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Research Paper

Determinants and frequency of pharmaceutical compounding in pharmacy practice in Palestine

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Abstract

Objectives The aims of this study were to determine the frequency of prescription compounding by community pharmacists, identify factors that influence pharmacists' decisions to provide compounding services, and evaluate physicians' perspectives on prescribing medications that require compounding.

Methods The study was a cross-sectional survey administered via face-to-face structured interviews with randomly selected community pharmacists and physicians from different areas of the West Bank.

Key findings Of the 260 community pharmacists who were contacted, 212 agreed to participate in the survey, giving a response rate of 81.5%. Overall, 153 (72.2%) of respondent pharmacists provided compounding services. Compounded prescriptions accounted for 1973 (1.55%) of 126 840 prescriptions dispensed in a typical month. Among the compounders, 112 (73.2%) pharmacists reported that their goal in providing full pharmaceutical care to their patients was the most important motivator. The most frequently reported reason for not providing compounding was 'I do not receive prescriptions that require compounding' by 43 out of 59 (72.9%) pharmacists. A total of 179 out of 220 physicians consented to participate in this study giving a response rate of 81.4%. The majority of physicians (142, 79.3%) did not prescribe compounded medicines. The most important reason for their decision to prescribe compounded medicines was the unavailability of the required dosage forms. The most commonly cited reason for not prescribing them was a lack of trust in the quality of the compounded formulations.

Conclusion While most respondent pharmacists provide a compounding service this represents only a small percentage of the total volume of dispensed prescriptions. Most responding physicians do not prescribe medications that require compounding because they lack trust in the quality of the compounded formulations.

Introduction

Pharmaceutical compounding is the combining, mixing or altering of ingredients to provide a customized medication for an individual patient required by a licensed practitioner.[1] Physicians may prescribe a medication requiring compounding for a patient with special health needs. Pharmacists providing compounding services can assist the patients and physicians by providing them with access to unique medications and dosage forms that can be helpful in designing and implementing the suitable therapeutic plan for the patient.

Compounded products are needed for patient-specific situations and can contribute to patient-tailored pharmacotherapy; for example, a product that is needed but which is not commercially available, a special dosage form or strength is required for infants and children, a patient is in need of a preservative-free medication or perhaps a combination of medications is needed in one dose.[2–5] For centuries, compounding was a core task of pharmacists. Compounded prescriptions as a fraction of total prescription volume decreased during the twentieth century, to an apparent low of less than 1% during the 1970s.[6] Within the past decade, compounding has increased.[1] This increase likely reflects expanding patients' needs, new drug-delivery technologies and the

unavailability of some commercially manufactured medications as orphan drugs. Therefore, attempts have been made to raise the standards of all compounding practices.[1,6]

According to Palestinian Ministry of Health (MOH) statistics in 2010, there are 2908 registered pharmacists in the West Bank, of whom 172 work in the MOH,[7] and a minority work in pharmaceutical companies or as medical representatives of medical products. The majority of pharmacists work in community pharmacies. There are 838 community pharmacies in the West Bank. The job description of the pharmacists include that they are allowed to perform pharmaceutical compounding.[8] Unfortunately, there are no regulations or details on how to perform this compounding and ensure good quality and safety. Data on the current status of compounding in pharmacy practice are lacking in Palestine. An understanding of the current prevalence of compounding in pharmacy practice is needed. Objectives of this study were to determine the extent of prescription compounding by community pharmacists in the West Bank, identify factors that influence the decision of pharmacists to provide compounding services and evaluate the physicians' perspectives on prescribing medications that require compounding.

Materials and Methods

The study was a cross-sectional descriptive survey administered as a face-to-face structured interview with randomly selected community pharmacists and physicians from different cities and villages in the 11 districts of the West Bank. The study was conducted between December 2009 and May 2010. The study consisted of two stages as a *pre-hoc* design: in the first stage the pharmacists were interviewed and then in the second stage the physicians were interviewed.

In the first phase, a list of all registered pharmacists (2838) was obtained from the Palestinian Pharmaceutical Association,[8] and a random-number generator using Matlab software[9] was used to choose a sample that represented around 10% of registered pharmacists (280). The pharmacists were contacted by telephone to explain the aims of the study and ask for a suitable time for an interview; 20 pharmacists were not working in community pharmacies, so they were excluded, leaving a sample of 260 pharmacists. A two-page questionnaire was modified from the one used by McPherson *et al*. in a similar study in the USA.[6] Pilot testing of the questionnaire was conducted on 20 randomly selected community pharmacists and some reasons for providing or not providing compounding services were added to the questionnaire based on their recommendations. The questionnaire asked about demographical data, whether compounding services were provided or not and numbers of total and compounded medications dispensed in a typical month. Respondents who indicated providing compounding services were asked to consider nine statements, representing reasons for providing compounding services, and to give their three most important reasons. Respondents who indicated they did not provide compounding services were asked to consider 11 statements, representing reasons for not providing compounding services, and to give their three most important reasons.

