SPECIAL ARTICLE

Severe Acute Respiratory Syndrome (SARS): The Pharmacist's Role

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Objectives. After two outbreaks of severe acute respiratory syndrome (SARS) occurred in Toronto, Ontario, Canada, from March–June 2003, we reviewed the unexpected role and responsibilities of pharmacists during these two crises, and present strategies for better crisis preparedness.

Methods and Results. Pharmacists were actively involved in battling the SARS crises. After conducting extensive literature searches and evaluations, pharmacists prepared administration and dosing guidelines for the two investigational drugs, ribavirin and interferon alfacon-1, that were being used to treat the syndrome. They provided direct patient care under modified conditions. They revised drug distribution procedures and developed new ones to meet more stringent infection-control standards. Collaborative teamwork with key stakeholders was important in accomplishing tasks in an efficient and timely manner. Regular communication with health care staff took place internally and externally. Education and updated information for pharmacists was crucial.

Conclusion. Pharmacists can play a vital role during crises in the areas of drug distribution, drug information, and direct patient care. Collaborative teamwork and close communication are keys to success. Pharmacists must be proactive and take a leadership role in assuming pharmacy-related responsibilities. By evaluating what worked and what didn't, pharmacists can develop procedures for future crises requiring pharmacy support.

Key Words: severe acute respiratory syndrome, SARS crisis, pharmacist's role, preparedness.

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Severe acute respiratory syndrome (SARS) has emerged as a new infectious disease that created a global public health emergency in 2003. The disease was first manifested in humans in China in November 2002 but subsequently spread to many countries.[1, 2] In Canada, most of the SARS cases occurred in the city of Toronto and the neighboring greater Toronto area. Severe acute respiratory syndrome is highly transmissible, putting close family members and people working in the health care environment at particular risk. In several countries and in Toronto, most cases occurred through nosocomial transmission.[1–3] The etiologic cause of SARS was identified as a coronavirus, now referred to as the SARS-associated coronavirus.[4–6]

Clinically, SARS presents as a flu-like illness typically characterized by fever, nonproductive cough, myalgia, dyspnea, diarrhea, and laboratory and radiologic chest abnormalities.[3, 7–9] The SARS

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incubation period is usually 3–10 days, and the illness has been associated with a mortality rate of 6.5%–30%. Several factors, such as age over 60 years, comorbid conditions such as diabetes mellitus, admission to an intensive care unit, and need for mechanical ventilation, predict a poor clinical outcome.[3, 7–9]

Optimal therapy for SARS remains to be established. Initially, treatment consisted of a super–broad-spectrum regimen of antibiotics, antivirals, and corticosteroids. This evolved to primarily supportive management, such as corticosteroids for worsening respiratory function. Antibiotics still are administered first to cover for community-acquired pneumonia until this cause is ruled out.

Ribavirin, an antiviral agent, initially was used because of its broad-spectrum activity against RNA viruses, such as the coronaviruses.[10] Because of considerable toxicity, lack of significant impact on clinical outcome, and poor in vitro antiviral activity, the use of ribavirin was abandoned.[1, 3] Subsequently, an engineered second-generation cytokine, interferon alfacon-1, was used empirically based on its antiviral and antiinflammatory effects.[1, 11] Preliminary results from its use in a small number of patients recently were published.[12]

Although much has been learned about SARS, many questions about its cause, transmission, and treatment remain to be answered through further research. When the SARS outbreak first occurred in various countries, health care institutions, local public health departments, and governments were not prepared to manage the outbreak. By examining what was done during the crises, we can be better prepared for managing future outbreaks of SARS or other communicable diseases. An example to follow would be our preparedness for dealing with biologic, chemical, and nuclear attacks of terrorism. Guidelines and recommendations for preparedness in these situations have been published.[13, 14] The role and importance of pharmacists in contributing to terrorism preparedness have been described.[14–18]

Based on our experience during two SARS crises in Toronto, we have found that every health care worker clearly plays an important role in providing care to patients with SARS. Pharmacists should take inventory of the challenges presented and actions taken, and determine the roles and responsibilities they must assume during future outbreaks of SARS or other communicable diseases.

We discuss the unexpected role and responsibilities undertaken by the pharmacy department at St. Michael's Hospital, one of several tertiary care, academic hospitals in Toronto that became involved in the two SARS crises. In addition, we present key principles and strategies that could be applied to similar events in the future. We do not address, however, the clinical management of SARS or the clinical pharmacology of the drugs used.

