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Original Article

Determination of pharmacy pharmacists and pharmacy employees' knowledge of and attitudes towards magistral drug preparation in Malatya/ Turkey

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ABSTRACT

Magistral drugs are preferred when present preparations are not sufficient. Even though their usage had decreased, it is predicted that magistral applications will be used more often in the future. In this study pharmacists and pharmacy employees working in 95 pharmacies in Malatya city center agreed to participate in the study (n=203) and filled in a questionnaire which was prepared according to literature. In the analysis of the obtained data, frequency and percentages were calculated using SPSS 24.0 program. It was observed that 11.1% of the pharmacies were close to a health center and 88.0% of the participants were preparing magistral drugs. 55.2% of the participants stated that they prepared magistral medications 1-2 times a week. According to the results, although the frequency varied with the localization of pharmacies, magistral drug preparation ratios were generally similar to those found in the literature. Preferred magistral drug forms were: creams (74.7%), pomades (69.8%) and solutions (54.7%). Of the participants who declared themselves to be inadequately skilled in magistral drug preparation, 19.5% said that the prescriptions were insufficient and 33.3% reported that the doctors' prescriptions were incomplete or unreadable.

Keywords: Magistral formulas, pharmacy workers, knowledge, preparation, Malatya/Turkey

INTRODUCTION

Magistral drugs are prepared by pharmacists according to the prescriptions of doctors (Geçgil 1991). Extemporaneous, compounding, off-label and unlicensed are terms also commonly used instead of magistral (Conroy et al. 2000; Kairuz et al. 2007). The common points for all terms are: they have at least one raw material, they are produced on a non-industrial scale and they are prepared in a suitable pharmaceutical form for the individual.

Industrial developments and advances in pharmaceutical technology has reduced the need and usage of magistral drugs. With such advances, more drugs can be produced in a shorter time and in a cheaper manner (Baytop 1997). However, genetic differences in people and the psychological motivations of a person based medication have received attention to magistral preparations again (Kairuz et al. 2007a; Ilgın Ruhi 2010). In cases where readymade preparations are insufficient, magistral applications are preferred for the patient-drug-dosage equilibration (Minghettiu et al. 2000; Martin et al. 2009; Schellekens et al. 2017).

The ability to prepare magistral formulas is considered an important skill for pharmacists in many countries (Täerel et al. 2014; Kristina et al. 2017). Although the frequency of magistral drug preparation in different countries has been reported to be 1-10% in recent years, these rates vary (Kristina et al. 2017). Difficulties in finding appropriate drug forms in newborn and childhood peri-

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ods, usage of some drugs in the treatment of rare diseases lead to the prescription of magistral formulas (Staubach and Metz 2013; Garcia 2015; Pérez 2016; Staubach and Weisshaar 2016; Schellekens et al. 2017). The ability to form different forms of drugs in essential doses alongside raw material procurement is an important advantage, but pharmacokinetic issues and certain other problems are faced in magistral drug preparations (Leal et al. 2012; Sklenár et al. 2013; Pereira et al. 2016).

The increasing importance of clinical pharmacy globally and in Turkey has made research into magistral drugs mandatory. Although there many global and European studies (Conroy et al. 2000; Brion et al. 2003; Kairuz et al. 2007a; Kairuz et al. 2007b; Neubert et al. 2008; Sellers and Utian 2014; Kristina et al. 2017), there are not enough studies in Turkey (Andaç et al. 2015). There is not sufficient data regarding the current state of the magistral drugs. Research into magistral medication will be important in increasing levels of pharmacist competence (Kristina et al. 2017).

The aims of this study are: to determine the scope of magistral drug applications, to establish the frequency of magistral drug applications, to identify the problems in preparing and providing magistral drug preparation among pharmacists. Similar studies will provide important viewpoints in the future of pharmaceuticals and pharmacies.