In the second phase, a list of all registered physicians from the West Bank and Gaza was obtained from the Medical Association.[10] Physicians from Gaza were excluded and physicians who work in MOH were also excluded because their prescriptions are dispensed from MOH and not from community pharmacies. A sample of 220 physicians was randomly selected (10% of the West Bank physicians from private hospitals and clinics). Another two-page questionnaire was developed by the authors and a pilot test conducted on 20 randomly selected physicians. The questionnaire was modified after the pilot study where the physicians were asked to add other reasons for prescribing or not prescribing medications that require compounding (if present). The questionnaire asked about demographical data, whether they prescribed medications that require compounding or not, numbers of prescribed medications that require compounding per month, the three most commonly prescribed compounded dosage forms and their reasons for prescribing or not prescribing these medications.

After collection of the filled forms, the data were entered and descriptively analysed using the Statistical Package for the Social Sciences (SPSS), version 16 (SPSS, Chicago, IL, USA).

Results

Pharmacists' responses

Among the 260 pharmacists who were contacted, 212 agreed to participate in the survey, giving a response rate of 81.5%. The respondent pharmacists were predominantly men 133 (62.7%) who had practised pharmacy for a mean of 14.2 years (range 1–45 years); bachelor of science was the highest pharmacy degree for 196 (92.5%) of them.

Of the 212 responses, 153 (72.2%) provided compounding services. Compounded prescriptions accounted for 1973 (1.55%) of the 126 840 total prescriptions dispensed per month by the 153 compounders. The majority of pharmacists (80.4%) did not dispense compounded medications without a prescription from a physician.

In the second section of the questionnaire, pharmacists were asked to rank the three most important reasons for their decision to provide compounding services. Among the compounders, 112 (73.2%) of pharmacists reported that their aim to provide full pharmaceutical care to patients was one of the most important reasons for providing compounding service. The second most common reason for providing

compounded prescriptions was 'Compounding is a factor that reinforces trust between patients and pharmacists' which was chosen by 86 (56.2%) pharmacists. 'I enjoy compounding' was the third most common reason for providing compounded prescriptions, indicated by 79 (51.6%) pharmacists.

Non-compounders were asked to rank the three most important reasons for their decision to not provide compounding services. This part was answered by 59 pharmacists. The most frequently cited reason by 43 (72.9%) pharmacists was 'I do not receive prescriptions that require compounding'. The other two reasons were 'The required equipment or supplies are not available in my pharmacy' which was chosen by 31 (52.5%) pharmacists and 'Ministry of Health discourages compounding' which was chosen by 16 (27.1%) pharmacists (Table 1).

Table 1 Pharmacists' demographics and reasons for providing or not providing compounding services (n = 212)

Pharmacists demographics	No. (%)
Sex	
Male	133 (62.7)
Female	79 (37.3)
Scientific degree	
Bachelor of science	196 (92.4%)
Pharm D	5 (2.4)
Master in clinical pharmacy	6 (2.8)
Others	5 (2.4)
Age (years)	
20–30	31 (14.6)
30–35	72 (33.9)
35–40	44 (20.8)
>40	65 (30.7)
Population the pharmacy serves	
<1000	42 (19.8)
1000–5000	133 (62.7)
>5000	37 (17.5)
Compounders' reasons for providing compounding services (n = 153)	No. (%)*
I want to provide full pharmaceutical care to my patients	112 (73.2)
Compounding is a factor that reinforces trust between patients and pharmacists	86 (56.2)
I enjoy compounding	79 (51.6)
Compounding is an intellectually stimulating part of pharmacy practice	54 (35.3)
Compounding helps in individualization of therapy	49 (32.0)
Compounding is a profitable business practice	39 (25.5)
Compounded medications are less expensive	32 (20.9)
MOH encourages compounding	4 (2.6)
PPA encourages compounding	4 (2.6)
Non-compounders' reasons for not providing compounding services (n = 59)	No. (%)*
I do not receive prescriptions that require compounding	43 (72.9)
The required equipment or supplies are not available in my pharmacy	31 (52.5)
MOH discourages compounding	16 (27.1)
Final cost is high	15 (25.4)
There are no regulations to ensure good quality and safety	15 (25.4)
There is no trust in compounded medications	14 (23.7)
I don't have enough time	11 (18.6)
Either my pharmacy staff or I lack appropriate training	10 (17.0)
It is too expensive or difficult to maintain compounding services	8 (13.6)
PPA discourages compounding	8 (13.6)
I do not enjoy compounding	6 (10.2)

*Multiple selections were allowed and hence numbers do not add up to 100%.

