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INSTRUCTIONAL DESIGN AND ASSESSMENT

Incorporation of Hands-On Sterile Technique Instruction in an Introductory Pharmacy Practice Experience

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Objective. To examine sterile technique and basic sterile compounding procedures among third-year pharmacy students.

Design. Third year pharmacy students participating in an introductory pharmacy practice experience (IPPE) in 2012 (n=126) and 2013 (n=119) performed a modified low-risk compounded sterile product (CSP) media fill challenge test, then prepared a 5 mg/mL vancomycin solution that was subsequently analyzed for accuracy.

Assessment. To identify deficiencies in sterile procedures, students were observed while performing a modified low-risk CSP media fill challenge test. In the first year of conducting the challenge test (2012), 3 deficiencies were identified: hand washing before compounding, cleaning items with alcohol prior to start, and cleaning work area upon completion. In 2013, significant improvements were observed in these 3 areas after students watched a demonstration video. Examination of CSPs revealed less than 1% contamination in both years. Analysis of compounded vancomycin solutions showed that 84% and 71% of students prepared solutions in 2012 and 2013, respectively, were within 10% of the targeted final concentration.

Conclusion. Hands-on sterile compounding exercises are typically delivered early in the pharmacy professional curriculum with minimal reinforcement in subsequent years. Providing opportunities for advanced pharmacy students to refresh and practice sterile compounding procedures allows students to refine their skills before entering pharmacy practice.

Keywords: sterile compounding, USP Chapter 797, introductory pharmacy practice experience

INTRODUCTION

Implementation of sterile compounding guidelines began in the early 1990s when several pharmacy organizations issued practice recommendations to assist pharmacists and technicians responsible for compounding sterile preparations. In 1995, the American Society of Health-System Pharmacists (ASHP) conducted a national survey of quality assurance for pharmacy prepared sterile products. [1] Results of this survey revealed that few pharmacies were equipped with adequately controlled compounding environments and highlighted the need for continued efforts to implement standard guidelines for sterile preparation.[1] In 2004, the US Pharmacopeia (USP) published "USP Chapter <797>, Pharmaceutical Compounding: Sterile Preparations," which described procedures and requirements for compounding sterile preparations and set standards applicable to all practice settings where sterile preparations are prepared and stored.[2] By law, USP 797 is enforceable and pharmacies may be subject to inspection by state boards of pharmacy, the Food and Drug Administration (FDA), and various accrediting organizations.[3] Unfortunately, only 20 states have adopted the USP chapter.[4] In 2013, a report by The PEW Charitable Trusts identified 20 pharmacy compounding errors associated with 1022 adverse events, including 75 deaths, that occurred between 2001 and 2012; contamination of sterile products was the most common compounding error associated with those reported events.[5] Following the 2012 fungal meningitis outbreak related to contaminated sterile products from the New England Compounding Center, the FDA increased its inspections of compounding pharmacies, focusing on those pharmacies the agency had previously identified as producers of "high-risk" sterile compounded drugs.[6] Thirty-one priority inspections were completed and warning letters issued outlining problems that create risk for contamination.[7] These inspections demonstrated that despite sterile preparation guidelines instituted by USP 797 almost

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10 years ago, there continue to be deficiencies in the preparation of sterile products that may pose significant risk to patients.

The preparation and compounding of sterile products is a competency required in pharmacy professional programs as specified by both the Accreditation Council for Pharmacy Education (ACPE) Guidelines (Appendix B)[8] and the North American Pharmacy Licensing Examination (NAPLEX).[9] Furthermore, in 2010 a joint ASHP-ACPE task force published "Entry level competencies needed for pharmacy practice in hospitals and health-systems," Appendix B of which listed competencies for hospital/health systems practice that should be achieved by all graduates.[10] Two competencies encompass the preparation of sterile products, and it is recommended that they be addressed in the curriculum through both didactic and practice laboratory exposure, as well as through IPPEs and advanced pharmacy practice experiences (APPEs).[10] All schools of pharmacy require a course in sterile compounding, in which students learn the basics of sterile preparation and become familiar with USP 797 guidelines. At our institution, this course occurs during the first year, and the techniques and principles are not revisited later in the curriculum. This format leaves open the possibility that upon entering the workforce, graduates 3 years removed from training may no longer possess the basic knowledge or skills of sterile preparation. The goals of this study were to examine sterile technique competency among third-year pharmacy students at our institution by incorporating hands-on laboratory exercises during a required IPPE and to assess the need for additional sterile technique instruction and opportunities to practice in the curriculum.

