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Research Article

Knowledge, Perceptions and Practices on Modified Release Tablets among Prescribers: A Preliminary Study

Fernando M.G.K.M., Priyadarshi K.I.J., Shanika L.G.T., Samaranayake N.R.*
Department of Pharmacy and Pharmaceutical Sciences, Faculty of Allied Health Sciences, University of Sri Jayewardenepura, Nugegoda, Sri Lanka

Abstract

Introduction: Modified release tablets (MRTs) are developed to achieve different therapeutic outcomes and are frequently prescribed. This study aims to evaluate the knowledge, perceptions and practices on using MRTs among a selected cohort of prescribers. Methods: A self administered online survey was conducted using a pre-validated questionnaire, prepared in-house to assess knowledge, perceptions and practices on using MRTs, among academics with an MBBS degree in medical faculties of State universities in Sri Lanka. Results: The response rate was 15.5% among 375 prescribers. Most were females (53.4%) and were 46-55 years (29.3%). Over 50% correctly expanded abbreviations related to MRTs. Most defined enteric coated (87.9%) and targeted release (77.6%) forms accurately. However, 87.0% mixed-up definitions of sustained release with controlled release. Most believed that inability to split tablets (70.7%) and high cost (70.7%), as disadvantages of MRTs. Nearly half did not identify the risk of dose dumping (53.5%) and inflexible dosing schedule (44.8%) as disadvantages. For frequency of administering MRTs, 86.2% referred the product information leaflet (PIL) while 29.0% depended on the frequency of the corresponding immediate release tablet. Most (79.3%) prescribed MRTs to increase patient compliance while 12.1% prescribed them to reduce cost. When problems regarding MRTs were encountered, most referred PILs (81.0%) and clarified with experts (75.9%). Conclusions: Although the response rate was low, a clear gap in knowledge, perceptions and practices on using MRTs were identified among prescribers who responded. Interventions are needed to improve the knowledge, perceptions, and practices on using MRTs among prescribers.

Keywords: Modified release tablets, Prescribers, Knowledge, Perceptions, Practices

Introduction

In the pharmaceutical industry, most drugs are designed as conventional dosage forms facilitating immediate delivery of the therapeutic agent to the target organ. However, immediate release dosage forms are associated with several drawbacks such as, drugs with short half-lives requiring frequent administration and poor patient compliance. Technical advancements have led to the development of modified release (MR) drug delivery systems to overcome such drawbacks [1]. When compared to the immediate release dosage forms, MR formulations offer diverse clinical benefits and convenience to patients including reduced adverse effects, drug concentration fluctuations, and dosing frequencies. As such,

*Corresponding author: nithushi@sjp.ac.lk

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MR formulations reduce misuse of drugs and increase patient compliance [2-4].

Due to the numerous advantages offered, it has become a common practice to prescribe and dispense MR tablets in the healthcare system [5]. However, MR tablets are also associated with potential safety hazards if not used appropriately [6,7]. Hence, healthcare professionals should be knowledgeable on the proper use of MR tablets.

There are numerous types of MR oral dosage forms that are widely used in healthcare. These differ based on the formulation technique and intended drug release characteristics. Table 1 summarizes definitions and commonly used abbreviations related to such MR dosage forms.

Table 1: Types of modified release dosage forms, definitions, and associated abbreviations

Type of MR dosage form	Definition	Abbreviations
Extended Release	These dosage forms are designed to release the active ingredient slowly. Thus, enables to maintain the plasma concentrations within the desired therapeutic level for an extended period [6].	ER, XR, XL
Controlled Release	These formulations are designed to release the medicament at a constant rate in order to achieve plasma concentration that remain nearly constant within time [6].	CR
Sustained Release	These dosage forms contain a first initial dose, which must be released immediately to achieve immediate on-set of action. This initial release of medicament is sufficient to provide a therapeutic dose soon after oral administration. The maintenance dose ensures the maintenance of plasma levels within the therapeutic range over an extended period of time [6].	SR
Targeted Release	These dosage forms release the medicament at or close to the intended site of action. A targeted release dosage form may have either immediate or extended release profile [6].	TR
Delayed Release	These formulations indicate that the drug is released later after oral administration. Enteric coated tablets are examples for this category as they are developed to release the drug in the intestine despite of stomach [6].	DR
Enteric Coated	Intended to delay the release of the drug (or drugs) until the dosage form has passed through the stomach. Enteric coated products are delayed release dosage forms [8].	EC