MOH, Ministry of Health; PPA, Palestinian Pharmaceutical Association.

Physicians' responses

Regarding the results of this study among physicians, 179 out of 220 physicians consented to participate in this study, giving a response rate of 81.4%. Most of the respondent physicians were males 118 (65.9%). About one-third of these physicians 54 (30.2%) were general practitioners, while the remaining were specialized physicians (dermatologists, gastroenterologists, internists, otologists, surgeons, residents, paediatricians, urologists, orthopedists, gynaecologists). Regarding the type of clinic, 61 (34.1%) were private hospital doctors, while 118 (65.9%) had private clinics. The majority of physicians 142 (79.3%) did not prescribe compounded medications. All physicians who prescribed medications that require compounding prescribed fewer than 20 prescriptions that needed compounding per month. The three most commonly prescribed dosage forms were topical preparations (36 out of 37 physicians, 97.3%), oral solution (29 out of 37 physicians, 78.4%) and oral suspension (16 out of 37 physicians, 43.2%).

The physicians were asked to choose from a list the three most important reasons for their decision to prescribe medications requiring compounding. This part was answered by 37 physicians who told that they prescribed medications that require compounding. The unavailability of the required dosage forms was the most important reason for 26 (70.3%) physicians. The unavailability of suitable paediatric medicines was a reason for 21 (56.8%) physicians, while the lack of the required strength commercially was the third important reason by 17 (46.0%) physicians.

Physicians who did not prescribe compounded medications were asked to rank their three most important reasons for this. Most physicians indicated lack of trust in the quality of the compounded formulations (138 out of 142, 97.2%) and a belief that the compounded formulations have poor patient compliance (134 out of 142, 94.4%). The third most

common reason was their belief that MOH does not allow compounded formulations (91 out of 142, 64.1%) (Table 2).

Discussion

The main findings of this study show that most community pharmacists (72.2%) dispensed prescriptions that require compounding. Compounded prescriptions accounted for 1.55% of prescriptions dispensed in a typical month. The majority of physicians (79.3%) did not prescribe compounded medicines. The most important reason for their decision to prescribe compounded medicines was the unavailability of the required dosage forms. The most commonly cited reason for not prescribing them was lack of trust in the quality of the compounded formulations.

The strength of this study is in providing baseline data about pharmaceutical compounding in the West Bank-Palestine which can be helpful in the development and regulating this field. This is the first study that has investigated pharmaceutical compounding in our country. Limitations of this study include lack of information about the acceptance and trust of patients towards compounded formulations and lack of information that assess the differences in quality and safety between commercial and pharmacy-compounded preparations. These limitations may be a potential area for future research. Also, we were unable to stratify physicians by place of work or specialty because the list that we had from the Medical Association included all doctors in alphabetical order. This might be a limitation because doctors from different specialties are not expected to have the same prescription profile, so future studies might concentrate on certain specialties, such as dermatologists.

The results show that compounding services are in demand, but it is not as prevalent as in other parts of the world. Schommer *et al*.[11] from the USA found that 'almost 98%' of surveyed Wisconsin pharmacists compounded prescriptions. McPherson *et al*.[6] from the USA also found that 94% of respondent community pharmacies provided compounding services at the time of their survey. Despite the fact that many Palestinian pharmacists provide a compounding service, the extent of compounding represents only 1.55% of the total prescriptions dispensed per month. A study in Dutch community pharmacies found that the overall frequency of prescriptions for pharmacy compounded medicines in relation to the total number of prescriptions was 3.4%.[3] It was 2.3% in McPherson *et al*.'s study from the USA.[6]

The goal of providing full pharmaceutical care to patients was the most frequently selected reason for providing compounding services by pharmacists. Despite this being the reason given by the pharmacists, pharmaceutical compounding would not be generally regarded as a component of

Table 2 Physicians' demographics and reasons for prescribing or not prescribing medications that require compounding (n = 179)

