup. Moisten pledgets with mitomycin C just prior to use. Make sure that the time is monitored appropriately. On average, the pledgets remain on the ocular surface from 1–2 minutes. Overexposure of mitomycin to the scleral bed may cause permanent cell damage. Confirm how much time is needed at the beginning of the procedure and again prior to applying the pledget to
the wound. The time may vary according to the tissue type (thin, scarred, etc.), race of patient and other diseases that may be present.

Always use separate instruments when handling pledgets or if they come into direct contact with the drug. Pledgets should be counted and all pledgets must be removed from the eye after the allotted time.

Drapes, gowns and gloves must be discarded in a yellow chemotherapy disposal bag. Unused mitomycin C should be disposed of in a yellow chemotherapy container. Some facilities may require the unused medication to be returned to the pharmacy for disposal in the hazardous substance "black container." Never dispose of mitomycin C in regular paper trash.

In the event of a spill of a hazardous substance such as mitomycin, the OESO (Occupational & Environmental Safety Officer) requires that an SOP (standard operating procedure) be in place to manage this incident. In other words, each institution must have a policy in place identifying how a spill should be handled. A chemical spill kit should be available in areas where chemotherapy agents are used. This kit contains PPE and necessary items needed to clean up a spill immediately.

Mitomycin C has proven to be effective for the treatment of glaucoma when used in trabeculectomy procedures. Caution should always be observed to prevent injury to the patient and health care providers.

References


Trabeculectomy and the Use of Antimetabolites

by Todd Sleep, MD

What Is Glaucoma?

Glaucoma is the leading cause of irreversible blindness worldwide. It affects an estimated 2.22 million U.S. citizens, or 1.86% of the people, and is expected to double by 2020. Glaucoma causes blindness by damaging the ganglion cell of the retina. As light hits the retina, information is transmitted through the retina to the ganglion cell. The ganglion cell connects the eye to the brain by a series of relay fibers called the nerve fiber layer. It is the collections of the nerve fiber layer leaving the eye that make up the optic nerve. Glaucoma causes premature ganglion cell death by a combination of risk factors such as genetics, age, vascular factors, and intraocular pressure. This progressive damage leads to visual loss that typically affects the peripheral vision first, and finally, the central vision. What makes glaucoma particularly dangerous is that the patient is usually not aware of the vision loss until late in the disease. Vision that is lost from glaucoma is permanent, so early detection is the key to glaucoma treatment.

Glaucoma Treatment

The goal of glaucoma treatment is to lower the intraocular pressure (IOP). Multiple studies have shown that lowering the IOP reduces the risk of glaucoma progression. IOP can be lowered through medical and/or surgical options. Medicines are typically very effective in lowering the IOP and consist of eye drops and occasionally oral agents. Although medicines work for many patients, some people may eventually require surgical interventions to lower the IOP. There are many types of surgical options for glaucoma, ranging from lasers to implantable devices. Although in the future this may change, the current gold standard for glaucoma surgery remains the trabeculectomy.

Overview of Trabeculectomy

The ultimate goal of the trabeculectomy is to lower the intraocular pressure of the eye by making a new passage for aqueous humor to drain from the eye. Essentially, we make an artificial fistula from the anterior chamber of the eye to underneath the conjunctiva. This leads to a small “blister,” or bleb, of aqueous to collect under the conjunctiva. Every surgeon has her or his way of accomplishing this fistula, but basically the surgical technique can be broken down into two categories. The names can be kept straight by thinking of the location of the conjunctiva left undisturbed. The two categories of trabeculectomy are fornix-based versus limbal-based. In the fornix-based trabeculectomy, the incision is made at the limbus, leaving the base of untouched conjunctiva in the fornix. In the limbal-based trabeculectomy, the incision is made in the fornix, leaving the limbal conjunctiva untouched.

