

Knowledge and Perception of Pharmacy Practitioners toward Sustained Release Dosage Forms in Benghazi Community Pharmacies

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ABSTRACT

Background: The term sustained release dosage form is used to describe the delivery system which slowly releases the drug in the circulation over a prolonged period of time. Sustained release formulations have many advantages over immediate release dosage forms. For instance, improvement of patient's compliance due to reduction in dose frequency. This study was carried out to evaluate and compare the knowledge and perception of pharmacy practitioners toward the sustained release medications in Benghazi community pharmacies.

Method: A cross sectional survey was conducted during January and February 2018 by distributing a questionnaire to a selected study sample of pharmacy practitioners. The collected data were analyzed using the Statistical Package for Social Sciences.

Results and discussion: The results demonstrated that oral sustained release medications are the most available and dispensed type in community pharmacies, where the central nervous system drugs accounted for the highest percentage then the cardiovascular system drugs (mainly angina). Interestingly, about (45%) of participants did not know the reasons for the presence of a few number of sustained release medications in the community pharmacies, and there was a significant difference between the participants ($P = 0.004$). Additionally, (41%) of participants believed that any drug can be formulated as a sustained release dosage form and there was no a significant difference between different groups of (participants ($P = 0.90$)).

Conclusion: The majority of pharmacy practitioners seem to have a good knowledge toward the sustained release dosage forms but there is a lack of knowledge in some concepts. The higher cost of the single course therapy of sustained release medications in comparison with immediate release medications can be compensated by better disease management and less drug side effects.

1. INTRODUCTION

Drugs are often administered with the aim of maintaining the therapeutic levels of drugs in plasma or tissue constant over a prolonged period of time. This can be achieved with different doses **and** dosing intervals. However, from the point of view of patient 's compliance, the dosage regimen of orally administered drug may be considered to be optimal when the therapeutic effect is maintained for the desired treatment period at the lowest frequency of administration. This can be achieved by using a sustained release dosage form (SRDF) [1, 2].

SRDFs involve any delivery system that produces slow release of drug over a long period of time [3, 4]. Indeed, these dosage forms are commonly administered only once or twice daily, compared to the counterpart immediate release dosage forms (IRDFs) that have to be taken three or four times daily to achieve the same effect [2]. The majority of oral pharmaceutical products are designed as IRDFs for rapid onset of action. IRDFs have various limitations including; poor patient's compliance due to frequent doses are required for drugs with short half-lives.

Additionally, fluctuations of steady state plasma drug concentrations can lead to a patient being over medicated or under medicated [5, 6].

Whereas sustained release medications have various advantages over immediate release medications. These include reduction in dose frequency thus patient's compliance improvement, and suitable for psychiatric patients who forget to take their medications and for chronic diseases [2]. Furthermore, drug plasma fluctuation is reduced, and steady state plasma drug concentrations can be maintained over a long period of time. Moreover, reduction in drug side effects owing to drug level in the plasma is maintained within a narrow window with no sharp peaks [5, 7].

However, SRDFs have limitations including; they do not allow for the prompt termination of therapy. Moreover, the main problem of these dosage forms is possibility of dose dumping (a phenomenon when large quantity of drug is released rapidly or at one time, which might be dangerous in case of drug with narrow therapeutic index), if the sustained release medication is improperly

formulated or swallowed [2, 8]. As well as, presence of variable physiological factors among patients such as transit time in gastrointestinal tract (GIT), and presence or absence of food and co-administration of other drugs. Furthermore, the manufacturing process of many SRDFs is costly. Overall, not all drugs are suitable candidates to be manufactured as SRDFs [6, 9]. Despite these problems the improvement in patient's compliance for long term therapy encouraged many pharmaceutical companies to develop sustained release medications for many pharmaceutically active ingredients. For example, there have been several financially successful passive SRDFs including those of carbamazepine, clarithromycin, verapamil, ciprofloxacin, clonidine and tramadol [2]. Hence, this study was conducted to evaluate the attitudes and knowledge of pharmacy practitioners toward sustained release medications in Benghazi community pharmacies, and to determine the availability of the SRDFs in Benghazi community pharmacies.