Methods

All relevant pharmacy-related events and tasks that were undertaken during the two SARS crises that occurred in Toronto from March–June 2003 were reviewed. Tasks were organized into five major categories: drug information, direct patient care, pharmacy operations, collaboration and communication, and personnel management. Key principles and strategies learned from this experience were identified.

Results

Drug Information

During the first SARS outbreak, the infectious disease specialists in Toronto decided to use a super–broad-spectrum regimen of antimicrobial agents for patients with suspected or probable SARS. Based on the drugs available in our hospital formulary, the regimen consisted of levofloxacin, azithromycin, imipenem, and oseltamivir, along with ribavirin, which was available through the Special Access Program, Health Canada (SAP). Guidelines for intravenous administration of all of the antimicrobials except ribavirin had been developed. Guidelines for dosing and administration of intravenous ribavirin were not readily available since it was not a marketed drug, and no research on its use for patients with SARS was available.

Dosage adjustment of ribavirin in patients with renal impairment presented an additional challenge due to the lack of fully published information regarding the pharmacokinetics of the drug in patients with different degrees of renal impairment. Pharmacists assumed responsibility for developing guidelines regarding preparation and administration of intravenous and oral ribavirin, dosage adjustment in patients with renal impairment, and monitoring. This was achieved by performing extensive literature searches, communicating directly with the drug manufacturer, and obtaining unpublished pharmacokinetic data from the manufacturer. Obtaining documentation of communication

from the drug manufacturer was important for reference and liability reasons. In addition, the pharmacists collaborated and shared information with pharmacy colleagues at other institutions who were also managing patients with SARS. Finally, a patient information sheet for ribavirin was developed in view of the underlying teratogenic and embryotoxic properties of the drug.[10]

At the start of the first SARS crisis, a SARS drug kit was created and stored in the hospital's emergency department. The kit provided readily accessible information on dosing of the various antimicrobial agents, guidelines on the preparation and administration of intravenous and oral ribavirin in patients with either normal or impaired renal function, a patient information sheet about ribavirin, and information about the SARS management algorithm. This kit was dynamic since information on patient management was continually evolving, especially during the first several weeks of the first SARS crisis. The types of drugs used were modified during the two crises. Pharmacists ensured that the kit was kept current.

When ribavirin therapy was abandoned, another investigational agent, interferon alfacon-1, was selected. Pharmacists again were involved in developing interim guidelines for intravenous administration of the drug while Toronto researchers were developing a formal research trial protocol.

With the implementation of strict infection-control procedures in the hospital during the SARS crises, administration of drugs by nebulizer was restricted for all hospital patients in order to eliminate another source of potential spread of SARS. Drugs normally administered by nebulizer, such as salbutamol and ipratropium, had to be administered by metered-dose inhaler. The drug information pharmacists prepared a chart to facilitate dosage conversion from nebulizer to metered-dose inhaler. Pharmacists intervened on orders written for nebulized drugs and collaborated with respiratory care practitioners to provide appropriate therapy.

Direct Patient Care

Pharmacists continued to provide direct care to patients with SARS under conditions of stress, urgency, and strict infection-control precautions. Health care staff who performed high-risk procedures (e.g., airway manipulation) were required to wear a fully protective outfit consisting of a fit-tested mask, a face shield, double gowns, goggles, double gloves, a hood/cap, and shoe covers (Figure 1). However, although the protective gown was essential for infection control, it hindered direct communication with the patient.

The approach to providing direct patient care needed modification because direct interaction between the patient and any health care provider was kept to a minimal level, and investigational tests were kept to the minimum required. Therapeutic plans needed to take into account the stringent infection-control precautions and the use of heavy sedation and paralysis to achieve minimal aerosol generation. Pharmacotherapy end points and monitoring plans were modified from those normally used for patients who do not have SARS. Use of the investigational agents required discussing risks versus benefits, counseling, and monitoring side effects. Monitoring the side effects of ribavirin therapy was important; anemia is a well-known

Figure 1. A proper protective outfit consisting of a fit-tested mask, a face shield, double gowns, goggles, double gloves, a hood/cap, and shoe covers was required for health care staff performing high-risk procedures.