DESIGN

Hands-on laboratory exercises that allowed advanced pharmacy students the opportunity to revisit skills and concepts required for the preparation of sterile products were integrated into a required IPPE in the third professional year. The first exercise required students to perform a modified low-risk CSP media fill challenge test in a simulated ISO 5 environment (classified clean room). Because of the high cost associated with commercially available media fill test kits and our large class size (120 students on average) the procedure was modified to use sterile serologic pipettes with a pipette aid and sterile polypropylene tubes. As these tools are not commonly encountered or used in a sterile pharmacy compounding setting, at the start of each laboratory session, instructors demonstrated how to use the motorized pipette aid with a serologic pipette to transfer 5-mL of water into a sterile 50-mL polypropylene tube. Students were provided with a handout outlining the actual procedure which consisted of transferring 5-mL of sterile tryptic soy broth (TSB, General Laboratory Products, Yorkville, IL) 4 times into each of 3 sterile 50-mL polypropylene tubes and were given the opportunity to practice using the pipette aid and serologic pipette prior to performing the actual exercise. In the 2nd year of conducting this exercise, 2 changes were introduced: (1) the students reviewed a video demonstrating the low risk CSP media fill procedure prior to the lab exercise, and (2) the students were given access via the online course learning management site (Moodle, Moodle Pty Ltd., West Perth, Australia) to copies of The ASHP Guide on USP Chapter 797 for Compounding Sterile Preparations[3] and "The Theory Behind Sterile Compounding," which was part of the first-year sterile compounding course. The video was produced by the instructors and made available one week prior to the laboratory session as well as during the classroom session preceding the laboratory.

During the media fill challenge test, each student was observed and evaluated by an instructor in 10 areas (Appendix 1): removing jewelry, hand washing to elbows, preparing work area, placing supplies in hood, and conducting manipulations in hood at arm's length (beyond 6-inch zone). At the end of the challenge test, students were instructed to label their CSPs with their initials and date. All CSPs were then placed in an incubator at 37˚C and inspected by instructors daily for 3 days, then at days 7 and 14 for turbidity; inspection times were logged and occurred at the same time of day. At the end of the 14-day incubation period, students were provided with individualized feedback, highlighting skills/areas in need of improvement. In the event of microbial contamination (solution turbidity), students were not required to repeat the test due to time constraints; however, instructors reviewed sterile technique with each student and identified steps in the procedure where contamination likely occurred. Solution turbidity did not affect course grade.

The second exercise required students to prepare a 5 mg/mL vancomycin solution that was subsequently analyzed for accuracy. Due to limited quantities of 500 mg vials of vancomycin for injection, teams of 4 students were formed and given a prescription for oral vancomycin and worksheet outlining a procedure for compounding an oral vancomycin solution for injection. The exercise was designed to provide students with the opportunity to practice the following skills: (1) interpreting orders/following directions, (2) doing pharmaceutical calculations, (3) reconstituting powdered drug in a vial and withdrawing it from the vial, (4) performing drug dilutions, and (5) working in a team. Additionally, one