METHODS

A cross sectional survey was conducted during January and February 2018 by distributing a questionnaire to a selected study sample of pharmacy practitioners including; pharmacists, pharmacist assistants and pharmacy students whom are working in community pharmacies in Benghazi city. A total of 120 valid forms were used as study sample, where the questionnaires were distributed and filled at the same time, therefore ensuring a 100 % response. In this study, the questionnaire was composed of fifteen questions including; two questions covering demographic information of participants (gender and type of degree or qualification), and thirteen questions covering their knowledge and attitudes regarding the sustained release medications. In addition, a list of SRDFs was collected which are available in the majority of Benghazi community pharmacies. The obtained data from the list of SRDFs were compared in some extent with opinions of the study participants.

2.6 STATISTICAL ANALYSIS

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 20. Descriptive statistics for each variable were represented as percentages and frequency. Chi-square test was used to test for significant differences among different groups of

study sample (pharmacists, pharmacy students and pharmacist assistants). A significance level (P-value) of < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

This study discussed an important issue in pharmacy practice; knowledge and attitudes among pharmacy practitioners toward the SRDFs which are available in the community pharmacies in Benghazi city. The data regarding SRDFs which are available in most of Benghazi community pharmacies were collected including; their brand and generic names, price in Libyan dinar, medicinal uses and type of dosage form. The list of these sustained release medications is summarized in table 1 and table 2. In order to compare and find whether these information are in an agreement with participants' opinions. The collected data have confirmed that, the approximate number of sustained release products in the majority of Benghazi community pharmacies is thirty two brands. In this regard, a previous study in Palestine stated that only fourteen different brands of SRDFs were found in the Palestinian market [2].

Based on the results of the current study, approximately two thirds of participants (65%) were males. Pharmacists represented more than one half of the study sample, then pharmacist assistants and pharmacy students as seen in table 3. Overall, this study demonstrated that the majority of participants (98.3%) know the term SRDFs and there was no significant difference among different groups of study sample (P value = 0.12). As well as, most of the participants (93.3%) know the difference between IRDFs and SRDFs, and there was no observed difference among the different groups of participants (P value = 0.87). More than one half of participants (55.93%) said that oral SRDFs are the most available type in their pharmacies, while they said that the remaining types of sustained release products (parenteral, topical and ophthalmic) accounted for 25.98%, 14.68% and 3.39% respectively. This was in an agreement to some extent with the data from the list of SRDFs where the order of types was the same but with different percentages. For example, the oral SRDFs were the most available type but with higher percentage approximately (90%), whereas the remaining types accounted for the lowest percentages (6.66%) & (3.33%) for parenteral and topical dosage forms respectively.

Table 1. List of SRDFs in the majority of Benghazi community pharmacies.

Trade name	Generic name	Medicinal use	Type of dosage form	Price in Libyan Dinar (LD)
Delay-tiazem™	Diltiazem HCL	Angina pectoris	Oral SR capsule /tablet	30
VASTAREL®MR	Trimetazidine	Angina pectoris & coronary heart disease	Oral modified release (MR) tablet	25
NITRO MAK® Retard	Nitroglycerin	Angina pectoris & coronary disorders	Oral SR capsule	20
Nitroderm TTS®	Nitroglycerin	Angina pectoris	Transdermal SR patches	40
Lopresor® SR	Metoprolol	Antihypertensive, Angina attack	Oral delayed release tablet	35
EPILAT® Retard	Nifedipine	Antihypertensive, Angina attack	Oral SR tablet	20
Adalat® chrono				
Loxen® LP	Nicardipine chlorohydrate	Antihypertensive	Oral prolonged release (PR) capsule	150
Isoptin® SR	Verapamil	Antihypertensive & heart attacks	Oral SR tablet	35
DIAMICRON®	Gliclazide	Oral anti-diabetic	Oral MR tablet	21
Lantus®	Insulin	Anti-diabetic	Injectable SR	120
Solostar®				
Kombiglyze™ XR	(Saxagliptin & Metformin)	Oral anti-diabetic	Oral extended release (ER) tablet	145
Tegretol®	Carbamazepine	Epilepsy	Oral ER tablet	40
Depakine® Chrono	Valproic acid & sodium valproate	Epilepsy	Oral PR tablet	35
Seroquel®XR	Quetiapine	Depression & Schizophrenia	Oral SR tablet	60
Anafranil®SR	Clomipramine	Depression	Oral SR tablet	45

Table 2. List of SRDFs available in the majority of Benghazi community pharmacies.