Trabeculectomy Technique

After the conjunctiva is incised, a dissection is carried down to the bare sclera. Antimetabolites are placed on the bare sclera underneath the conjunctival pocket and left to set for a desired time period. A partial thickness scleral flap is made. The scleral flap is lifted and dissected toward the limbus. The anterior chamber is entered
with a blade underneath the scleral flap. Ideally this opening is made through the cornea. To ensure the opening is made in the desired location, a crescent blade is used to tunnel into the cornea. The opening, or ostomy, is enlarged typically with a Kelly punch. Through this opening a small portion of iris is typically but not always removed by the surgeon. This process is called an iridectomy. The main purpose of an iridectomy is to keep the iris from clogging up the ostomy made by the Kelly punch. The disadvantage of the iridectomy is that the iris is very vascular. Removing a portion of it frequently causes bleeding and increases the amount of post-op inflammation. I prefer to make an iridectomy with a pair of jewelers forceps and Vannas scissors only if I feel there is a chance the iris will occlude the ostomy post-op. Having intraocular cautery available just in case the iris bleeds is always a good idea. A bipolar cautery system with a pencil tip should do the job. The scleral flap is then closed with 10-0 nylon sutures. The most dangerous time during the surgery is from the time the anterior chamber is entered to the time the scleral flap is closed. This is because the eye typically has a pressure of zero from loss of aqueous. The sudden pressure change in the eye or an unexpected cough can cause hemorrhaging from inside the eye called a suprachoroidal hemorrhage. This serious but rare complication can cause loss of vision or even loss of the eye. It is important to have all of the needed instruments available and ready so that the iridectomy and closure of the scleral flap occur in a timely fashion. Tension on the sutures closing the scleral flap is titrated to maintain the desired aqueous flow. To determine the desired flow of aqueous the surgeon will inject BSS through a paracentesis and watch the flow using Week-cell sponges around the scleral flap. Once flow is felt to be appropriate, the conjunctiva is closed and Week-cell sponges are used to ensure the closure is watertight so that aqueous is confined to the subconjunctival space.

Why Use Antimetabolites?

One of the hardest parts of performing a successful trabeculectomy is modulating the healing process. Ideally we want to limit the healing process so the fistula remains open to the level where the IOP stays at the surgical goal. Wound healing occurs by a complex interaction of hemostasis, inflammation, cell proliferation, and tissue remodeling. Attempts to modulate the healing process in glaucoma surgery by using the antimetabolites 5-fluorouracil (5-FU) and mitomycin C (MMC) began in the early 1980s. In the late 1980s the results of the landmark Fluorouracil Filtering Surgery Study were published. The study found lower IOP, longer time to failure, and decreased need for reoperations in patients receiving 5-FU during their trabeculectomy. This study was very demanding on patients, as they received...
TRABECULECTOMY AND THE USE OF ANTIMETABOLITES

a regimen of 21 post-op injections of 5 mg of subconjunctival 5-FU. Nonetheless, this study helped pave the way for the use of antimitabolite use in glaucoma. 5-FU works by blocking DNA synthesis by acting as a pyrimidine analogue and MMC is an alkylating agent that inhibits DNA-dependant RNA synthesis. Essentially, both of these antimitabolites modulate the healing process by inhibiting cellular proliferation. 5-FU and MMC are placed intra-operatively to the bare sclera typically by soaking polyvinyl acetate sponges in the antimitabolite and placing these sponges underneath the conjunctival pocket. Standard MMC concentrations are from 0.1 mg/ml to 0.5 mg/ml with a duration of 1 to 5 minutes. The duration and concentration can be varied according to surgeon preference. In patients with previous scarring, history of uveitis, or neovascular glaucoma the risk of failure from healing is higher. There is some evidence that varying the concentration has more effect than varying the duration and that these variables may want to be adjusted depending on the surgeon’s perceived risk of the patient to heal the fistula closed. This said, there is inadequate evidence at the present time to claim superiority of one regimen of MMC. 5-FU and MMC are powerful antimitabolites and as such caution must be used to ensure that the medication is applied only to the desired sclera and that the eye and any instruments that touch the medication are irrigated profusely after exposure. 5-FU and MMC have been associated with increased risk of bleb leaks post-operatively, suggesting a higher risk of endophthalmitis, corneal epithelial toxicity, and higher risk of cataract formation. A 2005 Cochrane review of intra-operative MMC use in glaucoma found that the risk of surgical failure of trabeculectomy was lower for patients who had lower IOPs post-operatively, and apart from cataract formation, patients did not have an increase in serious side effects. As such, most patients undergoing a trabeculectomy will have intra-operative MMC or 5-FU used as an adjunct to modulate the healing response.