MATERIALS AND METHODS

This research was carried out in order to determine the information/attitudes of pharmacy pharmacists and pharmacy employees towards the preparation of magistral drugs and the problems they encounter in preparing magistral formulations. The universe of the study was made up of those pharmacists and pharmacy employees working in the city center of Malatya between 2017-2018 (Malatya Eczacılar Odası, 2018). The aim of the study was to reach the entire universe without using a sample selection method. The research was completed with 203 pharmacists and pharmacy employees working in 95 pharmacies. Necessary permissions were obtained for conducting the research from the Malatya Clinical Research Ethics Committee (Ethics Committee no. 2018/7-5). After the visits to the pharmacies and the purpose-method of the study were explained, 203 pharmacists and pharmacy employees agreed to participate in the study on a voluntary basis. In the collection of data, a questionnaire form which was prepared by the researchers according to the literature was used. The questionnaire consisted of questions about the following: pharmacy-specific features, socio-demographic characteristics of the employees, the magistral drug preparation ability of the employees, magistral formula preperation frequency, knowledge and attitudes towards magistral drugs (Kairuz et al. 2007a; Kairuz et al. 2007b; Neubert et al. 2008; Zaid et al. 2012; Andaç et al. 2015). The questionnaires were completed in 5-10 minutes and the forms were collected by the researchers.

Statistical analysis

The data was analyzed using the IBM SPSS 24.0 program (IBM, Armonk, NY, USA), and the frequency and percentages were determined.

RESULTS

When the descriptive features of the pharmacies were investigated; 29.1% (n=58) were determined to be on the street, 28.6% (n=57) were on side streets, 25.6% (n=51) were near to hospitals and 11.1% (n=22) were near to health centers. The number of years the pharmacies had been operating differed from 1 to 76 and the average number of years was 14.87±13.36. No statistical significance was found when location and working years of the pharmacies were compared with magistral drug preparation status ($p>0.05$) (Table 1).

Of the pharmacy employees; 22.8% (n=46) were pharmacists, 7.8% (n=16) were technicians (associate degree), 69.2% (n=137) were male, 54.5% (n=110) were high school graduates and the average age was 34.23±10.22. When magistral drug preparation status was compared with the features of the pharmacy workers, pharmacy workers who had not graduated from university were determinated to prepare magistral drugs more ($p=0.016$) Also there was no statistical significance in working time of participants and self-sufficiency levels ($p>0.05$) (Table 2).

Among the pharmacy employees; 88.0% (n=176) stated that they prepared magistral drugs, 66.3% (n=122) pointed out that they only prepared prescribed preparations and 55.2% (n=100) said that magistral drug preparation frequency was 1-2 times a week. 19.5% (n=32) of the participants stated that they felt inadequately skilled in magistral drug preparation. While the main reasons for this status were prescription inadequacies (33.3%, n=12) and lack of adequate information resources (25.0%, n=9), 5.6% (n=2) of the participants stated that they had forgotten their knowledge on this topic.

Magistral prescriptions were determined to come from: state hospitals (75.0%, n= 138), private hospitals (72.8%, n=134), dermatology (95.3%, n=122), ear-nose and throat (ENT) (50.3%, n=69) and general surgery (17.0%, n=20) polyclinics (Table 3).

Table 1. Comparison of the magistral drug preparation status and the features of the pharmacies

		Magistral Drug Preparation Status				
		Yes		No		
		n	%	n	%	Significance
Location of the pharmacy	Not near to a health center	79	59.0	6	40.0	X^2=1.97
	Near to a health center	55	41.0	9	60.0	p=0.179
Working years of the pharmacy	1-9 years	47	43.9	4	36.4	X^2=0.23

Table 2. Comparison of magistral drug preparation status and the features of the pharmacy workers

		Majistral Drug Preparation Status				
		Yes		No		
		n	%	n	%	Significance
Working time of participants	<15 years	16	22.5	3	42.9	X2=1.42
	≥1 years	55	77.5	4	57.1	p=0.352
Education level	High school or less	61	74.4	4	36.4	X2=6.66
	University	21	25.6	7	63.6	p=0.016
Feeling self-sufficient	Yes	90	79.6	8	80.0	X2=0.73
	No	23	20.4	2	20.0	p=0.670

Table 3. From which polyclinics do frequently prescribed magistral formulas come?

Branches	N	%	Branches	N	%
Dermatology	122	95.3	ENT	69	50.3
General surgery	20	17.0	Internal medicine	21	17.2
Anesthesia and reanimation	16	11.7	Pediatrics	14	9.4
Infectious Diseases	10	6.4	Oncology	9	5.8
Neurology	7	4.7	Urology	7	4.7
Orthopedic	6	4.1	Ophthalmology	6	4.1
Transplantology	6	4.1	Gynecology	6	4.1
Psychiatry	5	3.5	Cardiology	4	2.3
Radiology	4	2.3	Gastrology	2	1.2

Table 4. Which pharmaceutical dosage forms are preferred as magistral formulations?