Trade name	Generic name	Medicinal use	Type of dosage form	Price in (LD)
Wellbutrin[®]	Bupropion	Antidepressant	Oral SR tablet	60
Trivastal[®] Retard	Piribedil	Parkinson's disease and cognitive depression problems	Oral SR tablet	60
Prianil[®] CR	Lithium carbonate	Manic-depression	Oral CR tablet	20
Trental SR[®]	Pentoxifylline	Cerebral and peripheral vascular disorders	Oral SR tablet	24
Oxybral[®]	Vincamine	Adapt the cerebral blood flow (regulates all brain functions).	Oral SR capsule	24
NATRILIX[®] SR	Indapamide	Diuretic	Oral SR tablet	45
LASILIX[®] retard	Furosemide	Diuretic	Oral SR capsule	24
Detrusitol[®] XL	Tolterodine	Overactive bladder syndrome	Oral PR capsule	120
Pinexel[®] PR	Tamsulosin	Benign prostatic hyperplasia	Oral PR capsule	45
Xatral[®] LP	Alfuzosine	Benign prostatic hyperplasia	Oral PR tablet	70
Bezalip[®]	Bezafibrate	In high cholesterol	Oral PR tablet	36
Depo-Provera[®]	Medroxyprogesterone	Contraceptive	Injectable SR	30
Dicloream[®] retard	Diclofenac sodium	Analgesic & antiinflammatory	Oral SR capsule	14
Ketofan[®] SR	Ketoprofen	Analgesic & antiinflammatory	Oral SR capsule	12
Indocin[®] SR	Indomethacin	Analgesic & antiinflammatory	Oral SR capsule	20
Quibron[®] SR	Theophylline	Asthma (Bronchodilator)	Oral SR tablet	30
DUSPATALIN[®]	Mebeverin	Abdominal pain (Spasm)	Oral SR capsule	36

Table 3. Demographic characteristics of participants.

Variable	Percentage
Gender	
Male	65%
Female	35%
Degree or qualification	
Pharmacist	55.8%
Pharmacist assistant	25.8%
Pharmacy student	18.3%

Furthermore, approximately two thirds of participants (67%) said that the most popular dispensed sustained release products in their pharmacies are the oral SRDFs, following that the parenteral products (18%) then the topical (11%) and the smallest percentage (4%) accounted by the ophthalmic dosage forms. This arrangement is in an agreement with their availability in the community pharmacies. Regarding types of SRDFs according to their medicinal uses which are available in the community pharmacies, the findings of participants showed that the highest percentage was accounted by central nervous system (CNS) drugs with approximately (30%), then antihypertensive drugs with about (16%), contraceptives with (12.65%), and cardiovascular system (CVS) drugs with (10%). While the remaining types including; anti-diabetic, pulmonary drugs, over the counter drugs (OTC), GIT drugs, diuretics, ophthalmic, anticancer and other drugs figure1.

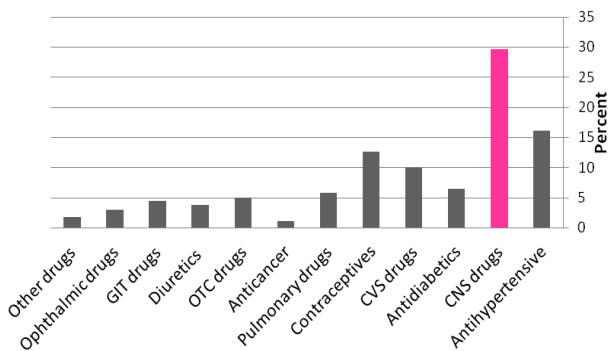


Figure 1. Distribution of SRDFs' types which are available in Benghazi community pharmacies according to participants' opinions.

