Determining the Risk of Sepsis Using Nurse-Compounded Elastomeric Pumps for Continuous Infusion in Outpatient Parenteral Antibiotic Therapy

Pauline M. Dobson, MHS, RN • Mark Loewenthal, MMedSci, MB, BS, FRACP, DTM&H • Lisa Harris, BSc (Hons), BPharm (Hons)

ABSTRACT

Limited availability of compounded antibiotics used for continuous infusion outpatient parenteral antibiotic therapy (OPAT) can delay or interrupt an OPAT course. To solve this problem, OPAT nurses at a hospital in Australia have been compounding elastomeric pumps for immediate use. The incidence of sepsis in 5014 patients before and after the introduction of nurse compounding was compared. There were no cases of laboratory-confirmed bloodstream infection among the nurse-compounded group compared with 2 cases (0.045/1000 catheter days) among the control group without nurse compounding ($P = .16$). No compounding medication errors occurred in more than 180 patient years of follow-up among the nurse compounding group. Nurse compounding can be a safe and convenient alternative when immediate access to preloaded elastomeric pumps is required.

Key words: antibiotic, aseptic, compounding, elastomeric, home infusions, infusion pumps, OPAT, technique

Traditionally, sterile compounding of anti-infective medications for administration as 24-hour continuous infusions in outpatient parenteral antibiotic therapy (OPAT) has been restricted to pharmacists following good manufacturing practice in a designated aseptic suite.

In Australia, a majority of OPAT services use commercially compounded elastomeric pumps that are generally provided as a week's supply of preloaded pumps containing antibiotic and intravenous (IV) fluid for daily administration. Depending on the length of therapy, the order is repeated weekly for the duration of the OPAT. Because there are a small number of commercial compounders of elastomeric pumps, the distance from the compounding facilities may result in a gap between ordering the patient-specific elastomeric pumps and their delivery to the OPAT service. This gap may extend to 4 days over long weekends and public holidays. The delay can prevent discharge from the hospital or emergency department to OPAT, incurring unnecessary, high-cost inpatient bed days. There is considerable pressure to transfer a patient to an OPAT service as soon as possible to reduce hospital length of stay and improve patient flow by freeing up inpatient beds.

In addition, new compounded elastomeric pumps are needed during OPAT when dose change is required because drug concentrations are found to be sub- or supratherapeutic, or when patients are not responding to a particular antimicrobial drug, or if patients develop an adverse drug reaction or allergy requiring a change of antibiotic. These scenarios necessitating immediate supply of

Author Affiliations: *John Hunter Hospital, Newcastle, New South Wales, Australia (Mss Dobson and Harris, Dr Loewenthal); and University of Newcastle, Newcastle, New South Wales, Australia (Ms Dobson and Dr Loewenthal).*

Pauline M. Dobson, MHS, RN, *is a clinical nurse consultant in the immunology and infectious diseases unit at John Hunter Hospital in Newcastle, Australia. She has 30 years' experience in the provision of home infusion therapy and established the unit's outpatient parenteral antibiotic therapy program in 1995. She is a conjoint lecturer in the faculty of health and medicine at the University of Newcastle, Australia.* **Mark Loewenthal, MMedSci, MB, BS, FRACP, DTM&H,** *is a staff specialist in infectious diseases and director of the immunology and infectious diseases unit at John Hunter Hospital, Newcastle, Australia. He is also a conjoint senior lecturer in the faculty of medicine and public health at the University of Newcastle, Australia.* **Lisa Harris, BSc (Hons), BPharm (Hons),** *is a clinical pharmacist in John Hunter Hospital's immunology and infectious diseases unit, with particular expertise in antibiotic administration and antimicrobial stewardship.*

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Corresponding Author: *Pauline M. Dobson, MHS, RN, Immunology and Infectious Diseases Unit, John Hunter Hospital, Lookout Road, New Lambton, NSW Australia 2305 (Pauline.Dobson@hnehealth.nsw.gov.au).*

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compounded elastomeric pumps are commonplace in the OPAT setting and were the catalyst for the service's search for alternative solutions.

For 24-hour continuous infusion, nurses admixing medications into IV fluids on a treatment room benchtop is an accepted practice in the hospital setting. The solution was to use this practice in the OPAT setting and initiate nurse compounding to cover the gap between ordering and delivery of compounded elastomeric pumps.