Pharmaceutical dosages form	N	%	Pharmaceutical dosages form	N	%
Cream	95	74.7	Ointment	96	69.8
Solution	82	54.7	Lotion	72	50.9
Shampoo	56	46.5	Powders	42	33.5
Emulsion	38	30.4	Suspension	37	28.4
Capsule-Cachet	31	25.9	Suppository	16	13.5
Pockets	14	10.7	Ovule	7	7.1
Liniment	8	5.9	Colloids	5	3.6

Table 5. Problems of pharmacy employees when preparing a prescription for magistral medication

	N	%
Non-payment of some prescriptions in the SGK system	129	82.7
Incomplete or unreadable prescription from doctors	100	67.8
Lack of raw materials	99	67.6
Inability to supply raw materials quickly	73	54.9
Unknown formula	60	45.8
Dissolution shortage	42	32.6
Calculation shortage	36	28.6
Too many pharmaceutical packaging forms	32	26.7

N: Number of respondents, %: Percentage of respondents.

The pharmaceutical forms of the desired magistral formulas were found to be: creams (74.7%, n=95), ointments (69.8%, n=96), solutions (54.7%, n=82), lotions (50.9%, n=72) and shampoos (46.5%, n=56), respectively (Table 4).

The answers to the question 'How often do you experience problems (as outlined in table 5), when preparing a prescription for a magistral drug?' were: payment problems with the Social Security Institution (SGK) system (82.7%, n=129), incomplete or unreadable prescriptions (67.8%, n=100), lack of raw materials (67.6%, n=99) and the inability to supply the raw material quickly (54.9%, n=73) (Table 5).

Pharmacy workers stated that they mostly consulted the 'Magistral Formulas Book' (14.2%, n=26) and professional experience (9.8%, n=18) in preparation of magistral formulas while 64.5% (n=118) stated they used more than one source (Table 6).

Of the pharmacy workers who said 'yes' to the question 'Is there a magistral formula that you do not want to prepare even though it is prescribed?'(19.1%), twentyseven (n=27) of them gave the reason for their answer as; technical hardware problems (33.3%, n=9), responsibilities of green and red prescriptions (22.2%, n=6) and raw material supply problems (18.5%, n=5) in order (Table 7).

Most of the pharmacies that did not prepare magistral formulas were experiencing raw material problems. The low frequency of prescriptions caused problems, both in supplying and maintaining raw materials (Table 8). Although most of the pharmacies often prepared frequently prescribed formulas, only a few pharmacies stated that they prepared rarely prescribed formulas. No one among the respondents stated that they did not trust themselves.

Pharmacy workers who said 'no' to the question 'Do you feel sufficient self-sufficiency in preparing a magistral prescription?' (19.5%, n=36) gave the reason for their answer as: insufficient prescriptions from doctors (33.3%, n=12) and lack of source books (25.0%, n=9) (Table 9).

Only one (0.6%) pharmacy employee answered the question 'What are the patients attitudes for non-prescribed magistral formulas?' as 'negative'. It was understood that patients did not usually give negative feedback on magistral formulas (Table 10).

Of the pharmacy employees, 44.7% (n=85) stated that vocational training programs in 'magistral formulas preparation' were organized, and 22.0% (n=42) said that these programs were sufficient. Of the employees, 89.5% (n=171) thought that vocational training programs should be organized in this regard.

When the thoughts of pharmacy workers regarding magistral formulas were questioned; 71.9% (n=133) stated that 'Magistral drug applications are useful applications for health professionals, pharmaceutical companies and health authorities', 62.2% (n=115) stated that 'Magistral drugs or drug mixes should not be made by employees without training', 60.5% (n=112) stated that 'More authority and responsibility should be given to pharmacists and pharmaceutics employees about magistral

Table 6. Source of information in preparation of magistral drug

	N	%
Book of magistral formulas	26	14.2
Based on professional experience	18	9.8
Books of medical formulas	7	3.8
Pharmacopeia and Codex	4	2.2
Consult with experienced colleagues	4	2.2
To consult doctor information	2	1.1
Internet	1	0.5

Table 7. The reasons for not preparing magistral formulas in pharmacies

	N	%
Technical hardware problems	9	33.3
Responsibilities in narcotic prescription and others	6	22.2
Raw material supply problems	5	18.5
Financial worries	4	14.8
Time problem	2	7.4
Distrust of patients towards magistral drugs	1	3.7

Table 8. Why do pharmacies not prepare prescriptions?