Post-operatively to limit the healing process patients are usually placed on high doses of topical corticosteroids. I will place patients on Prednisolone Forte 1% every hour while awake for the first week, and depending on my impression of healing at post-operative checks, will taper accordingly. If patients continue to heal aggressively on frequent Prednisolone Forte 1%, I will augment their surgery with an injection of 5 mg of subconjunctival 5-FU. It is not uncommon to give 5-FU more than one time in the post-operative period. If the intraocular pressure is too high, we commonly cut the scleral flap sutures with a laser (laser suture lysis). The most difficult portion of the trabeculectomy is managing the post-operative healing so that the intraocular pressure remains at the targeted goal. It is the combination of topical medications, subconjunctival injections, and suture lysing that help make this surgery successful.

Conclusion

As the prevalence of glaucoma continues to grow, the number of surgical procedures performed for glaucoma will also likely increase. A basic understanding of the principles of the trabeculectomy as well as a familiarity with antimitabolites used during surgery is important for anyone working in surgical ophthalmology.

References

The Use of Mitomycin C and Photorefractive Keratectomy: Role of the Nurse and the Technician

by Jane Katzen, RN, BSCN

- Mitomycin C is a powerful antibiotic and antimetabolite currently being used to treat and prevent corneal haze after surface excimer laser ablation.
- The medication is being used off-label and it can be extremely toxic unless it is carefully controlled. All ophthalmic personnel involved in the administration of the drug must be well trained in the safe handling of the medication.
- The patient should be consented on the use of mitomycin C and all questions regarding the use of the off-label application should be addressed by the physician prior to the day of surgery.
- Written policy and procedures should be in place, including safe transport, storage and handling of the medication to protect both the patient and ophthalmic personnel.
- The medication must be clearly labeled “hazardous” by the pharmacy and should be delivered in an opaque container, as it must be protected from light. It should be refrigerated if not used immediately.
- Personal protective equipment should be worn by all personnel administering the medication. The patient should be protected with the use of a plastic cap and protection for the skin and the eyes when the medication is irrigated from the eye.
- The nurse and/or technician should utilize a no-touch technique when applying the mitomycin C to a circular corneal light shield (sponge). The nurse and technician should be extremely careful when dispensing the medication to avoid contact or needle sticks. The medication must be clearly labeled. The exact duration of application and the concentration of the mitomycin C must be carefully monitored by the refractive team in order to reduce complications which could be induced by application of the drug. The use of 0.02% (0.2 mg/mL) applied to the central stromal corneal bed for a period of 12–120 seconds has been suggested in the literature. The eye is then irrigated with a minimum of 30 mL of balanced salt solution in order to remove most of the drug from the eye.
- Disposal of cytotoxic waste (needles, syringes, vials, ampules and remaining mitomycin) should be placed into a yellow puncture-resistant, leak-proof container which is labeled for cytotoxic waste. Contaminated disposable supplies must be discarded in a biohazard waste container.
- Terminal cleaning of all non-disposable equipment and surfaces should include a thorough cleansing with a mild detergent and thorough rinsing of all surfaces and equipment.
- A spill kit should be available in the procedure room with all supplies needed to clean up the spill. The contents of the kit should be labeled on the outside of the container.