Although the risk of microbial contamination of compounded elastomeric pumps is considered low,[1] anecdotally there has been widespread reluctance among pharmacists to allow nurse compounding because of the potential risk of contamination leading to sepsis. Because this OPAT service was the first in Australia to use nurse compounding, a prospective quality improvement study was conducted using SQUIRE 2.0 guidelines to provide evidence of the safety of the intervention by examining the occurrence of catheter-related bloodstream infections, a surrogate marker for poor aseptic technique,[2] and the incidence of medication errors in nurse-compounded elastomeric pumps. An initial trial demonstrated promising results and led to an extended period of follow-up, which is reported here.[3]

METHODS

The Setting

The OPAT service is an infectious diseases team-led service program based in a large tertiary teaching hospital. The service treats patients with serious infections who require long-term IV antibiotic therapy, such as prosthetic and native bone and joint infections, infective endocarditis, cystic fibrosis, and bacteremia. Patients receive their IV antibiotics at home; the majority are administered as continuous infusions through a variety of central vascular access devices (CVADs), comprising peripherally inserted central catheters (85%), implantable ports (10%), short-term CVADs (4%), and tunneled catheters (1%). Approximately half of the patients are seen at home daily by visiting nurses who change the elastomeric pump; the remainder of patients or their caregivers have been educated in self-administration techniques by an OPAT nurse. Patients admitted to the OPAT service have their demographic and clinical data entered prospectively in a clinical database, including all adverse events.

Medication errors are entered into a statewide, online incident monitoring system by nurses working on the OPAT team. Hospital policy dictates that all IV medications should have an independent double-check.

Patients and Controls

The service's clinical database contains information on all patients admitted to the OPAT service from October 1995 to the present. Nurse compounding was introduced in May 2007. The laboratory-confirmed bloodstream infection (LCBI) rate in patients receiving antibiotics via an elastomeric pump through a CVAD before the introduction of nurse compounding (Group A, control group) was compared with the LCBI rate in the same category of patients after the introduction of nurse compounding (Group B, intervention group).

Group A included patients who received commercially compounded anti-infective medications between October 21, 1995 and April 30, 2007. Group B comprised all patients receiving antibiotics between May 1, 2007 and December 14, 2015, after the initiation of nurse-compounded elastomeric pumps. Patients who received nurse-compounded elastomeric infusions were not uniquely identified in the clinical database, and therefore, Group B contained patients receiving antibiotics from both nurse-compounded and commercially compounded elastomeric pumps.

Detection of LCBIs

All bloodstream infections are investigated by the health service's infection prevention and control unit, which is independent of the OPAT service. The unit identifies all LCBIs based on a standard definition: a recognized pathogen identified in 1 or more blood cultures that is not considered a contaminant and is not related to infection at a site other than the CVAD.[4] There is a mandatory requirement to report LCBIs to the New South Wales Ministry of Health.

Nurse Compounding Procedure

Over the course of the study, 2 brands of elastomeric pumps preloaded with 200 mL 0.9% sodium chloride as a diluent were used (the LV-10 Infusor [Baxter Healthcare Australia, Old Toongabbie, Australia] and the MobiFUSER [MobiLIFE Medical, Mount Kuring-gai, Australia]) when immediate-use compounded antibiotics were required. The sodium chloride pumps had an extended expiration of 3 to 6 months when refrigerated, which ensured that there were sufficient supplies for periods of high demand and that they would be used before their expiration date. The compounding was undertaken in a clean benchtop area of the OPAT clinic (Table 1). The patient-specific antibiotic was added following the pump manufacturer's instructions, using aseptic nontouch technique.

Because sterility beyond 24 hours cannot be guaranteed if compounding occurs outside a sterile suite, all elastomeric infusions were compounded immediately before use. Only antibiotics with documented stability in the individual elastomeric pump were compounded by the OPAT nurses. The compounding components, such as the antibiotic, buffer (when applicable), dose calculation, and diluent, were independently double-checked by a second nurse. A label indicating admixture details, route, and expiration date was applied to each compounded elastomeric pump. Because of the time required to compound multiple elastomeric pumps, nurse compounding was restricted to fulfilling the need to supply immediate-use antibiotics for a single patient to fill the gap between ordering and delivery of patient-specific commercially compounded pumps.

Antibiotics most frequently compounded in the OPAT service are flucloxacillin, benzylpenicillin, piperacillin/tazobactam, and cephalosporins, including ceftazidime,

TABLE 1

Guidelines for Nurse Compounding of Elastomeric Pumps for 24-hour Infusion

The principles of nurse compounding of elastomeric devices:

- Antibiotics must be suitable for 24-hour infusion, with documented stability data for the specific elastomeric device used.
- Infusions are loaded immediately before use.
- The manufacturer's instructions for compounding are followed.
- Aseptic technique is used.
- Infusions are loaded in a clean clinical area.
- The infusion components, antibiotic order, dose calculation, and compounding are independently double-checked by a second nurse.
- Infusions are labeled to indicate drug dose, admixture details, and parenteral route.
- For benzylpenicillin infusions, the addition of a buffer is essential to maintain the stability of the antibiotic over 24 hours.
- Nurse compounding is an urgent stop-gap measure only, until a supply of commercially compounded elastomeric pumps is available.

cefazolin, and cephalothin. For continuous infusions of benzylpenicillin, a commercially prepared syringe containing a buffering solution (Baxter Healthcare Australia) was compounded along with the antibiotic to ensure drug stability over 24 hours.