Numerous abbreviations are used to categorize the various release mechanisms of MR dosage forms in literature. However, their definitions vary by the reference source. It has also been observed that manufacturers and healthcare professionals use abbreviations to denote MR dosage forms haphazardly, regardless of the mechanism of drug release. The resulting confusion, may lead to severe medication errors during prescribing, dispensing and administration of drugs [1,5].

Amongst the disadvantages associated with MR tablets, toxicities associated with dose dumping is a major life-threatening issue. Dose dumping is the phenomena of a large dose being released at once in the event of a failure in the drug delivery system, resulting in drug toxicity [2-4]. The main cause for dose dumping is crushing or splitting of a MR tablet. "The nature of controlled release (CR) drug delivery systems make it difficult and potentially dangerous to modify the dosage form, so nearly all CR medications are marketed as capsules or unscored tablets with instructions not to cut, crush or chew" [9]. A study by Schier et al. (2013) [7] cautions that crushing of CR tablets result in loss of its intended release profile and can increase the plasma levels significantly. Crushing may destroy the matrix system which is used to maintain the release mechanism of CR dosage forms. It has also been found that altering MR dosage forms can affect the intended release rate and drug absorption [10]. Limited awareness regarding this matter may result in ultimate patient harm [7].

Several studies have assessed the knowledge among healthcare professionals regarding crushing/splitting MR dosage forms. According to the study by Nguyen et al. (2014), [10] most healthcare professionals (prescribers, pharmacists and nurses) advised patients to crush or split only non-sustained release tablets, and observed that nurses often referred patients who had trouble in swallowing MR tablets to a pharmacist or a general practitioner [10]. However, a few healthcare professionals had recommended patients to crush sustained release dosage forms [10]. Another study too reported that MR dosage forms are still crushed in a few hospitals in Queensland as MR dosage forms were difficult to swallow, since the required doses were unavailable, or were needed in liquid form for tube feeding [11].

Only a limited number of studies have undertaken to evaluate the knowledge, perceptions and practices among healthcare professionals regarding the use of MR dosage forms. Zaid et al., (2010) [12] reported that most healthcare professionals in Palestine found sustained release dosage forms to increase patient compliance, were advantageous in psychiatric patients, and cost effective due to better disease management.

All prescribers, and pharmacists must take the lead role of training nurses to guide safe medicine modification practices especially in patients with swallowing difficulties [13]. Knowledge and practices of all healthcare professionals should be adequate to minimize potential medication related issues related to use of modified release oral solid dosage forms [13]. However, after an extensive literature search, it was evident to us that there is no standard reference for the use of abbreviations to indicate a specific type of MR dosage form. If abbreviations are used haphazardly, it could mis-lead the healthcare professional on the mechanisms of drug release. Further, poor knowledge, attitudes, and practices among prescribers about the different categories of MR dosage forms could result in significant patient harm. Following an extensive literature search, it was evident to us that there is no standard reference for the use of abbreviations to indicate a specific type of MR dosage form. Therefore, this study aims to assess the knowledge,

perceptions and practice of MR dosage forms among prescribers engaged in university teaching in Sri Lanka.

Methods

Study design

This was a prospective, descriptive, cross sectional study conducted in September, 2019.

Study population

Both men and women, with a MBBS degree qualification and working as academics in medical faculties of State universities in Sri Lanka were selected for the study. Among them, academics who did not use an electronic mail facility or whose email addresses were not available in a public domain were excluded.