While the data from the list of SRDFs showed that the CNS drugs come in the first place with (28.12%), and this is in an agreement with the participants' opinions. However, approximately (22%) was accounted by the CVS drugs (mainly angina) higher than those which represented by the participants' opinions then antihypertensive and anti-diabetic with (12.5%) and (9.37%) respectively. Additionally, the contraceptive drugs represented (3%) which less than those of the participants' opinions. Whereas the remaining types accounted for the smallest percentages as illustrated in figure 2.

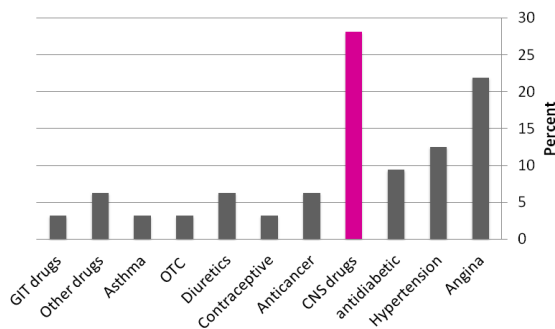


Figure 2. Distribution of SRDFs' types according to the data from the list of SRDFs.

Overall, the majority of participants said that the price of SRDFs is expensive (84.6%). However, the data from the list of SRDFs showed that about (43.33%) of the SRDFs have price between 14-30 Libyan dinar (LD). While the price range between 45-60 LD was accounted by approximately (40%) of the SRDFs, and about (16.65%) of the SRDFs have price range between 60–150 LD. Consequently, the price of SRDFs can be considered as relatively expensive. The higher cost of the single course therapy of SRDFs in comparison with IRDFs containing the same active ingredients was discussed in a previous study in Palestine. The study in Palestine found that the cost saving due to time saving of nurses who use sustained release medications in hospitals. This may result in a decrease in the number of employed nurses which return in cost saving for hospitals where most of pharmacists (63.1%) and physicians (63.5%) agreed with this issue. Furthermore, pharmacists and physicians consider the cost of the single course therapy, which is usually higher than the corresponding IRDFs. However, this cost can be compensated by better disease management and reduction in drug side effects and dose frequency thus patient's compliance improvement so cost saving for patient and society alike [2].

Approximately (57%) of participants said that the number of SRDFs in their pharmacies is between 1 to 10. While a small proportion of participants (6.8%) said that the number of SRDFs is more than 25. Overall, the data from the list of SRDFs have confirmed that the number of SRDFs in the majority of community pharmacies is small. Therefore, such observation requires further discussion. In general, there was a significant difference among the different groups of participants in their opinions regarding the reasons for the presence of a small number of SRDFs in the community pharmacies (P value = 0.004). Where approximately (45%) of participants did not know the reasons but about (16.3%) of pharmacists think that the SRDFs are expensive thus they are available in a small number, whereas this reason was represented only by (3.22%) of pharmacist assistants and similarly by pharmacy students. Interestingly, approximately (11.29%) of pharmacist think that there is no difference between IRDFs and SRDFs in their therapeutic effect while this was accounted by (3.22%) and (1.61%) of pharmacist assistants and pharmacy students respectively as shown in figure 3.

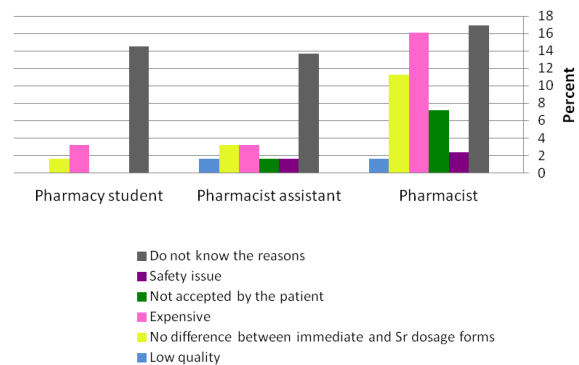


Figure 3. Distribution of participants' opinions regarding the possible reasons for presence of a small number of SRDFs in their pharmacies.