References
Mitomycin C: Use in Refractive Surgery

by Parag A. Majmudar, MD

Mitomycin C is an antimetabolite that initially burst onto the ophthalmic scene over twenty years ago, but has seen even greater increase in usage over the past several years. From glaucoma surgery to various corneal disorders, MMC appears to be a viable tool in the management of scar and haze formation. With the constant evolution of refractive surgery over the past 15 years, MMC has come to the forefront as a modulator of corneal wound healing after excimer laser surface ablation. In the latest ASCRS survey, 83% of refractive surgeons indicated that they routinely use MMC with their patients. This article will describe the various indications, techniques and current trends of MMC application in corneal refractive surgery.

Historical Perspective

Mitomycin C (MMC) is an antibiotic isolated from the broth of Streptomyces caespi- tatus which has been shown to have antimetabolic activity. It selectively inhibits the synthesis of deoxyribonucleic acid (DNA). The guanine and cytosine content correlates with the degree of mitomycin-induced cross-linking, resulting in suppression of DNA replication and cellular mitosis. As currently approved, MMC is indicated for intravenous administration in the treatment of stomach and pancreatic cancer. Its first reported use in ophthalmology was in 1967, when Murakami reported its use in pterygium surgery. Subsequent to this date, it has become a standard of care adjuvant in pterygium surgery and glaucoma filtration (trabeculectomy) surgery. As its method of action selectively inhibits fibroblast cell proliferation, ophthalmologists use it to control scarring and postoperative pathogenesis, as this prevention of fibroblast proliferation is the key pathophysiologic event in the formation of scarring. In recent years, the use of MMC in keratorefractive indications has been growing in acceptance, as stromal tissue can transform to myofibroblasts after laser surface ablation.

The end result is deposition of ground substance, abnormal collagen, and, ultimately, clinically significant haze. As a result, there has been increased utilization, both prophylactic and therapeutic, in excimer laser ablation applications, e.g., PRK, LASEK, Epi-LASEK. There also exist case reports documenting successful use of MMC in the treatment of LASIK flap complications, e.g., fibroblast in-growth.

The first non-clinical publication discussing the use of MMC in prophylaxis of corneal haze post-laser keratectomy occurred in 1991, when Talamo et al. documented the efficacy of MMC in prophylaxis of excimer laser PRK-induced haze in a rabbit model. In this study, eyes treated with MMC developed significantly less haze than eyes treated with only steroids and/or erythromycin. The first clinical publication in this regard was from Majmudar et al., describing a series of patients where subepithelial haze secondary to RK or PRK was successfully treated with epithelial removal, corneal debridement, and MMC application. The authors postulated that the anti-proliferative effect of MMC on the activated stromal keratocytes might prevent further abnormal collagen deposition and haze formation. As a result of this and subsequent studies, a protocol that is now widely accepted and in common use was developed for the therapeutic use of MMC post-surface laser ablation for the treatment of sub-epithelial haze.

The success and acceptance of MMC in its therapeutic applications in ablative refractive surgery led to the next step forward: the use of MMC in prophylaxis of haze
formation immediately following ablative refractive surgery. As the depth of ablation appeared to correlate to an increased risk of haze formation, the therapeutic protocol was expanded to include prophylactic use in patients undergoing PRK for high myopia (−6.00 to −10.00 diopters), prompted by a publication by Carones et al. in 2002.9

Current Trends

Subsequent to these initial reports, substantial data emerged validating the safety and efficacy associated with the prophylactic use of MMC for prevention of sub-epithelial haze following ablative refractive surgery. In a prospective study, Gambato et al. showed that high myopes treated with PRK and prophylactic MMC had significantly less postoperative haze at 12, 24, and 36 months when compared to the control eyes that were not treated with MMC.7 Control eyes showed significantly greater activated keratocytes and extracellular matrix the physiologic cause of the visual field disruption.