Study instrument

A self administered online questionnaire was prepared as a Google form to be circulated via electronic mail. The anonymity of each participant was ensured. The questionnaire was generated in-house and was validated via expert consensus (content validation) and a pilot study (face validation). Considering the feedback of both expert consensus and the pilot study, the questionnaire was modified and finalized. The questionnaire consisted of four basic parts.

Part 1 was on demographic information of participants. Part 2 assessed the knowledge on MR tablets based on three main aspects; ability to correctly expand abbreviations used to denote MR tablets, ability to correctly select the definition for each type of MR tablet, and knowledge on disadvantages related to MR tablets. Seven commonly encountered abbreviations, ER, XR, CR, SR, DR, TR and XL were included in the questionnaire to assess knowledge. Part 3 of the questionnaire assessed perceptions of prescribers on using MR tablets based on two main aspects; rationale for prescribing MR tablets, and possible causes for adverse drug events (ADEs) associated with MR tablets. Part 4 of the questionnaire included practice based questions on prescribing MR tablets and included two main aspects; determining the administration frequency of MR tablets, and practices when problems occurred related to MR tablets.

Data collection

Electronic mail addresses of academics included in the study were obtained via websites of respective universities. The questionnaire was sent as a Google form to every participant via electronic mail. Up to eight reminders were sent weekly to all the non-respondents. Along with the questionnaire, a brief description explaining the scope, purpose, risks and benefits of participation, and confidentiality was also sent. Therefore, participants who responded to the questionnaire were assumed to have consented to participate in the study. Demographic data of each respondent were reviewed separately to avoid duplications (as a result of weekly reminders).

Statistical analysis

Data were analyzed using the SPSS software (version 25). Descriptive statistics including means, frequencies, and percentages were calculated to present the data in a simple and meaningful form.

Ethical clearance

The study commenced after obtaining the ethics approval from the Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura (Ref: B.Pharm/03/18).

Results

Only 58 out of 375 academic prescribers responded resulting in a response rate of 15.5%. Many of the respondents were females (53.4%) and belonged to the age group 46–55 years (29.3%) (Table 2).

Table 2: Demographic data of participants (n=58)

Demographic variable	Frequency (n)	Percentage (%)
Gender		
Women	31	53.4
Men	27	46.6
Age group (years)		
Below 25	5	8.6
26-35	9	15.5
36-45	14	24.1
46-55	17	29.3
Above 55	9	15.5

Knowledge on modified release tablets among prescribers

Approximately fifteen percent (15.5%) of prescribers expanded all the seven abbreviations correctly while 30% expanded at least five of seven abbreviations correctly. Most prescribers could expand the abbreviations, SR (98.3%), CR (86.2%) and ER (91.4%) correctly.

None of the respondents could define all five types of MR tablets correctly (delayed release, sustained release, controlled release, targeted release, and enteric coated). Less than half of the participants (44.8%) defined three types of MR tablets correctly. Most prescribers defined, enteric coated (87.9%) and targeted release (77.6%) MR tablet types correctly. Only 5.2% of prescribers could correctly define "sustained release" tablets. Knowledge, perceptions and practices of prescribers regarding MR tablets are summarized in Figures 1, 2 and 3 respectively.