team member functioned as a "quality control officer" to ensure that the procedure was followed, check that calculations were correct, and visually inspect the final product prior to submitting for analysis. The "quality control officer" was required to initial the worksheet signifying that the requisite quality checks were conducted and to submit the worksheet together with the team's final product to the Pharmaceutical Sciences Research Institute (PSRI) at the McWhorter School of Pharmacy for analysis. In 2012, submitted samples were analyzed by Liquid Chromatography Mass-Spectrometry (LCMS) and in 2013 by High Pressure Liquid Chromatography (HPLC). This change in analytical methodology was made because of increased efficiency of the HPLC method. Additionally, the HPLC method is more amenable to having students participate in sample analysis in the future. Depending on the analytical method utilized, appropriate dilutions (1 to 100 for LCMS and 1 to 5 for HPLC) of each 5 mg/mL vancomycin solution were prepared in triplicate and analyzed against a standard curve. At the conclusion of all laboratory sessions, student teams were informed of the accuracy of their 5 mg/mL vancomycin solution and the submitted worksheet returned with comments/corrections where appropriate.

Prior to and at the conclusion of each session, students were asked to voluntarily and anonymously answer 2 questions: (1) Do you have prior experience in sterile compounding/using aseptic technique? Yes/No. If yes, please list in what setting (prelaboratory question); (2) Do you feel that you had enough prior knowledge/foundation to perform today's exercises? Yes/No. If you answered no, please explain (postlaboratory question). Appropriate exemption for the use of the data in this study was obtained from Samford University Institutional Review Board.

EVALUATION AND ASSESSMENT

All students, 126 in 2012 and 119 in 2013, enrolled in the spring semester IPPE course participated in and completed the modified low-risk media fill test exercise. Table 1 summarizes the performance of each class with 5 sterile compounding procedures: hand washing prior to commencing manipulation in the laminar flow hood, preparing work area, including proper cleaning of the laminar flow hood, cleaning supplies with alcohol prior to commencing manipulations, working in the laminar flow hood beyond 6-inch line and cleaning work area after completion. Pearson's chi-square was used to examine differences in student performance between 2012 and 2013 on the 5 procedures. Analysis was conducted using SPSS 19 (IBM, Chicago, IL); level of significance was predetermined to be ≤ 0.05. Statistical analysis revealed a significant improvement ($p \leq 0.05$) between students in 2013 and 2012 in 4 of 5 areas (Table 1) as follows: washing hands prior to start, proper preparation of the work area including proper technique for cleaning the laminar flow hood, cleaning of polypropylene tubes and the TSB jar with 70% alcohol prior to commencing manipulations, and cleaning work area following the completion of the exercise. With respect to working well within the laminar flow hood, no statistical difference between the 2 years was observed; 99% of students in 2012 and 97% of students in 2013 demonstrated proper technique. Contamination was less than 1% in both years. When contaminations occurred, microorganism growth was typically observed after 7 days of incubation.

Of the 32 vancomycin solutions analyzed in 2012, only 1 solution was out of range with a final concentration 1.5 times higher than the declared vancomycin concentration of 5 mg/mL. Errors in concentration for the remaining 31 solutions ranged from 0% to 12%: 17 (55%) fell within the 0-5% error range, 10 (32%) within the 6-10% error range, and 4 (13%) within the 11-12% error range. Similar error ranges were observed in 2013. One of 24 solutions assayed was out of range with a final concentration 2 times higher than the declared vancomycin concentration. Of the remaining 23 solutions, 11 (48%) fell within a 0-5% error range, 6 (26%) fell within a 6-10% error range, and the remaining 6 (26%) fell within the 11-15% error range.

Ninety-six percent and 93% of students in 2012 and 2013, respectively, answered both prelaboratory and postlaboratory questions. Approximately 25% of the class, in both years, indicated that they had no prior experience using aseptic/sterile technique, whereas 75% in both years indicated that they had prior experience, most often from sterile compounding laboratories during the first professional year, from sterile compounding laboratories in the first year combined with institutional IPPEs in the second professional year, or from institutional IPPEs in the second professional year. Hospital, research facility, or undergraduate microbiology laboratories were other settings identified.