Physicians' demographics	No. (%)
Sex	
Male	118 (65.9)
Female	61 (34.1)
Specialty	
General medicine	54 (30.2)
Dermatologist	8 (4.5)
Gastroenterologist	7 (3.9)
Internist	17 (9.5)
Otologist	9 (5.0)
Paediatrician	20 (11.1)
Urologist	8 (4.5)
Orthopedist	8 (4.5)
Gynaecologist	20 (11.1)
Others	28 (15.7)
Work	
Private hospital	61 (34.1)
Private clinic	118 (65.9)
Dosage forms prescribed	
Topical preparations	36 (97.3)
Oral solutions	29 (78.4)
Oral suspensions	16 (43.2)
Tablets	5 (13.5)
Capsules	13 (35.1)
Sterile products	6 (16.2)
Physicians' reasons for prescribing medications that require compounding (n = 37)	No. (%)*
Dosage form is not commercially available	26 (70.3)
Prepare paediatric dose from adult dose	21 (56.8)
Strength is not commercially available	17 (46.0)
I trust compounded formulations more than manufactured drugs	13 (35.1)
Combination of ingredients is not commercially available	9 (24.3)
Improve flavour of commercial products	9 (24.3)
Desired therapeutic outcomes are not met with manufactured products	8 (21.6)
Route of administration is not commercially available	5 (13.5)
Compounded formulations have high patient compliance	3 (8.1)
The product was discontinued by manufacturer	0 (0.0)
Physicians' reasons for not prescribing medications that require compounding (n = 142)	No. (%)*
Lack of trust in the quality of the compounded formulations	138 (97.2)
Compounded formulations have poor patient compliance	134 (94.4)
MOH does not allow compounded formulations	91 (64.1)
Compounded prescriptions are inconvenient economically	63 (44.4)

*Multiple selections were allowed and hence numbers do not add up to 100%.
MOH, Ministry of Health.

pharmaceutical care. Pharmaceutical care has evolved within the profession of pharmacy and it is defined as 'the process through which a pharmacist cooperates with a patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient'.[12] Other studies have shown that pharmacists described having a closer relationship with patients receiving compounded preparations than with patients receiving only manufactured products.[13] They perceived a greater responsibility in providing patient-centred care when dispensing a compounded medication compared with a manufactured product and reported greater follow-up with patients and physicians regarding therapy with compounded medications than manufactured products.[14] This idea is also reported in this study when pharmacists considered compounding as a factor that reinforces trust between patients and pharmacists. This trust may encourage patients to take their medications and may result in increased patient compliance. The enjoyment that pharmacists feel when they prepare compounded preparations was reported as a third reason for providing compounded prescription. This reason was interpreted by McPherson *et al*.[6] as decisions by the pharmacist to serve his/her own needs or desires.

Regarding the reasons for not offering a compounding service in the pharmacy, here the most frequently cited reason was 'I do not receive prescriptions that require compounding' as reported by other similar studies.[6] Interestingly, lack of time and training were not reported among the most important three reasons for not providing this service. The unavailability of the required equipment or supplies in the pharmacy, and that the MOH discourages compounding, were the second and third reasons respectively. The lack of raw materials (drugs, flavourings, etc.) can be solved by encouraging companies that are present in the Palestinian market, and which supply raw materials, to revise their policies to consider the needs of pharmacies that would like to provide compounding services.

McPherson *et al*.[6] reported that 'my compounding service is a response to demand by prescribers' as a second reason for providing compounding, which indicates that cooperation between physicians and pharmacists should be considered as an essential part of a successful therapy.

The majority of the interviewed physicians did not prescribe compounded medicines. This result is in accordance with the pharmacists' reports that they did not provide compounding due to lack of compounding requests by physicians. This is confirmed also by the very low number of prescriptions that physicians prescribed, which was fewer than 20 prescriptions per month. The most important reasons reported by physicians who did not prescribe compounded formulation were the lack of trust in the quality of the compounded formulations, and the belief that the compounded formulations have poor patient compliance. There are serious concerns regarding the quality of compounded products especially enteral and parenteral products. Improper compounding can lead to microbial contamination and serious infections.[15–17] Within the past decade, attempts have been made to raise the standards of all compounding practices through the efforts of the United States Pharmacopeia (USP) and the American Society of Health-System Pharmacists (ASHP).[2] The USP has put forth further procedures and requirements on compounding sterile and non-sterile preparations in an attempt to raise the standards of compounding and prevent the risk of patient harm.[18] In our country, there are no regulations at all to ensure the quality and safety of compounded medications. Efforts to improve pharmacy compounding practices should be commended. Adoption of standardized USP guidelines or any other suitable guidelines by regulatory bodies such as MOH have the potential to be a significant step forward in improving compounding pharmacy practices and ensuring the quality and safety of compounded products. Here, colleges of pharmacy, health regulatory bodies and pharmacists can cooperate through continuing education and compounding training to improve the skills of pharmacist.