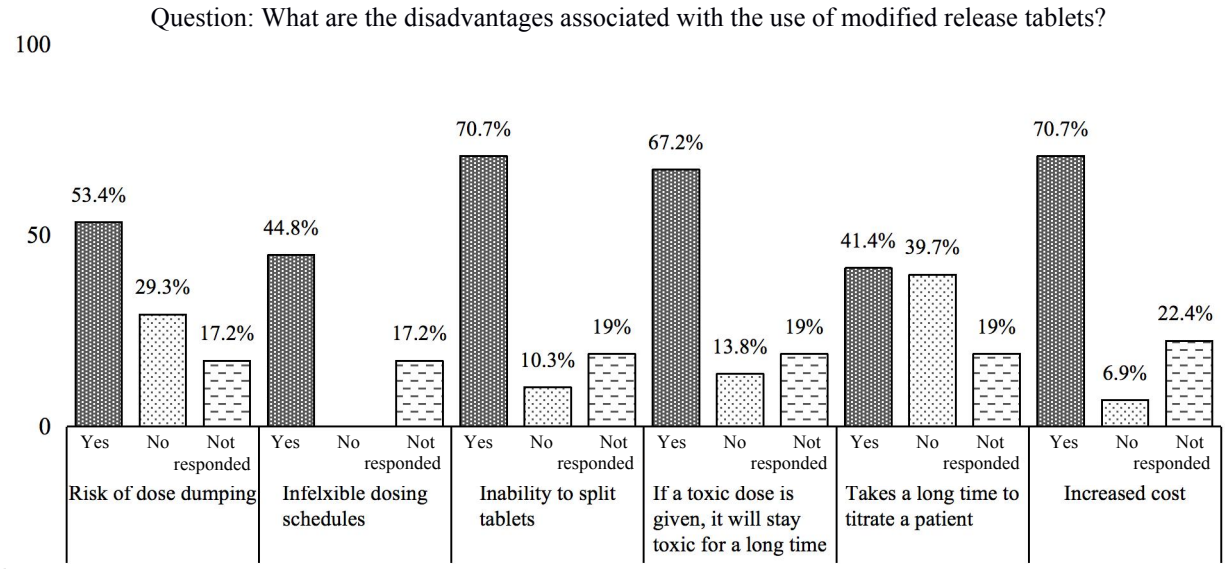

Figure 1: Knowledge among prescribers regarding modified release tablets (n=58)*

*Percentages may not add up to 100 because of rounding up

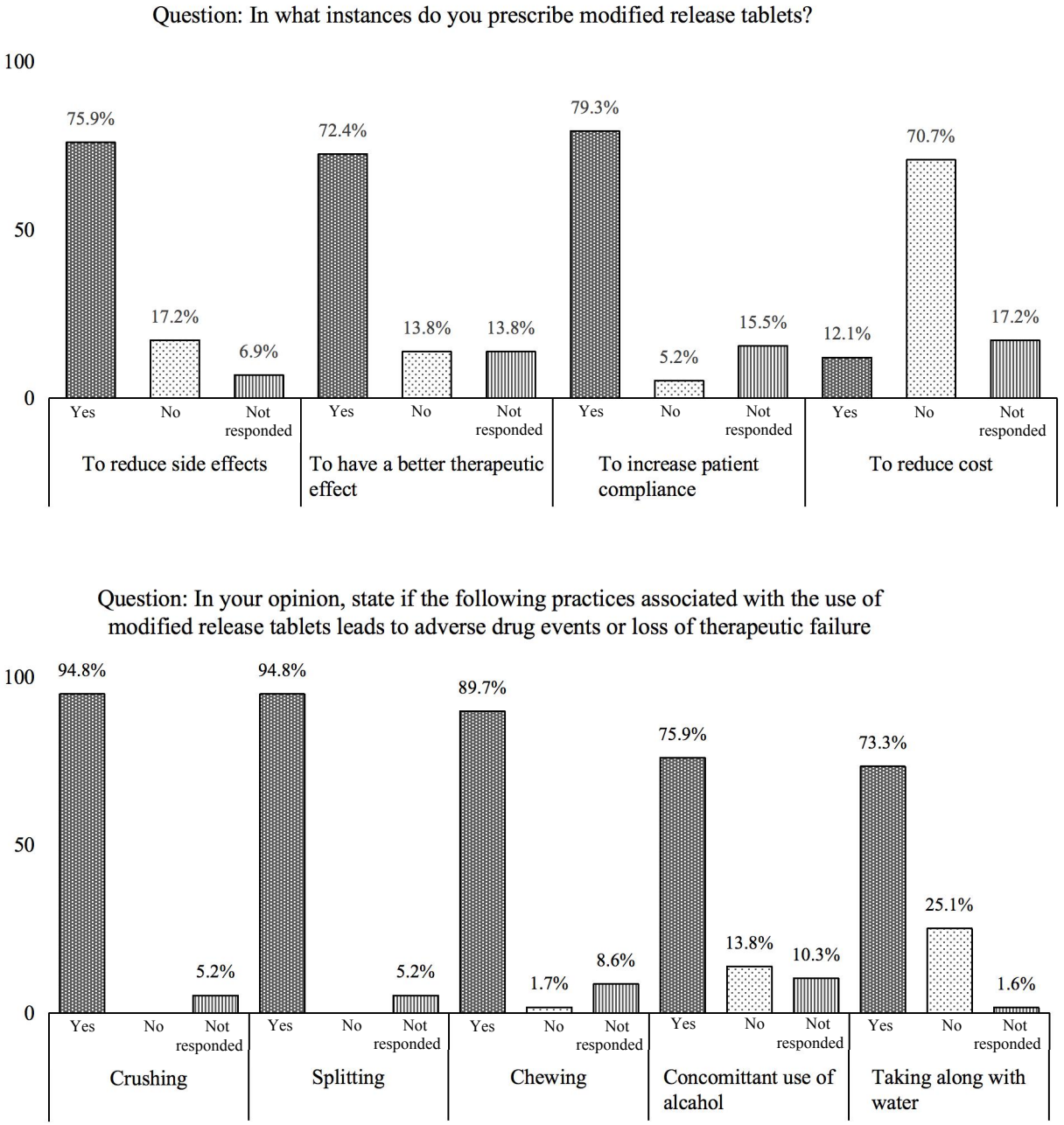

Figure 2: Perceptions on modified release tablets among prescribers (n=58)*

*Percentages may not add up to 100 because of rounding up

More than 65% of prescribers opted to prescribe MR tablets over immediate release tablets as they perceived MR tablets to have lesser side effects. Further, prescribers perceived that MR tablets improved therapeutic outcomes (72.4%) and patient compliance (79.3%). Prescribers also perceived that crushing, splitting, chewing, concomitant use of alcohol, and drug/food interactions as main influencing factors which lead to ADEs associated with MR tablets. It should also be emphasized that, 73.3% prescribers perceived taking MR tablets along with water also leads to ADEs/loss of therapeutic efficacy, which is incorrect.