Thirty percent of students in 2012 felt that they did not have enough prior knowledge to perform the laboratory exercises. In contrast, 5% of students in 2013 felt that they did not have enough prior knowledge to perform the exercises. When students explained why they felt that they did not have enough prior knowledge to perform the exercises, 58% said "A long time had passed between learning sterile compounding skills in the first year and having to use and think about those skills now."

Table 1. Student Performance During a Mock Low-Risk Media Fill Challenge Test

	2012, n=126	2013, n=119	
	n (%)	n (%)	*p* value
Washed hands before starting	81 (64)	119 (100)	<0.00 [a]
Prepared work area properly	105 (83)	119 (100)	<0.001[a]
Cleaned polypropylene tubes and TSB jar with alcohol before starting	25 (20)	101 (84)	<0.001[a]
Worked well within hood (beyond 6" line)	125 (99)	116 (97)	0.286
Cleaned work area upon completion	60 (48)	100 (84)	<0.001[a]
Percent of Contaminated CSPs	0.79 (3 out of 378)	0.84 (3 out of 357)	

[a] $p<0.05$.

DISCUSSION

Preparing and compounding sterile products is a competency requirement specified by both ACPE and NAPLEX and an entry-level competency expected of hospital pharmacy practitioners. In their study examining the extent of sterile compounding instruction in US schools of pharmacy, Hellums and colleagues reported that instruction among programs participating in the survey varied widely and that only 13% of respondents felt that students in their program had sufficient sterile compounding training.[11] By graduation, most students may not possess needed entry level competency in sterile compounding. For this reason, we examined sterile technique competency among our third-year pharmacy students using a modification of a low-risk media fill challenge test as outlined in USP Chapter 797.[2] The decision to modify the media fill challenge test was primarily driven by the high cost associated with commercially available kits; however, it is our opinion that proper sterile technique is a skill with wide application not limited to manipulations carried out with syringes, needles, and vials. In fact, our students required minimal instruction on how to use the serologic pipette to perform the tryptic soy broth transfers, and use of these tools did not appear to affect their basic sterile technique. However, conducting a side-by-side comparison between the modified media fill procedure and a typical low-risk media fill procedure would be needed to determine what effect, if any, the modification would have on basic sterile technique. Additionally, although the modification was no more complex than a typical low-risk media fill procedure, it did increase the risk for contamination as many items were open during the procedure, and it is much easier to contaminate the pipette tip during the media transfers. These differences challenged students to accomplish the media transfers in a timely manner while minimizing contamination risk. We noted, when working with closed vials, syringes, and needles, that it was difficult to contaminate the growth media, even when intentionally being careless and touching critical surfaces, such as the vial septum and syringe tip, and dropping the syringe with the needle uncovered. In fact, contamination was only achieved by removing the plunger and directly touching the rubber end with unwashed hands.

The most glaring deficiencies observed among students in sterile compounding procedures related to hand washing, cleaning supplies prior to commencing manipulations, and cleaning the work area upon completion. These deficiencies were greatest among students in 2012, the first year the sterile technique laboratory was integrated into the IPPE. Anecdotal student remarks and written responses to the postlaboratory question suggest that retention of key sterile compounding concepts learned in the first professional year was limited. To correct or remediate this, a 6-minute video demonstrating the media fill exercise from start (washing hands) to end (cleaning the work area at the end of the manipulation) was developed. This video was made available to students in 2013 one week prior to each laboratory session as well as in the classroom prior to the start of the laboratory sessions. When performance was compared between 2012 and 2013, significant improvement was noted among 2013 students in areas in which 2012 students were deficient. Anecdotal feedback from students indicated that the video was extremely helpful. The positive influence of this demonstration video was also reflected in responses to the postlaboratory question: "Do you feel that you had enough prior knowledge/foundation to perform today's exercises?" Only 5% of students in 2013 felt that they did not have enough prior knowledge/foundation to perform the laboratory exercises compared to 30% of students in 2012. Both classes experienced the same curriculum in the sterile compounding course in their first year and in institutional IPPEs in their second year. Since the number of students with prior sterile compounding experience in work settings in 2013 was not substantially more than that number in 2012, we believe that video demonstration of the media fill procedure explained the difference in responses between the 2 years.

