A Financial Evaluation of the Centralized Repackaging of Intracameral Moxifloxacin for Cataract Surgery and Its Impact on Cost Reduction

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Abstract

Background: Extensive evidence-based literature supports the use of intracameral (IC) moxifloxacin for the prevention of postoperative endophthalmitis after cataract surgery. The Aurora Pharmacy Packaging Center (APPC) has developed a process for centrally preparing IC moxifloxacin. **Purpose:** The aim of this study was to evaluate the centralized preparation of IC moxifloxacin production for quality assurance and to quantify a potential reduction in costs. **Methods:** The APPC's compounding procedure of IC moxifloxacin was evaluated using United States Pharmacopeia (USP) Convention 797 standard and compared with practices described in evidence-based literature. Patients who received IC moxifloxacin intraoperatively from one of 3 ophthalmologists during cataract surgery performed between February 15, 2016, and August 15, 2016, were identified using electronic health records. Cost savings were calculated by reviewing costs associated with drug supplies used by the APPC. **Results:** The APPC process for the centralized preparation of IC moxifloxacin was deemed compliant with USP 797's sterile compounding standards. USP 797 validation criteria included proper sterile technique, equipment, room sterility and pressure, beyond use dating, and storage. Implementation of the centralized production of moxifloxacin reduced the direct product cost per surgery from \$140 to \$20 (a cost savings of \$120 per surgery). There were 459 cataract surgeries analyzed during the study period, resulting in a savings of \$55 080 over 6 months. **Conclusion:** The APPC's centralized compounding procedure was found to be compliant with pharmacy compounding standards and to yield significant cost savings.

Keywords

compounding, cost effectiveness, eye, ear, nose, throat

Introduction

Cataracts are the leading cause of blindness and vision loss in the United States, with more than 20 million Americans over the age of 40 years affected with this condition.¹ Currently, approximately 60% of Medicare vision spending is due to cataract surgery.¹ It is estimated that the patient population needing cataract surgery will increase to 30 million by 2020, a near 50% increase.^{1,2} Cataract surgery is a significant risk factor for endophthalmitis, a serious ocular infection. Although rates of endophthalmitis are relatively low in the United States and Europe (0.40–2.65 per 1000 persons), this infection often leads to irreversible vision loss.²

The use of intraoperative intracameral (IC), an injection into the eye cavity, moxifloxacin for the prevention of endophthalmitis after cataract surgery has been endorsed for over a decade. The European Society of Cataract & Refractive Surgeon's (ESCRS) 2007 study on cataract

antibiotic prophylaxis reported a 5-fold increased risk of postoperative endophthalmitis (POE) for those who did not receive IC cefuroxime.³ There is ample evidence to support the safety and efficacy of IC moxifloxacin, but the literature lacks an adequate description of IC injection preparation.^{3–11} The widespread and increasing frequency of cataract surgery, in conjunction with the prevalent use of IC antibiotics for the avoidance of POE, has strengthened the importance for health care systems to identify the most appropriate and cost-effective preparation of IC antibiotics.

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Aurora Health Care - Central IV Pharmacy Compounding Batch Record
Moxifloxacin 0.25 mg per 0.05 mL syringe with 0.25 mL overfill – Refrigerate¹
 Use: Intracameral antibiotic injection given by eye surgeon at end of surgery^{2,3}

Production Date	Final Product	9 day Expiration	Batch Control/Lot #	Actual Yield	Tech	Theoretical Yield	% Yield (85-100%)	RPh
	Moxifloxacin (Vigamox) 0.25 mg/0.05 mL NDC 00065-4013-99							

Product Preparation

1. To determine total quantity of products and desired batch size needed for batch, refer to spreadsheet located at:
 Q:\Pharmacy Share\Central IV Prep\Inventory Management\Supplies Needed For Individual Batches.xls

Record desired batch size here: _____

Ingredients Needed:

Ingredients	SIZE	NDC	MFR	MFR LOT #	MFR Exp Date	QTY INTO ROOM	Tech	RPh*	ADD'L INTO RM	Tech/RPh*
Moxifloxacin hydrochloride (Vigamox)† Sterile Topical Ophthalmic Soln. 0.5% bottle	3 mL	0065-4013-03	Alcon							

†Only Vigamox (the no preservative additive-free version of moxifloxacin) can be used. Do NOT use Moxeza. The additives are associated with severe toxic anterior segment syndrome.³
 *Medication must be signed off by RPh prior to being brought into Central IV Prep Compounding Room.

Materials Needed:

Materials	SIZE	NDC	MFR	MFR LOT#	MFR EXP DATE	QTY INTO ROOM	TECH	RPH	ADD'L INTO RM	TECH
Fluid dispensing Connector			Braun							
Latex free black luer caps			BD							
5 mL syringes			BD							
19 g needles			BD							
1 mL TB sterile syringes**	REF: 309628		BD							
Sterile 70% Isopropyl Alcohol			Contec							

REASON FOR ADDITIONAL PRODUCTS IN ROOM: In case needed or other: _____

Last reviewed: 1/16 TM, 3/16 JWG
 Q:\Pharmacy Share\Central IV Prep\SOPs\Recipe\Moxifloxacin\Moxifloxacin eye compounding record 3.0.doc 1

Figure 1. Aurora Pharmacy Packaging Center compounding procedure for intracameral moxifloxacin preparation.

