Short Communication

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Profile of Centralization Practices for Preparation of Non-Hazardous Drugs in Quebec Hospitals

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Abstract

Background: The preparation of many drugs intended for parenteral administration is centralized in the pharmacy of healthcare institutions. However, no data are available describing the range of drugs with centralized preparation. The objective was to establish a profile of centralization practices for the preparation of non-hazardous drug doses in the pharmacy departments of Quebec healthcare institutions.

Methods: For this cross-sectional descriptive study, an e-mail survey was distributed in March 2017 to the directors of the pharmacy departments of Quebec healthcare institutions. Respondents were asked to estimate the percentage of parenteral drug doses that were prepared centrally in the pharmacy, the name of each drug prepared this way, the criteria used to select drugs for central preparation, and the barriers to centralizing preparation of drug doses. Only descriptive statistical analyses were performed.

Results: Of the 30 directors of pharmacy departments invited to participate, 27 (90 %) responded, representing a total of 40 Quebec healthcare facilities. Overall, 232 individual drugs were centrally prepared in one or more of these facilities, for an overall median of 22 drugs per facility (min: 1, max: 101).

Conclusions: This is the first survey in Quebec and indeed all of Canada to identify the many medications that are centrally prepared in hospital pharmacies. The survey showed that the selection of drugs for central preparation

differed widely across facilities. It would be desirable for pharmacy departments in this province to collaborate on standardizing practices for central preparations.

Keywords: sterile preparations, satellite pharmacy, contamination, centralized preparation

Introduction

In the healthcare institution setting, many drugs require special preparation for parenteral administration (e.g. by the subcutaneous, intramuscular, or intravenous route). Such preparation, also known as compounding, may include dilution of the active pharmaceutical ingredient and transfer of the required volume to be administered into the appropriate container (e.g. syringe or bag). Preparing medication doses entails various risks. For the operator, these may include a risk of occupational exposure (e.g. hazardous drugs), and for the patient there may be risks related to non-compliance with standard practice (e.g. poor preparation procedures, incorrect labeling), as well as the risk of errors (e.g. inappropriate choice of active ingredient, incorrect choice of diluent or dilution volume) and the risk of microbial contamination. To reduce these risks, many associations have published guidance on good pharmacy preparation practices [1–5].

Respondents to the 2016/17 edition of the Hospital Pharmacy in Canada Survey “indicated that the pharmacy department or organization was the primary provider of both non-hazardous (84 %, 155/184) and hazardous (92 %, 170/184) sterile compounding services” [6]. The pharmacy departments of most healthcare institutions have had in place the necessary infrastructure for compounding preparations, in compliance with regulations, for several years. However, no data are available to describe the range of drugs with centralized preparation. This study was undertaken to establish a profile of centralization practices for the preparation of non-hazardous drug doses in the pharmacy department of Quebec healthcare institutions.

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Materials and methods

This descriptive cross-sectional study targeted Quebec healthcare facilities with at least one site having acute care beds. The director of the pharmacy department of each institution was contacted by email and invited to respond to a survey (available through SurveyMonkey, Palo Alto, CA, USA) over a four-week period in March 2017. Two reminders were sent following the initial invitation.

The survey questions were developed during a brainstorming session. Specifically, we identified the various parameters of interest and established the questions to be asked to answer the main objective. To establish a detailed profile of practices, respondents were first asked to report the size their respective institutions and the number of facilities (sites). Given that centralization practices may vary between facilities within the same institution, participants were also asked to provide general answers for all facilities if practices were consistent across the institution or on the basis of individual facilities if there were differences. In addition, respondents were asked to estimate the percentage of parenteral drug doses that were prepared centrally in the pharmacy, the name of each drug prepared this way, the criteria used to select drugs for central preparation, and the barriers to centralizing preparation of drug doses.