Table 1. Pharmacy Policies and Procedure Changes Implemented as a Result of the SARS Outbreak

Policy	Procedure or Guideline
Unit-dose and central intravenous admixture processing for the SARS unit	Chart outlining SARS-related changes
Drug distribution to SARS patient care areas	Procedures related to modified distribution
Disposal of unused SARS drugs	Procedures for drug disposal under SARS precautions
SARS intubation drug kit	Information regarding contents of kits and procedures for handling
Code blue "S"pecial cardiac arrest drug trays	Procedures related to packaging and return of special cardiac arrest trays after a code blue incident
Drug procurement	Information on how to contact drug manufacturers and pharmacy departments at other hospitals to obtain special-access drugs such as ribavirin and interferon alfacon-1
Nebulizers	Recommendations about use of nebulizers in patients with SARS

SARS = severe acute respiratory syndrome.

significant side effect, and the ribavirin dosage was relatively high.

Pharmacy Operations

Implementing new or revised infection-control policies and procedures at our hospital during the SARS crises required major changes in various aspects of pharmacy operations (Table 1).

The SARS-designated patient care units, as well as the quarantined units, continued to receive unit-dose and central intravenous admixture services. However, these services were modified to meet new infection-control precautions. Any unused drug taken into an isolation room was discarded in biohazard containers in the room. This otherwise unnecessary wastage was tracked and reported to the hospital finance department to be considered for reimbursement by the government. New procedures determined when transfer of drugs from one area of the hospital to another was permissible, and when drugs could be returned to the pharmacy department for recycling. To minimize the number of staff entering the SARS-designated units, dedicated pharmacy technicians were assigned to handle unit-dose cart exchanges and ward stock replenishments.

A SARS intubation drug kit was created with input from the anesthesiologist and respiratory care practitioner. The kit was stocked on a mobile cart that contained special personal protective equipment for use by health care professionals performing high-risk procedures involving the patient's airway. If an intubation kit was opened for use in a patient with SARS, all remaining drugs and the plastic container were discarded as biohazard waste.

In addition, code blue (signifying cardiopulmonary arrest) "S"pecial carts were created in consultation with the cardiac arrest committee. The carts, which contained the usual cardiac arrest drug trays, were supplemented with additional neuromuscular blocking agents (to minimize aerosol generated during high-risk airway manipulation). After a code blue S incident, instead of returning the drug tray to the pharmacy as usual, all unused drugs were discarded, and the tray was sent in a biohazard plastic bag to the central sterile processing site for decontamination.

Detailed procedures were written for preparation and replacement of intubation kits and cardiac arrest drug trays, and for checking expiration dates. The pharmacy technician assisted in implementing the new or modified procedures. Nurses involved in intubation or cardiac arrest were oriented to the new policies and procedures. Auxiliary labels were used to remind staff of new procedures.

When a new exclusive SARS unit was constructed in less than 5 days, the pharmacy staff developed a specific drug delivery system for the unit, with all the infection-control measures in place. With the help of pharmacy technicians, ward stock drug lists were revised continually to meet the changing needs of this unit and of non–SARS care units affected by the reconfiguration of the patient population.

Procurement of ribavirin (intravenous and oral) and interferon alfacon-1 through SAP was coordinated by the drug-information pharmacist and the research pharmacy. Although oral ribavirin was a marketed drug (Pegetron; Schering Canada, Pointe Claire, Quebec), it was available only as part of the package containing interferon α-2b, specifically for treatment of hepatitis C. Therefore, another source for oral ribavirin (Copegus; Roche Pharmaceuticals,

Nutley, NJ) was obtained through SAP.

Procedures for shipment, turnaround time from approval to delivery, and costs were discussed with the drug manufacturers. Approval was obtained from SAP to borrow a small supply from another hospital, if necessary, before the drug shipment from the manufacturer arrived. Detailed procedures were written for how to obtain drugs during regular and off-hours of pharmacy operations, which SAP forms and inventory control sheets to complete, and contact numbers for SAP, the relevant drug manufacturers, and on-call pharmacists at other institutions.

Collaboration and Communication

To accomplish many of the tasks for which they were responsible, pharmacy staff collaborated with various key partners, such as the infectious disease consultant, microbiologist, anesthesiologist, cardiac arrest committee, and respiratory care practitioner. Many of the tasks had to be completed urgently and efficiently, with a multidisciplinary approach, and the pharmacists worked in close consultation with the respective stakeholders. Pharmacists and pharmacy technicians worked as a team to accomplish the various tasks within short time lines.