When examining student responses to the prelaboratory questions, it was surprising that approximately 25%

of students in both years indicated having no prior experience in sterile compounding/using aseptic technique despite having taken the sterile compounding course with laboratory instruction in the spring semester of their first year. Because students were not asked to explain their answer to this question, we hypothesized that this percentage of students may have interpreted the question to mean experience outside of the classroom. Since completion of the 2 questions prelaboratory and postlaboratory was voluntary and anonymous, correlating "no prior experience" responses with student performance in the media fill challenge test was not possible. It would be of interest to explore this correlation in the future and to formally assess the sterile compounding skills of students in the first professional year to examine potential relationships between perceived lack of experience, competency immediately following training in the first professional year, and performance on a media fill challenge test administered in the third professional year.

While 78% of vancomycin solutions prepared by student teams both years fell within 10% of the target final concentration, there was one solution each year that was substantially higher than the declared concentration. Examination of the submitted worksheets for the outlier solutions together with visual inspection of the solutions revealed that in 2012, the team correctly calculated the appropriate amount of diluent needed to achieve the desired final volume but then failed to add the calculated amount, resulting in a solution strength that was 1.5 times higher than the declared strength. In contrast, the outlier team in 2013 incorrectly calculated the amount of diluent required to achieve the desired final volume, resulting in a solution strength that was 2 times higher than the declared strength. In both cases the "quality control officer" failed to catch the errors. It should be noted that this was the first time that students were required to perform a quality assurance check for their compounded product and that an analytical component was incorporated.

In recent years, the importance of proper sterile technique in the compounding of medications has been reemphasized. Acquiring and refining these skills is best achieved through frequent exposure to the practice. Use of IPPEs in later years of the curriculum can provide hands-on opportunities for reinforcement of these skills and concepts learned in the first professional year. Results from our study highlighted the fact that a substantial number of students felt unprepared to perform sterile compounding with a first-year course as their only exposure to the practice. Conducting laboratory exercises after viewing a skills demonstration video in a required IPPE in the third professional year helped students review, practice, and refine their sterile compounding skills as they prepared to become entry-level practitioners.

SUMMARY

This study provided an opportunity not only to design laboratory exercises that incorporate sterile compounding/principles in a required IPPE in the third professional year, but also to improve the instructional design of the sterile compounding course offered in the first professional year. Based on the observations made in this study, the laboratory portion of the sterile compounding course in the first professional year incorporated a practical at the end of the course, in which the sterile technique of individual students was assessed through instructor observation. In addition, this study laid the foundation for incorporation of sterile compounding exercises into our Integrated Pharmacy Applications Laboratories in the second and third professional years.

Results of this study emphasize the need to provide advanced pharmacy students with opportunities to practice sterile compounding skills, review key concepts associated with sterile compounding, and experience firsthand the importance of quality control as they prepare to enter pharmacy practice. Increased exposure to sterile compounding may translate into better aseptic technique and more accurately prepared CSPs dispensed to patient populations among pharmacy students.

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Appendix 1. Evaluator Check List

Student Name _____

	YES	NO	Not Applicable
Student removed all visible jewelry			
Student secured/tied back his/her long hair			
Student washed hands to elbows			
Student dressed appropriately for sterile compounding			
Student cleaned laminar air flow hood correctly			
Student placed supplies in laminar air flow hood so that items received first air			
Student ensured he/she had all supplies needed prior to compounding			
Student performed manipulations well beyond the 6-inch line			
• Provided relevant comments as appropriate			
Student confirmed final product			
• Checked that volume per tube was correct			
• Appropriately labeled final product			
Student appropriately removed final product from the laminar air flow hood			
Student cleaned work area correctly upon completion			

Evaluator: _____