However, the presence of a few number of SRDFs in the community pharmacies can be attributed to the following reasons; not all the drugs are suitable to be formulated as SRDFs, cost issue as most of these dosage forms are expensive in production, also safety issues as these dosage forms have difficulty in termination of therapy in case of appearance any side effect. Moreover, sustained release medications have risk of dose dumping if any defect in formulation manufacturing occurs [6]. In this regard, a previous study in Palestine also had discussed the reasons for development a small number of SRDFs where questionnaires distributed to decision makers in pharmaceutical industry. The results have demonstrated that a high percentage of the questioned personnel (71.4%) thought that poor development of SRDFs may be due to either strategic company decisions or to the high cost of production. A small percentage (7.14%) of the interviewed decision makers believed that poor understanding of health professionals regarding the importance of SRDFs in the therapeutic field leads to their poor development [2].

The participants were asked whether patients prefer IRDFs or SRDFs, where a large proportion of participants (77%) said that the patients do not know the difference between IRDFs and SRDFs. Therefore, informing the patient regarding the benefits of SRDFs particularly reduction of dose frequency and better disease management is an important issue. Interestingly, approximately (41%) of participants believed that any drug can be formulated as a SRDF, and there was no a significant difference between different groups of study sample (P value = 0.90) as shown in figure 4. In contrast, the literature review stated that not any drug suitable to be formulated as a SRDF. Drugs which are not suitable candidates for sustained release formulations including; drugs with short half-life (less than 1 hour) and drugs with long half-life (more than 12 hour). Also, highly lipophilic or highly hydrophilic drugs are not suitable owing to these drugs will show either low flux or rapid flux into the tissues [6, 10, 11].

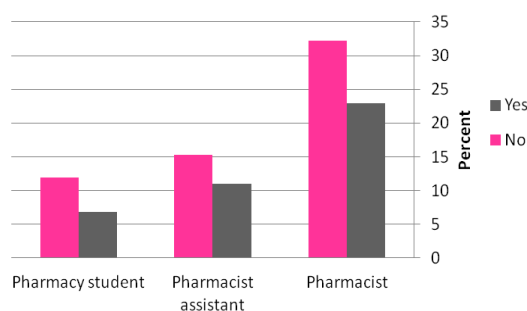


Figure 4. Distribution of participants' opinions regarding whether any drug can be formulated as a SRDF or it cannot.

CONCLUSION AND RECOMMENDATIONS:

This study demonstrated that the majority of pharmacy practitioners seem to have a good knowledge and attitudes toward the SRDFs. However, there is a lack of knowledge in some aspects of SRDFs such as the reasons for the presence of a few number of SRDFs in community

pharmacies, and there was a significant difference among the different groups of participants. As well as, a large percentage of participants believed that any drug can be formulated as a SRDF, but in deed not all the drugs are suitable to be formulated as SRDFs. The most available type of the SRDFs in Benghazi community pharmacies is the CNS drugs then the CVS drugs (mainly angina). Although, the price of SRDFs seems to be relatively expensive, the higher cost of the single course therapy of SRDFs in comparison with the IRDFs containing the same drug can be compensated by better disease management, patient's compliance and less drug side effects.

From the current study, it is recommended to give more attention to sustained release medications as a good choice for a wide variety of drugs. In addition, it is important to encourage the pharmaceutical companies to do more investments and scientific researches toward the SRDFs development. Moreover, in order to improve awareness and knowledge of pharmacy practitioners and physicians toward the SRDFs, introducing specific educational interventions particularly regarding the benefits and limitations of this type of dosage forms. If the patient considers only the economical part, the cost of SRDFs therapy may discourage him, thus it is necessary to educate patients regarding the benefits of SRDFs

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