	N	%
Difficulties in supplying raw materials	12	6.1
Lack of raw materials to meet the prescription	11	5.6
Low prescription frequency, need to buy raw materials and then having to expire them due to expiration dates	9	4.5
Not enough laboratory facilities	6	3.0
Difficulties in entering the prescription in the system and being afraid of SGK interruptions	4	2.0
Difficulties in supplying, recording and preserving toxic and separate substances	3	1.5
Considering that the written magistral formulation is incompatible with the diagnosis and not wanting to take responsibility	2	1.0
Difficulties in reading prescriptions	1	0.5
Unsuitable hygiene conditions in the pharmacy	1	0.5
Finding ready drugs more reliable when compared with magistral formulations	1	0.5

Table 9. Causes of not feeling sufficient in preparing a prescription for magistral medication

	N	%
Insufficient prescriptions of doctors	12	33.3
Lack of enough information resources in pharmacies related to these prescriptions	9	25.0
Lack of enough education about pharmaceutics in university	3	8.3
Contradiction between information sources	3	8.3
Having forgotten their knowledge over time	2	5.6
Other reasons	7	19.4

Table 10. What are the patients' attitudes towards non-prescribed magistral formulas?

	N	%
No negative feedback so far	117	69.6
Although we have a few problems, we usually receive positive feedback	27	16.1
There has been no positive or negative feedback so far	23	13.7
We have received negative feedback	1	0.6

Table 11. Thoughts about magistral formulas

	N	%
Magistral drug applications are useful applications for health professionals, pharmaceutical companies and health authorities	133	71.9
Magistral drugs or drug mixes should not be made by employees without training	115	62.2
More authority and responsibility should be given to pharmacists and pharmaceutics employees regarding magistral drugs	112	60.5
Herbal and alternative medicine products should be prepared and presented as magistral in pharmacies	106	57.3
Pharmacies should be able to receive academic or direct government support for the improvement and modernization of laboratory environments	105	56.8
Clinical studies on magistral formulas should be made and approved	104	56.5
Magistral formulas are more effective in terms of patient motivation when compared with readymade drugs	70	37.8
Good pharmaceutical manufacturing practices (GMP) standards are achieved in pharmacy laboratories	58	31.4
Definitions, laws and regulations about magistral drug applications are sufficient	50	27.0
There is no disadvantage to preparing magistral formulas for children or pregnant women	44	23.8
Magistral formulas should only be applied externally or peroral	27	14.6
There should be no need for magistral formulas, all drugs should be produced by pharmaceutical companies according to certain standards	23	12.4

Table 12. Thoughts on the necessity of magistral formulas

	N	%
Magistral formulas contribute to pharmacy turnover	135	79.9
Contribution to the motivation of colleagues as a morale factor	83	57.2
Provide facility in production of special personal drugs (intermediate dose, etc.)	80	53.7
Provide preparation of personal and home care medications	74	49.7
They are functional cosmetic products and supplements	59	42.4
Provide the production of medicines with new formulas and stability problems	60	42.3
Provides the production of drugs with import problems	54	37.5
Has strategic importance in social negativities such as war and economic crises	52	35.6
Provides advantages for the preparation of orphan drugs (less frequently sold drugs)	43	30.3
Provides access to non-industrial drugs at a cheap price	33	24.3

drugs', 57.3% (n=106) stated that 'Herbal and alternative medicine products should be prepared and presented as magistral in pharmacies' (Table 11).

The pharmacy workers stated; 'Magistral formulas contribute to pharmacy turnover', 'Magistral formulas contribute to the motivation of colleague as a morale factor', 'Magistral formulas provide facility in production of special personal drugs (intermediate dose, etc.)', 'Magistral formulas provide preparation of personal and home care medications' by 79.9%, 57.2%, 53.7%, 49.7% (Table 12).

DISCUSSION

In the research, although the frequency of magistral formula preparation varied with the localization of pharmacies, the results were generally compatible with Kristina (2017) and Martin (2009)'s studies (Martin et al. 2009; Kristina et al. 2017).