Data Analysis

Using Stata statistical software (StataCorp, College Station, TX),[5] exact binomial 95% confidence intervals (95% CIs) and 2-sided mid-*P* values were calculated for the difference in the LCBI incidence rate (infections per 1000 patient days of observation) between Group A and Group B.[5] Patient days of follow-up were converted to patient years by dividing the total number of days in each study group by 365.25.

RESULTS

Since May 2007, 1828 elastomeric pumps (average 18 elastomeric pumps/month) have been compounded with antibiotics by the OPAT nurses for continuous infusion. The outcomes of more than 5000 OPAT patients were included in the analysis (Table 2). The Group A period (October 1995-April 2007) incorporated 120 patient years of follow-up, with 181 patient years of follow-up in Group B. There were 2 confirmed infections in Group A and none in Group B after implementation of nurse compounding. There was no significant difference in infection incidence rates between the 2 groups. Infection incidence rates were 0.045 cases per 1000 patient days in Group A and 0 in Group B (difference −0.045; 95% CI, −0.018 to 0.11; $P = .16$). There were no medication errors resulting from the use of nurse-compounded elastomeric pumps.

DISCUSSION

The rate of LCBI in OPAT is very low. A large study is therefore required for adequate power to detect even a modest relative difference in LCBI due to any intervention.[6] In this study reporting more than 300 patient years of follow-up, no change in LCBI following institution of nurse compounding of 24-hour elastomeric infusion pumps was observed. Nurse compounding has reduced the number of inpatient days by facilitating timely admission to the OPAT service. For OPAT patients requiring immediate alterations to their treatment regimen, the ability to change doses or antibiotics on very short notice is now available, allowing for an uninterrupted course of infusion therapy. OPAT services outside of major metropolitan areas where commercial compounding facilities are located may benefit from the introduction of nurse compounding of elastomeric pumps to fill the gap between ordering and supply of OPAT medications.

TABLE 2

Outcomes Pre and Post Nurse Compounding

	Group A Control October 1995-April 2007	Group B Post Nurse Compounding May 2007-December 14, 2015
Patients	1962	3052
Patient days	44 049	66 348
Mean OPAT course (range)	22.4 days (1-167 days)	21.7 days (1-109 days)
Mean patient age (range)	51.1 years (2 months-96 years)	54.9 years (3 weeks-96 years)
Males (%)	1253 (64)	1932 (63)
Adult patients (%)	1750 (89)	2892 (95)
Cystic fibrosis (%)	182 (9)	223 (7)
LCBI incidence rate	0.045/1000 catheter days	0.0/1000 catheter days ($P = .16$)

Abbreviations: LCBI, laboratory-confirmed bloodstream infection; OPAT, outpatient parenteral antibiotic therapy.

REFERENCES

1. SHPA Manufacturing Working Party. SHPA guidelines for medicines prepared in Australian hospital pharmacy departments. *J Pharm Pract Res*. 2010;40(2):133-143. https://www.shpa.org.au/sites/default/files/uploaded-content/field_f_content_file/51._manufacturing_standards_0610.pdf. Accessed June 12, 2017.
2. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for QUality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. *BMJ Qual Saf*. 2016;25(12):986-992.
3. Cairns K, Dobson P, Lemessurier J, et al. Antibiotic compounding of 24-hour infusors as a stop-gap measure in home IV therapy. Paper presented at: 36th Society of Hospital Pharmacists Australia National Conference; November 11-14, 2010; Melbourne, Australia. https://issuu.com/conlog/docs/handbook_final_pdf. Accessed April 28, 2017.
4. US Centers for Disease Control and Prevention. National Healthcare Safety Network. National healthcare safety network (NHSN) surveillance definitions: central line-associated bloodstream infection & related sites. http://www.msic-online.org/pdf/NHSN_Definitions_CLABSI.pdf. Published June 2006. Accessed May 3, 2017.
5. Stata Statistical Software: Release 13. College Station, TX: StataCorp: 2013.
6. Moureau N, Poole S, Murdock MA, Gray SM, Semba CP. Central venous catheters in home infusion care: outcomes analysis in 50,470 patients. *J Vasc Interv Radiol*. 2002;13(10):1009-1016.