To illustrate the concept of centralization, we calculated the total number of drugs with central preparation, the number and percentage of hospitals where at least one drug had central preparation (by therapeutic class), the number of hospitals for which data were provided on the basis of individual drugs (not solely by therapeutic drug class) and the average number of drugs with central preparation per facility. Criteria for the selection of drugs for centralized preparation and barriers to centralization, as identified by respondents, are presented in decreasing order of importance. Only descriptive analyses were performed.

Results

Of the 30 directors of pharmacy departments in Quebec healthcare facilities who were invited to participate in this survey, 27 responded (participation rate 90%). These 27 respondents described practices in 40 separate facilities (78% [31/40] with fewer than 500 beds, 15% [6/40] with 500–1000 beds, and 7% [3/40] with more than 1000 beds).

Respondents provided usable data for 38 of these facilities, all of which provided centralized sterile preparation of medications.

Of the 38 facilities, 17 (45%) had central preparation for less than 25% of parenteral drug doses, 11 (29%) had central preparation for 25% to 49.9% of parenteral drug doses, 7 (18%) had central preparation for 50% to 74.9% of parenteral drug doses, and 3 (8%) had central preparation for 75% or more of parenteral drug doses. A total of 232 individual medications were centrally prepared in one or more of the facilities, for an overall median of 22 drugs per facility (min: 1, max: 101).

Larger facilities (in terms of number of beds) generally had central preparation for a higher number of drugs. For example, there were 23 facilities with central preparation of 15 or more drugs: 55% (16/29) of facilities with fewer than 500 beds, 83% (5/6) of facilities with 500–1000 beds, and 67% (2/3) of facilities with more than 1000 beds.

Table 1 presents the profile of centralization practices for preparation of non-hazardous drugs in Quebec healthcare facilities, by therapeutic drug class.

Table 2 lists the selection criteria used by pharmacy departments to determine the drugs for central preparation in the pharmacy.

Table 3 lists the challenges to centralization of sterile preparations in pharmacy, as reported by survey respondents.

Discussion

To our knowledge, this is the first study describing the profile of centralization practices for the preparation of doses of non-hazardous drugs in the pharmacy departments of Quebec healthcare facilities.

The benefits of centralized dose preparation are generally recognized as reductions in the risks of occupational exposure, poor compliance, errors and microbial contamination [1–5, 7]. Larmen-Beld *et al.* conducted a systematic review, which confirmed the importance of centralizing the preparation of drug doses in the pharmacy to reduce the risk of microbial contamination [8]. The contamination rate was 7.85% (95% confidence interval, 5.18%–10.53%, based on 13 studies) for doses of drugs prepared by nursing staff and 0.08% (based on 1 study) for doses of drugs prepared by technical staff in the pharmacy. Another literature review on the topic of microbial contamination with aseptic preparation was published previously with the same results [9].

Table 1: Profile of centralization practices for preparation of sterile non-hazardous drugs in Quebec healthcare facilities, by therapeutic drug class (n = 38 facilities).

Therapeutic drug class*	Examples	Total no. of centrally prepared drugs	No. (%) of facilities with ≥ 1 drug prepared centrally	No. of facilities providing data in terms of individual drugs	Average no. of drugs prepared per facility
Antihistamines	Diphenhydramine	1	3 (7.9)	3	1.0
Antibiotics	Aminoglycoside, antifungals, cephalosporins, penicillins, quinolones	54	33 (86.8)	22	11.1
ANS drugs	Baclofen, phenobarbital, cisatracurium	11	15 (39.5)	14	1.9
Anticoagulant	Heparin, argatroban	18	25 (65.8)	25	3.2
Cardiovascular medications	Epoprostenol, nitroglycerin, cariopegia solution	15	15 (39.5)	15	2.1
CNS drugs	Fentanyl, morphine, midazolam, bupivacaine	30	35 (92.1)	31	4.6
Electrolyte diuretics	Parenteral nutrition, calcium	25	29 (76.3)	27	3.6
ENT drugs	Chlorhexidine, lidocaine ophthalmic drops	7	14 (36.8)	4	1.8
GI drugs	Metoclopramide, octreotide, famotidine	8	16 (42.1)	16	2.0
Hormones and substitutes	Cosyntropin, dexamethasone, methylprednisolone	9	16 (42.1)	16	2.4
Immunizing agents	Infliximab, antithymocyte (rabbit and horse)	15	12 (31.6)	12	2.5
Antispasmodics	Oxytocin	1	1 (2.6)	1	1.0
Vitamins	Folic acid, multivitamin, thiamine	14	16 (42.1)	16	2.1
Enzymes	Alpha-glucosidase, rasburicase	6	4 (10.5)	4	0.5
Diagnostic agents	Tuberculin, L-arginine	3	2 (5.3)	2	0.5
Other	Methacholine, cyclosporine, zoledronic acid	15	13 (34.2)	12	2.3