Regular and frequent communication—up to twice/day in the early stages of the crises—became routine. The hospital SARS command center provided staff with e-mail updates. The pharmacy manager attended daily briefings provided by the hospital's chief executive officer or a delegate, and important messages were communicated to pharmacy staff. Through e-mail and ad hoc meetings, the pharmacy staff was kept immediately informed of new developments and changes pertaining to pharmacy issues. The on-call pharmacist of the day was directly apprised of any new drug-related information for that day. Various hospitalwide policies and procedures, treatment algorithms, and protocols were posted on the hospital's internal electronic network (Intranet).

Similarly, all pharmacy-related operational policies and procedures, as well as drug treatment guidelines, were posted on the pharmacy department's Intranet. A SARS binder was created to contain relevant information on treatment, drugs used, and dosing and administration protocols; relevant articles from the literature also were placed in the binder. The pharmacists communicated frequently by e-mail with pharmacists at other hospitals in the city involved in managing patients with SARS. The e-mail group of the Infectious Diseases Pharmacy Specialty Network (ID-PSN) of the Canadian Society of Hospital Pharmacists was used as a communication link for infectious disease pharmacists across the country. Other pharmacist networking groups also established links with the ID-PSN group to keep up with new information on drug protocol and dosing.

Personnel Management

Personnel management consisted of staff education, redeployment, and creative handling of new situations. In-service sessions were provided for pharmacy technicians regarding new procedures for pharmacy operations, and for pharmacists regarding SARS and its management. All pharmacy staff received orientation regarding infection-control precautions. During the second SARS crisis, a dedicated response team, known as the SARS tertiary acute response team, was formed. This team was dedicated to managing all hospitalized patients with SARS that was identified, probable, suspected, or under investigation. The team was multidisciplinary and composed of various health care professionals, including pharmacists. Every team member underwent extensive training in infection-control measures, such as proper procedures for putting on and removing the high-risk protective outfit shown in Figure 1.

Hospital admissions decreased, especially in the surgical units due to cancellations of elective surgical procedures, and because of closures of clinics and unavailable beds; thus, hospital staff was redeployed to areas of increased demand. For example, some pharmacists were redeployed to assist with SARS screening of patients and staff entering the hospital. Other pharmacists assisted with administrative, drug information, or drug-use evaluation projects. Examples of novel staff situations requiring creative management were temporary work restrictions to one hospital site, support of work-quarantined staff, fitting staff with customized masks, and dealing with increased rates of illness-related absenteeism mandated by the employee health unit.

Discussion

When the first SARS outbreak occurred in Toronto, the crisis created major challenges for the Public Health Department, health care institutions, and staff in managing the patients

with SARS. No previous experience existed elsewhere that could be drawn on to help manage the patients and contain the spread of SARS. With such a crisis, the pharmacist's role, like that of other health care team members, was scripted on an ad hoc basis. Guidance was not available from a written department policy, a procedure manual, or the published literature.

Pharmacy preparedness for management of crises from attacks of weapons of mass destruction and bioterrorism has been documented.[14–20] However, significant differences exist between the terrorism type of crisis and the SARS crisis, and generalization to management of SARS is not possible. Nevertheless, both types of crises invoke the expertise of pharmacists in providing direct and indirect patient care under stressful conditions.

Pharmacists played several key roles during the SARS crises in Toronto. By taking inventory of the challenges and actions, we evaluated our experience and identified key principles and lessons learned that could be applied to future similar events (Figure 2). One early lesson was the need to be cognizant of infection-control principles and to incorporate them into the drug delivery system. Infection-control procedures are always in place for intravenous and extemporaneous drug preparations. Infection control was an equally important consideration for drug distribution to the SARS-designated patient care units.

In consultation with the director of infection control, several new policies and procedures were developed to deal with drug delivery, decontamination of unit-dose carts, drug returns, and drug transfers during such an outbreak. Since pharmacists are responsible and accountable for the drug delivery system, they must take a proactive leadership role, ensuring that the system is safe from an infection-control point of view. Because of the urgency of a crisis situation, pharmacist responsibilities must be prioritized and accomplished efficiently and quickly. In addition, the contribution of pharmacy technicians is critical in developing and facilitating implementation of the new procedures.

Pharmacists are an important resource in providing drug information and developing guidelines for drug use and administration in a typical patient care setting. Our skills in carrying out these responsibilities were fully utilized during the SARS crises. This was demonstrated in our approach to searching for information regarding use and accessibility of the investigational drugs ribavirin and interferon alfacon-1.