In 2004, Hashemi et al. published on a similar cohort of patients. In 54 eyes of 28 highly myopic patients (≥ 5D, with a mean correction of −7.08 D), no eyes demonstrated measurable haze at 3 and 6 months. Furthermore, while contrast sensitivity decreased immediately following surgery, MMC (0.2 mg/mL)-treated patients showed an improvement of 1.5 at final follow-up.6 Continued use and investigation have resulted in an expansion of indications beyond mere prophylaxis in high-risk PRK patients. Complications secondary to primary failed keratorefractive procedures, e.g., LASIK, RK, PKP, such as buttonholed flaps, are often best treated with surface ablation procedures such as PRK. In this way, refractive functionality can be restored without the risks inherent to a flap, while the inclusion of prophylactic use of MMC within the surgical protocol has resulted in a reduced instance of sub-epithelial haze. Multiple independent studies have confirmed the efficacy of prophylactic MMC in surface ablation procedures in indications as varied as trans-epithelial phototherapeutic keratectomy (PTK)/PRK, wave-front guided PRK secondary to a previous buttonholed LASIK procedure,8 and PRK in an anisometropic hyperopic patient after PKP for keratoconus.8

MMC Protocol

Our current recommendation for haze prophylaxis with MMC is to initiate an informed consent discussion with all patients who may be at high risk for developing haze after PRK. In the past, high risk constituted patients with high myopia (≥ −6D), but newer excimer lasers and wavefront-guided procedures may result in deep ablations even in the setting of lower myopia. Since the development of haze is probably related to the total energy delivered to the cornea, and since this is directly proportional to the depth of ablation, our criterion is to consider the high-risk patient one who will have an ablation of 75 µm or greater. We use MMC 0.02% (or 0.2 mg/mL) applied to the stromal bed on a saturated corneal light shield for a selected exposure time after PRK. The main advantage of the shield is to help avoid contact with any other ocular structure and limit the contact of MMC to only the central cornea.

Toxicity?

Data from hundreds of published reports confirms that a single, intra-operative application of MMC appears safe and effective. However, as with any therapeutic agent, adverse events have been documented in the literature, which include reports of toxicity. There have been reports of corneal edema, glaucoma, corneal perforation, iritis, and photophobia following the use of MMC in pterygium surgery.10 Likewise, a case report of permanent corneal edema secondary to PTK and prolonged MMC use was documented by Pfister.11 However, this case report is instructive, in that the patient was treated postoperatively with 0.02% MMC a total of 14 drops over a period of 6 days subsequent to PTK for recurrent erosions secondary to basement membrane dystrophy. Mitomycin is believed to be toxic to the corneal endothelium, and such extended exposure is likely to have resulted in dysfunctional endothelial cells, a low endothelial cell count, permanent corneal edema, and, ultimately, corneal transplant. The literature shows a correlation between adverse events and the use of MMC in high concentrations, prolonged exposure/administration, and/or when delivered in limbal applications. Likewise, there has been a single, non-clinical (rabbit) demonstration of dose-dependent increased corneal thickness, reduced corneal clarity, and endothelial apoptosis after a single application of MMC.12