The Aurora Pharmacy Packaging Center (APPC) is a 503A compounding pharmacy within Aurora Health Care that repackages bulk pharmaceuticals into unit doses for distribution within the health care system. The sterile repackaging is done at Aurora St. Luke's Medical Center of Aurora Health Care Metro, Inc. The APPC began the centralized compounding of IC moxifloxacin in February 2016 per the request of physicians, due to the increased demand of IC injections and the need for sterile preparation of the product. Reasons to support this practice included limiting the on-site preparation of IC injections and prohibiting between-room transfer of stock antibiotic eye drops for infection control purposes. The APPC procedure involves simple manipulation of the commercially available product into 1-mL syringes, documentation of equipment/products used, and appropriate labeling and storage. The APPC has implemented a compounding procedure outlining their process (Figures 1-3).

To our knowledge, there are few published descriptions detailing the preparation of IC moxifloxacin.^{4,6} Articles reviewed by this evaluation do not correlate the direct financial benefit of such practice.⁴⁻¹¹ This financial evaluation was developed to describe the centralized repackaging of IC moxifloxacin in compliance with the United States Pharmacopeia (USP) 797 standards,¹² and to identify the impact on product cost savings.

Methods

Evaluation of Production Quality

The APPC's centralized compounding procedure of IC moxifloxacin was evaluated using USP 797 standards and compared with evidence-based literature. A systematic literature search using OvidSP and Ovid Medline platforms was used to identify evidence-based literature (limited to publications in English from after the year 2000, with the following primary search terms: intracameral, moxifloxacin, antibiotics, endophthalmitis, safety, efficacy, and cataract). Articles were chosen based on relevance, date of publication, and outcomes. USP 797 criteria were also reviewed and summarized. The final criteria for evaluation are described in Table 1. Pharmacy leadership within the hospital and APPC reviewed the evaluation criteria with respect to the centralized compounding practice, and the procedure was deemed compliant with USP 797 standards per expert consensus.

Cost Savings

Patients who received IC moxifloxacin intraoperatively from one of 3 ophthalmologists during cataract surgery between February 15, 2016, and August 15, 2016, were identified using data from the APPC. Standard procedure involved running weekly reports through EPIC health care software to determine

Product Preparation (cont'd)

****RPh to verify the lot of BD syringes was NOT made using alternative stopper.**
Go to: <http://www1.bd.com/alerts-notice/> and enter either catalog number OR lot number into appropriate box. Click search and review results. Print sheet. Above lots were NOT made with alternative stopper as of last update (USA) _____ (Date according to website).

Performed by _____ (RPh Initials/Date)

2. Printing Batch labels for Final Product:

- Print batch labels using the McKesson/Aesync computer with attached tadpole label printer located on the east side of the 7th Floor Pharmacy, near C-II Safe. (Print enough batch labels to use one for the outer brown bag as well.)
- Log into Aesync program using your username/password. Click under Packaging tab, and locate product name by typing in Moxifloxacin.
 - Label should include the following components:
 - NDC 0065-4013-99
 - moxifloxacin 0.5%
 - 0.3 mL Ophth Inj
 - PACKAGED BY AURORA HEALTH CARE
 - Lot number (Today's date & initials)
 - Expiration date: (9 days from today's date)

Check labels for legibility and correctness as compared to the moxifloxacin formula. Attach a copy of the label from this batch to this sheet. Attach refrigerate auxiliary label here. *Note: If not enough labels are printed in 1st print run, place a label from any subsequent print runs on this sheet as well.*

Of Labels Printed _____ Label Check Performed by: _____ (Tech initials) Verified by: _____ (RPh initials)

Attach Finished Product Labels Below:

PLACE FINISHED PRODUCT LABEL HERE

IF ADDITIONAL LABELS PRINTED

PLACE Refrigerate AUX LABEL HERE

- Transport all supplies needed to ANTE ROOM for disinfection.
- Prior to disinfecting products, clear CIV Prep High Risk Room of any non-moxifloxacin essential products.
- Clean and disinfect countertops and Laminar Flow Hood in accordance with Aurora Policy and USP <797> Standards.
- Verify Laminar Flow Hood # 72366

Performed by: _____ (Tech initials)

- Record temperature, humidity, air pressure and cleaning according to logbook located in CIV Prep High Risk Room.

Performed by: _____ (Tech initials)

Figure 2. Aurora Pharmacy Packaging Center compounding procedure for intracameral moxifloxacin preparation continued.