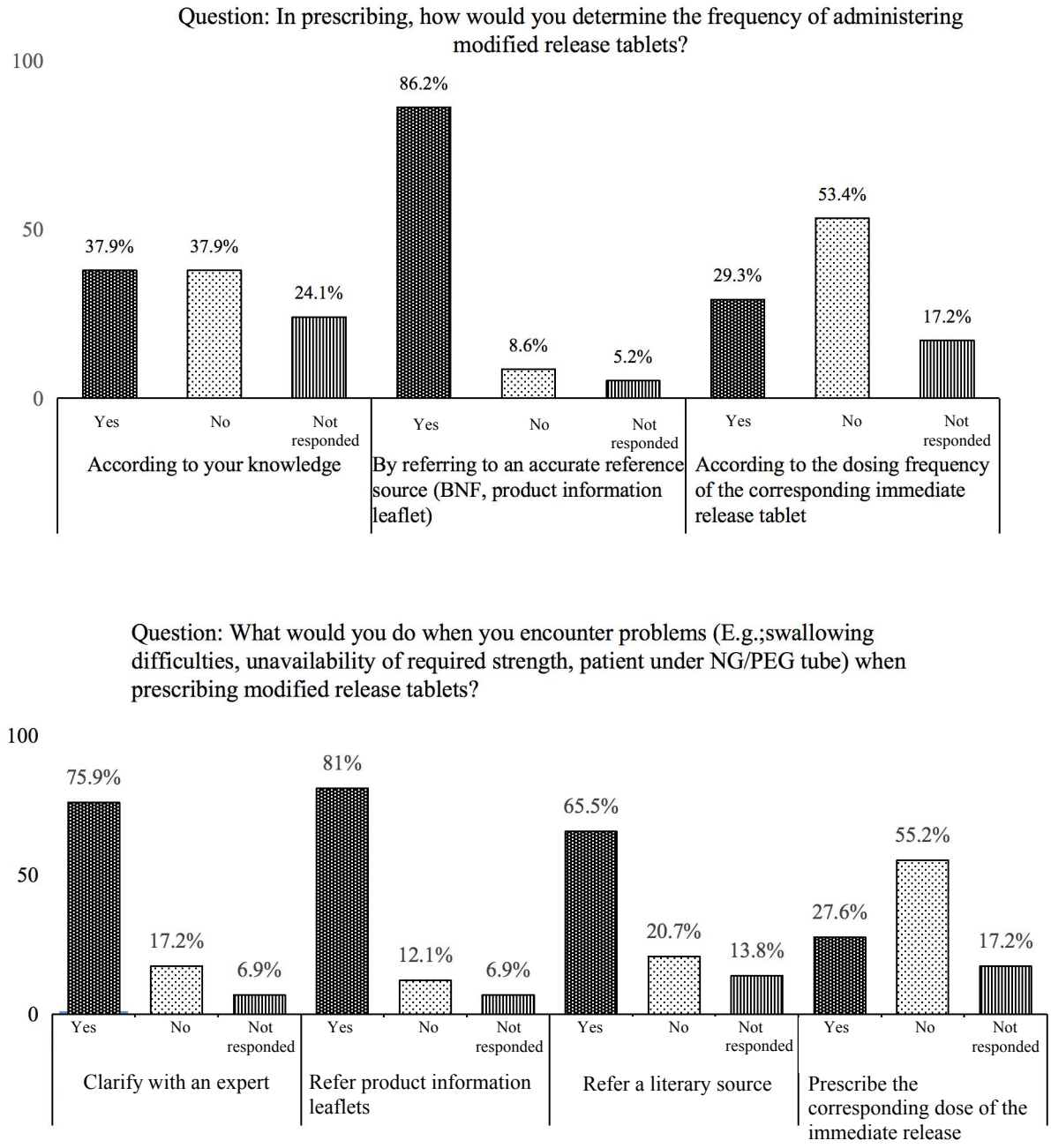

Figure 3: Practices on modified release tablets among prescribers (n=58)*

*Percentages may not add up to 100 because of rounding up

BNF- British National Formulary, NG/PEG -Naso Gastric/Percutaneous Endoscopic Gastrostomy

As a practice, 86.2% of prescribers used the British National Formulary or Product information leaflets to determine the frequency of MR tablets when prescribing. However, 37.9% of prescribers used their knowledge to determine frequency of MR tablets and 29.3% used dosing frequency of the corresponding immediate release tablets to determine the frequency of MR tablets.

When prescribing modified release tablets, 81.0% of prescribers referred the respective product information leaflet of the MR tablet while 75.9% clarified with experts to overcome problems such as swallowing difficulties, unavailability of required strength, and prescribing for patient under NG/PEG (naso gastric/percutaneous endoscopic gastrostomy) tube.

Discussion

MR dosage forms are a novel drug delivery system that is widely utilized in modern-day healthcare. Along with the numerous advantages, they could also cause a variety of hazards if not used carefully with a good knowledge of the formulation characteristics and release mechanisms [1].