We regard these reports as instructive, in that they highlight the risks associated with the use of MMC in high concentrations and/or with extended exposure. These complications can be dramatically reduced by limiting use to a single application of low-concentration MMC, delivered to the central avascular cornea for a brief period of time, followed by copious irrigation of the treatment site with a minimum of 30 mL of balanced salt solution. Observing these protocols within our practice has shown toxic adverse events reduced to zero, documented by twelve years of follow-up. Unpublished data from several researchers supports the confocal evidence from Gambato et al. that there is no endothelial toxicity, and no separate effect on keratocyte density compared to PRK alone, but longer follow-up is needed.
Our current protocol for the prophylactic use of MMC is to use a 0.02% concentration for 12 seconds. The therapeutic protocol, in the presence of existing haze, is for application of a 0.02% concentration, but for two minutes, subsequent to removal of the haze. This protocol is supported by literature demonstrating reduced toxicity tied to lower concentration and decreased exposure time. The reduced exposure time was supported by no difference in corneal haze scores and/or refractive outcomes, regardless of exposure time, randomized to 12 seconds, 60 seconds, and 2 minutes. There have been reports of the successful prophylactic use of 0.01% MMC with no toxic adverse events, and non-clinical (rabbit) demonstration of effectiveness in concentrations as low as 0.002% and exposure times ranging from 12 seconds to 2 minutes. Additionally, a single report has shown that ultra-low-concentration MMC (0.002%) can be effective in preventing haze in low corrections, but not as effective as 0.02% when used on patients requiring higher correction.

Summary

The role of MMC continues to expand in ophthalmology. There is undoubtedly strong interest in its role in refractive surgery. Current studies indicate that MMC is a viable and safe adjunctive treatment in preventing and treating scar formation in eyes previously affected by visually disabling complications. While longer follow-up is needed to validate the future role of MMC in refractive surgery, recent developments have corroborated past findings and shown great promise in its continued success.

References

Conclusion

The positive outcomes associated with the off-label use of mitomycin C (MMC) in ophthalmic procedures have led to FDA approval of Mitosol (ophthalmic mitomycin C). It is likely that the use of MMC will increase as more ophthalmologists are trained to use this medication for these procedures and additional uses are explored. Knowledge of the safe handling, use, and disposal of MMC is critical to assure the safety of healthcare providers and patients. When posted in the Operating Room, tips for the safe use of MMC such as those on the tip sheet that follows, may decrease the possibility of injury.
OPHTHALMIC MITOMYCIN C:
TOP TIPS FOR SAFE HANDLING, USE, AND DISPOSAL

Mitomycin C (MMC) is an antimetabolite used in ophthalmic procedures for its antifibrotic effect. MMC is a toxic and potentially hazardous chemotherapeutic drug that must be handled with care to protect healthcare providers and patients. The following steps are recommended to prevent injury and document appropriate use:

STORING OF MITOMYCIN C
Store MMC according to the manufacturer’s directions.

PREPARING FOR MITOMYCIN C USE
Document the planned use of MMC on the operative consent.
Include the planned use of MMC in the preoperative time out.
Wear appropriate Personal Protective Equipment including gloves, mask, face shield and impervious gown. MMC should not be handled by anyone breastfeeding, pregnant or trying to conceive.
Check the expiration date.
Prepare the MMC according to the manufacturer’s directions.

ADMINISTERING MITOMYCIN C
Follow the steps for safe drug administration:
• Correct patient
• Correct drug
• Correct dose/strength
• Correct route/site
• Correct application time
Avoid exposure to unintended tissue.
Irrigate MMC copiously from the eye following administration.

DOCUMENTING THE USE OF MITOMYCIN C
Document the following information on the O.R. record:
• Strength of MMC administered
• Amount of time MMC was administered
• Number of MMC saturated sponges placed in and removed from the patient’s eye.
• Lot number from MMC package

DISPOSING OF MITOMYCIN C
Dispose of MMC container, soaked sponges, and surgical waste materials that have come in contact with MMC (gowns, gloves, patient drapes) in an appropriate chemotherapy disposal container.

HANDLING INSTRUMENTS USED WITH MITOMYCIN C
Restrict the instruments used to handle MMC sponges from use in other parts of the surgical procedure.
Rinse and clean instruments used to handle MMC prior to sterilizing them for use on a subsequent case. Consider using disposable instruments to handle MMC sponges.