The third reason for not prescribing compounding formulation was the physicians' belief that the MOH doesn't allow compounded formulations. This last point can be resolved by contacting the regulatory body in the MOH to clarify the regulations and inform the physicians and pharmacists regarding these regulations.

Compounding is a critical part of providing care to patients with special and individualized needs who may be underserved by industrial product formulations. However, pharmacists are obligated to ensure that the medications they compound are safe, effective and of exceptional quality.[2] Pharmacy graduates provided with relevant compounding experience will be better equipped to optimize patient outcomes than graduates who are not trained in compounding.[19] Efforts to improve training and education of pharmacy staff, environmental control, quality assurance and sterilization practices will result in safe compounded medications.[1]

Conclusion

Most responding pharmacists provide a compounding service, but at a low prescription volume. Most responding physicians do not prescribe medications that require compounding because they lack trust in the quality of the compounded formulations. Regulations that cover compounding practice are needed to ensure good quality and safety of compounded products.

Declarations

Conflict of interest

The Authors declare that they have no conflicts of interest to disclose.

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References

1. Pegues DA. Improving and enforcing compounding pharmacy practices to protect patients. *Clin Infect Dis* 2006; 43: 838–840.
2. Treadway AK *et al*. Practices of pharmacies that compound extemporaneous formulations. *Am J Health Syst Pharm* 2007; 64: 1403–1409.
3. Buurma H *et al*. Frequency, nature and determinants of pharmacy compounded medicines in Dutch community pharmacies. *Pharm World Sci* 2003; 25: 280–287.
4. Brown S. Prescribing flexibility through prescription compounding. *Tech Reg Anesth Pain Manag* 2008; 12: 19–121.
5. Loyd A. Does a limited distribution system fit the definition of commercially available? *Int J Pharm Compound* 2011; 8: 9.
6. McPherson TB *et al*. Prevalence of compounding in independent community pharmacy practice. *J Am Pharm Assoc (2003)* 2006; 46: 568–573.
7. Ministry of Health. Health Status in Palestine 2010. http://www.moh.ps/attach/297.pdf (accessed 7 August 2011).
8. Palestinian Pharmaceutical Association. Registered pharmacists in the West Bank districts. (language: Arabic). http://www.ppa.ps/med_index/pharmacist.html (accessed 7 August 2011).
9. MathWorks. Matlab help. 2009, www.mathworks.com/help/techdoc/ref/rand.html;jsessionid=HGKgNWtDhbVhm19qcfxB30KlhXRj071FJqk2KNgNK2Nhtwc8hpQn!-1738074165 (accessed 4 August 2011).
10. Medical Association-Jerusalem Center. Name, Specialization, and Address of doctors. (language: Arabic). www.jma.ps/en/#doctors (accessed 4 August 2011).
11. Schommer JC *et al*. Prescription compounding in Wisconsin pharmacies. *Wisc Pharm* 1990; 59: 24–25.
12. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm* 1990; 47: 533–743.
13. Yancey V *et al*. Perceptions of pharmaceutical care among pharmacists offering compounding services. *J Am Pharm Assoc (2003)* 2008; 48: 508–514.
14. McPherson T, Fontane P. Patient-centered care in the community-based compounding practice setting. *J Am Pharm Assoc (2003)* 2010; 50: 37–44.
15. Austin PD, Elia M. A systematic review and meta-analysis of the risk of microbial contamination of aseptically prepared doses in different environments. *J Pharm Pharm Sci* 2009; 12: 233–242.
16. Civen R *et al*. Outbreak of Serratia marcescens infections following injection of betamethasone compounded at a community pharmacy. *Clin Infect Dis* 2006; 43: 831–837.
17. Gebhart F. Fatal meningitis links to compounding by California pharmacy. *Drug Topics* 2001; 13: 32.
18. United States Pharmacopeial Convention, eds. *The United States Pharmacopeia, 27th Rev., and the National Formulary*, 22nd edn. Rockville, MD: US Pharmacopeial, 2004.
19. Martin KS *et al*. Independent community pharmacists' perspectives on compounding in contemporary pharmacy education. *Am J Pharm Educ* 2009; 73: 54.