Product Compounding

- Wipe each ingredient bottle/solution bag with Sterile 70% Isopropyl Alcohol, place in tote with labels and batch record, then pass into clean room.
- Compounding technician will verify that components, labels and batch record are for the same batch prior to the start of the compounding process.

Performed by: _____ (Tech initials)

ACTIVITY	Tech	RPh
1. In sterile compounding area, draw moxifloxacin bottle into 5 mL syringe using a 19 g needle.		
2. Attach fluid dispensing connector to 5 mL syringe, attach on other end 1 mL tuberculin syringe.		
3. Withdraw 0.3 mL into each tuberculin syringe.		
4. Cap with black luer cap. Repeat steps 1 through 3 until batch is complete.		
5. Solutions should be clear/colorless with no particulates, and minimal air bubbles are acceptable.		
6. Document waste here: # OF UNUSED MOXIFLOXACIN BOTTLES Returned: _____		
# OF mLs OF MOXIFLOXACIN WASTED: _____		
# Final Product Syringes WASTED (use tally marks): _____		

Figure 3. Aurora Pharmacy Packaging Center compounding procedure for intracameral moxifloxacin preparation continued.

the anticipated number of cataract surgery cases per week and then compounding the corresponding number of syringes. The number of cases per physician and number of syringes dispensed weekly were recorded in a production log. After the study period, cost savings were calculated by reviewing costs associated with drug supplies. Descriptive statistics were calculated.

Results

Evaluation of Production Quality

The APPC's current process was validated as compliant with USP 797's sterile compounding standards. USP 797 validation criteria included proper sterile technique,

Table 1. Evaluation of Aurora Pharmacy Packaging Center Compounding Procedure With USP 797 Standard Criteria.¹²

	Evaluation	797 standards ¹²
Equipment	Compliant	Laminar Horizontal Flow Hood (ISO class 5)
Technique	Compliant	Compounding personnel are adequately skilled, trained, and educated to correctly perform and document the following activities: <ol style="list-style-type: none"> 1. Perform aseptic hand cleansing and disinfection of nonsterile compounding surfaces 2. Complete aseptic gloved fingertip testing 3. Select and appropriately don protective garb 4. Maintain or achieve sterility of CSPs in ISO class 5 PEC devices and protect personnel and compounding environments from contamination 5. Identify, weigh, and measure ingredients 6. Manipulate sterile products aseptically, label, and quality inspect CSPs
Environment	Compliant	ISO class 7 clean room
Sterility/risk	Compliant	Medium risk: Batching; 9 days refrigerated ¹²
Evidence-based literature	Consistent	Lane et al, ⁷ Arbisser, ⁸ and Espiritu et al ⁹

Note. CSP=Compounded Sterile Products; PEC= Primary Engineering Control.

equipment, room sterility and pressure, beyond use dating, and storage.¹² Sterile technique by technicians was supported by aseptic technique training, media fill testing, and gloved fingertip testing. These results are documented and stored via templated production logs (Figures 1-3). The potency and purity of the product under refrigerated conditions over the specified time frame (9 days) were determined by high-performance liquid chromatography (HPLC) by an independent laboratory. All samples were within the USP-specified range for moxifloxacin ophthalmic solution.

Cost Savings

Prior to centralized production, a vial of moxifloxacin was dispensed for each surgery at a direct cost of \$140/surgery. After implementing centralized production, a vial of moxifloxacin produced 9 IC injections and therefore reduced the direct cost to \$20/surgery. Direct cost savings to the organization was \$120/surgery. There were 459 surgeries during the study period, resulting in a savings of over \$55 000 over 6 months and a projected annual savings of over \$100 000 for the health system.

Discussion

Implications

This study described the magnitude of a small operational change, and how it can save an organization a substantial amount of money while maintaining quality. The implementation of the usage of centralized IC moxifloxacin syringes during cataract surgery will save this organization over \$100 000 dollars over its first year. As more ophthalmologists accept this practice, there will be a greater demand for its production, and further savings. This study will help support the transition to the centralized production of IC moxifloxacin by providing evidence on continued quality and adherence to best practices through centralized production, with an added cost savings advantage.

Future research could evaluate the financial benefit of the centralized production of additional IC antibiotics for ocular surgery. Moxifloxacin was an appropriate first choice for investigation as it has clinical advantages which may outweigh the cost savings with using alternative antibiotics. These advantages include a broader spectrum of antibacterial activity against common ocular pathogens, compatibility with intraocular tissues, its preservative-free formulation, and commercially available status reducing the complexity of compounding.^{6,7,13}

Limitations

This study was limited by its short duration of 6 months. With a longer study duration, there would have been no need to estimate potential cost savings. Despite this limitation, the consistency of the production and documentation practices supports the extrapolation of reported data. In addition, the cost savings were calculated based solely on direct costs, not considering production time and labor costs. Finally, although the use of IC moxifloxacin has been established and supported in the evidence-based literature, it should be noted that the use of moxifloxacin as an IC injection is off-label.

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