MANAGING ACCIDENTAL RELEASE (SPILL) / HUMAN EXPOSURE
Prevent exposure with personal protective equipment including gloves and safety glasses.
Absorb the spill with paper or cloth.
Dispose of contaminated items in an appropriate chemotherapy disposal container.
Refer to the Material Safety Data Sheet (MSDS) for specific first aid measures if human exposure occurs.

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For information on related continuing education please visit www.actioned.org.

Printing of this document is supported by an unrestricted educational grant from Mobius Therapeutics.™
For additional information on the use of Mitomycin C in ophthalmology see the Education section at http://www.mobiustherapeutics.com/education/education.cfm.

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Test Your Knowledge

Mitomycin C: Indications for Use and Safe Practice in Ophthalmology

Post-Test Preview

ASORN offers learners the opportunity to earn continuing education credits by completing a post-test that has been developed to complement this educational resource. The post-test preview is included below. Continuing education credits may be obtained by accessing the post-test on the ophthalmology continuing education web site www.actioned.org. The type and number of credits is noted in the product detail associated with this activity on the ACTIONED site and also on the ASORN web site at www.asorn.org. ASORN-provided nursing contact hours may be used toward recertification for the Certified Registered Nurse in Ophthalmology (CRNO) designation. Other types of credits may also be available. Please review the activity details located in the Course Catalog at www.actioned.org, contact the ASORN office for an update, or check the ASORN web site at www.asorn.org.

To receive continuing education credits for this activity, read all articles included in the publication, submit your registration payment and complete the evaluation and post-test available at www.actioned.org. Available continuing education credits will be awarded to individuals who achieve a score of 80% or higher.

At www.actioned.org the learner will select the most appropriate response for each test question that follows below.

1) All of the following are potential risks when using mitomycin C for ophthalmic procedures except:
   A. corneal or sclera thinning
   B. retinal detachment
   C. secondary glaucoma
   D. sudden onset mature cataract

2) Mitomycin C is a/an:
   A. emollient
   B. lubricant
   C. vesicant
   D. desicant

3) Surgical preparation begins in the
   A. surgical scheduling office
   B. operating room
   C. pre-surgical area
   D. physician’s office

4) A spill kit for cytotoxic material clean up is
   A. opened for each procedure
   B. disposed of in the regular trash
   C. used to dispose of items from the surgical procedure
   D. immediately available in the event of a spill of MMC

5) Who is responsible for monitoring the MMC at all times on the sterile field?
   A. the circulating nurse
   B. the scrub person
   C. the physician
   D. the physician’s assistant

6) Safe handling of MMC includes
   A. rinsing instruments with saline or balanced salt solution
   B. wearing a high filtration surgical mask
   C. using a biohazard label for paper waste
   D. disposing of waste items exposed to MMC separately
7) Accidental exposure to MMC is minimized by
A. wearing two pair of surgical gloves
B. washing hands with soap and water
C. completing hand-off communication
D. practicing universal precautions

8) Which of the following is an indication for pterygium removal?
A. Decreased visual acuity
B. Corneal haze
C. Scleral thinning
D. Epithelial down-growth

9) The time duration for MMC application on a primary pterygium excision is
A. 1 minute
B. 2 minutes
C. 3 minutes
D. 4 minutes

10) A serious side effect of MMC application is
A. scleral thinning
B. increased intraocular pressure
C. decreased visual acuity
D. fibroblastic cell proliferation

11) The usual material used as a graft following pterygium removal is a
A. scleral patch graft
B. limbal stem cell graft
C. conjunctival auto-graft
D. lamellar corneal graft

12) Post-operative topical drops includes the use of a(n)
A. miotic
B. mydriatic
C. anesthetic
D. steroid

13) Mitomycin C is classified by the FDA as a/an:
A. anti-inflammatory used to treat inflammation
B. antineoplastic agent used to treat cancer
C. antibiotic used to treat infections
D. anti-emetic used to treat nausea

14) The inappropriate handling of mitomycin C can cause
A. heart failure
B. kidney failure
C. birth defects
D. auto-immune disease