ANS = autonomic nervous system; CNS = central nervous system; ENT = ear, nose, and throat; GI = gastrointestinal.

*Each drug class includes associated medications.

The data from our survey study align with data from the 2016/17 Hospital Pharmacy in Canada Survey, in which most Quebec pharmacy departments (41/43) reported offering centralized preparation services [6]. These results are not surprising, given that many drugs have been prepared centrally since the 1980s [10].

However, our survey has revealed wide diversity in the types and numbers of drugs with centralized preparation. All of the common therapeutic classes were represented, with the largest average numbers for antibiotics (11.1 drugs prepared/facility) and central nervous system drugs (4.6

drugs prepared/facility). Centralized preparation of non-hazardous drugs was initiated in the 1980s with parenteral nutrition preparations [11]. This type of preparation incorporates many ingredients (including amino acids and dextrose) and carries a high risk of microbial contamination, given the vehicles used and the duration of infusion (typically 24 hours). Over time, centralization of these preparations has continued, but compounded is now accomplished with the help of multi-channel pumps.

Subsequently, several antimicrobial drugs have been added to the list of centralized preparations of various

Table 2: Profile of criteria used to select sterile medications for central preparation in Quebec healthcare facilities.

Selection criterion*	No. (%) of facilities (n = 36)
Complexity of preparation	23 (64)
Cost	15 (42)
Frequency of use	14 (39)
Tendency for preparation errors in care units	11 (31)
Stability data compatible with centralization	12 (33)
Hazardous or high-alert drug	11 (31)
Route of administration	11 (31)
Risk of contamination	9 (25)
Specific drug class (antibiotics, electrolytes, etc.)	8 (22)
Specific drug container (bag, syringe, etc.)	3 (8)
Existence of a standard dose	3 (8)
Intended patient population	3 (8)
Drug availability	3 (8)
Need for quick access	2 (6)
Optimization of drug circuit	1 (3)
Risk of occupational exposure of healthcare providers	1 (3)
Historical practices of the facility	1 (3)

*In decreasing order of importance. Respondents were asked to list all criteria that applied in their respective facilities.

Table 3: Challenges to centralization of sterile compounding in the pharmacy in Quebec healthcare facilities (n = 34).

Challenge to centralization*	No. (%) of facilities (n = 34)
Insufficient staff (e. g. lack of human or financial resources)	29 (85)
Limited beyond-use date (according to guidelines)	17 (50)
Limited space	14 (41)
Instability of the medication after central preparation	11 (32)
Need for non-standardized doses	9 (26)
Management of parameters during batch preparation	4 (12)
Other**	7 (21)
– Substandard compounding installation	
– Not a priority for management	
– Need for harmonization among facilities	
– High cost in light of limited number of sterile preparations required	
– Increased workload for pharmacy staff	

*In decreasing order of importance. Respondents were asked to list all challenges that applied in their facilities.

**Based on manual coding of free-text answers.

facilities, because of the associated savings [12]. More specifically, centralizing the preparation of antimicrobials leads to cost savings associated with using bulk formats (e. g. cefazolin 10 g, piperacillin 36 g-tazobactam 4.5 g).