- Be proactive and flexible in assuming new responsibilities that are in the realm of the pharmacist's expertise.
- Maintain collaborative working relationships and communication with key players, such as the medical microbiologist.
- Seek efficient and timely methods to achieve goals in a dynamic work environment.
- Keep staff well informed through frequent e-mail communications, ad-hoc meetings, and the Intranet; provide a forum to address questions and concerns.
- Collaborate in sharing information with pharmacists at other institutions who are experiencing the same crisis. Use pharmacist network groups to keep colleagues at other institutions abreast of new information, guidelines, and issues.
- Determine mechanisms for obtaining drugs that are not available on the market; ensure that pharmacists and physicians know how to access these drugs during off-hours; secure a supply chain of such drugs.
- Perform comprehensive literature searches and evaluations on drugs that are being used. Communicate with drug manufacturers to obtain unpublished information on file.
- Prepare a kit containing the necessary information, such as management algorithms, drug dosing and administration guidelines, and pharmacist contact numbers; make this kit available in relevant patient care units, such as emergency departments and intensive care units.
- Develop or revise policies and procedures pertaining to the drug delivery system to meet more stringent infection-control precautions.
- Ensure that appropriate drug administration and dosing guidelines are available to guide medical, nursing, and pharmacy staff.
- Continue to provide direct patient care; modify approach as specific circumstances require.
- Manage staff creatively and flexibly to accommodate revised or expanded responsibilities.
- Collaborate to develop emergency preparedness for pharmacy services for potential future outbreaks of communicable disease.

Figure 2. Strategies for pharmacists in crisis management situations of communicable disease.

For example, the lack of published literature regarding ribavirin dosing in patients with renal impairment required the pharmacists to use various resources to derive dosing guidelines that were as evidence-based as possible.

With respect to providing direct care to patients with SARS during a crisis, the pharmacists' responsibilities were generally consistent with those that apply in a noncrisis situation; that is, patient assessment, monitoring, and counseling. However, an important difference was the conditions to which the pharmacists had to adapt in providing care, such as stringent infection control, high stress, and modified pharmacotherapy end points and monitoring plans. The pharmacists had to retain the essence of direct patient care while modifying or adapting the usual therapeutic and monitoring plans to meet the unique needs of these patients, since the degree of direct patient interaction was minimized to involve only what was essential.

The critical importance of collaboration and communication was clearly demonstrated during the SARS crises in Toronto. The success of pharmacists in fulfilling their various roles was possible only through close collaborative working relationships with various players in the hospital. This was exemplified by the multidisciplinary team effort in efficiently developing the SARS intubation kit and establishing the special SARS unit. Also vital in a crisis situation, all staff must be kept apprised of any new or evolving information on policies and procedures pertaining to drug delivery, drug guidelines, and protocols. Timeliness in dissemination of information is crucial, and it is useful to have the information available both electronically and in print format.

The pharmacy manager must play a key role in relaying information in a timely manner from the corporate level (such as the central command center) to staff. Lines of communication with staff members must be kept open throughout the crisis so that they feel reassured and free to ask questions or discuss issues or concerns. We also recognized the value of networking with pharmacists at other institutions in the city. Networking allowed us to share information, especially regarding the use of investigational drugs since the literature offered little information.

The experience gained from the SARS crises provided useful strategies that may be applied in similar crises in the future. Since each outbreak is different, pharmacists must be creative in fulfilling their responsibilities in order to meet specific needs effectively. However, the lessons we learned could be used to organize the pharmacy profession in becoming better prepared for future communicable disease outbreaks. We need to follow the example of pharmacy preparedness for handling attacks of bioterrorism or weapons of mass destruction.[14–20]

No specific requirements or regulations address the roles and responsibilities of pharmacists during an outbreak of a communicable disease or an attack of terrorism. The time has come for the profession to collectively develop an approach for pharmacy preparedness at the local, regional, and national levels. A leadership role needs to be established to spearhead pharmacy preparedness before the next crisis occurs.

Conclusion

Our experience demonstrates that pharmacists play a major role during crisis management with respect to drug delivery, drug information, and direct patient care. Pharmacists must be proactive and resourceful, taking the initiative to assume pharmacy-related responsibilities and accomplish them in an efficient and timely manner. Teamwork through collaboration and close communication is vital to success. Increased awareness of the importance of incorporating infection control into drug delivery is also required. By taking a leadership role in fulfilling and exceeding their professional responsibilities, pharmacists not only contribute significantly to management of a specific crisis, but also further demonstrate their value and foster their image. Continuing pharmacist contributions to emergency preparedness initiatives may be an opportunity to enhance and expand our role in patient care.

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