15) Standards for safe handling of chemotherapeutic agents are published by:
A. Occupational Safety and Health Administration (OSHA)
B. Center for Disease Control (CDC)
C. World Health Organization (WHO)
D. National Institute for Occupational Safety and Health (NIOSH)

16) Personal protective equipment should:
A. be available in case of large spills only
B. include gowns, lead aprons and safety goggles
C. be worn when handling mitomycin C
D. not be worn in appropriately ventilated cabinets

17) Instruments that are used to handle mitomycin C should be
A. kept separate from the other instruments
B. disposed of in the sharps containers
C. cleaned immediately with alcohol
D. instruments that are not used often

18) The goal of the trabeculectomy procedure is to
A. increase intraocular pressure
B. prevent neovascularization
C. decrease intraocular pressure
D. place a permanent drainage tube

19) Wound healing occurs by a complex interaction of
A. hemostasis, inflammation, cell proliferation and tissue remodeling
B. inflammation, cell proliferation, tissue remodeling and miosis
C. hypotony, inflammation, tissue remodeling and hemostasis
D. hemostasis, neovascularization, tissue remodeling and miosis
20) Another antimetabolite used for wound healing modulation is
A. methotrexate  
B. 6-Mercaptopurine  
C. clofarabine  
D. 5-Fluorouracil

21) Antimetabolites were first used in glaucoma surgery in
A. the 1960s  
B. the 1970s  
C. the 1980s  
D. the 1990s

22) After mitomycin C has been applied for the prescribed amount of time the eye should be
A. examined for excessive bleeding  
B. irrigated profusely with balanced salt solution  
C. irrigated with an antibiotic solution  
D. observed for 5 minutes for signs of infection

23) Mitomycin C is an antibiotic/antimetabolite used in corneal refractive surgery to
A. treat and prevent haze formation after surface excimer laser ablation  
B. stabilize post treatment refraction  
C. prevent regression  
D. reduce postoperative pain

24) Written policies and procedures for mitomycin C
A. are not required since it is a topical medication  
B. are not required in a laser only center  
C. should address medication exposure time  
D. should cover issues that affect personnel and patient safety

25) Cytotoxic waste, including needles and syringes, should be disposed of
A. in the regular trash along with other items from the procedure  
B. in a yellow, puncture resistant, leak proof container  
C. by double bagging in red bags  
D. in a clear plastic container so the contents can be visualized

26) Mitomycin C was initially approved for intravenous use in the treatment of
A. ocular melanoma  
B. haemophilus influenza  
C. stomach and pancreatic cancer  
D. staphylococcus epidermis

27) The first reported use of mitomycin C in ophthalmology was for
A. pterygium surgery  
B. glaucoma filtration surgery  
C. oculoplastics surgery  
D. refractive surgery

28) The first clinical application of mitomycin C in keratorefractive surgery was for
A. prevention of epithelial down-growth post LASIK  
B. treatment of sub-epithelial haze post RK or PRK  
C. prophylaxis of haze post PRK for high myopia  
D. prevention of epithelial down-growth post ALK

29) Extended corneal exposure to mitomycin C is likely to result in
A. epithelial down-growth post LASIK  
B. increase in refractive error post PRK  
C. basement membrane dystrophy  
D. dysfunctional endothelial cells, low endothelial cell count and corneal edema

30) Research states that a safe and effective regimen for the application of mitomycin C in corneal refractive surgery is
A. 14 drops of 4% mitomycin C placed on the cornea for a period of 6 days  
B. 0.02% of mitomycin C applied to the corneal stroma for a minimum period of 5 minutes  
C. a single application of low concentration mitomycin C applied to the central cornea for a very brief period of time and followed by a minimum irrigation of 30 ml of balanced salt solution  
D. 2.0% mitomycin C drops two times a day for a period of 3 days
American Society of Ophthalmic Registered Nurses

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