For central nervous system drugs, centralization of preparation is important because of concerns about drug safety and risks of microbial contamination (e. g. preparation of fentanyl-bupivacaine mini-bag used for obstetric deliveries, preparation of opiate bag for palliative care or

for medical assistance in dying). Various other preparations have been centralized to support compounding of medications for critical care units. In the 1990s, satellite pharmacies were set up in some intensive care units [13]. However, with the recent normative framework suggested by the United States Pharmacopeia (e. g. General Chapters 797 and 800), preparation of these medications has had to be returned to fully conforming production units in the central pharmacy (e. g. clean rooms).

Centralization of drug preparation in the pharmacy has certain disadvantages [14, 15]. Preparing drug doses in advance can increase the risk of microbial growth, given the time lag between drug preparation and administration. For example, during the outbreak of fungal meningitis in the United States from 2012 to 2015, doses of methylprednisolone prepared in a pharmacy and intended for epidural administration resulted in 753 infections and 64 deaths [16]. The US Food and Drug Administration responded by questioning the rules that apply to compounding pharmacies. In Canada, manufacturing is regulated by Health Canada, whereas compounding is regulated by provincial pharmacy regulatory authorities. Both levels of oversight have high standards, taking into account the beyond-use dates applicable to end products and the risks associated with these dates.

Centralization of drug preparation implies a close relationship between healthcare staff and the pharmacy to plan required production in real time and to avoid wastage and errors. Centralization also involves setting up quality controls and quarantine while waiting for the results of quality testing. In addition, centralization is based on the development of a standard compliance infrastructure, which can represent significant financial investment for an institution. Centralization may not be cost-effective at a small scale, and smaller institutions may find it necessary to outsource the production of certain drugs [17]. Centralization also involves training the pharmacy team and periodic certification of skills and good practices. In addition, centralizing the preparation of drug doses can increase loss and wastage.

This survey has highlighted the need to standardize practices and to prioritize medicines for which preparation should be centralized in the pharmacy. The decision to centralize preparation of a particular drug is usually made by the director of the pharmacy department or by the pharmacy team. Participants mentioned 17 potential criteria for selection of drugs suitable for centralized preparation in pharmacy, and more than a dozen barriers to centralization. Hennebicq *et al.* proposed three criteria: the distribution of doses, the frequency of use of each doses, and anticipated needs [18]. Injectable drugs at higher risk of microbial contamination can also be identified for inclusion on this list. Beaney *et al.* proposed a method for identifying drugs suitable for centralized preparation [19]. In our opinion, priority for centralized compounding should be given to parenteral nutrition preparations and hazardous drugs (group 1, 2 and 3 of National Institute for Occupational Safety and Health [20]). It may be useful to also prioritize high-risk drugs,

along with drugs for which centralization may yield with cost-saving benefits.

In light of our survey results, we believe it would be useful for directors of pharmacy departments in Quebec healthcare institutions to work together to identify and prioritize criteria for the centralization of drug preparation. Greater consistency across facilities would be beneficial for patients and would likely also facilitate the planning of future facilities and resources.

This survey study had some limitations. Some of the respondents provided answers on the basis of drug classes, not by individual drug, which limited our ability to calculate the number of drugs with central compounding. The survey did not ask respondents to report the total number of drug units produced, but such information would allow better description of the extent of central compounding in Quebec. A broader consultation through a Delphi technique or another survey, could be used to develop the list of drugs to be prioritized for central compounding at the pharmacy level.

This is the first survey to highlight the profile of drugs that are centrally prepared in hospital pharmacies in Quebec. Although many drugs are centrally prepared in the hospital setting, the particular selection of drugs is not consistent across facilities. It would be desirable for pharmacy departments to standardize practices in this regard.

Conflict of interest statement: The authors state no conflict of interest. The authors have read the journal's Publication ethics and publication malpractice statement available at the journal's website and hereby confirm that they comply with all its parts applicable to the present scientific work.

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