According to the results of the research, no statistical significance was found when magistral drug preparation status was compared with location of the pharmacies, working years of the pharmacies, working time and ability of participants in preparing magistral formulas (Table 1, Table 2). However, magistral drug preparation status was significantly lower in university graduates when compared with graduates of high school or lower (Table 2). Ergün et al. (Ergün et al. 2010) determined that, most of the magistral drugs examined in their study were inappropriate. When this study is assessed with the research's findings, the reason for inappropriate magistral drug production may be interpreted as the result of lower education levels of the pharmacy workers who prepare magistral drug. These topics are important points to research further.

It was found that magistral prescriptions mostly came from dermatology (95.3%) and ENT (50.3%) polyclinics (Table 3). Dermatology and ENT polyclinics commonly prefer magistral formulas (Martin et al. 2009; Staubach and Metz 2013; Staubach and Weisshaar 2016; Kristina et al. 2017). The results of the research regarding this topic are generally compatible with reference studies (Martin et al. 2009; Kristina et al. 2017).

Martin et al. determined the topical and transdermal formulas preparation rate of at least once a week to be between 30% and 46% in their study (Martin et al. 2009). In this study, the rate

of magistral drug preparation (mostly topical and transdermal) was found to be as 55.2%, (Table 4). The results are compatible with reference studies. We think that the low rate in oral magistral drug preparation is due to the non-inclusion of hospital pharmacies (Gubara et al. 2016; Gubara et al. 2018).

In the study, of the participants who found themselves insufficiently trained in preparing magistral preperations, 19.5% stated that the prescriptions were inadequate and 33.3% said that the prescriptions were incomplete or unreadable (Table 9). In addition to this, a high frequency of technical equipment problems, a shortage of raw materials and supply problems (Table 7) are compatible with reference studies (Minghettiu et al. 2000; Leal et al. 2012).

In the study, the suggestion that magistral drugs should not be carried out except by pharmacists and pharmacy employees was approved by 62.2% (Table 11). This rate is close to the result of 69% from the compilation of Kristina et al. (Kristina et al. 2017).

In Martin et al.'s study regarding preparing a magistral formula, consulting 'an experienced colleague' comes first, 'reference book' and 'experience' afterwards (Martin et al. 2009). This study shows a partial similarity with Martin et al.'s study (Table 6).

Of the participants, 88% stated that they prepared magistral drugs. This rate is significantly higher than Taerel et al.'s study in Bucharest (Tăerel et al. 2014). We think that the reason for the difference is that those pharmacies that did not prepare magistral prescriptions refused to participate in the research (Neubert et al. 2008; Gubara et al. 2016; Gubara et al. 2018)

The most common problems encountered by pharmacies in preparing magistral formulas are the problems experienced with refund institutions (SGK) (82.7%), incomplete or unreadable prescriptions (67.8%) and lack of raw materials (67.6%) (Table 5).

The reasons for not preparing magistral formulas were stated as; having difficulties in supplying the essential raw materials (6.1%), having difficulties in preserving raw materials for the prescriptions (5.6%), the need for buying the raw materials each time the prescription comes because of the low prescription rates, discarding the raw materials because of the expiration dates (4.5%) and inadequate laboratory facilities (3.0%) (Table 8).

Of the participants, 89.5% think that vocational training programs should be organized for the preparation of magistral drugs, and this result is similar to the results of Martin et al's study (Martin et al. 2009).

CONCLUSION

The quality of magistral drugs is important (Kristina et al. 2017). In Leal et al.'s study concerning the control of the magistral drugs prepared in Brazil, it was reported that 70% of the required criteria could not be determined. The cause of this situation was defined as: active substance differences, raw material quality, inadequate raw material control and procedures (Leal et al. 2012). However, magistral drugs prepared under appropriate conditions show the same effects as fabricated forms (Olguín et al. 2009).

The preparation of magistral products which have not been prescribed by the physician and the lack of formulations according to the standards are also problems encountered in Turkey (Emmerton et al. 2005; Ergün et al. 2010; Özbek and Kırmızı 2016).

In this study, it is understood that pharmacies prepare magistral products, but they should be supported, with training, technical facilities and procedures, to achieve the desired quality standards. Making raw materials easier to be obtained in smaller packages and support of pharmacies in terms of laboratory facilities will help in solving these problems. Quality control research into magistral products with similar studies will contribute to further improvements in the health sector.

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