The assessment of knowledge, perceptions and practices regarding MR tablets among prescribers only had a response rate of 15.5% which is low. However, among the respondents, an average of 50.5% of prescribers expanded the associated abbreviations accurately. Interestingly, 98.3% expanded the abbreviation "SR" correctly, although some used the word 'sustained release' and some used 'slow release' (both were taken as correct as meanings are similar). Similarly, the abbreviation, "TR" was expanded as 'targeted release' by some and 'timed release' by others (considered as "correct" in this study although meanings were different). Most respondents were incapable of correctly expanding "XL" and "XR" as 'extended release'. Given that only half of the prescribers correctly recognized abbreviations used for MR tablets, and resorted to use the same abbreviation to denote different types of MR tablets e.g. TR, our study highlights a major safety issue in using abbreviations to denote MR tablets.

It was also observed that there is a clear gap of knowledge among prescribers on defining the specific types of MR tablets. There was only an average of 50% accuracy in identifying the correct definition of MR tablets. Only 5.2% correctly defined "sustained release" tablets, as most confused it with the definition of "controlled release". The correct definition for sustained release; "the drug is released as one portion immediately, and the other over an extended period", was often confused with the definition for controlled release, which is, "the drug is released constantly over an extended period".

It was observed that, most prescribers (79.3%) prescribed MR tablets to improve patient compliance. A similar study conducted in Palastein by Zaid. A.N. (2010), [12] found that 89.2% physicians used sustained release dosage forms to improve patient compliance. They [12] also reported that, 77% of physicians had agreed that sustained release dosage forms maintain therapeutic activity during the night which is similar to our findings where 72.4% of respondents agreed that MRTs should be prescribed in patients who require long hours of therapeutic effect.

It is encouraging that 86.2% of prescribers used reference sources such as the British National Formulary or the respective product information leaflets to determine the frequency of MR tablets when in doubt. However, it was disturbing to find that 29.3% of prescribers referred to the dosing frequency of the corresponding immediate release tablet to determine the frequency of the MR tablets which is inappropriate and unsafe.

This study revealed that prescribers referred to experts (75.9%), the relevant product information leaflets (81.0%), or referred reliable sources such as book, journal (65.5%) when problems regarding MR tablets were encountered. This emphasizes the need for a reliable, comprehensive, and standardized, source of information on MR dosage forms for healthcare professionals. During the literature survey, we observed that it was difficult to find information on all types of MR tablets in one single reference. Further, nearly half of the product information leaflets that were assessed prior to the study did not contain essential information related to the use of MR tablets for healthcare professionals. Based on the findings of this study, it is important to highlight that healthcare professionals lack a

usable and reliable reference sources to educate themselves on MR tablets.

One of the major limitations of this study is the poor response rate of prescribers to the online questionnaire. We only achieved a response rate of 15.5% which is poor, despite weekly reminders. This study was not restricted to one specific area (district) with the intention of increasing the generalizability of findings. However, considering academics holding MBBS degrees as our population affects the generalizability. We failed to include the knowledge, perceptions and practices of practicing prescribers who are not attached to a university due to practical issues of obtaining email addresses. The prescriber study was an online study, and there is a possibility that the participants might have referred other sources to fill the questionnaire. To identify this phenomenon, we incorporated a separate question to state the sources they referred but this step did not eliminate the response biases. We were compelled to conduct this survey as a self administered questionnaire study as we intended to include prescribers from all over the country due to practical difficulties in approaching the respondents individually.

However, there are only a limited number of studies that have been conducted on knowledge, perceptions and practices on MR dosage forms among healthcare professionals, especially prescribers. The findings of this study reveal the timely necessity for more studies to enhance the proper use of MR dosage forms and hence, patient safety.

Conclusions

It is evident that there is a clear gap of knowledge, perceptions and practices on prescribing MR tablets among prescribers. The use of abbreviations to denote MR tablets also seems to be haphazard and no standardized and comprehensive reference source exists to refer. In order to address this gap of knowledge, perceptions and practices on MR dosage forms among prescribers, we believe that there is an urgent need to implement policy changes in both national as well as international contexts for promotion of safe use of MR dosage forms. A larger study of a similar nature will enable to identify more specific needs required for improving the appropriate use of MR dosage forms.

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